



STEP IN MRCP I & II

NOTES FOR

# MRCP I & II

FROM PAST PAPERS & REAL EXAMS

*Revision Notes (Latest Guidelines) 2021-2022*

NOTES FOR  
MRCP I & II

Revision Notes  
2021-2022

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## GASTROENTEROLOGY

### 1. **Chromosome 5 - APC tumour suppressor Gene -**

Adenomatosis Polyposis Coli : Colonic cancer

2. Chromosome 6 - HFE gene : Haemochromatosis

3. Chromosome 13 - ATP7B gene : Wilson's disease

4. JAK STATA mutation : Primary Polycythemia rubra vera

5. Mild UDP Glucuronyl transferase deficiency : Gilbert's syndrome

6. Absolute UDP Glucuronyl transferase deficiency : Crigler Najjar type 1 & 2

7. Peutz Jeghers syndrome - gene : Serine Threonine Kinase LKB1 or STK11

8. **Haemochromatosis** - Transferrin saturation is correct. The patient has haemochromatosis. Typical clinical features of this condition include secondary osteoarthritis (with **hook-like osteophytes at the 2nd and 3rd digits at the metacarpophalangeal joints being pathognomonic**) and a **slate-grey appearance of the skin**. A transferrin saturation > 55% is typical in untreated disease and this is the best marker to monitor treatment response.

9. **Hypogonadotrophic hypogonadism** occurs due to pituitary gland involvement in haemochromatosis. Iron deposits within the pituitary gland impair its ability to secrete gonadotropins, which leads to hypogonadotrophic hypogonadism. This condition typically presents as impotence in men and amenorrhea in women. Unfortunately, this endocrine dysfunction is not usually reversible with treatment as it's due to permanent damage of the pituitary gland.

10. **Diabetes mellitus** develops when pancreatic beta cells are damaged by iron deposits, resulting in insulin deficiency. Despite treatment for haemochromatosis, diabetes mellitus may not be reversible because of irreversible damage to pancreatic beta cells.

11. **Arthropathy**, specifically a degenerative arthritis affecting the metacarpophalangeal joints (most commonly the second and third), is another common manifestation of haemochromatosis. This arthropathy results from direct joint damage caused by iron deposition and is not generally reversible with treatment.

12. Finally, **Liver cirrhosis** occurs due to hepatic iron overload causing fibrosis and eventually cirrhosis if left untreated. Once cirrhosis has developed it cannot be reversed even after successful de-ironing treatments for haemochromatosis; however progression can be halted or slowed significantly with appropriate management.
13. Coeliac disease - Patients with coeliac disease require regular immunisations due to functional hyposplenism. The spleen plays a crucial role in the immune system, particularly in filtering bacteria and producing antibodies. In patients with coeliac disease, there can be a decrease in splenic function, which increases their susceptibility to certain infections, especially those caused by encapsulated bacteria such as *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, and *Neisseria meningitidis*. Therefore, it is essential for these patients to receive regular immunisations against these organisms.
14. HNPCC - Lynch syndrome - gene involved - MSH2 and MLH1 - these genes are involved in DNA mismatch repair leading to micro satellite instability. The MSH2 gene is involved in the process of DNA mismatch repair, which is essential for maintaining genomic stability. This mechanism corrects errors that occur during DNA replication by removing and replacing incorrectly paired nucleotides. In hereditary non-polyposis colorectal cancer (HNPCC), also known as Lynch syndrome, mutations in the MSH2 gene lead to a defective DNA mismatch repair system. As a result, cells accumulate errors in their genetic code, increasing the risk of developing various types of cancer, particularly colorectal and endometrial cancers.
15. Elevated subtypes of Ig and corresponding hepatobiliary disease:
- Alcoholic LD = IgA
  - Primary biliary cirrhosis = IgM
  - Autoimmune hepatitis = IgG
16. Laxative abuse. The histological finding of pigment-laden macrophages in the colon, often referred to as 'pseudomelanosis coli', is indicative of chronic laxative use. Anthraquinone laxatives such as senna and cascara are culprits, leading to a brown-black discolouration of the colonic mucosa due to the accumulation of lipofuscin pigment in macrophages within the lamina propria.

17. MEN-I - parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia; pituitary (70%); pancreas (50%, e.g. Insulinoma, gastrinoma); also: adrenal and thyroid.

18. **Nicotinic acid test.** Gilbert's syndrome is a common, benign liver condition in which the liver doesn't properly process bilirubin. It's caused by a mutation in the gene for the enzyme glucuronyl transferase, which helps to break down bilirubin in the liver. The nicotinic acid test can confirm this diagnosis as it leads to an exaggerated and prolonged increase in serum unconjugated bilirubin levels in patients with Gilbert's syndrome due to impairment of hepatic uptake and conjugation of bilirubin.

19. The **Bromsulphthalein excretion test** is not the best option here as it tests for hepatic function by measuring the ability of the liver to take up, conjugate and excrete bromsulphthalein. While it may show some abnormality in Gilbert's syndrome due to impaired conjugation, it isn't specific or sensitive enough for diagnosing this condition.

20. The **Ammonium chloride acidification test** is used to evaluate renal tubular acidosis rather than liver function. This test involves checking urine pH before and after administering ammonium chloride orally. In cases of renal tubular acidosis, there will be an inability to adequately acidify urine.

21. A **Urine analysis** would not typically help diagnose Gilbert's syndrome as this condition primarily affects bilirubin processing in the liver and does not cause significant changes in urine composition unless there is concurrent jaundice due to other causes.

22. Lastly, **Faecal fat excretion testing** is used for assessing malabsorption syndromes such as steatorrhoea (excessive fat in stools) seen with conditions like coeliac disease or chronic pancreatitis. It does not play a role in diagnosing Gilbert's syndrome which does not affect fat absorption or digestion.

23. Fulminant hepatitis - necrosis; viral hepatitis - apoptosis

24. SBP - most common organism - *E.coli* followed by *Klebsiella*; most common gram positive organism - *Streptococcus pneumonia* followed by *Streptococcus viridans* & *Staphylococci*.

25. Patient with diarrhoea \_ history of carcinoid tumour - treatment : Octreotide

26. Patient with diarrhoea with history of scleroderma - suggestive of bacterial overgrowth - Metronidazole

27. Patient with diarrhoea + terminal ileal resection - bile salt malabsorption - treatment with Cholestyramine

28. Hepatocellular carcinoma (HCC) should be managed according to the Barcelona Classification for Liver Cancer Treatment System. Patients with Child-Pugh A cirrhosis without signs of portal hypertension who have single lesions <2cm in size should be treated with surgical resection.

For those patients with Child-Pugh A and B cirrhosis and 2-3 tumours  $\leq 3$  cm or 1 tumour  $\leq 5$  cm without vascular invasion or extrahepatic spread should be considered for liver transplantation. As a bridge to liver transplantation these patients can be treated with TACE or RFA.

For those patients who have Child-Pugh A or B cirrhosis, good performance status, and evidence of vascular, lymphatic or extrahepatic spread the multiple tyrosine kinase inhibitor, Sorafenib, has been shown to prolong survival.

Those with Child-Pugh C cirrhosis have end-stage liver disease and are poor candidates for therapy as they lack any hepatic functional reserve to tolerate either resection, TACE or RFA. These patients are best treated symptomatically. Early involvement of community and/ or hospital palliative care teams should be considered. Best supportive care is therefore the correct option here.

29. Peutz Jegher Syndrome is caused by mutations in nuclear genes (specifically STK11/LKB1) - autosomal dominant

30. VIPomas are a type of neuroendocrine tumour that primarily arise from the non-beta islet cells of the pancreas. The name 'VIPoma' comes from vasoactive intestinal peptide, which these tumours excessively secrete leading to a syndrome known as Verner-Morrison or WDHA syndrome (Watery Diarrhea, Hypokalemia, Achlorhydria).

31. Li-Fraumeni syndrome is a rare autosomal dominant condition associated with germline mutations in the TP53 tumour suppressor gene. While individuals with this syndrome have an increased risk of developing multiple types of cancer including breast, brain, sarcomas and adrenocortical carcinomas throughout their lifetime, colorectal cancer is not specifically one of the more common manifestations.

32. Fanconi syndrome refers to a group of conditions resulting in impaired renal tubular function; it does not predispose to colorectal

cancer. The term 'Fanconi Syndrome' may also refer to Fanconi Anaemia - a rare genetic disease leading to bone marrow failure and increased risk for leukaemia but again there's no specific link with colorectal cancer.

33. Hereditary non-polyposis colorectal carcinoma (HNPCC), also known as Lynch syndrome. This is the most common type of inherited colorectal cancer, accounting for approximately 3-5% of all cases. It is an autosomal dominant disorder characterised by early onset colorectal cancer and an increased risk of other malignancies such as endometrial, ovarian, gastric, urinary tract, and small bowel cancers.

34. Pseudomembranous colitis. This condition is characterised by the presence of multiple white plaques or pseudomembranes on the gastrointestinal mucosa, typically as a result of overgrowth of the bacterium *Clostridium difficile* following antibiotic use. The patient's symptoms, particularly diarrhoea, and sigmoidoscopy findings are classic for this diagnosis.

35. The Glasgow-Imrie criteria are listed below. Each criterion met scores 1 point. 3 or more points indicate a high risk for severe pancreatitis.

PaO<sub>2</sub> <7.9 kPa

Age >55 years

White blood cells >15 x 10<sup>9</sup>/L

Serum calcium <2 mmol/L

Serum urea >16 mmol/L

Serum LDH >600 IU/L

Serum albumin <32 g/L

Serum glucose >10 mmol/L

36. Lactulose. According to the National Institute for Health and Care Excellence (NICE) guidelines, lactulose should be avoided in patients with irritable bowel syndrome (IBS) as it can exacerbate symptoms. Lactulose is a synthetic disaccharide that works by drawing water into the bowel, softening stools and increasing bowel movements. However, it can also cause bloating, flatulence, and abdominal discomfort, which are common symptoms of IBS.

37. In patients with ulcerative colitis, the risk of developing colorectal cancer is directly proportional to both the extent and

duration of colonic involvement. Therefore, disease confined only to the rectum is associated with a significantly lower risk compared to more extensive disease.

38. Factors increasing risk of cancer-

- disease duration > 10 years
- patients with pancolitis
- onset before 15 years old
- unremitting disease
- poor compliance to treatment

39. Angiodysplasia is associated with aortic stenosis and can cause gastrointestinal bleeding. The combination of these two conditions is known as Heyde's syndrome.

40. Facial flushing. Carcinoid syndrome is a paraneoplastic syndrome associated with carcinoid tumours, which are neuroendocrine tumours. The symptoms are due to the release of vasoactive substances, such as serotonin and kallikrein, into the systemic circulation. Facial flushing is often the first symptom of carcinoid syndrome and occurs in up to 90% of patients. It is usually episodic and provoked by alcohol, stress, or certain foods.

41. According to the UK National Health Service, approximately 10% of individuals with a positive faecal occult blood test (FOBT) will be found to have colorectal cancer on subsequent colonoscopy. This percentage falls within the range of 5 - 15%, making it the most accurate answer. It's important to note that while only around 10% of people with a positive FOBT will have colorectal cancer, many others may have other significant findings such as polyps or inflammatory bowel disease which also require further management and treatment. Therefore, even if the chance of having cancer is relatively low, it's still crucial for patients to undergo further investigation if they receive a positive result from their screening test.

42. Biliopancreatic diversion with duodenal switch is a primarily malabsorptive procedure and reserved for patients who are very obese. Causes significant malabsorption. Reserved for patients with BMI >60 kg/m<sup>2</sup>

43. Coeliac disease is strongly associated with HLA-DQ2 (95% of patients) and HLA-DQ8 (80%).

44. Haemochromatosis -

- 1) Most specific investigation : Transferrin saturation
- 2) Investigation of choice : Transferrin saturation
- 3) General population : Transferrin saturation
- 4) Best screening test : HFE gene
- 5) Family member : HFE gene

45. Typical iron study profile in patient with haemochromatosis

- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

46. Dubin-Johnson syndrome results in a conjugated hyperbilirubinaemia, not an unconjugated one. In this condition, there is a defect in the canalicular multispecific organic anion transporter (MRP2), which hinders the excretion of conjugated bilirubin into bile. This leads to a buildup of conjugated bilirubin in the liver cells and its subsequent leakage into blood, causing a conjugated hyperbilirubinaemia. 'Runs a benign course' - This is true. Dubin-Johnson syndrome typically has a benign course with patients usually living normal life spans without clinical impairment. The main manifestation of the disease is intermittent jaundice, which does not cause significant morbidity.

47. HBeAg is a marker of infectivity. The Green Book guidelines advise giving both the vaccine and immunoglobulin in this situation. If the patient had antibodies against HBe (anti-HBe), rather than the HBe antigen as in this scenario, then only the vaccine would need to be given.

48. There is a suspicion here that the patient may have Heyde's syndrome, with aortic stenosis and angiodysplasia resulting in chronic gastrointestinal blood loss. The repeated negative upper and lower GI endoscopies suggest that small bowel angiodysplasia may be the cause, in an area which is difficult to image via conventional endoscopy. In this situation capsule endoscopy has a



higher yield and would be the appropriate next step. The pathophysiology of angiodysplasia in this situation isn't known, although it may be due to changes in pressure within the mesenteric venous plexus, as the condition often resolves once the valve is treated.

49. Colorectal carcinoma is one of the only oncological diseases where the presence of a metastatic deposit can be treated with curative intent. A solitary liver lesion should be surgically resected. In fact, the purpose of following patients with CEA is to identify patients with solitary metastatic lesions amenable to surgical resection.

Transarterial chemoembolization & Radiofrequency ablation are used as palliative procedures when the lesions are too numerous or large to resect.

50. Pancreatic cancer risk factors - Mutations in certain genes - including but not limited to BRCA2 - can increase an individual's susceptibility to pancreatic cancer. BRCA2 mutations are more commonly associated with breast and ovarian cancers but these individuals also have an estimated two-fold increased lifetime risk for developing pancreatic cancer compared to those without the mutation. Other genes implicated include BRCA1, PALB2 and certain mismatch repair genes associated with Lynch syndrome (MLH1, MSH2).

#### Associations

- increasing age
- smoking
- diabetes
- chronic pancreatitis (alcohol does not appear an independent risk factor though)
- hereditary non-polyposis colorectal carcinoma
- multiple endocrine neoplasia
- BRCA2 gene
- KRAS gene mutation

|                         |                                  |
|-------------------------|----------------------------------|
| 51. Disease             | Associated raised immunoglobulin |
| subtype                 |                                  |
| Alcoholic liver disease | IgA                              |

|                           |     |
|---------------------------|-----|
| Primary biliary cirrhosis | IgM |
| Autoimmune hepatitis      | IgG |

52. to provide 50% of normal energy and protein requirements for the first 2 days. This approach helps to prevent refeeding syndrome, a potentially fatal complication that can occur when reintroducing nutrition to a severely malnourished patient. Refeeding syndrome is characterized by rapid shifts in electrolytes, particularly phosphate, potassium, and magnesium, which can lead to cardiac and neurological complications. By providing only 50% of the patient's normal energy and protein requirements initially, it allows their body to gradually adapt to the increased nutritional intake while minimizing the risk of refeeding syndrome.

53. The Alvarado score can be used to suggest the likelihood that a patient has acute appendicitis. It consists of eight different criteria (symptoms, signs and laboratory results) and divides patients into appendicitis unlikely, possible, probable and definite.

54. A non-cardioselective B-blocker (NSBB) is used for the prophylaxis of oesophageal bleeding. This is a non-selective beta-blocker which decreases portal venous pressure by reducing cardiac output and splanchnic blood flow. According to the British Society of Gastroenterology guidelines, non-selective beta-blockers (NSBBs) such as Propranolol are first-line treatment for primary prevention of variceal bleeding in patients with medium or large oesophageal varices that have not bled.

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## INFECTIOUS DISEASES & STIs

1. Amoebiasis : Metronidazole + Diloxanide Furoate
2. Animal & Human bites : Co-amoxiclav; Penicillin allergic : Doxycycline + Metronidazole
3. Anthrax : Ciprofloxacin
4. **Urinary Tract & Antibiotics -**
  - Lower UTI : Trimethoprim? Nitrofurantoin
  - Acute Pyelonephritis : Broad spectrum cephalosporin / Quinolone

- Acute prostatitis : Quinolone for 14 days or Trimethoprim

## 5. Respiratory system & Antibiotics

- Exacerbations of chronic bronchitis - Amoxicillin or Tetracycline or Clarithromycin
- Uncomplicated CAP - Amoxicillin; Penicillin allergic - Doxycycline/Clarithromycin; Flucloxacillin if Staphylococcus spp is suspected
- Atypical Pneumonia - Clarithromycin
- Hospital acquired pneumonia : ≤ 5 days of admission - Co-amoxiclav/Cefuroxime;  
>5 days of admission - Piperacillin + Tazobactam/  
Ceftazidime/Ciprofloxacin.

## 6. Skin & Antibiotics -

- Impetigo : Topical Hydrogen peroxide/ Oral Flucloxacillin / Erythromycin widespread disease
- Cellulitis : Flucloxacillin (Clarithromycin/Erythromycin/ Doxycycline if penicillin allergic)
- Cellulitis near the eyes or nose : Co-amoxiclav
- Erysipelas : Flucloxacillin
- Animal/human bite : Co-amoxiclav; Doxycycline + Metronidazole if penicillin allergic
- Mastitis during breast feeding : Flucloxacillin

## 7. ENT & Antibiotics -

- Throat infections : Phenoxymethylpenicillin; Penicillin allergic - Erythromycin
- Sinusitis : Phenoxymethylpenicillin
- Otitis media : Amoxicillin
- Otitis externa : Flucloxacillin
- Periapical/Peridontal abscess : Amoxicillin
- Gingivitis (acute necrotising ulcerative) : Metronidazole

## 8. Genital System & Antibiotics

- Gonorrhoea : Intramuscular Ceftriaxone
- Chlamydia : Doxycycline/ Azithromycin
- PID : Oral Ofloxacin + Oral Metronidazole (OR) IM Ceftriaxone + Oral Doxycycline + Oral Metronidazole
- Syphilis : Benzathine Penicillin (OR) Doxycycline (OR) Erythromycin
- Bacterial Vaginosis : Oral/Topical Metronidazole (OR) Topical Clindamycin

## 9. GIT & Antibiotics

- Clostridioides difficile : Vancomycin → Fidaxomicin → Oral Vancomycin + IV Metronidazole
- Campylobacter enteritis : Clarithromycin
- Salmonella (non typhoid) : Ciprofloxacin
- Shigellosis : Ciprofloxacin

10. Cryptosporidium is a parasite that can cause gastrointestinal and respiratory illness. It is spread by farm animals and contaminated water. A modified Ziehl-Neelsen stain reveals red cysts in the stool of infected individuals, highlighting cryptosporidium oocytes.

Congo red stain is used to detect amyloid deposits or the cell walls of plants or fungi. It would not aid the identification of *Cryptosporidium*.

Fite's Faraco is a stain used to identify mycobacterium leprae.

11. Aerosolized pentamidine prophylaxis for Pneumocystis jirovecii pneumonia in patients with the acquired immunodeficiency syndrome (AIDS) may often not be effective. Bullous changes and pulmonary cysts can form in lung apices from repetitive inflammation and cytotoxicity of HIV on the pulmonary macrophages. These changes persist in spite of prophylaxis against recurring pneumocystis infection with aerosolized pentamidine which increases the risk of spontaneous pneumothorax.

12. Entamoeba Histolytica is the correct answer. Amoebiasis typically occurs 2-4 weeks after infection with Entamoeba Histolytica although can occur months to years later. It is a cause of dysentery. This is a type of gastroenteritis that results in bloody diarrhoea.

13. Giardia Lamblia is incorrect. The incubation period of this infection is 3-40 days so this could be consistent. However, this classically causes chronic intermittent 'explosive' diarrhoea without blood. Given there is no blood, it would not be classified as dysentery and therefore is the wrong answer.

14. *Campylobacter jejuni* is incorrect. This is another cause of dysentery but the incubation period is 2-4 days rather than 3 weeks

15. The correct answer is blocking integrase enzymatic activity. Raltegravir is an integrase inhibitor. There are five classes of medications involved in the treatment of HIV. The NICE guidelines recommend triple therapy for the treatment of HIV. A backbone treatment of two nucleoside reverse transcriptase inhibitors (NRTIs) with an additional third medication. The third medication is recommended to be either an integrase inhibitor (INI), a protease inhibitor (PI) or a non-nucleotide reverse transcriptase inhibitor (NNRTI).

HIV can be targeted at five points in the cell's cycle with drug treatments currently.

Entry inhibitors are a class of medication which interfere with the binding, fusion and entry of HIV-1 into host cells. An example of this type of medication includes maraviroc. Maraviroc works by targeting the CCR5 receptor on T-helper cells, reduces the HIV virus' ability to enter the host CD4 cells. Indeed, some individuals may have a mutation of the CCR5 delta gene which results in natural protection from viral cell entry. Nevertheless, caution should be used when administering maraviroc as a tropism of the HIV virus can allow the HIV virus to target an alternative receptor CXCR4 - bypassing maraviroc's mechanism of action.

HIV is an RNA virus and the genetic code be 'reverse' transcribed into DNA in order to be incorporated into the human cell. The conversion of RNA to DNA is not done by mammalian cells and is performed by a viral reverse transcriptase enzyme. This makes it an opportune target for drug therapies. Nucleoside reverse-transcriptase inhibitors act as nucleoside analogues which compete with natural deoxynucleotides for incorporation to DNA to prevent reverse transcription. Examples of this class of medications include emtricitabine and tenofovir disoproxil.

Reverse transcription can also be inhibited by non-nucleoside reverse-transcriptase inhibitors. These medications bind to the

reverse transcriptase enzyme and inhibit its function (acting as allosteric modulators). Examples of this class of medications include efavirenz and nevirapine.

Integrase inhibitors (of which raltegravir is one) block integrase enzymatic activity which is involved in inserting the viral genome into the DNA of the host cell . Integrase is a viral enzyme and hence is a reliable target.

Finally, protease inhibitors block the viral protease enzyme activity necessary to produce mature virions from budding from the membrane . Viral particles produced in the presence of protease inhibitors are mostly non-infectious and defective. Examples of this class of medications include ritonavir and lopinavir.

14. **Macrolides** are a class of antibiotics commonly employed to treat various bacterial infections, including respiratory tract infections (such as bronchitis and pneumonia), skin infections, and certain sexually transmitted. Examples include azithromycin, clarithromycin and erythromycin. Their mechanism of action involves binding to the 50S subunit of bacterial ribosomes, specifically interfering with protein synthesis. By attaching to this ribosomal subunit, macrolides disrupt the elongation of the growing protein chain, ultimately preventing the bacterium from producing essential proteins for its survival and replication. This inhibitory action halts the bacterial infection, helping the body's immune system clear the pathogen.

15. Aminoglycosides are a class of antibiotics commonly used to treat severe bacterial infections such as those affecting the urinary tract and respiratory system. The mechanism of action of aminoglycosides involves disrupting bacterial protein synthesis. They bind to the 30S subunit of bacterial ribosomes, not the 50S subunit, interfering with the reading and translation of genetic information. This leads to the production of faulty or incomplete proteins within the bacterial cell, ultimately causing cell death. Aminoglycosides are particularly effective against gram-negative bacteria and are often used in combination with other antibiotics for a synergistic effect in treating serious infections.

16. **Tetracyclines** are a class of antibiotics used to treat a wide range of bacterial infections, including respiratory, urinary tract, skin, and gastrointestinal infections. Examples include doxycycline, minocycline, and tetracycline. The mechanism of action of tetracyclines involves inhibiting bacterial protein synthesis. They bind to the bacterial ribosome's 30S subunit, not the 50S subunit, preventing the attachment of aminoacyl-tRNA to the ribosome's A site. This interference disrupts the elongation of the protein chain during translation, leading to the production of incomplete or nonfunctional proteins within the bacterial cell. Ultimately, this inhibitory action hampers bacterial growth and replication.

17. **Cephalosporins** are a class of antibiotics commonly used to treat a wide range of bacterial infections, including respiratory tract infections, skin and soft tissue infections, and urinary tract infections. Notable examples include cephalexin, ceftriaxone, and cefuroxime. The mechanism of action of cephalosporins is similar to that of penicillins. They disrupt bacterial cell wall synthesis by binding to and inhibiting enzymes called penicillin-binding proteins (PBPs). This interference weakens the bacterial cell wall, leading to cell lysis and death. Cephalosporins do not affect bacterial ribosomes.

18. **Quinolones** are a class of antibiotics commonly used to treat various bacterial infections, including respiratory, urinary tract, and gastrointestinal infections. Notable examples include ciprofloxacin, levofloxacin, and moxifloxacin. The mechanism of action of quinolones involves targeting bacterial DNA replication and repair processes. They inhibit enzymes called DNA topoisomerases, particularly DNA gyrase and topoisomerase IV. By blocking these enzymes, quinolones prevent the unwinding and resealing of DNA during replication, which ultimately leads to the breakage of bacterial DNA strands and cell death.

19. Cardiac conduction abnormalities, including first, second, and third-degree arrhythmias, are rare complications in cases of atypical pneumonia, such as those caused by *Mycoplasma pneumoniae*. Although the precise underlying mechanisms are not entirely known, it is hypothesised that these complications may arise due to autoimmune reactions. Importantly, these cardiac

complications have not been linked to infections with *Streptococcus pneumoniae*.

20. *Streptococcus pneumoniae* is not commonly linked to dermatological complications, making maculopapular rashes rare in association with this bacterium. However, in certain instances, a severe and potentially life-threatening skin condition known as **purpura fulminans** can occur. **Purpura fulminans** is characterised by purple or black skin discolouration resulting from bleeding into the skin and underlying tissues.

21. Syphilis can be present without any symptoms at either an early or a late stage; these are called 'early latent' (less than 2 years since last negative syphilis test) and 'late latent' (more than 2 years since last negative test). Whether the syphilis is latent or causing symptoms does not alter the treatment; this is only affected by whether syphilis has not been tested for in the last 2 years, in which case further doses are required, or if neurosyphilis is suspected. Many patients with syphilis are unaware of having had a chancre and this is sometimes picked up incidentally on clinical examination. There is no known clearance of *Treponema pallidum* without antibiotic treatment

22. Tetanus High risk wounds include :  
> 6hrs , > 1cm deep , Foreign body , Infection ischemia or necrosis

23. Chickenpox infection during the first 20 weeks of pregnancy can cause foetal varicella syndrome. In the second or third trimester chickenpox can cause severe maternal disease. In late pregnancy infection (near delivery) there is a risk of neonatal varicella.

If a woman is exposed to chickenpox during pregnancy, a history should be taken of whether she has previously had chickenpox or varicella vaccination. If she has, no further action is needed.

If the woman is unsure about previous chickenpox or has never had chickenpox, a blood test for varicella zoster virus (VZV) antibodies should be performed.



For susceptible women (negative antibodies) exposed in the first 20 weeks of pregnancy, varicella zoster immunoglobulin (VZIG) is recommended.

For susceptible women (negative antibodies) exposed from 20 weeks of pregnancy, either VZIG or aciclovir from days 7 to 14 after exposure is recommended.

**Oral aciclovir** should be prescribed for pregnant women with symptomatic chickenpox if they present within 24 hours of the onset of the rash and if they are 20+ weeks' gestation. Use of aciclovir before 20 weeks can be considered but should be discussed with obstetrics.

24. **Silver stain**, as it is the most appropriate staining method to demonstrate the presence of *Pneumocystis carinii* in bronchoalveolar lavage samples. Silver stains, such as **Gomori methenamine silver** (GMS) or **Grocott's methenamine silver stain**, are commonly used to visualize fungi and other pathogens in tissue samples. In the case of *Pneumocystis carinii* pneumonia, these stains provide **excellent contrast** between the organism's cysts and surrounding lung tissue, allowing for clear identification.

25. **Rubeanic acid** is not the correct choice, as it is a reagent used to detect copper in tissues. It forms a **green complex with copper ions** and can be useful in diagnosing Wilson's disease or assessing copper levels in liver biopsies. However, it is not relevant for visualizing *Pneumocystis carinii*.

26. Rose Bengal can be applied to corneal scrapings to diagnose **fungal keratitis** or **Acanthamoeba infections**, but it is not the best choice for demonstrating *Pneumocystis carinii* in bronchoalveolar lavage samples.

27. Congo red staining is also an incorrect option. This stain is used to identify **amyloid deposits** in tissues by binding to beta-pleated sheet structures present in amyloid fibrils. Congo red-stained amyloid appears as red-orange birefringent material under polarized light microscopy.

28. Artesunate acts rapidly against the blood-stage parasites, leading to a faster reduction in parasite load and subsequent clinical improvement.

29. This patient is presenting with the classic features of Lymphogranuloma venereum (LGV). This tropical sexually

transmitted disease can be caused by multiple serovars of *Chlamydia Trachomatis*. The bacterium gains entry through breaches in the epithelial/mucous membranes, travelling through the lymphatics via macrophages to local nodes. It is endemic to Africa, India, Caribbean, central America and southeast Asia.

The disease presents in two stages:

Primary stage: Self-limiting painless genital ulcer at the site of inoculation 3-12 days later.

Secondary stage: Presents 1-6 months later with unilateral painful lymphadenitis/lymphangitis. The site of inoculation dictates symptomatology, if rectally, then tenesmus, proctocolitis, strictures and fistulas can ensue. Cervicitis and urethritis are also common features. Enlarged lymph nodes are known as buboes, they are often painful and can lead to thinning of the overlying skin causing abscesses. Groove sign is separation inguinal nodes by the inguinal ligament and is characteristic of the disease.

Diagnosis is achieved by enzyme linked immunoassays or polymerase chain reaction of infected sample areas/pus. Acute and convalescent sera can be used, but requires two samples 2 weeks apart.

Treatment involves antibiotics, either doxycycline or macrolides (azithromycin or erythromycin) and potential surgical drainage/aspiration of the buboes or abscesses.

Complications of the disease include: genital elephantiasis, hepatitis, infertility, pelvic inflammatory disease, arthritis and fitz hugh curtis syndrome.

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Complications of the disease include: genital elephantiasis, hepatitis, infertility, pelvic inflammatory disease, arthritis and Fitz-Curtis syndrome.

30. This patient has presented with the human parasitic infection strongyloidiasis caused by the helminth *Strongyloides stercoralis*. Following the larvae penetrating the skin, commonly via patients walking barefoot, the parasite makes its way to the intestines where it lays eggs. Unlike in other soil-transmitted helminth infections, these eggs hatch into larvae still within the intestines. Although most of these larvae will be excreted in stool, a portion of the larvae can mature and penetrate the intestinal wall or skin around the anus, immediately re-infecting the patient, a process known as auto-infection. These larvae can travel around the host body including reaching the lungs causing respiratory symptoms and eosinophils accumulation known as Löfller's syndrome. This

auto-infection means without treatment a patient may remain infective with *Strongyloides stercoralis* for life. Treatment of *Strongyloides stercoralis* is with the antiparasitic ivermectin which interferes with the nervous and muscular functions of helminths. As ivermectin only kills the adult form of the worm and not the larvae, repeat dosing may be required to properly eradicate the infection.

31. Causes of bloody diarrhea (CASE)

- *Campylobacter* (Macrolide)
- Amoebiasis (Metro + diloxanide furoate)
- *Salmonella* (ciprofloxacin)
- *Shigella* (ciprofloxacin)
- E.Haemorrhagic *E coli* (supportive)

32. Tetracyclines are often prescribed for acne and can cause a photosensitive skin rash. This appears as a red rash on areas of skin exposed to the sun. Other skin reactions to tetracyclines include exfoliative dermatitis and Stevens-Johnson syndrome.

33. This patient has symptoms of a lower urinary tract infection which should be treated with antibiotics. The clue to finding the correct answer is the fact that despite being leucocyte positive, the urine dipstick is nitrite negative. Gram negative organisms test positive on the nitrite test as they convert nitrates to nitrites for energy. Gram positive organisms are unable to reduce nitrate to nitrite and therefore, test negative. As *Staphylococcus* species are the only gram positive organisms of the answers given, this is the correct answer.

34. The correct answer is to destroy liver hypnozoites and prevent relapse. Primaquine is an 8-aminoquinoline antimalarial drug used primarily for the radical cure of *Plasmodium vivax* and *Plasmodium ovale* infections. These species can form dormant liver stages known as hypnozoites that can reactivate weeks to months after the initial infection, causing a relapse. Primaquine targets these hypnozoites, thereby preventing subsequent relapses.

35. The likely diagnosis here is one of scrub typhus, which is caused by the obligate intracellular bacteria *Orientia tsutsugamushi*

and is one of a group of related conditions collectively known as the 'tropical rickettsial infections'.

Scrub typhus is the most common tropical rickettsial infection in South-east Asia, where it is a common cause of febrile illness. It is transmitted by the bite of a 'chigger' which live in dry grassy areas. It presents as a vasculitis-like illness with regional or generalised lymphadenopathy and there is typically a black crusted lesion at the site of the bite called an 'eschar'. Complications include hepatic and renal failure, myocarditis and (as seen in this case) meningoencephalitis.

The diagnosis of scrub typhus is almost invariably a clinical one and rests on plausible epidemiology and compatible symptoms. Given that the clinical spectrum of disease is wide this can often be difficult and a very careful search for the eschar (often at the joins of clothing where the chigger mite is unable to climb further) is warranted as its discovery all but seals the diagnosis.

Doxycycline is effective against all of the tropical rickettsial infections and may initially may need to be given down an nasogastric tube.

36. 1) Offensive discharge: Bacteria Vaginosis, Gram variable (mostly +ve) coccobacilli), treat with Metronidazole

2) Offensive but greenish discharge : Trichomonas, parasite , treat with metronidazole

3) non-offensive discharge + easily bleeding: Chlamydia, intracellular, treat with Doxycycline

4) non-offensive discharge + disseminated infection: Gonorrhoea, gram -ve cocci, treat with Ceftriaxone

37. Chlamydia testing - Women : Volvo vaginal swab, Men : urine sample

Mx : Doxycycline; Alternative Mx : Azithromycin

Pregnant - Azithromycin/ Erythromycin/ Amoxicillin

38. Primaquine - Non falciparum malaria to destroy liver hypnozoites and prevent relapse

Since *Plasmodium vivax* and *Plasmodium ovale* species both have hypnozoite stages in the liver, these need to be eradicated with an additional therapy to prevent relapse of malarial illness. Primaquine is the appropriate treatment for this.

39. Animal Bite - Co-Amoxiclav  
Penicillin allergic - Doxycycline + Metronidazole

40. HHV 3 = Varicella zoster HHV 4 = EBV HHV 5 = CMV

41. Sporadic Creutzfeldt-Jakob disease (CJD) is a subacute spongiform encephalopathy that presents with rapidly progressive dementia and is the most frequent among rare prion diseases. In such a patient like this with rapidly progressive dementia and focal neurological signs, CJD should be the first-line diagnosis given the triad dementia, myoclonus, and rigidity. An MRI of a CJD patient usually demonstrates hyperintense signal changes in the striatum or thalamus on T2-weighted images.

Herpes Simplex Encephalitis typically affects the temporal lobes and the frontal cortex predominantly while JE affects thalamus, basal ganglia and brainstem more commonly.

42. The correct answer is hypoadrenalism. The case described is suggestive of tuberculosis (TB), caused by *Mycobacterium tuberculosis*. This infection is endemic in areas such as India and causes a subacute illness characterised by constitutional symptoms such as fever, weight loss and night sweats. Pulmonary involvement is most common and presents with cough which may include haemoptysis. Radiographic changes are most commonly apical and may include cavities. Tuberculous adrenalitis is a well-described complication, usually resulting from the haematogenous spread of bacilli from other sites. Untreated, it causes progressive destruction of the adrenal glands leading to hypoadrenalism.

43. This patient has bacterial meningitis as indicated from the CSF analysis. NICE guidelines recommend treating bacterial meningitis with dexamethasone if lumbar puncture reveals either: purulent CSF, white cell count  $> 1000$  cells/ $\mu\text{L}$ , raised white cell count plus protein count  $> 1\text{g/L}$ , or bacteria on gram stain. Dexamethasone should be given within 4 hours of starting antibiotics and should be avoided if the duration from starting antibiotics is beyond 12 hours.

44. Praziquantel is the correct answer. The clinical history suggests a diagnosis of 'Katayama fever', which is the acute form of schistosomiasis. It is characterized by fever, myalgia, cough, diarrhoea and clinical evidence of an urticarial rash and hepatosplenomegaly associated with blood eosinophilia and radiological evidence of pulmonary infiltrates.

swimming history -> snail in water -> nail is intermediate host of schistosomia

skin skin penetration -> acute schistosomiasis syndrome/

### **Katayama fever**

C/F : Hepatomegaly , splenomegaly, diarrhoea, cough, pulmonary infiltrates on CXR, fever, urticaria, angioedema, arthralgia, myalgia, eosinophilia

45. Klebsiella is associated with cardiomyopathies and alcoholics, with upper lobar involvement.

Mycoplasma occurs in epidemics with skin changes and some haematological involvement.

Legionella typically is a water borne infection with hyponatraemia and gastroenterological symptoms.

This patient is most likely to be suffering from pneumonia secondary to streptococcal pneumoniae. It is the most common cause of community acquired pneumonia and further clues to this being the diagnosis is the evidence of a cold sore and the blood stained sputum.

46. MRSA can be differentiated from MSSA in the microbiology lab by using a rapid PCR test. This enables the identification of MRSA before culture and sensitivity results are available.

Drugs used Vancomycin > Teicoplanin > Linezolid

Relatively new antibiotics such as linezolid, quinupristin/dalfopristin combinations and tigecycline have activity against MRSA but should be reserved for resistant cases

47. Visceral lavra migrans- toxocara canis; Mucocutaneous lavra migrans-anylostoma braziliense; Larva currens- strongiloides stercolaris

48. *E. coli* O157:H7 is a particular strain associated with severe, haemorrhagic, watery diarrhoea. It has a high mortality rate and can be complicated by haemolytic uraemic syndrome. It is often spread by contaminated ground beef.

49. *Clostridium tetani* causes a spastic paralysis.

*Clostridium perfringens* commonly causes skin infections and gas gangrene.

*Clostridium difficile* does cause diarrheal illness but does not cause paralysis.

*Clostridium sordellii* is a very rare cause of post-partum and post-termination sepsis.

50. Measles is the correct answer. This patient presents with cough, coryzal symptoms, conjunctivitis and fever in association with a rash and Koplik spots, allowing his general practitioner to make a clinical diagnosis of measles. Koplik spots (small white lesions on buccal mucosa) are pathognomonic for measles. There is a lower uptake of the measles, mumps and rubella vaccine in some groups (including members of the Roma community).

51. *Trichomonas vaginalis*. This protozoan infection typically presents with a green, frothy, and malodorous vaginal discharge, accompanied by vulvar itching and dyspareunia (pain during sexual intercourse). The symptoms described by the patient align very closely with this diagnosis.

52. Intravenous dexamethasone should be given prior to or with the first dose of antibiotic to reduce the risk of neurological sequelae by reducing cerebrospinal inflammation. If pneumococcal meningitis is suspected or confirmed from clinical features, cerebrospinal fluid parameters or culture results, then dexamethasone should be continued for 4 days. It should be stopped if another causative organism is strongly suspected or confirmed.



53. *Bartonella henselae* causes cat scratch disease. Patients typically develop low-grade fever, fatigue and malaise and regional ipsilateral lymphadenopathy. Diagnosis can be confirmed by microbiology through serology or culture, or histopathology through visualisation of bacilli in Warthin-Starry staining.

54. Trimethoprim is an antibiotic, mainly used in the management of urinary tract infections.

It inhibits dihydrofolate reductase, cannot give to patients on Methotrexate as both act in the same way.

Adverse effects of Trimethoprim - myelosuppression, transient rise in creatinine as it competitively inhibits tubular reabsorption of creatinine

trimethoprim blocks the ENaC channel in the distal nephron, causing a hyperkalaemic distal RTA (type 4).

55. Pregnancy - elective caesarean section at term is advised if a primary attack of herpes occurs during pregnancy at greater than 28 weeks gestation

—> women with recurrent herpes who are pregnant should be treated with suppressive therapy and be advised that the risk of transmission to their baby is low

56. No vaccine is available but treatment is successful in the majority of patients. There is currently no vaccine for Hepatitis C, despite ongoing research. However, treatment has significantly improved over the years with the introduction of Direct-Acting Antivirals (DAAs). These medicines have a success rate of over 90% and can cure the disease within 8 to 12 weeks.

Management of chronic infection

- treatment depends on the viral genotype - this should be tested prior to treatment
- the management of hepatitis C has advanced rapidly in recent years resulting in clearance rates of around 95%. Interferon based treatments are no longer recommended
- the aim of treatment is sustained virological response (SVR), defined as undetectable serum HCV RNA six months after the end of therapy

- currently a combination of protease inhibitors (e.g. daclatasvir + sofosbuvir or sofosbuvir + simeprevir) with or without ribavirin are used

57. Anthrax is caused by the gram-positive soil organism *Bacillus anthracis*. Cutaneous anthrax represents over 90% of cases and it results from direct inoculation. Other forms include inhalation, injection and ingestion anthrax.

Anthrax is typically acquired from infected animals. Hence being a farmer is a risk factor. It is a very rare disease, but is most common in Central and South America, sub-Saharan Africa, central and southwestern Asia, and southern and eastern Europe.

It typically presents with a pruritic vesicle that develops two to five days after the time of inoculation, and then rapidly develops into a black painless ulcer and eschar. There is normally marked oedema surrounding the lesion, which can lead to compartment syndrome or necrotising fasciitis. In about half of cases, there is regional lymphadenopathy. If left untreated cutaneous anthrax has a mortality rate of 20%.

Mx - Ciprofloxacin

58. HIV-1/2 Ab/Ag Immunoassay (fourth generation) is correct. This fourth-generation assay should be used to screen individuals for HIV as it will detect HIV-1 and HIV-2 antibodies (Ab) and antigens (Ag) with high sensitivity within a short window period (technically still 45 days as per BHIVA guidelines).

59. Blocks enzymatic insertion of the viral genome into host DNA is correct. This is the 'gravir' class of medication, which are integrase inhibitors. The current BHIVA (British HIV Association) guidelines recommend bictegravir/tenofovir-alafenamide/emtricitabine - 'Biktarvy' - as first-line treatment for HIV in the absence of contraindications and drug-drug interactions. This regimen has a high barrier to resistance and is the optimal choice during the coronavirus pandemic where access to baseline testing for resistance may be less than normal. This patient has normal renal and hepatic function and is not on any other medications. Therefore, this combination is the typical initial choice.

Non-competitive inhibition of HIV reverse transcriptase is incorrect. This is the mechanism of action of non-nucleoside analogue reverse transcriptase inhibitors. This class of medication includes nevirapine and efavirenz. This would be another suitable choice in normal circumstances to add to a combination of two NRTIs. However, during the pandemic, the above combination is recommended.

Antagonism of CCR5 is incorrect. This is the 'entry inhibitor' class of medication. This includes maraviroc and enfuvirtide. This is typically not part of a standard starting regimen for treatment-naive patients and is usually only used if patient-specific factors dictate its use.

Competitive inhibition of HIV reverse transcriptase is incorrect. This is the mechanism of action of the nucleoside analogue reverse transcriptase inhibitors (NRTI). This class of medication includes emtricitabine and tenofovir. Typically, starting HIV medication regimens use two NRTIs and another medication class in combination.

Blocking proteases is incorrect. This is the protease inhibitor class of medication. Examples include ritonavir and indinavir. This would usually be a possible choice for initial combination therapy in HIV. However, given the current pandemic situation, an integrase inhibitor is preferred as the 3rd drug.

60. Rifampicin is an RNA synthesis inhibitor. It specifically inhibits bacterial DNA-dependent RNA polymerase. In doing so, elongation is physically blocked and so, without adequate RNA, bacteria cannot translate proteins.

61. This patient is most likely to have adrenal TB given her clinical history. Symptomatic anaemia would explain her fatigue, but not her electrolyte imbalance.

62. Amoebic colitis is caused by the anaerobic parasitic Amoebozoa *Entamoeba histolytica*. The diagnosis can be hard and often requires the input of a specialist infectious diseases lab. *Entamoeba histolytica* can be identified by stool microscopy only if

this is sent as a 'hot stool' and examined within 15 minutes of passage; after this the trophozoites encyst and become indistinguishable from the common and non-pathological *Entamoeba dispar*. In the scenario above it is impossible that the stool sample would arrive at the infectious diseases centre in time. Stool leukocytes are characteristically reduced due to suppression by parasite.

63. *Chlamydia psittaci* is incorrect. Psittacosis is an infection of birds caused by the bacterium *C. psittaci*. The disease has been described in many species of birds, particularly in parrots, parakeets, budgerigars and cockatiels. It typically causes flu-like symptoms (fever, headache, muscle aches) but can lead to severe pneumonia. The pneumonia is usually atypical with perihilar patchy reticular or reticulonodular opacities.

64. Pneumonia + Alcoholic + Cavitation = *Klebsiella*  
Pneumonia + cavitation = Staph, *Klebsiella*  
Pneumonia + Prior Flu = Staph Pneumonia  
Pneumonia + Chicken Pox Rash = Varicella  
Pneumonia + Hemolytic Anemia = *Mycoplasma*  
Pneumonia + Hyponatraemia + Travel History = *Legionella*  
Pneumonia + Fleeting opacities = Cryptogenic Pneumonia  
Pneumonia + Fits/LOC = Aspiration Pneumonia  
Pneumonia + HSV oral lesion = Strep Pneumonia  
Pneumonia + parrot = *Chlamydia psittaci*  
Pneumonia + farm animals = Q fever (*Coxiella burnetii*)  
Pneumonia + HIV = think PCP but if straight forward case strep pneumonia is still most common  
Pneumonia + Cystic fibrosis = consider *Pseudomonas*/  
*Burkholderia*  
Pneumonia + COPD or exac = *C1::Haemophilus Influenza*  
Commonest cause of CAP = Strep Pneumonia

65. The correct answer is yellow fever . This is caused by the yellow fever virus, which is a member of the Flaviviridae virus group and is transmitted by the *Aedes* mosquito. It is found in sub-Saharan Africa and South America.

The incubation period is short at 3-6 days following a mosquito bite. The first stage classically causes a non-specific illness which is often described as 'flu-like' with fever, malaise, nausea, myalgia and headache. This stage is due to the circulating virus in the bloodstream (viraemic stage). There is then a recovery stage when the viraemia clears. Most patients recover completely following this stage and do not progress to the third stage. Around 15% of patients progress after about 3-7 days after the onset of symptoms which presents with fever, nausea and vomiting, acute kidney injury, hepatitis with jaundice, and haemorrhage.

66. Of the non-falciparum malaria species, *Plasmodium knowlesi* has the shortest replication time. Its full replication cycle lasts just 24 hours, explaining the daily temperature spikes described in this scenario. No other malaria species could be attributed to a cyclical fever with a 24-hour interval. *Plasmodium knowlesi* is mostly found in Southeast Asia.

*Plasmodium falciparum* replication takes approximately 48 hours. This patient's daily cyclical fever is more in keeping with *Plasmodium knowlesi* infection.

*Plasmodium malariae* has a replication cycle of approximately 72 hours. A cyclical fever of this duration, rather than 24-hourly, would therefore be expected.

*Plasmodium ovale* has a replication cycle of 48 hours, with a corresponding cyclical fever of this duration. This is double the length of the replication cycle of *Plasmodium knowlesi*.

*Plasmodium vivax* also has a replication cycle of 48 hours. As such, it is unlikely to be the cause of the 24-hour cyclical fever here.

67. erythema multiforme in mycoplasma pneumonia; erythema chronica migrans in lyme ; erythema marginatum in rheumatic fever

68. This question is examining your knowledge of one of the important side effects of commencement of HAART - immune reconstitution inflammatory syndrome (IRIS). This condition

features a paradoxical worsening of a pre-existing chronic (or latent) condition. In this case, the patient had previous tuberculosis (TB) infection, which is hinted at by his chest x-ray findings and previous work in an endemic area. The presentation with haemoptysis, fevers, and shortness of breath, as well as the new opacities on the repeat radiograph, suggest a worsening or reactivation of the latent TB.

The pathophysiology of IRIS is not fully understood but is thought to feature excessive immune activation as CD4 counts rise.

69. The correct answer is enzyme-linked immunosorbent assay (ELISA). This patient has presented with symptoms of Lyme disease without the characteristic rash of Lyme disease. If there is clinical suspicion but no characteristic rash, the first line investigation is ELISA for IgM and IgG. If there is high clinical suspicion consider starting antibiotics.

70. An aspergilloma may arise in a lung cavity that developed secondary to previous tuberculosis

71. Factors which reduce vertical transmission (from 25-30% to 2%)

- maternal antiretroviral therapy
- mode of delivery (caesarean section)
- neonatal antiretroviral therapy
- infant feeding (bottle feeding)

Screening - NICE guidelines recommend offering HIV screening to all pregnant women

Antiretroviral therapy - all pregnant women should be offered antiretroviral therapy regardless of whether they were taking it previously

Mode of delivery - vaginal delivery is recommended if viral load is less than 50 copies/ml at 36 weeks, otherwise caesarian section is recommended

a zidovudine infusion should be started four hours before beginning the caesarean section

Neonatal antiretroviral therapy - zidovudine is usually administered orally to the neonate if maternal viral load is <50 copies/ml.

Otherwise triple ART should be used. Therapy should be continued for 4-6 weeks.

Infant feeding - in the UK all women should be advised not to breast feed

72. The most appropriate next step in treatment for this 23-year-old woman with recurrent genital warts is topical imiquimod.

Imiquimod is an immune response modifier that stimulates the production of cytokines, such as interferon-alpha, which can help to clear human papillomavirus (HPV) infections and reduce the size and number of genital warts. It has been shown to be effective in treating genital warts, particularly when other treatments have failed.

73. The CSF lymphocytosis combined with a glucose greater than half the serum level points towards a viral meningitis. TB meningitis is associated with a low CSF glucose

74. *Neisseria gonorrhoeae* can disseminate and cause the typical triad of dermatitis, migratory polyarthritits, and tenosynovitis. This is an exam favourite. The tendon and joint involvement are thought to be due to immune complex deposition, which results in an inflammatory response. They typically yield negative synovial fluid and joint cultures and rarely leads to significant joint destruction. The rash typically affects the trunk, limbs, palms and soles, and usually spares the face, scalp and mouth. This patient's joint pains and tendon pain coupled with the skin rash make this the most likely diagnosis.

**75. New Delhi metallo-beta-lactamase 1 is the mutation that leads to carbapenem resistance. Typically found in *Klebsiella pneumoniae*, *Escherichia Coli* (E. Coli), *Enterobacter cloacae* and others. First line of management is the old antibiotic colistin and second line may be tigecycline.**

D-alanyl-D-lactate variation leading to loss of affinity to antibiotics is the mechanism of VRE (vancomycin resistant enterococci). Vancomycin binds to D-ala-D-ala.

The presence of MexAB-OprM efflux pumps is one of the mechanisms by which *Pseudomonas aeruginosa* is resistant to  $\beta$ -lactams, chloramphenicol, fluoroquinolones, macrolides, novobiocin, sulfonamides, tetracycline, and trimethoprim.

Alteration to the penicillin binding protein 2 is the mechanism behind methicillin-resistant *Staphylococcus aureus*. Mutations in the *MEC* gene which codes the penicillin binding proteins give *Staphylococcus aureus* its resistance.

76. The correct answer in this case is Brucella serology. Brucellosis, also known as Malta fever or Mediterranean fever, is caused by the Gram-negative bacteria of the genus *Brucella*. The most common species affecting humans are *Brucella melitensis*, *Brucella abortus*, and *Brucella suis*. The infection can be transmitted through contact with infected animals or consumption of unpasteurised dairy products. In this case, the patient's recent stay on a Cypriot sheep farm suggests potential exposure to the bacteria.

Serological tests for Brucellosis detect antibodies against *Brucella* antigens in the patient's blood. These tests have high sensitivity and specificity, making them useful for confirming the diagnosis. The most commonly used serological test is the Rose Bengal Test (RBT), followed by confirmation using standard tube agglutination (STA) or enzyme-linked immunosorbent assay (ELISA).

77. The correct answer is Normal CSF result. The cerebrospinal fluid (CSF) findings in this case are within normal ranges. CSF glucose is typically 60-70% of serum glucose, so a value of 4.1 mmol/l with a serum glucose of 5.9 mmol/l is normal. Protein levels below 0.45 g/l are also considered normal and the white cell count is not elevated, indicating no infection or inflammation in the central nervous system.

Normal Lumbar puncture results

Appearance: clear and colourless

White blood cells (WBC): 0 – 5 cells/ $\mu$ L

No neutrophils present, primarily lymphocytes

Red blood cells (RBC): 0 – 10/mm<sup>3</sup>



Protein: 0.15 – 0.45 g/L (or <1% of the serum protein concentration)

Glucose: 2.8 – 4.2 mmol/L (or ≥ 60% plasma glucose concentration)

Opening pressure: 10 – 20 cm H<sub>2</sub>O

78. The presence of pus cells on urethral swab suggests a diagnosis of non-specific urethritis, which commonly presents with symptoms similar to these. BASHH recommend treating with oral doxycycline. The window period for Chlamydia and Gonorrhoea tests is generally 2 weeks so the home test he did is likely to be accurate; while retesting may be appropriate it should not delay treatment, and should not be delayed further.

79. This is a typical presentation of measles, a highly contagious airborne viral infection. Given the child's travel history and uncertain immunisation status, he is particularly susceptible.

A prodromal phase (which develops 10-12 days after contracting the virus) usually lasts for 2-4 days before the characteristic maculopapular skin rash develops. This prodromal phase includes fever, malaise, cough, rhinorrhoea and conjunctivitis.

Koplik's spots are pathognomonic for measles and may appear on the buccal mucosa at the end of the prodromal phase, around the same time as the rash, and disappear over the next couple of days. These consist of 2-3 mm red spots with white or blue-white centres.

In terms of the skin rash, it tends to appear on the face and behind the ears first, before spreading downwards and becoming confluent over the following 3-4 days before fading away usually within 1 week.

80. The correct answer is Albendazole. Albendazole is an anthelmintic (anti-worm) medication that works by preventing newly hatched insect larvae (worms) from growing or multiplying in the body. It is considered as the first line treatment for hydatid disease, also known as Echinococcosis, which is caused by

infection with the larval stage of *Echinococcus granulosus*, a species of tapeworm found in dogs and other carnivores.

**Sodium stibogluconate** is also not the right answer. Sodium stibogluconate is an antimonial compound used in the treatment of leishmaniasis, a disease caused by protozoan parasites spread by sandfly bites, rather than for treating tapeworm infections such as hydatid disease.

81. Cavitating pneumonia- *Klebsiella*, *Staph aureus*  
*Staph aureus* pneumonia followed a recent viral illness

***Staphylococcus aureus* infection** is correct. The patient presents with fever and shortness of breath and has chest x-ray evidence of pneumonia. The superimposed areas of lucency suggest cavitation. There are a number of causes of cavitating pneumonia but pneumonia caused by *Staphylococcus aureus* often follows a recent viral illness and therefore this is the likely cause in this presentation.

82. **Monod's sign** is similar to the **air-crescent sign**, which is a classic radiographic feature of air around a ball of fungus (in this case, an aspergilloma). Monod's sign is more specific for an aspergilloma whereas an air-crescent sign is an improving angioinvasive aspergilloma. The difference between the two signs is picked up by acquiring a chest X-ray in the prone position. Monod's sign implies the presence of a mobile mass, and so in the prone position would shift, whereas the air-crescent sign is fixed, and implies a reduction in the size of a fixed invasive aspergilloma mass.

Approximately 20% of immunocompetent individuals who had pulmonary tuberculosis, left with a cavity measuring above 2cm, develop a form of aspergilloma. Symptoms typically are chronic in immunocompetent hosts rather than more rapid and aggressive forms seen in the immunocompromised.

83. Lassa fever is contracted by contact with the excreta of infected African rats (*Mastomys* rodent) or by person-to-person spread. Treatment : **RIBAVIRIN**

Marburg Virus - hemorrhagic fever similar to Ebola, Risk factors for transmissions include caves/bats and primates.

84. In certain parts of South-East Asia there is widespread chloroquine resistance. Chemoprophylaxis using atovaquone + proguanil (Malarone), mefloquine (Lariam) or doxycycline is therefore recommended.

Chloroquine & Mefloquine should be avoided in this patient due to his history of epilepsy.

85. Interferon-alpha -> Hep B treatment

Interferon-beta -> Multiple sclerosis treatment

Interferon-gamma -> TB test

TB Test - Type IV delayed Hypersensitivity reaction

86. The cerebrospinal fluid (CSF) results show a clear sample with a lymphocytosis, normal protein and no polymorphs. This is all in keeping with a viral cause. Of the viruses listed, only mumps is known to cause a CSF result with low glucose. The other viral causes of meningitis would produce normal/near-normal glucose (60-80% of the serum glucose).

87. Intravenous drug use may cause acute skin infection, often caused by Streptococcal or Staphylococcal species (both gram-positive cocci). Rarely, heroin may be contaminated with *Bacillus anthracis* or *Clostridia* species, including *C. botulinum*, *C. perfringens* and *C. novyi*.

*Bacillus anthracis* (anthrax) is a spore-forming, aerobic gram-positive bacillus. Although treatment would be based on sensitivities, cutaneous anthrax is typically treated with ciprofloxacin or doxycycline.

88. Painless genital ulcers - 1) Syphilis 2) lymphogranuloma venereum 3) donovanosis (granuloma inguinale)

Granuloma inguinale caused by *Klebsiella granulomatis*

Painful genital ulcers 1) Herpes 2) Hemophilus ducreyi Chancroid disease

Chancroid associated with unilateral, painful inguinal lymph node enlargement; chancroid ulcers - ragged/undermined edges

Lymphogranuloma venereum - stage 1 : painless pustule

Stage 2 : painful inguinal lymphadenopathy

Stage 3 : proctocolitis

MX - Doxycycline

89. The correct answer is hepatitis E infection. This patient has severe transaminitis in the first trimester of pregnancy. This should make candidates consider hepatitis E infection, as pregnant patients tend to experience a more severe course of infection than other patient groups. Additional factors supporting the diagnosis of hepatitis E infection include thrombocytopenia, which is a recognised extra-hepatic manifestation of this infection, and the history of recent attendance at a barbecue (hepatitis E is often contracted from undercooked pork).

90. herpes simplex virus 1 and 2 -> cold sores, genital herpes

—> VZV - HHV 3 -> chickenpox, shingles

—> CMV (HHV 5) -> Glandular fever, CMV retinitis / colitis / oesophagitis in HIV

—> HHV 6 -> Glandular fever, roseola infantum

—> EBV (HHV 4) : Glandular fever, lymphoma, nasopharyngeal CA

—> HHV 7 -> Glandular fever, roseola infantum

—> HHV 8 -> Kaposi sarcoma

91. Needle stick injury Hep B 20-30%

Needle stick injury HIV **0.2%**

Needle stick injury Hep C - 2%

Vertical transmission Hep C - 6%

Sexual intercourse Hep C - 2%

92. Oseltamivir, an antiviral medication most commonly used in the treatment and prevention of influenza A and B (flu), works by

**inhibiting the activity of neuraminidase.** Neuraminidase is an enzyme found on the surface of influenza viruses that allows newly formed virus particles to be released from infected cells. By blocking this enzyme, oseltamivir prevents new viral particles from being released, which in turn limits the spread of infection.

93. Tetanospasmin - GABA is the correct answer. The features of lock-jaw and muscle spasms following an injury in soil which likely contained *Clostridium tetani* are most likely due to a diagnosis of tetanus toxin release. This tetanospasmin at the synaptic membrane between the lower motor neurone and the neuromuscular junction blocks the release of the inhibitory neurotransmitter GABA, thus the motor neuron is causing uninhibited excitation of the muscles resulting in muscular paralysis from over-stimulation. If left untreated this can lead to problems swallowing and diaphragmatic paralysis, which in turn can cause respiratory paralysis, a medical emergency.

94. The most appropriate investigation to exclude an HIV seroconversion illness in this case is the p24 antigen test. This is because the p24 antigen test can detect the presence of the HIV virus during the acute phase of infection before antibodies have had time to develop. The p24 antigen is a viral protein that is produced early in the course of HIV infection, and its detection can help to diagnose acute HIV infection.

95. Meningitis - If the patient has a history of immediate hypersensitivity reaction to penicillin or to cephalosporins the BNF recommends using chloramphenicol.

96. Long incubation period- amoebiasis - Metronidazole  
long duration of illness- giardiasis - Metronidazole  
acute- E.coli

Acute bloody diarrhoea in UK - *Campylobacter* - Ciprofloxacin

Long bloody diarrhoea - amoebiasis

long watery diarrhoea - giardiasis

Shorter bloody diarrhoea - *Campylobacter*

V Short bloody diarrhoea - E. Coli

97. Adults who have had an unplanned splenectomy should be vaccinated against Pneumococcus, meningococcus type B and C, and Haemophilus type B initially.

These vaccines should be given at least 14 days post-splenectomy for maximal efficacy. They should also receive the influenza vaccine if during the autumn or winter months.

They should also have meningitis ACWY and a further dose of meningitis B after 2 months.

98. Parasite burden is evaluated from **thick** blood films, while thin films allow for speciation.

**Thin** peripheral blood films allow for better visualisation of the parasites and therefore speciation.

99. MAC infection - A minimum of two drugs should be given: clarithromycin plus ethambutol. In severe disease, rifabutin can be added. This is recommended due to fewer side-effects than rifampicin however rifampicin is still widely used as the third drug in severe disease due to its cheaper cost. Azithromycin can be also substituted for clarithromycin in severe disease.

100. This patient has presented with clear features in keeping with pneumonia (respiratory symptoms and chest x-ray changes etc). They also have features indicating a potential atypical pneumonia with extra-pulmonary symptoms in the form of gastrointestinal (GI) upset, although these are non-specific findings.

**The key feature in this case is the peripheral blood smear showing red blood cell (RBC) agglutination making Mycoplasma pneumoniae the most likely diagnosis.**

This agglutination is a result of the surface of the RBC becoming coated with antibodies and typically occurs in cold agglutinin disease, a form of autoimmune haemolytic anaemia which can be triggered by specific infections.

**Cold agglutinin disease** is a well-recognised feature of Mycoplasma pneumoniae.

101. Aciclovir is phosphorylated after entry into herpes infected cells to form aciclovir triphosphate. The first step in this process is dependant on the presence of HSV-coded thymidine kinase.

Aciclovir triphosphate acts as an inhibitor of, and substrate for, the

herpes-specific DNA polymerase, preventing further viral DNA synthesis without affecting normal cellular processes. It is 10-30 times more specific for viral DNA polymerase versus the human enzyme.

102. This patient is presenting with symptoms typical of Brucellosis; Fluctuating temperatures, transient arthralgia and myalgia, hyperhidrosis with a 'wet hay' smell. The clue in the history is his exposure to unpasteurised cheese.

*Brucella melitensis* is the bacteria found in contaminated unpasteurised milk that causes brucellosis.

103. The correct answer is doxycycline. This patient is presenting with fever, headaches, and a rash which started on his trunk and spread over his limbs with sparing of his palms and soles. There is also possible exposure to fleas given the history of vermin. This raises the suspicion of typhus. There is an increasing incidence of typhus across South and Southeast Asia, particularly scrub typhus. This intracellular pathogen must always be considered in the differential diagnosis of travellers presenting with fever within three weeks of their return. Antibiotics should be initiated as soon as possible, usually before serological confirmation of the diagnosis.

104. Genital wart treatment

- multiple, non-keratinised warts: topical podophyllum
- solitary, keratinised warts: cryotherapy

Topical podophyllum, a cytotoxic agent that inhibits cell division and DNA synthesis,

105. Listeria infection - spread via contaminated food through unpasteurised milk products

Risk factors - immunocompromised, elderly, neonates

C/F : Gastroenteritis - diarrhoea, bacteremia - flu like illness, CNS - meningoencephalitis, ataxia, seizures

INV : Blood cultures shows **tumbling** motility

CSF - pleocytosis - lymphocytes predominant, raised protein, reduced glucose

Mx : Sensitive to Amoxicillin/Ampicillin, Listeria meningitis in elderly treated with IV Amoxicillin + Gentamicin

Pregnant woman 20 times higher risk of infection

Complications - chorioamnionitis, miscarriage, premature labor, stillbirth

105. HIV: anti-retrovirals - P450 interaction

nevirapine (a NNRTI): induces P450

protease inhibitors: inhibits P450

106. While certain strains of E. coli, including O157:H7, can be foodborne, they are most commonly associated with contaminated beef products or raw milk rather than shellfish. This particular strain produces Shiga toxins and can cause severe gastrointestinal illness and haemolytic uraemic syndrome.

107. Erythema infectiosum', 'fifth disease' and 'slap cheek' are the same condition which are all possible manifestations of parvovirus B19 infection. It is associated with fetal abnormalities and commonly causes a characteristic rash in children and in adults it can additionally cause arthralgia.

Infection in a pregnant woman can lead to fetal hydrops and spontaneous miscarriage, particularly in the first trimester. This can be managed with the use of fetal blood transfusion.

In patients with sick-cell disease, aplastic crisis may be precipitated by parvovirus. Immunocompromised individuals are also at risk.

108. The patient is asymptomatic so we can say she does not have active TB. However, she may have latent TB. TB is not easily caught and requires prolonged close contact. The recent NICE guidelines state that the initial screening test is the Mantoux test. The interpretation has also changed in the recent guidelines. A diameter of 5 mm is considered positive regardless of BCG history.



109. A history of Intravenous drug use coupled with a descending paralysis, diplopia and bulbar palsy is characteristic of infection with **Clostridium botulinum**

**Presenting features typically include difficulty speaking or slurred speech, blurred or double vision, and/or dysphagia. Other features include ptosis and facial muscle weakness. Without treatment, paralysis may progress to the upper limbs, trunk, lower limbs and respiratory muscles.**

Intravenous drug users are particularly at risk of developing infection with clostridium botulinum, through injecting contaminated drugs into skin or muscle. Botulism spores are found naturally in the environment (such as in soil), so they can contaminate supplies of drugs such as heroin.

NO FEVER OR LOSS OF SENSATION OR LOSS OF AWARENESS.

110. Staphylococcal toxic shock syndrome

Centers for Disease Control and Prevention diagnostic criteria

- fever: temperature  $> 38.9^{\circ}\text{C}$
- hypotension: systolic blood pressure  $< 90$  mmHg
- diffuse erythematous rash
- desquamation of rash, especially of the palms and soles
- involvement of three or more organ systems: e.g. gastrointestinal (diarrhoea and vomiting), mucous membrane erythema, renal failure, hepatitis, thrombocytopenia, CNS involvement (e.g. confusion)

111. Clarithromycin is the correct answer. This patient likely has a Campylobacter infection given his presentation of bloody diarrhoea, fevers, and consumption of unpasteurised milk. Campylobacter infections are typically associated with the consumption of undercooked poultry or unpasteurised milk.

112. Chikungunya - Prominent symptoms are severe joint pain and abrupt onset of high fever. Other symptoms include general flu-like illness of muscle ache, headache, and fatigue. The disease shares its symptoms with dengue but tends to have more joint pain which

can be debilitating. A rash may develop as with other viral illness and swelling of the joints is not uncommon.

**113. Spiramycin may reduce the risk of toxoplasmosis transmission from mother to fetus in pregnancy.**

114. This concept was tested in the MRCP, specifically recognising the association between rhabditiform larvae and strongyloidiasis. This patient has symptoms and eosinophilia consistent with a gastrointestinal parasite. The rhabditiform larvae are diagnostic of strongyloidiasis, and the life-cycle of this worm involves passage through the lungs which causes the intermittent cough. Ivermectin is the most effective treatment for strongyloidiasis, and a single dose regime is highly effective.

115. The correct answer is Orf. Orf, also known as contagious ecthyma, is a zoonotic infection caused by the Parapoxvirus. It is common in sheep and goat farmers. The disease presents with a small, red papule that enlarges over time to form a larger lesion which can be haemorrhagic and flat-topped as described in the question. The history of the patient being a sheep farmer and the clinical presentation make Orf the most likely diagnosis.

116. Tularemia is a zoonotic infection involving the microorganism *F. tularensis* commonly transmitted through lagomorphs such as rabbits, hares and pikas but also in aquatic rodents - beavers and muskrat - and ticks. It can present in a variety of forms. Commonly, it produces an erythematous papulo-ulcerative lesion at the site of the bite with reactive and ulcerating regional lymphadenopathy. It is treated with antibiotics such as doxycycline.

117. testing for anti-HBs is only recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease. In these patients anti-HBs levels should be checked 1-4 months after primary immunisation

- around 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine. Risk factors include age over 40 years, obesity, smoking, alcohol excess and immunosuppression

118. MRSA will be resistant to all beta-lactam-based antibiotics, including cephalosporins and carbapenems because it produces a mutated protein (penicillin-binding protein 2a) to which beta-lactams can no longer bind and therefore cannot affect their action. It will be sensitive to glycopeptides, including vancomycin and teicoplanin, which have different mechanisms of action. They also interfere with cell wall synthesis but do so by binding to the D-ala-D-ala terminal of the pentapeptide chain and blocking the further extension of the chain.

119. This patient has acquired typhoid whilst in Sri Lanka and has followed a fairly typical course. Abdominal pains are common and constipation predominates over diarrhoea. When they occur, severe manifestations such as typhoid delirium/encephalitis and abdominal perforation (which the patient in the vignette has experienced) typically occur in the third week of illness. Leukopenia is sometimes seen but the white cell count is normally within the normal range. Rose spots are insensitive and their absence does not exclude the diagnosis. A relative bradycardia (Faget sign) is typical of typhoid fever.

The test of choice is a large volume blood culture (the large volumes are needed to increase the yield as few bacteria are circulating). The Widal test is commonly used globally but is not recommended for clinical use due to low sensitivity and specificity. Bone marrow cultures have increased sensitivity compared to blood cultures and are considered in exceptional circumstances.

120. Worldwide, enterotoxigenic *E. coli* (ETEC) is the most common cause of diarrhoea in travellers. There is, however, geographical variation - *Campylobacter* is more common in travellers in South East Asia.

121. The correct answer is Steroids. According to the British HIV Association and British Thoracic Society guidelines, adjunctive corticosteroid therapy is recommended for patients with moderate to severe *Pneumocystis carinii* pneumonia (PCP) who have a  $pO_2$  of less than 8 kPa or an A-a gradient greater than 35 mmHg. Steroids work by reducing the intense inflammatory response in the lungs caused by the organism, which can lead to respiratory failure.

122. Relative bradycardia, also known as Faget's sign, is a clinical feature of typhoid fever caused by *Salmonella typhi*. It refers to the presence of a pulse rate slower than would be expected for a given elevated body temperature. This paradoxical presentation is not exclusive to typhoid fever but it is commonly associated with it.

123. *Shigella* infection is usually self-limiting and does not require antibiotic treatment; antibiotics are indicated for people with severe disease, who are immunocompromised or with bloody diarrhoea. This patient sounds fairly well; hospital admission would be inappropriate and *Shigella* is only notifiable if food poisoning is suspected. Antimotility drugs are not recommended in infective diarrhoea

124. The correct answer is serology for *Aspergillus* precipitins. Aspergilloma, a fungal ball within a pre-existing lung cavity commonly caused by *Aspergillus fumigatus*, is often suspected based on radiological findings and clinical symptoms. The most appropriate next test to confirm the diagnosis is serologic testing for *Aspergillus* precipitins. This test detects antibodies in the patient's serum that react with *Aspergillus* antigens, indicating an immune response to the fungus. It has high sensitivity and specificity, making it an excellent diagnostic tool.

125. This child has received the BCG vaccine. This is the only UK vaccination that is based on the risk factors of the individual child. All infants aged 0-12 months who have a parent or grandparent born in a country with an incidence of TB greater than 40 per 100,000 people should receive the BCG. All infants living in areas of the UK with incidence  $> 40/100,000$  are also offered the BCG.

The BCG vaccine does not prevent primary infection with tuberculosis or prevent the reactivation of latent TB. It does not provide reliable protection against any forms of TB in adults. It is still used because it is protective against severe diseases in children, particularly TB meningitis and disseminated TB in children. It is thought to prevent 60 - 80% of cases of TB meningitis in children who received BCG as neonates.

126. The BNF now says at least two years rifampicin + dapsons + clafazimine for multibacillary.

Paucibacillary remains those two agents for 6 months.

Multi bacillary >6 lesions

127. **Egg protein** is present in clinically significant quantities in the yellow fever vaccine.

Anaphylaxis to egg protein is also a contraindication to the use of propofol.

Egg embryos are also used in the production of the MMR and some rabies vaccines.

128. ETEC- TRAVELLERS WATERY DIARRHHEA  
EHEC,Shigella -TRAVELLERS BLOODY DIARRHOEA

129. The Meningococcal vaccines, including the MenACWY and MenB vaccines, are examples of conjugate vaccines. Conjugate vaccines are those that use a protein that attaches to the polysaccharide outer coat of the pathogen to make it more immunogenic. This is because polysaccharides alone are not very immunogenic, especially in infants and young children. By linking these polysaccharides to a protein, the immune system can recognise and respond more effectively to the pathogen.

Other conjugate vaccines - Pneumococcus, H.influenza B, Meningococcus

Sub unit vaccines - Hepatitis B, Human papillomavirus

130. Latent TB - Mantoux test

Interferon gamma test is used if Mantoux test is equivocal or positive or in people where tuberculin test is falsely negative.

131. Cryptosporidium is the most common infective cause of diarrhoea in HIV patients. It is an intracellular protozoa and has an incubation period of 7 days. Presentation is very variable, ranging from mild to severe diarrhoea. A modified Ziehl-Neelsen stain (acid-fast stain) of the stool may reveal the characteristic red cysts of

Cryptosporidium. Treatment is difficult, with the mainstay of management being supportive therapy\*

132. The patient has presented with a typical history of bacterial vaginosis. There is a white homogenous discharge which is foul-smelling. Bacterial vaginosis occurs where there is an overgrowth of anaerobic bacteria, leading to a loss of lactic acid-producing lactobacilli. This leads to a rise in pH to above 4.5. Whilst bacterial vaginosis is not a sexually transmitted infection. It is more commonly seen in people who are sexually active.

The most commonly seen organism is *Gardnerella vaginalis* a peptidoglycan walled coccobacillus which can appear as both gram-positive or occasionally gram-negative due to its very thin wall.

133. Human bites organisms -

*Streptococcus*

*Staph aureus*

*Eikenella*

*Fusobacterium*

*Prevotella*

134. Vancomycin is a glycopeptide antibiotic, which works by blocking cell wall subunit assembly (separate from beta lactams). The antibiotic has extensive gram positive cover and is commonly used to treat MRSA and *Clostridium difficile*.

The characteristic side effects include: Ototoxicity, nephrotoxicity and red man syndrome.

**Red man syndrome** is associated with flushing or a maculopapular rash. The proposed mechanism is **non IgE mediated mast cell degranulation**.

Red man syndrome is more common with higher flow rates of infusion.

Treatment includes **antihistamines**.

**135.** This patient's presentation of malaise, fever, and extensive painful oral ulceration with submandibular lymphadenopathy is classic for primary herpes simplex virus (HSV) infection. HSV typically presents as painful ulcers after an incubation period of 2-20 days following exposure. Fever and malaise are common

systemic symptoms. Lymphadenopathy can be present due to the body's immune response to the infection.

136. Erythema multiforme target lesions - Mycoplasma pneumoniae, Pneumococcus

**137.** MRSA tackling in hospitals - hand hygiene most effective

**138.** The correct answer is to Arrange an anti-HCV antibody test. This is because Hepatitis C Virus (HCV) infection is commonly associated with intravenous drug use. The risk of acquiring HCV from this practice in the 1990s was particularly high due to less stringent needle hygiene practices. An anti-HCV antibody test would be the first step in diagnosing a current or past infection with hepatitis C. If positive, it would then be followed by a HCV RNA test to confirm ongoing viral replication and need for treatment.

**139.** painless ulcer painless LN = syphilis

Single painless ulcer painful LN = LGV

Indolent painless ulcers 'regional lymphadenopathy is rare' >>  
Granuloma inguinale

Multiple painful ulcer with ragged edges painful LN = chancroid H. ducreyi

Multiple painful blisters/ulcers with tingling pain neuropathic type pain and tender inguinal lymph nodes + systemic symptoms=  
Genital herpes simplex

**140.** Zanamivir (Relenza) is an antiviral medication used to treat and prevent influenza. It works by inhibiting the neuraminidase enzyme, thus preventing the release of new virus particles from infected cells. However, it can cause bronchospasm in patients with underlying respiratory diseases such as asthma or chronic obstructive pulmonary disease (COPD). UK guidelines recommend caution when prescribing zanamivir in patients with these conditions due to the risk of exacerbation of their symptoms.

**141. Erysipelas** is an acute infection typically with a skin rash, usually on any of the legs and toes, face, arms and fingers. It is primarily caused by Streptococcus pyogenes, also known as Group A Streptococcus (GAS). This organism is highly virulent and can cause a wide range of infections, including pharyngitis, impetigo, cellulitis, necrotising fasciitis and erysipelas. The characteristic features of erysipelas are a well-demarcated

erythematous rash with raised borders and systemic symptoms such as fever.

142. Acute toxoplasmosis is difficult to diagnose and the definitive diagnosis requires histopathological identification of the organism and is rarely obtained. It is typically diagnosed by serology with IgM levels rising 5 to 14 days after infection, peaking after 2-3 months and returning to normal shortly thereafter.

The most likely source of her toxoplasmosis is undercooked meat from her BBQ. Although cat faeces are a well known source of toxoplasmosis (and could equally be the source here) consumption of undercooked meat is common and often under appreciated as a route of infection.

**143. Spiramycin is the drug of choice if toxoplasmosis is diagnosed in the first or second trimester of pregnancy, as it has been shown not to have teratogen properties. Treatment of toxoplasmosis is important in pregnancy to prevent potential congenital toxoplasmosis complications.**

144. Live vaccines

- BCG
- MMR
- Influenza (intranasal)
- Yellow fever
- Oral polio, rota, typhoid

So basically, the vaccines ALWAYS contraindicated in HIV are

2 GI infection -> cholera, polio

2 lung infection -> BCG (TB), intranasal Influenza

Contraindicated < 200 are those cause rash

- Yellow fever (petechial rash)
- MMR
- Chicken pox

145. The most appropriate answer is serum cortisol. The patient's history of tuberculosis, non-compliance with treatment, symptoms of fatigue and weight loss, and postural hypotension with hyponatraemia and hyperkalaemia suggest the possibility of adrenal insufficiency. This can occur as a result of adrenal tuberculosis, which may have developed due to her discontinuation of anti-TB therapy. The most appropriate next step would be to



check her serum cortisol levels to confirm or exclude this diagnosis. Other investigations listed may be relevant for different clinical scenarios but are less likely in this case based on the information provided.

146. Hepatitis E is associated with faecal-oral spread, commonly affecting shellfish and pork products. Blood results show elevated bilirubin and significant transaminitis.

147. The correct answer is ciprofloxacin. This quinolone antibiotic has good efficacy against gram-negative organisms including *Pseudomonas aeruginosa*. Its use is well-recognised to promote the acquisition of MRSA.

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## CLINICAL PHARMACOLOGY & TOXICOLOGY

### 1. Drugs causing thrombocytopenia -

- Quinine
- Antibiotics - Penicillins, Sulphonamides, Rifampicin (inhibits RNA synthesis)
- NSAIDs
- Heparin
- Abiciximab
- Furosemide
- Anti convulsants - carbamazepine, valproate

### 2. Drugs causing Impaired glucose tolerance :

Thiazides, Fursomedie  
Steroids, Interferon-alpha  
Tacrolimus, Cyclosporin  
Nicotinic acid

### 3. Drugs causing urinary retention -

- Opioids                      - Anti cholinergic
- NSAIDs                      - Dipyridamole                      - TCA - Amitryptiline

### 4. Alpha-1 agonist - Phenylephrine, Oxymetazoline -

#### **Decongestant**

Alpha-2 agonist - topical Briminodine - Glaucoma

Alpha 1a antagonist - Tamsulosin - Benign Prostatic Hyperplasia  
Alpha 1 antagonist - **Doxazosine** - Hypertension

5. Beta 1 agonist - **Dobutamine** - Heart failure

Non selective beta-1 blocker - **Atenolol, Bisoprolol**

Beta 2 agonist - **Salbutamol** - Asthma

6. Dopamine agonist - **Bromocriptine, Cabergoline, Ropinirole**  
Parkinson's disease, Prolactinemia

Dopamine antagonist - **Haloperidol, Metoclopramide, Domperidone**

**Haloperidol** - Schizophrenia

**Metoclopramide, Domperidone** - Anti emetics

7. GABA Agonist - **BZD, Baclofen** - muscle spasticity  
Antagonist - **Flumazenil** (BZD overdose)

8. Histamine - 1 antagonist - antihistamines - **loratadine**  
Urticaria, DRESS

9. Histamine - 2 antagonist - **antacids** - Ranitidine

10. Muscarinic agonist - **Pilocarpine** - Glaucoma

Muscarinic antagonist - **Atropine** (Bradycardia)

**Ipratropium bromide, Tiotropium Bromide** (COPD)

**Oxybutynin** (Urge incontinence)

11. Nicotinic agonist - **Varenicline** (smoking cessation)  
**Suxamethonium** (depolarising muscle relaxant)

Nicotinic antagonist - **Atracurium** - non depolarising muscle relaxant

12. Oxytocin - Agonist - **Synoctin** - inducing labor

Antagonist - **Atosiban** - Tocolytics

**13.** Serotonin - Agonist - **Triptan** - Migraine

Antagonist - Anti emetics - **Ondansetron**

**14.** Drugs causing lung fibrosis -

1. **Amiodarone**
2. Cytotoxic agents - Busulphan, Bleomycin
3. **Nitrofurantoin** (UTI treatment - 1st trimester)
4. Ergot derived dopamine agonists - Bromocriptine, Cabergoline, Pergolide

Ergot derived dopamine agonists - high risk of cardiac, retro peritoneal and pulmonary fibrosis.

**15.** Drugs causing ocular problems -

- Cataracts - Steroids
- Corneal opacities - **Amiodarone**, Indomethacin
- Optic neuritis - **Ethambutol** (anti TB), **Amiodarone**, **Metronidazole**
- Retinopathy - **Chloroquine** (anti malarial), **Quinine** (anti malarial)

Digoxin toxicity - green yellow discolouration

Sildenafil - **blue discolouration, non arteritis ischemic neuropathy**

**16.** Drugs causing photosensitivity -

- Thiazides
- **Tetracyclines**, sulphonamides, ciprofloxacin
- Amiodarone
- NSAIDs - Piroxicam
- Psoralen's
- **Sulphonylureas - Metformin**

**17. AMIODARONE** - hypothyroidism, hyperthyroidism type 1, hyperthyroidism type 2, photosensitivity, corneal opacities, lung fibrosis, optic neuritis

**18. Serotonin agonist** -

- Sumatriptan : 5-HT<sub>1D</sub> receptor agonist : acute migraine
- Ergotamine - partial agonist of 5-HT<sub>1</sub> receptor

Serotonin Antagonists -

- **Pizotifen** : 5-HT<sub>2</sub> receptor antagonist : prophylaxis of migraine attacks
- Methysergide : 5-HT<sub>2</sub> receptor antagonist : rarely used due to risk of retroperitoneal fibrosis
- Cyproheptadine : 5-HT<sub>2</sub> receptor antagonist : control diarrhoea in patients with carcinoid syndrome
- Ondansetron : 5-HT<sub>3</sub> receptor antagonist : anti emetic

**19. Ecstasy overdose**

Clinical features :

CNS - agitation, anxiety, confusion, ataxia, dilated pupils, lock jaw, bruxism (teeth grinding)

CVS - tachycardia, hypertension

Hyponatremia - due to SIADH or dilution hyponatremia

Hyperthermia

Rhabdomyolysis

Seizures

Mx - supportive, dantrolene in case of hyperthermia

This patient has presented with 3,4-methylenedioxymethamphetamine (MDMA) also known as ecstasy toxicity.

MDMA's mechanism of action involves releasing and inhibiting the reuptake of serotonin, leading to increased serotonin levels. It also stimulates dopamine and norepinephrine release and directly binds to related receptors, contributing to its mood-elevating and stimulating effects.

MDMA toxicity can induce **hyponatremia** by triggering the syndrome of inappropriate antidiuretic hormone secretion (SIADH),

leading to excessive water retention and sodium dilution.  
Additionally, MDMA increases thirst which can cause users to consume excessive amounts of water, overwhelming the body's ability to excrete, again resulting in sodium dilution.

## 20. Ethylene glycol poisoning

Stage 1 : similar to alcohol intoxication - confusion, slurred speech, dizziness

Stage 2 : metabolic acidosis with high anion gap and high osmolar gap; tachycardia, hypertension

Stage 3 : acute kidney injury

Poisoning with ethanol or methanol :

The British Association for Accident & Emergency Medicine (BAEM) guidelines suggest that an elevated osmolar gap ( $>10$  mOsm/kg H<sub>2</sub>O) may indicate poisoning with these alcohols or their metabolic products.

MX : Fomepizole - inhibitor of alcohol dehydrogenase

Previously - ethanol was used as it competitively inhibits for enzyme alcohol dehydrogenase

21. Amiodarone-induced thyrotoxicosis (AIT) can be categorised into two types: AIT type 1 and AIT type 2. Type 1 is associated with an underlying thyroid disease and is treated with antithyroid drugs, whereas type 2 is a form of destructive thyroiditis and is typically managed with corticosteroids according to UK guidelines.

22. Methanol poisoning : alcohol effects (intoxication, nausea) and visual problems (blindness, optic neuropathy).

Effects are due to accumulation of formic acid.

MX : Fomepizole (competitive inhibitor of alcohol dehydrogenase) or Ethanol

Hemodialysis

Co-factor therapy with Folinic acid to reduce visual complications

## 23. MONOCLONAL ANTIBODIES

- Infliximab : anti TNF - Rh arthritis, Crohn's
- Rituximab :anti CD20-Rh arthritis, Non-Hodgkin's Lymphoma
- Cetuximab : Epidermal growth factor receptor antagonist - Metastatic colon cancer, Head & Neck cancer
- Trastuzumab : HER2/neu receptor antagonist - metastatic breast disease
- Alemtuzumab : anti CD52 - Chronic lymphocytic leukaemia
- Abciximab : Glycoprotein IIb/IIIa receptor antagonist - Percutaneous coronary interventions

Abiciximab - can cause thrombocytopenia

- OKT3 : anti CD3 - used to prevent organ rejection

Cetuximab & Panitumumab - metastatic colon cancer

Infliximab and Adalimumab - Crohn's disease

24. Mercury poisoning is correct. The patient ingests extremely large amounts of albacore tuna, which is a type of fish that has a large amount of mercury (up to 33 parts per million of mercury).

Symptoms and signs of chronic mercury poisoning include visual field defects, hearing loss, and paraesthesia, peripheral neuropathy.

Treatment is with avoidance of the source and chelation.

25. Lead poisoning - can cause peripheral neuropathy but is unlikely to cause a visual field defect. Additionally, it often causes constipation and vomiting and blue lines may be noted on the gums (known as Burton's lines).

A typical exposure would be lead paint in a poorly maintained house rather than excessive tuna.

26. Manganese Poisoning - acute : visual hallucinations and anxiety

Later stages - can mimic Parkinson's disease - tremors, gait disturbances, low volume speech

Typical exposure - fume inhalation while working with steel

27. Zinc poisoning - GI distress, abdominal pain, nausea

Chronic toxicity - spastic gait, sensory ataxia

28. Amlodipine side effects - gingival hyperplasia, ankle swelling, flushing, headache

29. Stimulants : similar to MDMA, Amphetamines, Cocaine - high levels of Serotonin, Dopamine and Noradrenaline

Example - Mephedrone 'bath salt' 'M-CAT' 'meow-meow'

Benzyl piperazine 'Exodus' 'Legal X' 'Legal E'

Risk of serotonin syndrome, adverse effects similar to cocaine

30. Hallucinogenics - either dissociative or psychedelics

Dissociative similar effect to ketamine

Psychedelics - similar effect to LSD

31. Octreotide - somatostatin analogue

Somatostatin - inhibits the release of Growth Hormone, insulin and glucagon

Uses - acute variceal bleeding treatment, acromegaly, carcinoid syndrome, VIPomas, refractory diarrhoea, following pancreatic surgery

Adverse - gall stones due to biliary stasis

32. Oculogyric crisis - dystonic reaction to drugs or metabolites

C/F - restlessness, agitation, involuntary upward deviation of eyes

Causes - 1) anti psychotics 2) Metoclopramide 3) post encephalitis  
Parkinson's disease

MX - IV antimuscarinic - Benztropin / Procyclidine / Trihexiphenidyl

33. Cortical necrosis is a rare cause of acute kidney injury caused by renal vascular spasm and microvascular injury. It frequently occurs in pregnancy.

34. Zero order kinetics : Phenytoin, Salicylates

35. Phase I reactions - oxidation, reduction, hydrolysis

## Phase II reactions - conjugation

Drugs showing first pass metabolism :

- Aspirin
- Isosorbide dinitrate, Isosorbide trinitrate
- Glyceryl trinitrate
- Lignocaine AKA Lidocaine
- Propranolol
- Verapamil
- Isoprenaline
- Testosterone
- Hydrocortisone

Zero order kinetics drugs -

- Phenytoin
- Salicylate - high dose aspirin
- Heparin
- Ethanol

Drugs affected by acetylator status - due to deficiency in Hepatic N-acetyl transferase

- Isoniazid
- Dapsone
- Procainamide
- Hydralazine
- Sulfasalazine

36. PHOSPHODIESTERASE TYPE 5 INHIBITORS - causes vasodilation through increase in cGMP leading to smooth muscle relaxation

Sildenafil - Viagra : short acting, 1 hour before sexual activity

Tadalafil - Cialis : longer acting than Sildenafil, once daily

Contraindications :

1. Patient taking nitrates and related drugs such as Nicorandil
2. Hypotension
3. Recent stroke or MI - wait period of 6 months

Uses - Erectile dysfunction, Pulmonary Hypertension



Adverse - blue discolouration, non arteritic anterior ischemic optic neuropathy  
nasal congestion  
flushing  
GI side effects  
headache  
Priapism

37. Conjugation of paracetamol becomes saturated in overdose. Paracetamol is primarily metabolised in the liver via conjugation with sulphate and glucuronide, which are then excreted by the kidneys.

However, a small fraction is also metabolised by the cytochrome P450 system to form a toxic metabolite called N acetyl-p-benzoquinone imine (NAPQI). Under normal circumstances, NAPQI is immediately detoxified by glutathione. When an overdose of paracetamol occurs, the conjugation pathways become saturated leading to more metabolism through the P450 system and subsequently excessive production of NAPQI.

This depletes glutathione stores causing accumulation of NAPQI which leads to hepatocellular damage.

38. G protein coupled receptor - Opioid receptor, Beta receptors

Ligand gated ion channels - nicotinic acetylcholine, GABA receptors

Tyrosine kinase - Insulin

Nuclear receptors - Hydrocortisone, Levothyroxine

Levothyroxine is transported into the target cells via a transporter, before binding on to a nuclear receptor to directly influence gene transcription and translation. This kind of signal transduction is slow compared to others but tends to lead to a more prolonged effect.

39. Caustic ingestion usually occurs accidentally and is of little consequence clinically.

However, in the case of deliberate self-harm or suicide attempts, larger quantities may be consumed.

As well as clarifying the precise substance ingested, it is important to follow general management principles including an ABCDE approach.

This patient is symptomatic - experiencing nausea, vomiting and odynophagia. As such, she warrants urgent upper GI endoscopy to assess the degree of ulceration.

40. In paediatric patients, there are at higher risk of **hyponatraemic encephalopathy**.

This is most noted in those who receive hypotonic intravenous fluids such as **0.45% sodium chloride**.

There is a second reason for the hyponatraemia in this patient, a well documented cause of SIADH is trauma and stress.

ADH secretion lowers serum sodium levels through opening aquaporin channels allowing water to move into the intravascular space.

41. **Potassium sparing diuretics** - 2 types :

- Epithelial Sodium Channel Blockers
  - A. Amiloride : blocks the Epithelial Na channel in DCT; weak diuretic, usually given in combination with thiazide or loop to counter hypokalaemia
  - B. Triamterene
- Aldosterone antagonists - Spironolactone, Eplerenone
  - a) Spironolactone : acts in cortical collections duct
    - i) Ascites - patients with cirrhosis develop secondary hyperaldosteronism
    - ii) Heart failure
    - iii) Nephrotic syndrome
    - iv) Conn's syndrome

42. Drugs to avoid in renal failure -

- A. Antibiotics - tetracycline, Nitrofurantoin
- B. NSAIDs
- C. Lithium
- D. Metformin

Drugs which require dose adjustment in CKD -

- Antibiotics - penicillins, cephalosporins, Vancomycin, Gentamicin, treptomycin
- Digoxin
- Atenolol
- Methotrexate
- Sulfonyureas
- Furosemide
- Opioids

Drugs safe in CKD - Erythromycin, Rifampicin, Diazepam, Warfarin

#### 43. Quinine toxicity - Cinchonism

Used as anti-malarial drug, prophylaxis against leg cramps.

Toxicity can be fatal due to cardiac arrhythmia and flash pulmonary edema.

Arrhythmia - prolonged QRS and QT interval, ventricular fibrillation

Hypoglycemia - quinine stimulates pancreatic secretion of insulin.

Flash pulmonary edema - hypoxia

Classical hallmarks : tinnitus, visual blurring, flushed dry skin, abdominal pain, visual defects

MX - supportive fluids, inotropes, bicarbonate, positive pressure ventilation

44. Quinolone - inhibits bacterial DNA synthesis - inhibits topoisomerase II (DNA gyrase) and topoisomerase IV

Ciprofloxacin, Levofloxacin

Ciprofloxacin —> P450 inhibitors

Adverse effects -

- lowers seizure threshold in epileptics
- Achilles tendon rupture
- Cartilage damage
- QT prolongation

AVOID in - pregnant, breast feeding, G6PD deficiency

#### 45. Salicylate overdose - mixed respiratory alkalosis + metabolic acidosis

Early stimulation of respiratory centre - resp. Alkalosis

Direct renal effect of salicylates with acute renal failure - acidosis

C/F :

- A. Hyperventilation
- B. Tinnitus
- C. Lethargy
- D. Sweating, pyrexia
- E. Nausea, vomiting
- F. Hyperglycaemia & hypoglycaemia
- G. Seizures
- H. Coma

Pyrexia - salicylates causes uncoupling of oxidative phosphorylation leading to decreased ATP production, increased oxygen consumption, increased CO<sub>2</sub> and heat production

MX : urinary alkalinisation with IV HCO<sub>3</sub>, hemodialysis

Indications for hemodialysis in salicylate overdose -

- Serum concentration >700 mg/L
- Metabolic acidosis resistant to treatment
- Acute renal failure
- Pulmonary edema
- Seizures
- Coma

#### 46. Serotonin Syndrome

Causes :

- Monoamine Oxidase inhibitors
- SSRI - St Johns Wort - OTC for depression
- Ecstasy
- Amphetamines

### **Clinical features :**

- Neuromuscular excitation - hyperreflexia, myoclonus, rigidity
- ANS excitation - hyperthermia, sweating
- AMS - confusion
- Increased reflexes, clonus, normal pupil size

MX : IV Fluids, BZD, severe cases - cyproheptadine and chlorpromazine

**Cyproheptadine uses** - to control diarrhoea in carcinoid syndrome, serotonin syndrome

Neuroleptic malignant syndrome -

- Caused by anti psychotics
- Tachycardia, hypertension, pyrexia, diaphoresis
- Increased Creatine kinase
- Slower onset
- Decreased reflexes, lead pipe rigidity, normal pupils
- Mx - Dantrolene

47. Side effects of anti anginal drugs -

1. CCB - Headache, flushing, ankle oedema; **Verapamil - constipation**
2. Beta blockers : bronchospasm (asthma), fatigue, cold peripheries, sleep disturbances
3. Nitrates - headache, postural hypotension, tachycardia
4. Nicorandil - headache, flushing, **anal ulceration**

48. Side effects - diabetes drugs :

- a) Metformin - GI side effects (diarrhoea, nausea), lactic acidosis

- b) Sulfonylureas (glimepiride) - hypoglycaemia, increased appetite, weight gain, SIADH, liver dysfunction (cholestatic)
- c) Glitazones (Pioglitazone) - weight gain, fluid retention, liver dysfunction, fractures (CI in heart failure)
- d) Gliptins - pancreatitis

49. **QT Shortening** - Hypercalcemia, Hypermagnesemia, Digoxin, Thyrotoxicosis

**QT Prolongation** - MATCHES OPQ

M - Methadone/Metoclopramide

A - Amiodarone

T - TCA (Citalopram, Escitalopram); Tefenadine/Tramadol,

C - Chloroquine/Clarithromycin

H - Haloperidol

E - Erythromycin

S - Sotalol

O - Ondansetron

P - Procainamide

Q - Quinolones

50. **Cocaine overdose** - palpitations, agitation, chest pain, mydriatic pupils, elevated pulse rates

Cocaine - sympathomimetic drug which stimulates the release of Noradrenaline and dopamine.

Causes increased HR, increased BP and vasoconstriction.

Coronary vasospasm - acute chest pain

**Cannabis overdose** - relaxation, euphoria, slowed reaction time, red eyes

**LSD overdose** - mydriasis, altered mental state

Heroin - respiratory depression, miosis, sedation, hypotension, bradycardia

Ketamine - dissociative anaesthetic agent by antagonist to NMDA receptors in brain

51. Motion sickness —> hyoscine > cyclizine > Promethazine

Prochlorperazie - nausea and vomiting associated with surgery, cancer chemotherapy, radiotherapy

Adverse effects - extra pyramidal symptoms

Domperidone - dopamine antagonist - nausea and vomiting affecting gastric motility

52. Calcineurin - decreased clonal proliferation by reducing IL-2 release

Also binds to FKBP forms a complex - inhibits calcineurin which is a phosphatase that activates various transcription factors in cells

Tacrolimus - commonly used as immunosuppressant to prevent transplant rejection.

Adverse effects - impaired glucose tolerance, nephrotoxicity

53. Tamoxifen - SERM which acts as oestrogen receptor antagonist and partial agonist

Mx of ER +ve breast cancer.

Adverse effects :

- Menstrual disturbances - vaginal bleeding, amenorrhea
- Hot flushes
- Venous thromboembolism
- Endometrial cancer (due to partial agonist activity on oestrogen receptors causing endometrial hyperplasia and increased risk of neoplasia)

Raloxifene - pure estrogen receptor antagonist - lower risk of endometrial cancer.

## 54. Teratogens

- A. ACE inhibitors - renal dysgenesis, crania-facial abnormalities
- B. Alcohol - cranio-facial abnormalities
- C. Aminoglycosides - ototoxicity
- D. Carbamazepine - Neural tube defects, craniofacial abnormalities
- E. Chloramphenicol - Gray baby syndrome
- F. Cocaine - IUGR, preterm labor
- G. Lithium - Ebstein anomaly (atrialized right ventricle)
- H. Maternal DM - Macrosomia, Polyhydramnios, Preterm labor, caudal regression, neural tube defects
- I. Diethylstilbestrol - vaginal clear cell adenocarcinoma
- J. Smoking - preterm labor, IUGR
- K. Tetracyclines - discoloured teeth
- L. Thalidomide - limb reduction defects
- M. Valproate - neural tube defects
- N. Warfarin - craniofacial abnormalities

55. Retinopathy - Hydroxychloroquine, Ethambutol, Vigabatrin, AMiodarone

BP monitoring - Cyclosporin

Urine analysis - Gold, Penicillamine (both to look for protein due to increased risk of membranous glomerulonephritis)

Urine analysis - Cyclophosphamide (blood due to fish of hemorrhagic cystitis & bladder cancer)

Therapeutic levels - Tacrolimus, Cyclosporin

**56.** Activated charcoal administration helps to achieve gastric decontamination by adsorbing the **salicylate** in the gastrointestinal tract. Initial treatment should include the use of oral activated charcoal, especially if the patient presents **within 1-hour of ingestion**.



## 57. Heparin induced thrombocytopenia diagnosis : Serotonin Release Assay or Heparin - PF4 Antibody ELISA test

HIT : immune mediated complication of heparin therapy. Formation of antibodies against complexes of platelet factor 4 and heparin, which activates platelets and causes **thrombosis**.

HIT less common with LMWH due to their weaker ability to form immunogenic complexes with PF4.

Treatment of HIT : Stop all heparin products, start treatment with direct thrombin inhibitors.

## 58. Macrolides - act by inhibiting bacterial protein synthesis by blocking translocation.

Adverse effects -

- QT prolongation
- GI side effects are common
- Cholestatic jaundice
- P450 inhibitor
- **Azithromycin** - hearing loss, tinnitus

## 59. **Trastuzumab** - HER2/neu Receptor monoclonal antibody

**Trastuzumab** (AKA **Herceptin**) + Cisplatin + Capecitabine or 5-fluorouracil. —> recommended option for HER2 positive metastatic adenocarcinoma of stomach.

Anthracyclines - Doxorubicin and Epirubicin - known to have cardiotoxic effects due to generation of reactive oxygen species which leads to myocardial damage.

Cardiotoxicity presents as reduced LVEF, heart failure, arrhythmia.

Cisplatin & Carbaplatin - nephrotoxicity and ototoxicity; these two form intrastrand and interstrand DNA crosslinks leading to apoptosis.

**Paclitaxel & Doclitaxel** - Taxanes drugs - peripheral neuropathy via microtubule function

**Topoisomerase I inhibitors** - **Irinotecan** and **Topotecan** - diarrhoea and myelosuppression.

**Cetuximab** —> **monoclonal antibody** against **HER1 receptor**; HER1 receptor mutations are associated with colorectal and squamous cell cancers

**VEGFR** - receptor which stimulates angiogenesis, **Bevacizumab** inhibits this receptor.

**PDGFR** - monoclonal antibody against this receptor —> **Imatinib** and **Dasatinib**

60. Drugs causing urticaria -

- 1) aspirin
- 2) Penicillins
- 3) NSAIDs
- 4) Opiates

61. Carbon Monoxide Poisoning - oxygen dissociation curve shifts to the left, it means that the haemoglobin saturation is achieved at a lower partial pressure of oxygen. Downward shift of the curve reflects the reduced oxygen binding capacity of haemoglobin since CO occupies one of the four heme groups.

62. Amitriptyline - **increase** serotonin and noradrenaline

**Blocks** histamine, cholinergic and alpha 1 receptors  
TCA - cardiotoxic prolongs QT interval and widens QRS complexes leading to ventricular arrhythmia and seizures.

Also causes metabolic acidosis.

Overdose of amitriptyline - anti cholinergic effects

- Dilated pupils
- Dry skin

- Confusion
- Urinary retention
- Tachycardia

63. This patient has a number of the classic features of organophosphate poisoning.

Organophosphates **inhibit acetylcholinesterase enzymes**, leading to upregulation of cholinergic transmission.

As acetylcholine is the principal neurotransmitter for postganglionic neurons in the parasympathetic nervous system, a number of features of organophosphate poisoning represent **over-activation of the parasympathetic nervous system** (e.g. the excessive urination, defaecation, borderline bradycardia and miosis seen in this patient).

In addition to this, the post-ganglionic fibres of sweat glands use cholinergic transmission, explaining the **presence of diaphoresis** in this patient.

64. The combined oral contraceptive pill (COCP) is a highly effective form of birth control made up of both oestrogen and progestogen. As naturally occurring oestrogen and progesterone levels are known to affect the occurrence of certain cancers, research has confirmed the use of the COCP can increase and decreased specific cancer risks. Studies have confirmed the use of the COCP is associated with a decreased risk of endometrial cancer which is thought to be due to the COCP suppressing endometrial cell proliferation.

Research has shown that breast cancer risk is increased with prolonged COCP use. It has been proposed that breast cancer expresses receptors for oestrogen and/or progesterone hormones and therefore additional, synthetic versions of these female hormones may stimulate the development and growth of breast cancer.

Similar to breast cancer, research has shown an increased risk of cervical cancer associated with the use of the COCP, not a decrease. It has been proposed that the use of the COCP may change the susceptibility of the cervical cells to persistent human

papillomavirus infections which is the cause of nearly all cases of cervical cancer.

65. **Fomepizole**, also known as **4-methylpyrazole**, works by **competitively inhibiting** the enzyme **alcohol dehydrogenase**. This enzyme is critical in the metabolism of both ethanol and methanol. By inhibiting this enzyme, fomepizole prevents the conversion of methanol to its toxic metabolites, formaldehyde and formic acid, thereby reducing toxicity and preventing further damage.

66. Sildenafil is a phosphodiesterase-5 (PDE5) inhibitor used for the treatment of erectile dysfunction.

It works by enhancing the effect of nitric oxide in the body, which leads to vasodilation and increased blood flow into the penis during sexual stimulation.

**Nicorandil**, on the other hand, is a potassium channel activator with a nitrate component.

The concurrent use of sildenafil and nicorandil can lead to an excessive drop in blood pressure due to their combined vasodilatory effects.

This could potentially result in life-threatening hypotension or **myocardial infarction**, especially in patients with underlying ischaemic heart disease.

#### 67. Drugs which worsen heart failure -

1. Pioglitazone
2. NSAIDs
3. Non Dihydropyridine CCB - Verapamil, Diltiazem
4. Non cardio selective Beta blockers
5. Alpha blockers used for urological problems

#### 68. Cholinergic overdose symptoms - DUMBBELLS

- D - diarrhoea
- U - Urination
- M - Miosis
- B - Bradycardia
- B - Bronchospasm
- E - Emesis

- L - Lacrimation
- L - Lethargy
- S - Salivation, Sweating

SLUDGE - Salivation, Lacrimation, Urination, Defecation, GI Upset, Emesis

69. **Aminophylline** is a bronchodilator used in the management of symptoms of asthma and COPD.

It works by relaxing the muscles around the airways so that they open up and breathing becomes easier.

The action of aminophylline can be reduced by smoking because **tobacco smoke induces hepatic enzymes**, particularly **CYP1A2**, which metabolises aminophylline, leading to a **decrease in its serum levels and hence reducing its effectiveness**.

70. Drugs causing photosensitivity -

PQRST AND CNG

P - phenothiazines

Q - Quinine, Quinolones, Quinidine

R - Retinoids

S - Sulphonamides, Sulfonylureas

T - Tetracyclines, Thiazides

A - Amiodarone

N - NSAIDs - Piroxicam, Celecoxib

D - Dapsone

C - Chloroquine, Chlorpromazine

N - Nalidixic acid

G - Griseofulvin

- Thiazides
- Tetracyclines
- Sulphonamides
- Ciprofloxacin
- Amiodarone
- NSAID - Piroxicam

- Psoralen's
- Sulfonylureas

71. Zero Order elimination drugs -

### **WATT Power**

Warfarin; Aspirin; Alcohol; Theophylline; Tolbutamide; Phenytoin

72. **Tacrolimus**, a calcineurin inhibitor, is known to cause impaired glucose tolerance and can lead to new-onset diabetes after transplantation (**NODAT**). The mechanism involves both decreased insulin secretion by pancreatic beta cells and peripheral insulin resistance. This side effect is particularly important in transplant patients who are already at an increased risk of metabolic complications.

73. A recognised adverse effect of **amiodarone**, normally with prolonged or high dose use, is **vortex keratopathy**. This is characterised as **white, yellow, or brown corneal opacities**, observed beneath the cornea apex, disrupting visual acuity.

### 74. **Flecainide**

Vaughan Williams class Ic anti-arrhythmic

Slows action potential conduction by blocking sodium channel (Nav 1.5 sodium channel)

Causes widening of QRS complex and prolongation of PR interval.

Indications - 1) atrial fibrillation 2) SVT associated with accessory pathway - WPW syndrome

Contra-indications : 1) post MI 2) structural heart disease - heart failure 3) sinus node dysfunction - second degree or greater AV block 4) atrial flutter

Adverse effects :

1. Negatively inotropic

2. Bradycardia
3. Proarrhythmic
4. Oral parenthesis
5. Visual disturbances

**75. Ethanol** reduced calcium-dependent secretion of anti-diuretic hormone by blocking channels in the neurohypophyseal nerve terminal.

Nausea during hangover is due to vagal stimulation of vomiting centre.

Increased tremors due to excess alcohol is due to increased glutamate production by neuros to compensate for previous inhibition by alcohol.

76. PDE 5 inhibitors side effects -

- Visual disturbances - blue discolouration, non arteritis anterior ischaemic neuropathy
- Nasal congestion
- Flushing
- GI side effects
- Headache
- Priapism

77. Renal failure - dosing of anti TB drugs needs changing in Ethambutol .

78. Phase I reactions - oxidation, reduction, hydrolysis, deamination, dealkylation

79. Anaphylaxis 0.5 mg - 0.5 mL 1:1,000 IM

Cardiac Arrest - 1mg - 10mL 1:10,000 IV (or) 1mL 1:1,000 IV

80. Drugs to be avoided in pregnancy -

- Tetracyclines
- Aminoglycosides
- Sulphonamides

- Trimethoprim
- Quinolones - ciprofloxacin
- ACE inhibitors, ARBs
- Statins
- Warfarin
- Sulfonylureas
- Retinoid - including topical
- Cytotoxic agents
- Anti epileptics - valproate, carbamazepine, phenytoin

#### 81. Precipitating factors for Digoxin toxicity -

- Hypokalaemia
- Increasing age
- Renal failure
- Myocardial ischaemia
- Hypomagnesaemia
- Hypercalcaemia
- Hyponatraemia
- Acidosis
- Hypothermia
- Hypothyroidism
- Drugs - Amiodarone, Quinidine, Verapamil, Diltiazem, Spironolactone, Ciclosporin, Thiazides, Loop diuretics

Spironolactone competes with Digoxin for excretion in DCT hence leading to higher digoxin levels

Hypokalaemia - digoxin and potassium bind to Na/K ATPase hence lower potassium levels means more digoxin binding and effect.

82. Frusemide, also known as furosemide, is a loop diuretic that works by inhibiting the sodium-potassium-chloride cotransporter in the thick ascending limb of the loop of Henle. This leads to increased excretion of sodium, chloride, and water, but it can also cause increased urinary excretion of potassium and magnesium. Hypomagnesaemia (low serum magnesium) is a well-known side effect of frusemide therapy.

#### 83. **Hypomagnesaemia** -



- Drugs - diuretics, PPI
- TPN
- Diarrhoea
- Alcohol
- Hypokalaemia
- Hypercalcemia - secondary to hyperparathyroidism
- Metabolic disorders - Gitelman's and Bartter's.

84. Calculating anion gap =  $(Na + K) - (Cl + HCO_3)$

Calculating osmolar gap =  $(2 \times Na) + \text{glucose} + \text{urea}$

Normal anion gap = 8 to 14

Normal osmolar gap = less than 10

85. Mercury poisoning -

- Peripheral neuropathy
- Reduction in visual fields
- Sensorineural hearing loss
- Hyperchloraemic metabolic acidosis consistent with renal tubular acidosis
- Irritability

86. Thallium poisoning - causes non specific features of GI upset, delirium, convulsions, coma, MODS.

87. Iron poisoning - due to ingestion of excess iron. Common features include vomiting, diarrhoea, hepatotoxicity, bowel obstruction, multi organ failure.

88. Methanol poisoning -

Alcohol effects : intoxication, nausea

Visual problems and blindness - due to optic neuropathy because of accumulation of formic acid in the eyes

MX. : Fomepizole or Ethanol, Hemodialysis

Cofactor therapy with Folinic acid to reduce ophthalmological complications.

**89. Drugs precipitating acute intermittent porphyria :**

- Barbiturates
- Halothane
- Benzodiazepines
- Alcohol
- Oral contraceptive pill (by increasing synthesis of porphyrin precursors, as they increase demand for hepatic cytochrome P450 enzyme system which in turn increases heme synthesis and depletes heme stores to provoke an attack of acute intermittent porphyria)
- Sulphonamides

**Drugs safe to use in acute intermittent porphyria :**

- Paracetamol
- Aspirin
- Codeine
- Morphine
- Beta blockers
- Penicillin
- Metformin
- Chlorpromazine

**90. NIVOLUMAB** - PD-1 (Programmed cell death) inhibitor. PD-1 receptors are found on surface of T cells.

When a T-cell is alerted to cancer cell, the cancer cell can express the PD-L1 Protein. This is a ligand protein which binds to T cell receptor and deactivates it.

PD-1 inhibitor are antibodies which blocks this receptor, leaving T-cells active and alerts other immune cells to cancer cells.

Adverse Effects : hypophysitis, hypothyroidism

EGFR - **Erlotinib** (Tarceva)

PDGR monoclonal antibody - **Olaratumab**

VEGF inhibitors - **Bevacizumab**

ALK-1 inhibitor. - drugs that act on anaplastic lymphoma kinds - **Crizotinib**

CTLA-4 inhibitor - **Ipilimumab**

91. Nifedipine, Amlodipine, Ciclosporin - gingival hyperplasia

92. Anti lipidemia drugs causing myositis - statins, nicotinic acid, fibre

Single best drug to avoid in combination with statins in view of myopathy - **FIBRATE**

93. Cocaine clinical features :

1) Cardiovascular :

- coronary artery spasm
- myocardial ischemia
- myocardial infarction
- Tachycardia and bradycardia
- QRS widening and QT prolongation
- Aortic dissection

2) Neurological :

- Seizures
- Mydriasis
- Hypertonia
- Hyper-reflexia

3) psychiatric affects

- Agitation
- Psychosis
- Hallucinations.

4) others :

- Ischaemic colitis

- Hyperthermia
- Metabolic acidosis
- Rhabdomyolysis

94. The correct answer is blockage of the Nav1.5 sodium channel. **Flecainide** is a class I antiarrhythmic drug according to the Vaughan-Williams classification system. Specifically, it falls into class Ic, having the strongest effect on the initiation phase of depolarisation.

The **Cav1.2** unit is part of **L-type calcium channels**. Blockage of these is the method of action of class IV antiarrhythmic drugs, including verapamil and diltiazem. **Amiodarone** also exhibits some calcium-channel blocking effects.

Blockage of the Cav2.3 calcium channel is incorrect. This refers to R-type calcium channels, which are poorly understood and sparsely found in the body. Flecainide does not block these.

Blockage of the **Kv11.1 potassium channel** refers to the effect of **amiodarone** (among other effects), a class III antiarrhythmic drug according to the Vaughan-Williams classification system.

Inhibition of the **If current** is incorrect. This refers to the action of **ivabradine**, which is not routinely used as an antiarrhythmic drug (although can be used for tachycardia); rather, it is used in the management of stable angina.

**95.** Adrenaline induces **hyperglycemia**, **hyperlactatemia** and **hypokalaemia**.

Because insulin secretion is suppressed by alpha adrenergic stimulation, plasma concentration of insulin remains low.

Hyperglycemia is induced by an increase in glucose production caused by an increase in hepatic glycogenolysis and an increase in gluconeogenesis.

There is also a marked increase in oxygen consumption.

In skeletal muscle, epinephrine **increases glycolysis** and **glycogenolysis**, inducing an **upsurge in lactate**.

Muscular lactate serves as a substrate for hepatic neoglucogenesis (Cori cycle).

Epinephrine also **increases lipolysis** and **decreases muscular proteolysis**.

**96. Hypomagnesaemia** is often found in conjunction with hypokalaemia, particularly in patients with a history of alcohol excess. This is because both magnesium and potassium homeostasis are closely linked.

In terms of physiology, the renal handling of magnesium and potassium are interconnected. Hypomagnesaemia can cause functional hypokalaemia due to an increase in renal potassium wasting. This happens because magnesium deficiency leads to a decrease in intracellular potassium, which results in an increased secretion of potassium into the urine by the renal tubules.

Furthermore, alcoholism can contribute to both hypomagnesaemia and hypokalaemia due to poor dietary intake, gastrointestinal losses (such as vomiting or diarrhoea), and increased urinary excretion facilitated by alcohol. Alcohol-induced damage to the gut lining also hinders absorption of these electrolytes.

Additionally, treatment for alcohol withdrawal often includes loop diuretics which can further exacerbate losses of both magnesium and potassium.

Therefore, it is crucial that levels of both electrolytes are monitored closely in patients with a history of alcohol excess presenting with one or more electrolyte imbalances. Treatment should aim at correcting all detected imbalances to prevent potential complications such as cardiac arrhythmias or seizures.

**97. Monoclonal antibody constant region - Fc region - human in origin.** Human constant origin reduces immunogenicity and increases half life compared to mouse antibodies.

98. Drugs causing lung fibrosis -

- 1) amiodarone
- 2) cytotoxic agents - bleomycin, busulphan
- 3) anti Rh arthritis drugs - sulfasalazine, Methotrexate
- 4) nitrofurantoin
- 5) ergot based dopamine agonists - bromocriptine, cabergoline, pergolide

99. Drugs cleared by hemodialysis :

BLAST

B - barbiturate

L - lithium

A - alcohol

S - salicylates

T - theophyllines

100. **Glycopeptide antibiotics - Teicoplanin and Vancomycin**

These antibiotics inhibit peptidoglycan synthesis

101. **Erythromycin**, a macrolide antibiotic, acts as a motilin receptor agonist in the stomach. Motilin is a hormone that increases gastrointestinal motility and **stimulates gastric emptying**, which is **beneficial** in **conditions** like **gastroparesis** where there is delayed gastric emptying.

102. Drugs that cause **agranulocytosis** -

- Anti thyroid drugs - Carbimazole, Propylthiouracil
- Anti psychotics - atypical anti psychotics
- Anti epileptics - Carbamazepine
- Antibiotics - Penicillin, Chloramphenicol, Co-trimoxazole
- Anti depressant - Mirtazapine
- Cytotoxic drugs - Methotrexate

**103.** treatment with hyperbaric oxygen (HBO) in the following circumstances :

- CO level >25 percent
- CO level >20 percent in pregnant patient

- Loss of consciousness
- Severe metabolic acidosis (pH <7.1)
- Evidence of end-organ ischemia (eg, ECG changes, chest pain, or altered mental status)

104. Causes of Normal anion gap metabolic acidosis NAGMA include ('ABCD'):

Addison's

Bicarbonate loss: GI (e.g. diarrhoea) or renal (e.g. renal tubular acidosis)

Chloride excess

Diuretics (e.g. acetazolamide)

Causes of NAGMA include ('ABCD'):

- Addison's
- Bicarbonate loss: GI (e.g. diarrhoea) or renal (e.g. renal tubular acidosis)
- Chloride excess
- Diuretics (e.g. acetazolamide)

### 105. **Buy AT 30 - aminoglycosides, tetracyclines**

CCEL for 50 - chloramphenicol, clindamycin, erythromycin (macrolide) linezolid

106. Flecainide is a class IC antiarrhythmic that works by slowing the conduction of electrical impulses in the heart. However, it should not be used in patients with structural heart disease, such as ischaemic heart disease and chronic heart failure, due to an increased risk of arrhythmia and mortality. This has been established by studies like the Cardiac Arrhythmia Suppression Trial (CAST) which found an increased risk of death or nonfatal cardiac arrest in post-myocardial infarction patients treated with class IC antiarrhythmics.

The following medications may exacerbate heart failure:

- thiazolidinediones
  - pioglitazone is contraindicated as it causes fluid retention
- verapamil
  - negative inotropic effect
- NSAIDs/glucocorticoids

- should be used with caution as they cause fluid retention
- low-dose aspirin is an exception - many patients will have coexistent cardiovascular disease and the benefits of taking aspirin easily outweigh the risks
- class I antiarrhythmics
  - flecainide (negative inotropic and proarrhythmic effect)

107. HLA-B\*5801 allele testing is the most appropriate next step in management. This patient with gout is at high risk for allopurinol sensitivity. His risk factors include diuretic use, ethnicity (Thai descent), and chronic kidney disease. Allopurinol hypersensitivity is characterized by DRESS (drug reaction, eosinophilia, and systemic symptoms) syndrome and can result in kidney failure and death.

Allopurinol should be avoided in patient with mild to moderate chronic kidney disease.

Probenecid should be avoided in patients with chronic kidney disease, as the drug requires intact kidney function.

**108. Oxycodone is a safer opioid to use in patients with moderate to end-stage renal failure as it is mainly metabolised in the liver.**

**109. Beta 2 adrenoceptor stimulation effects -**

1. Arteriolar dilatation
2. Bronchodilation
3. Decreased bronchial secretion
4. Relaxation of pregnant uterus
5. Decreased gut motility
6. Lipolysis, gluconeogenesis, glycogenolysis.

**110. Iron poisoning -**

**Pathophysiology :**

- Cellular toxicity impairs oxidative phosphorylation and causes mitochondrial dysfunction leading to **cellular death** and **anaerobic metabolism**.



- Ingested iron has **corrosive effects** on GI mucosa.
- Iron affects the liver, and also heart causing myocardial siderosis
- **Metabolic acidosis** happens due to result of hypoperfusion due to volume loss from vomiting/diarrhoea, vasodilation and negative chronotropic effects of iron which all cause **lactic acidosis**.
- Clinical features : vomiting, diarrhoea, upper & lower GI bleeding.
- Severe cases - metabolic acidosis, multi organ failure.

Stages of Iron poisoning -

- **Stage 1** : gastrointestinal phase - nausea, diarrhoea, abdominal pain. Upper/lower GI bleeding, hypovolemia, shock
- **Stage 2** : latent phase - 6-12 hours after ingestion, GI symptoms may resolve, metabolic abnormalities rise including hypotension, metabolic acidosis and coagulopathy
- **Stage 3** : Shock and Metabolic acidosis : metabolic acidosis, organ failure, CNS - coma
- **Stage 4** : Hepatotoxicity - 12 to 96 hours after ingestion Elevated liver enzymes and bilirubin levels with coagulopathy. Hypoglycemia and liver dysfunction
- **Stage 5** : Bowel obstruction - 2-8 weeks after ingestion, gastric outlet obstruction due to scarring, vomiting, abdominal pain.

Diagnosis :

- Serum iron levels >500 micro gram/dL - aggressive
- Abdominal X ray may reveal radiopaque pills
- Glucose - elevated due to hepatic dysfunction - can cause hypoglycaemia later
- FBC - anemia
- LFT - hepatic dysfunction

Serum iron levels >90 —> moderate to severe toxicity

**Management :**

- Mld GI symptoms with serum concentration < 500 —> **Observe**
- IV Fluids
- IV Deferroxamine : binds ferric iron and promotes urinary excretion.

**Indications of Deferroxamine :**

- 1) severe symptoms - AMS, hemodynamic instability, persistent diarrhoea and vomiting
- 2) Anion gap metabolic acids
- 3) Serum iron >500
- 4) Significant number of pills on radiography

111. **Ethambutol** - neuritis, central scotoma, red-green colour blindness.

**Sildenafil** - blue green discolouration of vision : activation of PDE-6 receptors located in rod and cone cells of retina - this happens at a high dose which is not seen when Sildenafil is being used for erectile dysfunction.

**Digoxin** - green yellow discolouration of vision.

112. **Fiansteride** - 5 alpha reductase enzyme inhibitor

5 alpha reductase converts testosterone to dihydrotestosterone. DHT more active than testosterone and binds stronger to cytoplasmic receptors to stimulate prostate growth, DHT promotes development of benign prostatic hyperplasia in elderly.

Androsterone is also converted to DHT by **hydroxytestosterone dehydrogenase**; NOT by Fiansteride.

113. NSAID overdose : upto 10% of patient will have seizures after NSAID overdose, particularly with **Mefenamic Acid**.

Large ingestions - Acidosis, renal impairment, GI heorrhage, CNS effects (drowsiness, coma, cerebellar signs).

GI symptoms occurs due to inhibition of COX enzymes.

NSAID causes direct damage to gastric mucosal barrier by depleting mucosal PGE levels - NSAIDs decrease the gasproduodenal defence mechanisms and cytoprotective effect of PGE —> resulting in mucosal injury, erases and ulceration.

#### 114. **Salicylate Overdose :**

Mild poisoning - nausea, vomiting, tinnitus, dizziness  
(concentration <300)

Moderate 300-700 : sweating, restlessness, tachypnea, bounding pulse

Severe >700 : cardiac arrhythmia, pulmonary edema, hypoglycemia, cerebral edema, seizures, confusion, hyperpyrexia, cardiac failure, coma, renal failure

**ABG** : mixed respiratory alkalosis + metabolic acidosis.  
Resp alkalosis - direct stimulation of respiratory centre

Metabolic acidosis - accumulation of lactic acid and fatty acid metabolites due to uncoupling of oxidative phosphorylation.

**INV** : urgent plasma salicylate levels measurement -  
Taken two hours after overdose in symptomatic, four hours after overdose in asymptomatic.

MX -

- Activated Charcoal
- IV fluids, dextrose
- IV sodium bicarbonate to alkalinise urine and serum
- Hemodialysis if presenting with -
  - A. Salicylate concentration >900
  - B. Salicylate >700 with metabolic acidosis
  - C. Coma

115. Digoxin loading dose - large volume of distribution and readily penetrates tissues including heart, brain, erythrocytes, skeletal muscle and crosses the blood brain barrier.

Concentration of digoxin is higher in myocardium than plasma.

Volume of distribution is decreased in patients with renal impairment and hypothyroidism, increased in patients with hyperthyroidism.

116. Warfarin - vitamin K Antagonist - inhibits carboxylation of vit K dependent factors - factor II, factor VII, factor IX, factor X, protein C.

Half life of Warfarin - 44 hours, highly protein bound, negligible quantities in breast milk.

Initial loading dose is given because of more rapid onset of action, not related to half life.

117. Factors that increase risk of Tendonitis with Ciprofloxacin use

-

- 1) age > 60 years
- 2) Concomitant use of steroids
- 3) Renal impairment
- 4) Solid organ transplant
- 5) Previous tendon rupture
- 6) Women have higher risk than men
- 7) BMI 20-25 associated with higher risk of tendinitis

Rheumatoid arthritis - increases the risk of heart valve regurgitation in patients who use Fluoroquinolones.

Moxifloxacin - new generation of Fluoroquinolones that is bactericidal by interfering with DNA synthesis.

Adverse effects -

118. Normal anion gap metabolic acidosis -

- Diarrhoea, vomiting
- Pancreatic fistula
- Renal bicarbonate loss
- Kidney disease
- Hypoaldosteronism
- Acetazolamide - causes renal sodium and  $\text{HCO}_3$  loss
- Renal tubular acidosis

Raises anion gap metabolic acidosis - MUDPILES

- Methanol poisoning
- Uraemia
- Diabetic ketoacidosis
- Paraldehyde
- Isoniazid, iron overload
- Lactic acidosis (can be due to metformin)
- Ethylene glycol intoxication
- Salicylate overdose

119. Anabolic steroids effects -

BP elevation, Increased LDL, decreased HDL

Prolonged use - hematocrits increased which causes prothrombotic tendency, plasma fibrinogen concentrations decrease

120. Heroin withdrawal -

Sweating; diarrhoea; nausea; vomiting; irritability; restlessness; muscle ache

MX : methadone or buprenorphine maintenance programs to prevent dangers of heroin withdrawal.

121. Most common drugs associated with adverse effects in elderly -

- Diuretics
- Digoxin
- Anti hypertensives
- Anti inflammatory agents
- Drugs acting on CNS

Older individuals are much at risk for volume depletion and hyponatremic effects of diuretics.

122. Ethanol - fetal alcohol syndrome  
Diethylstilbestrol - vaginal carcinoma

Phenobarbital - cleft lip

Thalidomide - phocomelia

Androgen - deformities

Drugs to be avoided in pregnancy -

- Excessive caffeine
- Excessive alcohol
- Cocaine
- Marijuana
- ACE inhibitors
- Acebutolol
- Fluoxetine (SSRI)
- Sulphonamides
- Iodine
- Warfarin - chondrodysplasia punctata
- Isotretinoin
- Androgens & diethylstilbestrol
- Methotrexate
- Lithium - neonatal goitre, hypothyroidism causes heart defects, Ebstein anomaly, neonatal thyroid problems, floppy baby syndrome
- Anti convulsants - phenytoin, carbamazepine (microcephaly), sodium valproate (neural tube defects), trimethadione/paramethadione

Drugs contra indicated during breast feeding -

- Amiodarone
- Anti neoplastics
- Chloramphenicol
- Ergotamine
- Iodides
- Methotrexate
- Lithium
- Tetracyclines
- Cabergoline
- Pseudoephedrine
- All recreational drugs
- Clozapine (fetal agranulocytosis)

- BZD - cleft lip, cleft palata

Drugs safe in breast feeding -

- Paracetamol
- Flucloxacillin
- Erythromycin/clarithromycin - only if benefits outweigh the risks
- Fluconazole
- Domperidone and metoclopramide - can be used to improve milk supply by increasing prolactin

123. Fungal infections :

- Oral candidiasis - Miconazole oral gel or nystatin mouthwash ; severe infection - oral fluconazole
- Oesophageal candidiasis - ketoconazole
- tinea infection : Terbinafine topical
- invasive aspergillosis - Amphotericin B
- Aspergilloma : oral voriconazole
- cryptococcal meningitis : amphotericin B

124. Cyclophosphamide -

Prodrug that is metabolised by liver to 4-hydroxyl cyclophosphamide

Which further breakdown into chloroacetaldehyde + acrolein

Acrolein - chemical hemorrhagic cystitis

Ifosamide - chemical hemorrhagic cystitis

Co administration of Mesna - decreased risk of bladder toxicity by binding to acrolein and toxic metabolise of Ifosamide.

125. Ciclosporin levels are increased with co-administration of these drugs

- FLuconazole
- Ketoconazole
- Itraconazole
- Voriconazole
- Methyl prednisolone high dose
- Allopurinol
- Protease inhibitors
- Colchicine

126. Doxorubicin - anti tumor activity derives from triggering of topoisomerase II dependent DNA breakage

- Cardiotoxicity
- Cardiomyopathy
- Acute arrhythmia
- Congestive heart failure
- Dose dependent impairment of LVEF
- Myocardial dysfunction.

127. Tamoxifen -

Decreased LDL cholesterol, no change in HDL —> decreases risk of CHD

Endometrial sampling is recommended for women as risk of endometrial cancer is 2-3 times more with long term use.

Prior hysterectomy is not a pre-requisite.

Yearly PAP smear is not advised - no risk of cervical cancer.

128. Amphotericin B - nephrotoxicity

Tubular toxicity - wasting of potassium

Metabolic acidosis may occur due to type 1 Renal Tubular Acidosis

- polyuria may also occur due to nephrogenic diabetes insipidus.

Reversible effect.



### 129. **Eplerenone** -

Aldosterone antagonist that improves survival (morbidity and mortality) when added to existing therapy after MI in stable patients with **ejection fraction <40%**.

**Common adverse effects** - **hyperkalemia**, dizziness, **hypotension**, diarrhoea, nausea

Can be affected by P450 inducers/inhibitors.

### 130. Infantile spasms - **Vigabatrin**

**Adverse effects** - aggression, alopecia, **retinal atrophy**, reduced peripheral vision.

### 131. **Vincristine** -

Peripheral neuropathy - neurotoxic feature

C/F : Foot drop, parenthesis, loss of ankle jerks, wrist drop.

Vincristine - biochemical picture resembling syndrome of inappropriate antidiuretic hormone (SIADH) & hyponatremia.

Other adverse effects - mucositis of GIT and bleeding

Bleomycin - interstitial pneumonia

Cyclophosphamide - hemorrhagic cystitis

Doxorubicin and Daunorubicin - cardiomyopathy

Methotrexate - hepatic and pulmonary fibrosis

### 132. **Actions of insulin**

- Promotes glucose uptake
- Inhibits glucose generation or release
- Inhibits glucose conversion into storage molecules - glycogen and triglycerides

- Increases protein synthesis
- Promotes glycogen synthesis
- Inhibits gluconeogenesis
- Promotes lipogenesis
- Decreases serum potassium levels.

### 133. **Cannabis overdose**

C/F : 1) impairment in reaction time  
2) red eyes 3) distorted sense of time and space 4) mood changes

Adverse health effects - anxiety; paranoid reaction; increased risk of schizophrenia; increased risk of using other drugs

MX : CBT

Opioid misuse

C/F : 1) euphoria 2) analgesia 3) drowsiness 4) bradycardia 5) hypotension 6) respiratory depression 7) pupillary constriction 8) constipation 9) lowering of body temperatures

Heroin withdrawal C/F : 1) cravings 2) restlessness 3) insomnia 4) sweating 5) abdominal pain, diarrhoea, vomiting 6) dilated pupils 7) runny nose 8) tachycardia 9) yawning

Withdrawal Heroin Mx with Methadone / Naltrexone / Clonidine.

Heroin Overdose : Unconscious,; pinpoint pupils; hypotension; shallow breathing; snoring

Amphetamine Misuse

Enhances dopamine, Noradrenaline & serotonin

C/F : enhanced mood, excessive speech, increased energy, insomnia

Sign : hypertension, dilated pupils, dry mucous membranes

Complication : Paranoid psychosis with prolonged use

Clinical uses - treating narcolepsy and ADHD

**Cocaine intoxication** - presents with symptoms similar to mania or psychosis  
Grandiose ideas

Cocaine hallucinations - **auditory** or **tactile** variety

Cocaine can also cause - agitation, tachycardia, hypertension, arrhythmia, coronary artery spasm. (Chest pain and aortic dissection, Myocardial infarction )

**MDMA/Ecstasy** : hyperpyrexia, acute renal failure, acute psychosis

**Hallucinogen / Psychedelic - LSD** : effects begin 2 hours after consumption, and can last 8-12 hours

C/F : distorted sensory perception, hallucination, out of body experiences, panic/agitation in severe cases

Mx - BZDs

**Phencyclidine/Ketamine** - hallucination, agitation, disorientation by antagonising NMDA glutamate receptor  
Can cause - nystagmus, tachycardia, hypertension, seizures.

134. All conventional CCBs work on L type calcium channels. CCBs bind to L type calcium channels in heart and smooth muscle of peripheral vessels.

The L type calcium channels are found on a tubular network of sarcolemma of muscle called Transverse T tubules.

135. **Anti retroviral insulin resistance syndrome** -

Long term use of Protease inhibitors associated with redistribution of body fat in patients.

HIV lipodystrophy follows an insulin resistance pattern with a loss of fat on face, increasing abdominal fat and deposition of subcutaneous fat on back.

Other features are - 1) low HDL and High triglyceride levels  
2) hypertension 3) impaired glucose tolerance precedes the development of type 2 DM.

**135. Paroxysmal Nocturnal Hemoglobinuria** - clonal red cell abnormality, leaves erythrocytes open to complement mediated attack.

Can occur in paroxysms resulting in hemolysis.

**Eculizumab** - orphan drug for PNH which inhibits C5 - stops complement mediated erythrocyte destruction.

**136. Slow acetylators - isoniazid - peripheral neuropathy**

**Rapid acetylators - isoniazid - hepatitis**

137. Beta blocker - Bisoprolol - Hypoglycemia, IUGR, Fetal bradycardia

Thiazide - neonatal electrolyte and thrombocytopenia disorders

**138. Imipramine - overdose with TCA**

Side effects -

Anti cholinergic - dry mouth, tachycardia, mydriasis

Sodium channel blockade - QRS prolongation, arrhythmia, seizures

Others - grossly abnormal reflexes, loss of consciousness, divergent eye movements

**138. Theophylline and smoking**

Theophylline - bronchodilator used to treat Obstructive airway diseases

Adverse effects - nausea, vomiting, **hypokalaemia, metabolic acidosis.**

Hypokalaemia - due to beta agonist effects of theophylline and acidosis usually lactic acidosis.

Narrow therapeutic window - drug monitoring needed to minimise risk of toxicity

Target concentration of drug - 10 - 20 mg/L

Regular smoking - up-regulates hepatic enzyme activity and cessation of smoking causes increased theophylline concentrations.

Other factors that increase theophylline concentrations - heart failure, liver cirrhosis, acute viral infection, increased age, enzyme inhibitor or inducer.

### **139. Ventricular tachycardia - polymorphic**

- Broad complex tachycardia - numerous ventricular foci that leads to polymorphic QRS complexes
- Most common type - tornadoes de pointes
- Aetiology :
  - A. Inherited
  - B. MI
  - C. Drug induced
  - D. Congenital Long QT syndrome - Romano Ward, Jervell and Lange-Nielson syndrome
  - E. Electrolyte disturbances - low K, low Mg, Low Ca
- Torsades de pointes : prolonged QT interval indicates longer time needed for myocytes to repolarise due to channelopathy - causing premature after-depolarisations.
- **C/F** : light headedness, palpitations, dizziness, sudden cardiac death. Can progress to VF or cardiac arrest.
- Bidirectional VT - DIGOXIN

- MX : IV Magnesium is the drug of choice : 1-2g in 30 to 60 seconds, repeated in 5-10 minutes.
- Avoid these drugs
  - A. Anti arrhythmia - Amiodarone, Sotalol, Procainamide
  - B. Anti psychotics - Haloperidol
  - C. Antidepressants - Citalopram
  - D. Antibiotics - Erythromycin, Trimethoprim
  - E. Antihistamines - Terfenadine
  - F. Antifungals - Ketoconazole, Fluconazole

140. Digoxin - water soluble - major determinant of any loading dose is patient's renal function.

Adjustment of loading and maintenance dose is necessary because the normal half-life of 36 hours is lengthened.

Digoxin binds to Na/K ATPase pump on the membranes of cardiac myocytes.

#### 141. **Digoxin specific antibodies**

Indications - Digoxin toxicity with severe hyperkalemia that has failed to respond to fluid resuscitation and administration of insulin and dextrose.

Also indicated in patients with significant arrhythmia and hypotension

Digoxin antibodies need good renal function as it is really excreted

Rare adverse effect - **serum sickness**

#### 142. **SIADH**

- SIADH - excess production of ADH/Vasopressin causing body to retain water
- Causes dilution hyponatremia
- Diagnosis requires : Confirming requires serum osmolality  $<275$  and urine osmolality  $>100$  and Urine sodium  $>30$ 
  - concentrated urine Na  $>20$
  - hyperosmolality  $>100$  mOsm/kg

- hyponatremia plasma Na <125 mmol/L
- absence of hypovolemia/edema/diuretics
- Etiology :
  - Malignancy - small cell lung Ca, pancreatic cancer, prostate cancer, lymphoma
  - CNS disorders : meningoencephalitis, abscess, stroke, head injury, SAH
  - Respiratory disease : tuberculosis, pneumonia, abscess
  - Drugs : opiates, SSRI
  - Endocrine : Hypothyroidism
- ADH stored in **posterior pituitary** and released in response to high plasma osmolality and acts on **distal tubule and renal collecting ducts** to increase water permeability.
- Causes water reabsorption and urine becomes more concentrated.
- **C/F : Mild** - anorexia, nausea, malaise vomiting; **moderate** - personality change, muscle cramps, fatigue; **severe** - reduced GCS, seizures
- MX ; non pharmacological - fluid restriction
- Pharmacological : Hypertonic saline, loop diuretics with saline, Demeclocycline, Vasopressin receptor antagonist **Tolvaptan**

#### 143. **Insulin & enzymes :**

- I. Inhabits enzymes involved in gluconeogenesis : pyruvate carboxylase
- II. Stimulation of glycogen synthesis
- III. Stimulates Glucose 6 phosphate dehydrogenase in Hexose monophosphate shunt
- IV. Activates acetyl CoA carboxylase to increase FFA production
- V. Activates citrate lyase to increase free fatty acids production

#### 144. **Gynecomastia :**

Causes -

- Pathological :
  - Chronic renal failure, chronic liver disease
  - Tumors producing HCG/Estrogen - teratomas, bronchial carcinoma
  - Male breast cancer

- Gonadal failure - Klinefelter syndrome
- Metabolic : hyperparathyroidism/hypothyroidism
- Drugs :
  - Raised oestrogen : **Digoxin, Opiates**
  - Anti androgen activity : **Spironolactone, Cimetidine, Cyproterone**
  - Others - Metronidazole, Domperidone, PPI, Anti retrovirals, Anabolic steroids
- MX : Pharmacological
  - Medications -
    1. Danazol : inhibits secretions of gonadotrophin, reducing androgen synthesis
    2. Tamoxifen : anti estrogen acting directly on breast
    3. Testosterone - direct inhibitor of mammogenesis
  - Surgical : mastectomy

#### 145. **Warfarin - decreased efficacy**

Pharmacokinetic factors :

- Cholestyramine - decreased absorption
- CYP450 inducers - St Johns Wort

Pharmacodynamic factors :

- Excess dietary vitamin K
- Oestrogen's
- Griseofulvin
- 6-mercaptopurine (Azathioprine)

#### 146. **Tumour Lysis Syndrome**

- **Oncological emergency**
- Metabolic disorder - complication of malignant diseases
- Hyperuricaemia + hyperkalemia + hyperphosphatemia
- Hypocalcemia
- Raised urea and creatinine levels due to acute renal failure
- Hyperuricemia - crystallisation of uric acid in renal tubules - obstructive uropathy
- Associated with malignancies -
  1. Non Hodgkin's lymphoma
  2. Solid tumours



### 3. ALL

### 4. AML

- Associated with steroid administration, monoclonal antibodies, biologics - Thalidomide, Paclitaxel, Zoledronic acid
- Hypocalcemia - arrhythmia, tetany, seizures
- C/F :
  - Dyspnea, orthopnea, tachypnea
  - Dysuria, flank pain, hematuria
  - Nausea, vomiting, seizures, tetanic spasms
  - Abdominal distension
  - Facial edema
  - Palpitations
  - Lethargy
- **Management** : Rapid expansion of intravascular volume - IV fluids started 48 hours before initiation of chemotherapy
- Allopurinol - can decrease production of uric acid - used in low risk patients
- Recombinant urate oxidase : Rasuricase - treats hyperuricemia associated with leukaemia and lymphoma - used in high risk patients
- Sodium Bicarbonate - for urine alkalinisation
- Calcium - Calcium chloride, calcium gluconate

#### 147. **Elderly - drug metabolism factors -**

- Diminished renal function
- Proportions of body, fat, and water
- Reduced cardiac output
- Altered hepatic metabolism
- Disease
- Concomitant medication use

#### 148. **Drugs causing nephrogenic diabetes insipidus**

- Lithium
- Demeclocycline
- Amphotericin
- Glibenclamide

#### 149. **Methaemoglobinemia - Isosorbide mononitrate**

### 150. **Crack Cocaine**

Associated with condition known as crack lung

C/F of crack lung - chest pain, cough with hemoptysis, dyspnoea, and bronchospasm.

Snorting cocaine - hemoptysis as a result of pulmonary and bronchial constriction and ischemia resulting in interstitial and alveolar haemorrhages

Coronary artery vasospasm in cocaine overdose - treat with nitrates or CCBs.

### 151. **Serotonin Syndrome**

- SSRI/SNRI + serotonin enhancing agents such as TCA, St Johns Wort, MAO
- C/F :
  - Hypomania
  - Agitation
  - Drowsiness
  - Hyperthermia
  - Myoclonus
  - Tachycardia
  - Labile blood pressure (happy drunk state)
  - Early features : tremor, akathisia, diarrhoea
  - Followed by : hypomania, agitation, drowsiness, coma, myoclonus, hyperthermia, seizures
  - Pronounced autonomic symptoms - tachycardia, high BP, sweating, mydriasis, hyperactive bowel sounds
- Mx : IV fluids for hyperthermia, rhabdomyolysis
- BZDs to manage sedation
- Hyperthermia - Dantrolene

### 152. **Trimethoprim - adverse effects**

- Pancytopenia
- Isolated leucopenia
- Megaloblastic anaemia

- Thrombocytopaenia
- Agranulocytosis

Dihydrofolate reductase inhibitor - decreased folic acid incorporation into bone marrow.

**153. Drugs causing seizures -**

- IV penicillin - high doses
- quinolones- ciprofloxacin
- TCA
- Mefenamic acid
- Class I anti arrhythmics
- Anti convulsants

**154. Drugs causing hyperprolactinemia -**

- Dopamine receptor antagonists - Domperidone, Metoclopramide
- Antidepressants - TCA, MAO inhibitors, SSRI
- CCB - Verapamil
- Opiates
- Protease inhibitors
- Bezafibrate
- H2 receptor antagonists
- Oestrogens, anti androgens
- Cocaine
- Cyproheptadine

**155. Drug induced hepatitis -**

- Fenofibrate
- Anti TB drugs
- Methyldopa
- Carbamazepine
- Nitrofurantoin
- Isoniazid

156. Inhibitors of CYP 3A4 with Cyclosporin - increased risk of nephrotoxicity

- Verapamil
- Diltiazem
- Imidazole anti fungals
- Macrolide antibiotics

### 157. **Green blue urine**

- Pseudomonas urinary tract infection
- Amitriptyline
- Indigo carmine
- IV cimetidine
- IV promethazine
- Methylthioninium Chloride
- Triamterene

### **Brown tinged urine -**

- Levodopa
- Metronidazole
- Nitrofurantoin
- Fava beans

### 158. **Drugs associated with intra cranial hypertension -**

- Tetracyclines
- Amiodarone
- OCP
- Withdrawal of steroid therapy

### 159. **Carbimazole - Adverse effects -**

Carbimazole — converts into Methimazole —> **inhibits iodination of tyrosine and blocks the coupling of Iodotyrosine.**

Methimazole : minor immunosuppressive action —> leading to reduction in serum thyroid stimulating hormone antibody (TRAb).

Adverse effects - 7 to 28 days after starting treatment - stop the drug if they develop any fever or sore throat.

Other rare complications : hepatitis, cholestatic jaundice.

### 160. **Pyrimethamine - Schizontocide**

Anti malarial that act on erythrocytic phase of schizogony are called schizontocides.

**Pyrimethamine** - treatment on uncomplicated malaria, mainly Chloroquine resistant *P.falciparum*.

**Pyrimethamine** - fast acting, high efficacy blood schizontocides

**Doxycycline** - slow acting anti malarial.

Acts on both erythrocytic and hepatic phases of infection, inhibits dihydrofolate reductase in the parasite and prevents biosynthesis of purines and pyrimidines and stops the process of DNA replication, cell division and reproduction.

### 161. Glycoprotein 2b/3a inhibitors

Abciximab, Eptifibatide, Tirofiban

The receptor mediates platelet aggregation.

Inhibited by these drugs - leads to decreased thrombus formation.

ADP receptor antagonism - Clopidogrel, Prasugrel, Ticagrelor

### 162. Statins - drug interactions :

- Antacid and anti fungal agents interact with Atorvastatin.
- All statins interact with Cyclosporine and Nicotinic acid.
- All statins should be used in caution with patients on fibrate therapy as the risk of rhabdomyolysis is increased.

### 163. P-glycoprotein

**P-glycoprotein** - encoded by **Multidrug resistance gene (MDR1)** and is ATP dependent drug transporter molecule found on the cell surface that accelerates efflux of drugs and toxins from cells.

It is expressed at high levels in some cancer cells, reducing the effects of cytotoxic actions of chemotherapeutic agents.

Another molecule involved in cytotoxic drug resistance - **Multidrug resistance protein MRP**

#### 164. **Chemotherapy side effects**

1. Ciclosporin - nephrotoxicity, hepatotoxicity, increased K, Na, hypertrichosis, gum hypertrophy, increased BP, fluid retention
2. Cyclophosphamide - bone marrow suppression
3. Methotrexate - pulmonary fibrosis, pancytopenia, bone marrow suppression, mucositis
4. Vincristine - neurotoxicity
5. Doxorubicin - cardiotoxicity

#### 165. **Propylthiouracil**

- Propylthiouracil (PTU) and carbimazole are both derivatives of thiourea with similar chemical structure, mechanisms of action and adverse effects.
- Both are capable of inhibiting organification of iodine at the thyroid gland.
- Neither drug affects iodine trapping and neither drug inhibits the release of preformed thyroid hormone.
- A key distinction is that PTU also blocks conversion of T<sub>4</sub> to T<sub>3</sub> in peripheral tissues (does not inactivate existing T<sub>4</sub> and T<sub>3</sub> stores in circulating blood and the thyroid and does not interfere with replacement thyroid hormones).
- This may give PTU a modest therapeutic advantage because it reduces the proportion of active thyroid hormone as well as total T<sub>4</sub>.
- Both PTU and carbimazole are excreted in very small quantities in breast milk, so breast feeding is not advised with either.
- Thiourea derivatives have several side-effects, including a maculopapular rash, hepatocellular damage and vasculitis.
- The most serious side-effect of both agents is agranulocytosis, although it is more common to see a fall in, rather than total absence of white cells.

#### 166. **Long QT drugs associated -**

- Amiodarone
- Sotalol
- TCA, SSRI (Citalopram)

- Methadone
- Chloroquine
- Terfenadine
- Erythromycin
- Haloperidol
- Ondansetron
- Cisapride (pro kinetic drug - increases gastric motility and enhances gastric emptying time; prolonged QT higher risk if combined with erythromycin or ketoconazole) - Anti cholinergic blocks the effects of Cisapride

#### 167. Salmeterol

- Long acting Beta-2 agonist used in asthma
- Paradoxical bronchospasm is a rare but recognised complication of salmeterol
- Can sometimes cause tachycardia due to direct stimulation of beta-1 and beta-2 receptors
- Bronchospasm **more common** with **inhaled disodium chromoglycate**
- Recognised side effects of Salmeterol and Formoterol (LABAs) - hypokalaemia, caution in severe liver disease, breast feeding, pregnancy

#### 168. Phenytoin - protein binding

- Phenytoin and Warfarin are highly protein bound drugs.
- Phenytoin levels measure free and bound drug levels added together.
- Toxicity happens when proportion of free to bound drug are increased.
- Factors which increase this proportion -
  - States of hypoalbuminemia - pregnancy, malnutrition, nephrotic syndrome, malignancy
  - Uraemia
  - Neonates
  - Elderly individuals
  - Hyperbilirubinemia

#### 169. Pioglitazone

Cytochrome pathway P450 enzyme responsible for Pioglitazone -  
**CYP2C8**

Gemfibrozil and trimethoprim inhibit activity of CYP2C8 isoenzyme and increases Pioglitazone concentration.

Adverse effects - weight gain, fluid retention, heart failure, reduced bone mineral density.

**CYP3A4** - simvastatin metabolism

Can be inhibited by protease inhibitors and macrolides.

**CYP2C9** - NSAID metabolism and Warfarin

Inhibited by Ketoconazole

**CYP2D6** - metabolism of antipsychotics

Inhibited by SSRI Fluoxetine and Paroxetine

CYP3A2 - conversion of testosterone to 6-beta-hydroxytestosterone

Inhibited by Macrolides

#### 170. **Nitrofurantoin - neuropathy**

Peripheral neuropathy with symptoms of motor neuropathy and sensory, reported with use of Nitrofurantoin.

Other neurological complications - optic neuritis, diplopia, nystagmus, vertigo.

171. Torticollis/acute dystonia - prochlorperazine or Metoclopramide

MX - Procyclidine or Benztropine

#### 172. **Animal / human bite Mx -**

First line - Co-amoxiclav

Penicillin allergic : Doxycycline + Metronidazole



Infection : **Capnocytophaga canimorsus** has been associated with severe infections in immunocompromised patients including meningitis, endocarditis, kidney disease and septicaemia.

173. Prolactinemia drug causes :

- A. Phenothiazines
- B. Butyrophenones
- C. Risperidone
- D. Metoclopramide
- E. Methyldopa
- F. Isoniazid
- G. TCA
- H. MAO inhibitors
- I. Verapamil

174. **Isoniazid - Acetylator status**

Slow acetylator of Isoniazid - peripheral neuropathy (higher drug concentrations)

Rapid acetylator status - hepatic toxicity (more extensive metabolite formation and metabolites of Isoniazid plays a key role in liver injury)

175. **Drugs - adverse effects**

**Methotrexate** - pneumonitis, pulmonary fibrosis, hepatic fibrosis, folate deficiency

**Ciclosporin** - nephrotoxic, cholestasis, hypertrichosis, gingival hyperplasia, tremor, nausea, vomiting

**Prednisolone** - used as treatment for fibrosing alveoli's

**Sulfasalazine** - can cause pulmonary fibrosis, myelosuppression, decreased sperm count, hepatitis, oral ulcers, rash, haemolytic anemia.

Azathioprine - dose related myelosuppression, hair loss, hypotension, cholestatic jaundice, arrhythmia, hypersensitivity reactions

#### 176. Donepezil - adverse effects

- Donepezil - cholinesterase inhibitor - potentiates the actions cholinergic neurons
- Adverse effects - nausea, vomiting, diarrhoea
- Cardiac adverse effects - bradycardia, AV block
- Other side effects - urinary incontinence, hepatitis

#### 177. Theophylline - adverse effects

- Headache, insomnia
- Agitation
- Seizures
- Severe nausea and vomiting
- Metabolic disturbances - hypokalaemia, metabolic acidosis
- Theophylline toxicity - hypotension, hypokalaemia, ventricular & supra ventricular arrhythmia

#### 178. Anti epileptics - OCP

- Lamotrigine - most correct choice as it does not interfere with effectiveness of OCP
- Carbamazepine - powerful enzyme inducer and decreased OCP effectiveness, and increased risk of unintended pregnancy
- Clonazepam - causes sedation
- Topiramate - decreases Estrogen levels - reduces pill effectiveness; also has a ten-fold risk of cleft lip compared to other people
- Phenytoin - causes weight gain, powerful enzyme inducer - can cause congenital malformations - cleft lip, cleft palate, neural tube defects

#### 179. Breastfeeding & contra indicated drugs -

- Aiodarone
- Anti neoplastics
- Chloramphenicol
- Ergotamine

- Idodies
- Methotrexate
- Lithium
- Tetracyclines
- Cabergoline
- Pseudoephedrine
- Aspirin - high risk of Reye's syndrome

180. **Breast feeding & safe drugs :**

- Ibuprofen
- Warfarin
- Heparin
- Emergency contraception - Levonelle
- Paracetamol
- Flucloxacillin
- Erythromycin/clarithromycin
- Fluconazole
- Domperidone, Metoclopramide

181. Digoxin overdose

Cardiac features :

- A and AV block
- Premature ventricular contractions
- PR prolongation
- ST depression

Non cardiac features :

- GIT - nausea, vomiting, diarrhoea
- Vision - blurred, yellow green discoloration
- CNS - weakness, dizziness, confusion, apathy, malaise, headache, depression, psychosis
- Haematological - thrombocytopenia, agranulocytosis
- Gynecomastia

MX : Digoxin specific antibody fragments (Fab) fragments

Symptomatic bradycardia - atropine

Hypotension - fluid replacement

## 182. **Drugs - high first pass metabolism**

Drugs which undergo high first pass metabolism :

1. Propranolol
2. Verapamil
3. Morphine

All these drugs to be used in caution with liver impairment  
Poor hepatic functioning → accumulation of drug because of increased bioavailability.

## 183. **Rosuvastatin - metabolism**

- **Rosuvastatin** - substrate for **hepatic uptake transporter OATP1B1** and **efflux transporter breast cancer resistance protein (BCRP)**
- Agents which interfere with the function of either of these two transporters can therefore lead to significantly elevated levels of Rosuvastatin.
- CYP3A4 inhibitors - do not impact the metabolism of statins.
- CYP3A4 inhibitors impact metabolism of Simvastatin & Atorvastatin - which are affected by CYP3A4 inhibitors like Itraconazole and Clarithromycin.
- Ciclosporin - inhibitor of OATP1B1
- Other drugs inhibiting OATP1B1 -
  1. Gemfibrozil
  2. Rifampicin
  3. Ritonavir
  4. Saquinavir
  5. Indinavir
  6. Nelfinavir
  7. Quinidine
  8. Verapamil
  9. Digoxin
  10. Pantoprazole

## 184. **Adverse drug reactions - types**

- **Type A** - anticipated effect arising from a particular pharmacological property. They are dose related - e.g., bradycardia as an adverse effect of Beta-blocker
- Type B - unpredictable adverse events, not related to a predictable pharmacological effect of the drug. They are idiosyncratic - unexpected - usually rare, may be serious.
- Type C - These occur in the setting of prolonged drug use - e.g., analgesic nephropathy or visual-field defects with Vigabatrin - these are unpredictable in nature. Visual field defects are an absolute contraindication to Vigabatrin use.
- Type D - these occur late after treatment - e.g., teratogenic or carcinogenic reactions such as - phocomelia after administration of Thalidomide in pregnancy
- Type E - adverse reactions related to drug withdrawal. e.g., SSRI cessation and agitation or opioid withdrawal syndrome.

185. Cranberry Juice & Pomegranate juice - inhibitors of 2C9 - main P450 isoenzyme responsible for metabolism of drugs like Warfarin.

Warfarin - 2C9 metabolism - 30% increase in INR on Cranberry juice

Liver and plants of Brassica family - sprouts - recognised to contain large amounts of vitamin K - inhibits the pharmacological effects of Warfarin - decrease in INR

Grapefruit juice - contains chemical which inhibits enzyme 3A4 - drugs metabolised are usually simvastatin, cyclosporin.

186. Digoxin overdose - drugs

- Amiodarone
- Diltiazem
- Verapamil
- Trazodone
- Carvedilol
- PPI
- Macrolides
- Tetracyclines

- Trimethoprim

**ECG of Digoxin at therapeutic levels** - PR prolongation, Scooped ST segment

**ECG of Digoxin toxicity** - increased automaticity, premature ventricular response, slowed ventricular response, AV nodal blockade

### 187. **Toxicity with Hydrofluoric Acid**

- Both hydrogen ions and fluoride ions are capable of hydrolysing proteins.
- Hydrogen ions - superficial corrosion, coagulative necrosis, eschar formation
- Fluoride ions - majority of injuries; lipophilic and penetrates deep into tissues - causing liquefactive necrosis.
- Fluoride ions can also bind to calcium and magnesium - resulting in hypocalcemia and hypomagnesemia.

188. Beta agonists & angiotensin II - promote proto-oncogene expression - which then stimulates protein synthesis and induces synthesis of fetal forms of actin and myosin, leading to hypertrophy of smooth muscle.

Therefore - Beta blockers, ACE inhibitors, ARBs can be used for reversal of hypertrophy.

189. **Drug fever** - isolated phenomenon can occur with penicillins, phenytoin, hydralazine, and Quinidine.

Fever is usually low grade, and subsides within few days of stopping the drug.

### 190. **OAT-1 renal transporter**

- Methotrexate - substrate for OAT-1 renal transporter
- Levels are affected by decreased renal function
- OAT-1 inhibitors - **Probenecid** should not be used in conjunction with Methotrexate.

- **Omeprazole** - inhibition of breast cancer resistance protein - which is helpful in Methotrexate transport in the kidney.

### 191. **Activated Charcoal** -

- Multiple doses of activated charcoal aid in the elimination of some drugs that are prone to enterohepatic circulation.
- Activated charcoal adsorbs drug excreted in bile and prevents reabsorption in small bowel.
- Examples - aspirin, Quinine, Carbamazepine, Phenobarbital, Theophylline
- Adverse effects - nausea, vomiting, constipation, abdominal fullness, abdominal pain
- Repeated doses can cause bowel obstruction

192. Erythromycin is a CYP 3A4 inhibitor; as such it potentiates the action of warfarin, simvastatin and other drugs metabolised by this cytochrome. The interaction between erythromycin and warfarin causes an increased INR and bleeding risk. Other agents capable of inhibiting warfarin metabolism include allopurinol, disulfiram, ketoconazole, omeprazole, cimetidine, glibenclamide, metronidazole and amiodarone.

### 193. **Acetazolamide**

- Inhibitor of carbonic anhydrase enzyme
- Used to treat patients with hydrocephalus after intracerebral haemorrhage, to reduce ICP in Idiopathic intracranial hypertension and to reduce intraocular pressure in glaucoma
- Adverse effects -
  - A. Metabolic acidosis due to  $\text{HCO}_3^-$  loss in PCT and DCT through inhibition of reabsorption
  - B. Hypokalaemia
  - C. Acute interstitial nephritis
  - D. agranulocytosis
  - E. Thrombocytopenia

### 194. **Docetaxel**

- Reversibly binds to microtubules with high affinity

- Leads to decrease in availability of free tubule and thus preventing mitotic cell activity
- Microtubules also accumulate within the cell, increasing the rate of apoptosis.
- Docetaxel also has a further action in **blocking bcl-2**.

- Alkylating agents - disrupt DNA
- Sodium Azide & Dinitrophenol - inhibits mitochondrial energy production
- Anti-60S anti-ribosomal antibodies - inhibits RNA production

#### 195. Paracetamol metabolism -

- Key pathways responsible for metabolism are - 1) glucuronidation  
2) sulfation
- In acute overdose - these pathways become saturated and increasing quantity is being metabolised via non-specific P450 oxidative metabolism.
- Excess paracetamol - forms toxic metabolite - NAPQI
- NAPQI - rapidly conjugated with Glutathione and is really exerted.
- Excess NAPQI levels causes it to bind to vital proteins and lipid bilayer of hepatocyte membranes.
- This causes hepatocellular death and centrilobular liver necrosis.

#### 196. Drug induced hemolysis

- G6PD - Quinolones, dapsons, primaquine, Aspirin
- Acquired autoimmune haemolytic anaemia - Methyldopa, Penicillin, Quinine, Quinidine
- Lead exposure - can cause direct red cell toxicity

#### 197. **Drug induced Parkinsonism :**

- Sodium valproate
- Lithium
- Tetrabenazine
- Prochlorperazine
- Metoclopramide
- Anti psychotics



- Butyrophenone - haloperidol, droperidol
- Phenothiazines

### 198. **Ecstasy adverse effects** -

- Nausea
- Muscle pains
- Confusion
- Ataxia
- Hyperkalemia
- Hyponatremia
- Metabolic alkalosis
- CVS collapse
- Acute respiratory distress
- Hyperthermia
- Rhabdomyolysis

### 199. **Migraine - drugs used**

- Amitriptyline - patients with a frequency of 3-4 episodes per month or those with headaches that impair the quality of life should be offered prophylaxis.

First line agents - Propranolol & Amitriptyline.

- Propranolol - contraindicated In patient with asthma
- Sumatriptan - contraindicated in patients with stroke
- Topiramate - used in cases of idiopathic intracranial hypertension - contraindicated in patients who are of child bearing age as it is teratogenic.

### 200. **Theophylline toxicity**

- Nausea & vomiting
- Seizures
- Myoclonus
- Hyperthermia
- Rhabdomyolysis
- Acute kidney injury
- Hypokalaemia
- ECG - sinus tachycardia, ventricular arrhythmia, prolongation of QT and QRS intervals

- Metabolic acidosis
- Hyperglycaemia

## 201. Itraconazole

- Symptomatic patients - hemoptysis - surgical management by lobectomy
- Alternative treatments - bronchial arterial embolisation & long term oral **Itraconazole**.
- Pre and post operative systemic anti fungal treatment is also preferred.
- Treatment options include - amphotericin with flucytosine/ itraconazole / voriconazole.

**Fluconazole** - candidiasis and CNS infections with *Cryptococcus neoformans*

**Griseofulvin** - tinea capitis in adults and children; effective against infections caused by **Trichophyton tonsurans** and **Microsporum spp.**

**Nystatin** - oral, vaginal and enteric candidiasis; only topical; systemic route too toxic

Terbinafine - superficial mycoses - dermatophyte infections

## 202. Diuretics - site of action

- C - carbonic anhydrase inhibitors - proximal convoluted tubule
- O - osmotic diuretics - at loop of Henle
- L - loop diuretics - ascending limb of loop of Henle
- T - thiazide diuretics - at proximal distal convoluted tubule
- P - Potassium sparing - at distal portion of distal convoluted tubule

Spironolactone - pharmacological antagonist of Aldosterone, acting through competitive-binding of receptors at aldosterone-dependent Na-K exchange site at distal section of DCT.

Spironolactone causes increased amount sodium and water to be excreted, while potassium is retained.

203. Amiodarone - Corneal Microdeposits  
Presents as night-time visual glare.

Amiodarone - contains iodine and may result in hypo- or hyper-thyroids.

Other adverse effects - pneumonitis, pulmonary fibrosis, hepatotoxicity

204. **Statins**

- Inhibits HMGCoA reductase - rate limiting step in cholesterol synthesis
- Statins lead to increased hepatic LDL receptor and decrease hepatic VLDL synthesis
- Statins also increase VLDL clearance.
- Adverse - myositis, abnormal liver function

205. Dilated pupils = Mydriasis —>

Caused by :

- 1) drugs with sympathomimetic actions - cocaine, amphetamine, pseudoephedrine
- 2) Anticholinergic drugs - antihistamines, atropine, tricyclic antidepressants

206. Atorvastatin and Pravastatin can be used safely with Warfarin.

207. Vigabatrin - visual field defects

Visual field assessment before starting the drug

208. **Orlistat**

- Orlistat - pancreatic lipase inhibitor.
- Orlistat is isolated from bacterium **Streptomyces toxytricini**.
- Orlistat in addition to lifestyle modifications lose about 2-3 kgs in a year

- Orlistat decreases the risk of T2D by 40% in obese people
- Orlistat reduces blood pressure

MOA :

- Orlistat blocks the breakdown and absorption of dietary fat.
- Patients have to maintain low fat diet - or else they can suffer from distressing, oily diarrhoea.

## 209. **Ciclosporin MOA** -

Two main modes of action -

1. Arrest the activity of resting lymphocytes in G0 or G1 phase of growth cycle
2. Cytokine inhibition - IL-2

- Ciclosporin concentrations affected by renal function and co-administration of drugs that interfere with CYP3A4 enzyme activity.
- Contraindicated drugs with Ciclosporin - Statin, Macrolides

## 210. **Tirofiban; Eptifibatide; Abciximab** - Gly IIb/IIIa receptor antagonist

Main side effects of these - thrombocytopenia, risk of bleeding

## 211. Co-trimoxazole - Steven Johnsons syndrome

Steven Johnson syndrome = erythema multiforme;

Occurs most strongly after antibiotic use of Sulphonamides including Sulfomethoxazole.

Infection of skin and mucous membranes

## 212. **Drugs causing SIADH** -

- Vinca alkaloids
- Cyclophosphamide
- Carbamazepine

- Phenothiazines
- Thiazide diuretics
- TCA
- Morphine
- Nicotine

### 213. **Drugs increasing theophylline toxicity -**

- Allopurinol - inhibitory effect of P450 system
- Carbimazole
- Ciprofloxacin
- Clarithromycin
- Diltiazem
- Disulfiram
- Erythromycin
- Fluconazole
- Interferon
- Isoniazid
- Methotrexate
- Thiabendazole
- Verapamil

### 214. **Tamoxifen - cytochrome P450 enzyme CYP2D6**

Drugs which inhibit P450 system inhibits Tamoxifen breakdown.

Tamoxifen breaks down into Endoxifen

Decreased Tamoxifen metabolism can cause reduced efficacy

Potent CYP2D6 inhibitors - Fluoxetine, Paroxetine, Quinidine, Bupropion

### 215. **Carbamazepine - CYP3A4 - Autoinduction**

- Carbamazepine induces expression of CYP3A4, which is responsible for its own metabolism and certain other drugs.
- Therefore, small dose increases may be required after the initial starting dose of 100-200 mg/day; the usual maintenance dose is

0.8-1.2 g/day and plasma concentrations can be used to guide dosing.

- Adverse effects that require cessation of therapy include skin reactions, including risk of Stevens-Johnson syndrome, blood dyscrasias, and deranged liver biochemistry.
- Carbamazepine metabolism may be inhibited by a number of agents, including cimetidine, macrolide antibiotics and calcium channel blockers, thereby causing toxicity.

## 216. Drugs which increase radiation therapy sensitivity -

- Dactinomycin - radio sensitiser agent which increases cellular response to radiation treatment
- Metronidazole
- 5-Fluorouracil
- Gemcitabine
- Cisplatin
- Hydroxyurea
- Paclitaxel
- Mitomycin C
- Topotecan

AMIFISTONE - protects against radiation therapy

## 217. Ondansetron

- Selective antagonist of 5-HT<sub>3</sub> receptor.
- Cytotoxic chemotherapy and radiotherapy are associated with **release of Serotonin** from enterochromaffin cells of small intestine - initiating a **vomiting reflex** by stimulation of 5-HT<sub>3</sub> receptors on **vagal afferents**.
- Activation of vagal efferents also causes a **central release of Serotonin** from the CTZ of area postrema, located on **floor of fourth ventricle**.

## 218. Theophylline

- Adenosine blockers

- Blocking of adenosine receptors has the following effects -
  - A. Relaxation of bronchial smooth muscle
  - B. Constriction of cerebral blood vessels
  - C. Stimulation of cardiac pace maker
  - D. Stimulation of gastric secretions
- In addition to adenosine receptor blockade, theophylline also **inhibits Phosphodiesterase** - causing calcium ion release from sarcoplasmic reticulum in skeletal and cardiac muscle - thus enhancing their contractility.
- Theophyllines is highly protein bound >90%
- Theophyllines may assist in respiration
- 10% of the drug is excreted unchanged in the urine
- Majority of drug **metabolised in liver**
- Theophylline is subject to saturable liver metabolism pathways - small increase in dose can provoke toxicity

#### 219. Gitelmann syndrome

- Low levels of chloride
- Low levels of potassium
- Low levels of magnesium
- Decreased calcium excretion in urine
- C/F : muscle cramps, weakness, numbness, thirst, waking up at night to urinate, salt cravings
- Mx : potassium sparing diuretic - Amiloride or Spironolactone

#### 220. Methotrexate

- Antimetabolite that exerts its effects by inhibiting dihydrofolate reductase
- This interferes with tetrahydrofolate store required for synthesis of purines and thymidylate in inflammatory cells

#### 221. Drug induced cholestasis -

- Phenothiazines - Chlorpromazine
- Erythromycin
- Ciclosporin
- Cimetidine
- Nifedipine

- Nitrofurantoin
- Imipramine
- Azathioprine
- Dextro-propoxyphene

Danazol - prolonged use - can hepatic adenomas or HCC

222. Loop Diuretics & Thiazide diuretics - metabolic alkalosis

Carbonic anhydrase inhibitors - metabolic acidosis

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## INFECTIOUS DISEASE - PASSTEST

### 1. Amoebic Liver Abscess

- Routine Blood tests : raised TLC, deranged LFT; raised inflammatory markers
- **Amoebic serology : >90% sensitive**
- Most patients with Amoebic Liver abscess will have **negative stool microscopy**
- **Medical Rx** : Metronidazole OR Tinidazole

### 2. Staphylococcus - Gram positive

- Further sub-divided into coagulase test :
  - 1) coagulase negative : Staph epidermidis
  - 2) coagulase positive : Staph aureus
- Infections caused by Staph. Aureus -
  - Skin & soft tissue - carbuncles, cellulitis, impetigo, erysipelas, necrotising fasciitis
  - Bone : osteomyelitis, septic arthritis
  - Necrotising cavating pneumonia - associated with Panton-Valentine Leukocidin (PVL Staph. Aureus)
  - Food poisoning : within 6 hours of ingestion ( like Bacillus cereus)
  - Toxic shock syndrome
  - Infective Endocarditis

### 3. Rocky Mountain Spotted Fever



- RMSF : febrile illness - *Rickettsia rickettsii*
- History of tick bite 65%, fever 100%, rash 90% of patients
- C/F : fever, headache, malaise, myalgia
- Macular rash - starts on hands and feet and progresses proximally towards trunk.
- Macules evolves into papules, petechiae, ecchymoses.
- Severe cases - necrosis & gangrene
- Diagnosis - confirmed by 4-fold rise in titres over 2 week period
- Treatment : **Tetracycline**

#### 4. Trachoma

- Caused by *Chlamydia trachomatis* - obligate intracellular bacterium
- Leading infectious cause of blindness worldwide
- **Serovars A, B, Ba, C** - associated with conjunctival infection
- Transmission through 5 routes - 5 F's - flies, fomites, fingers, within family, long close friends
- Acute infection seen in children - inflammatory conjunctivitis, punctate keratitis
- Mx : Azithromycin single dose
- WHO elimination strategy - SAFE (Surgery, Antibiotics, Facial cleanliness, Environmental improvement)

#### 5. Lyme disease

- *Borrelia burgdorferi*
- Three main stages - erythema migrans, development of arthritis
- First line Treatment - Doxycycline or Amoxicillin for 3 weeks
- Stage 1 - initial infection - due to ticks carrying the bacteria infecting the patient; localised inflammatory & infective response
- Stage 1 C/F : erythema migrans, 5% can have central pustule/vesicle. Target like appearance, regional lymphadenopathy, fever, headache
- Stage 2 & 3 - bacterial dissemination
- Rash, myalgia, 25% arthritis, 15% neurological [ meningitis, cranial/peripheral neuritis] can have facial palsy
- 5% cardiac involvement - heart block, pericarditis
- Chronic complications - chronic oligoarthritis, chronic neurological disease

- **Acrodermatitis chronic atrophicans** - dermal atrophy + peripheral nerve involvement + dermal sclerosis
- Rare manifestations - keratitis, uveitis
- MX : **early** stages - **oral Doxycycline**
- Later stage - IV Ceftriaxone

#### 6. **Mediterranean Spotted Fever**

- C/F : Fever, headache, myalgia, rash
- Caused by ***Rickettsia conorii***
- Skin lesion - Eschar, forms around the site of initial infected tick bite

7. Protease Inhibitors - Ritonavir - adverse effects - Hypertriglyceridemia, diarrhoea, asthenia, oral paresthesia, impaired glucose metabolism

8. HSV Keratitis - Topical Acyclovir

#### 9. **Strongyloidosis**

- Infection by parasitic roundworm - Strongyloides stercoralis
- Caught by walking barefoot in soil contaminated with larvae
- Marked eosinophilia in blood tests
- Pathophysiology : larvae enter the skin via direct contact; filariform larvae travel via bloodstream into lungs and migrate to pharynx; swallowed and reach the GIT; auto infection occurs due to rhabditiform larvae and re-enter lungs via bloodstream
- C/F : larva currens - linear pruritic rash.
- Pulmonary infection can lead to pneumonitis - Loeffler syndrome - cough, bronchospasm, SOB, rarely pulmonary hemorrhage.
- Chronic infection in GIT - malabsorption, weight loss, intermittent diarrhoea
- DX : FBC for eosinophilia, Stool for M/c and culture for cysts and parasites
- CXR can show pulmonary infiltrates
- MX : Albendazole and Ivermectin. **Ivermectin 1st line**
- **Albendazole dose - 400mg**
- Antihistamines in case of skin itching

#### 10. **Actinomyces**

- Cervicofacial actinomycosis - most commonly seen
- Risk factors : dental extractions, jaw fractures, periodontal abscess, tonsillar crypts
- C/F : acute, odontogenic abscess or cellulitis of the floor of mouth, (or) as a painless reddish swelling
- Subacute to chronic course : regression of central suppurative foci while the infection progresses peripherally; can spread to other parts of head and neck, can involve meninges.
- Actinomyces - sulfur granules, **anaerobic conditions**
- Nocardiosis - sulfur granules +/- **aerobic** conditions
- Prolonged courses of Amoxicillin >6 months

### 11. Cutaneous Nocardiosis

- Following previous trauma to skin
- Presents with a painless swelling followed by an area of ulceration
- Nocardia cultures - slow growing, **does not grow under anaerobic conditions. USE PARAFFIN BAIT FOR GROWING**

### 12. Intestinal Anthrax

- Intestinal anthrax - develops following consumption of raw meat contaminated with Bacillus anthracis
- Occurs in familial cluster - presents with fever, severe pharyngitis and neck oedema
- Neck swelling - lymphadenopathy + subcutaneous oedema; upper group of jugular chain of lymph nodes are commonly involved
- Inflammatory lesion in the oral cavity or oropharynx - inflamed mucosa —> necrosis & ulceration; pseudomembrane over ulcer
- Subcutaneous edema can extend to chest wall and axilla - overlying skin showing signs of inflammation
- Treatment - combination of antibiotics

### 13. Listeria food poisoning

- Listeria - non spore forming, facultatively anaerobic, Gram positive bacilli
- Can multiply in temperatures of 0-40 degree
- Presents in people who eat refrigerated foods without cooking

E.coli and Staph aureus - multiply at 37 degrees

14. **Ribavirin** - common side effect - **Haemolytic anaemia** - decrease in Hb could be upto 20 g/l.

Avoid Ribavirin in older adults or those with pre-existing haematological disorders

**Ribavirin - teratogenic** - pregnancy prevented during and after treatment upto 1 year for both males and females .

**Side effects of IFN therapy** - flu like syndrome, emotional lability, mood changes, thyroiditis.

#### 15. **Infectious Mononucleosis**

- IM - EBV infection - adolescents and young adults
- C/F : fever, pharyngitis, fatigue, lymphadenopathy
- Other findings - splenomegaly, palatal petechiae
- Cervical lymphadenopathy - posterior chain of lymph nodes
- Generalised maculo-papular, urticarial or petechial rash
- Inv : Heterophile / Monospot test

#### 16. **Pneumocystis pneumonia - PCP**

- **Elevated 1,3 beta-d gluten levels** - polysaccharide present in the walls of fungi cysts
- Screening option for PCP pneumonia
- High sensitivity of 96%; high negative predictive value

Ground glass opacities on HRCT -

- A. PCP infection
- B. Eosinophilic pneumoniae
- C. Idiopathic interstitial pneumonias
- D. Sarcoidosis
- E. Pulmonary edema
- F. ARD
- G. Hypersensitivity pneumonitis

#### 17. **HSV keratitis**

- C/F : acute pain, blurred vision, conjunctival injection, photophobia

- Corneal examination - dendritic ulcer : ulcer with linear branching pattern, terminal bulbs, swollen epithelial borders and central ulceration through the basement membrane
- Branches of the ulcer follows nerve pattern of cornea
- Dendritic ulcers are only observed after staining with fluorescein
- HSV keratitis - corneal blindness
- Mx : **Trifluridine and topical acyclovir**
- \*topical steroids contraindicated\*

#### 18. **Giardiasis**

- C/F : malabsorption, bloating, flatulence, diarrhoea, abdominal cramps, weight loss
- Infection through contaminated food and water
- Malabsorption due to loss of brush border enzyme activity
- INV : stool M/C, fecal immunoassays
- Mx : Metronidazole or Tinidazole

#### 19. **Hepatitis C Treatment**

- Daclatasvir & Sofosbuvir - treatment of Hep. C genotype 1 or 4; with or without compensated cirrhosis.
- Daclatasvir - NS5A inhibitor which stop Hepatitis C replication

20. Guidelines for people with TB infection who are wanting to travel - wait for 2 weeks of therapy

Only individuals who have evidence of drug susceptible disease or no signs of drug resistance

And

Do not have a clinical or public health need for admission to hospital

#### 21. **Fungal keratitis**

- Mycotic keratitis
- Associated with trauma
- **Ulcerative lesion** in cornea, base is raised with **creamy infiltrate**
- Slough off the ulcer appears dry with a **feathery border** surrounded by a **yellow line of demarcation**.
- R/F : patients with immunosuppression
- Mx : antifungals such as Amphotericin B, Itraconazole, Natamycin

22. **Yellow Fever** vaccine even though it is a live vaccine - **recommended** in patient who have **CD4 >200**.

Shingles, Chicken pox, MMR also given in patients with CD4 >200

23. Tenofovir - adverse effects : renal impairment, osteoporosis

Renal tubular damage - particularly in high risk patients - older group, diabetes, hypertension

Co-administration of ACE inhibitor - further increases risk of renal disease - regular renal parameters monitoring

Peripheral Neuropathy - Stavudine (not used in UK)

Hyperlipidemia - Protease inhibitors

Nightmares - Efavirenz

24. Acute epididymo-orchitis -

Men >35 years, stable partner - caused by enteric bacteria : treat with Ofloxacin

Men <35 years, multiple sexual partners, ?STI cause - treat with Ceftriaxone

25. Yellow Fever - 17D strain - contraindicated in :

- I. Under six months age
- II. Previous confirmed anaphylactic reaction to vaccine
- III. Previous confirmed anaphylactic reaction to any of the vaccine components
- IV. Previous confirmed anaphylactic reaction to eggs
- V. With a thymus disorder
- VI. Immunocompromised patients

26. Mefloquine toxicity

- Presents as acute psychosis
- Mefloquine may induce psychiatric symptoms such as anxiety disorder, paranoia, depression, hallucinations and psychosis
- Psychiatric symptoms - nightmare, acute anxiety, depression, restlessness or confusion are considered prodrome

- Sometimes - suicide, suicidal ideation and self harm behaviour
- Adverse reactions after discontinuation of drug - depression, vertigo, loss of balance
- Mefloquine prophylaxis Contra indicated in patients with active psychiatric illness or history of psychiatry disorder

## 27. **Hantavirus infection**

- Hemorrhagic fever with renal features
- Endemic in Korean, Balkans, Scandinavia
- C/F : fever, myalgia, shock, conjunctival haemorrhage with epistaxis, elevated creatinine, elevated urea

Haemolytic Uraemia syndrome will be associated with kidney disease and thrombocytopenia + hypertension (NO SHOCK)

28. Q fever - *Coxiella burnetii* - transmission to humans by inhalation of infected dust and aerosols, drinking unpasteurised milk from cows

C/F - high fever, headache, malaise

Complications - pneumonia, hepatitis, myocarditis

29. **Mycobacterium tuberculosis** - pleural effusions more commonly seen as primary presentation in adults; **replicates 18-24 hours.**

*Escherichia coli* - divides every 20 minutes

*Staph aureus* divides every 30 minutes

*Treponema pallidum* divides every 1-2 days

*Mycobacterium leprae* - divided every 14 days

## 30. **Trypanosomiasis**

- African Trypanosomiasis :
  - A. Caused by protozoa transmitted by **tsetse fly**.
  - B. West Africa - Trypanosome *Brucei* *ambience*
  - C. East Africa - Trypanosome *brucei* *rhodesiense*
  - D. Early C/F : fever, headaches, arthralgia, pruritis
  - E. Later stages : meningoencephalitis, personality change, agitation, severely disordered sleep
  - F. INV of choice : thick and thin blood films. CSF M/C, serology

G.MX : T. brucei ambiense —> **Pentamidine**

H.MX : T. Brucei rhodisense —> **Suramin**

I. **CNS involvement Rx changes**

J. **CNS T. brucei ambiense - Nifurtimox & Elfornithine**

K. **CNS T.brucei rhodisense - Melasprolol**

- Trypanosome cruzi - South American Trypanosomiasis
  - Transmitted by reduviid bugs
  - Cardiac : cardiomyopathy dilated, myocarditis, cardiac arrhythmia - complete heart block
  - Mega oesophagus & megacolon - due to destruction of parasympathetic nerves; recurrent aspiration, bloating, severe constipation.
  - MX : **Benznidazole** or **Nifurtimox**

### **31. Toxic Shock Syndrome**

- Diagnosis requires five criteria -
  1. Fever >38.9
  2. Hypotension
  3. Widespread erythematous, macular rash
  4. Subsequent desquamation of affected skin areas, palms and soles
  5. Involvement of at least 3 organ systems -
    - GIT - diarrhoea, vomiting
    - Muscular - severe myalgia, raised CK
    - Renal : raised urea, raised creatinine
    - Hepatic : impaired liver function
    - Blood : thrombocytopenia
    - CNS : disorientation, confusion without focal neurology
    - Mucous membranes : hyperaemia of conjunctiva, pharynx or vagina

### **32. Loa loa**

- Nematode infection
- Called as African eye worm
- Microfilariae travel across the eye
- Skin lesions confined to extremities - arms and legs
- Calabar swellings - overlying areas of urticaria where muscle cysts occur around tendon sheaths
- Systemic microfilariasis - severe itching, myalgia, arthralgia, tiredness, urticaria



- Diagnosis is by demonstration of adult worms/microfilariae or antibodies
- Treatment - **Diethylcarbamazine**
- Sensitivity reactions to filarial antigen both local and systemic - common and can stimulate acute manifestation reactions
- Treatment - 1mg/kg on first day - increasing over 3 or more days to 6mg/kg in divide dose - dose is continued for 21 days
- Heavy filariasis - DEC can trigger encephalitis - treatment with Albendazole is recommended

### 33. Dermatophyte infections

- 1) Microsporum - single microconidia or multiseptate macroconidia
- 2) Trichophyton spp. - multiple small microconidia
- 3) Epidermophyton spp. - do not produce conidia

### 34. **Acute Hepatitis B infection - anti Hbc IgM**

### 35. Eculizumab - monoclonal antibody

- Monoclonal antibody to complement factor C5 which backs complement activation
- Shiga toxin associated HUS - associated with complement activation particularly of **C3** and **C9**
- Earlier intervention with Eculizumab is most effective and is associated with improved neurological outcomes.

### 36. Brucella melitensis - zoonotic infections of sheep, cattle.

Transmission to humans is by direct animal contact via inhalation or breaks in skin or by eating infected, unpasteurised dairy products

### 37. Taenia solium / Taenia saginata

- Taenia solium - pork tapeworm
- Taenia saginata - beef tapeworm
- Gravid proglottids - passed during defecation, often in short chains; free eggs also occur in faeces
- Mx : single morning dose of **2 g Niclosamide** given on an empty stomach for adults and children
- Alternative treatment - Praziquantel - single dose 10-20 mg/kg after a light breakfast

- Failure of proglottids to reappear within 3-4 months indicates cure

### 38. HIV infection

- Total number of B lymphocytes = appears normal counts
- HIV patients shows hypergammaglobulinemia with an increase across all immunoglobulin classes
- Depletion of CD4 positive lymphocytes
- **Lymphocytes are defective in their response 1)to soluble antigen and 2)to mitogenic substances** such as **phytohemagglutinin** and **concanavalin A**
- NK cells are decreased in number and are functionally impaired

### 39. Malignant Otitis Externa

- Malignant form - involves invasion of temporal bone and base of skulls and can be rapidly progressive
- Life threatening condition
- All most all cases are caused in diabetics
- Majority of diseases - caused by - **Pseudomonas**

### 40. Sporothrix schenckii

- S.schenckii lives on soil and plant matter; enters the skin through a cut or scrape
- Cutaneous sporotrichosis - most common form of infection
- Begins as reddish, non tender, macula-papular lesion at the site of inoculation.
- Similar nodules form along proximal lymphatic channels
- These break to form a row of ulcers
- Diagnosis - culture of biopsy samples on Sabouraud dextrose agar
- Treatment - Itraconazole - severe infections : IV Amphotericin B

### 41. Typhoid fever

- Systemic infection caused by Salmonella type or paratyphoid
- Incubation period of few days to few weeks after initial infection
- Short period of diarrhoea or constipation at the beginning of the illness
- C/F - fever, headache, myalgia, maculopapular rash - Rose spots on chest or abdomen

- **GI bleeding** may occur - due to **ulceration of Peyer's patches** in the ileum
- Blood cultures more likely to be positive early in the disease; stool and urine cultures later
- Neutropenia - common
- Empirical antibiotic therapy is recommended - **IV Ceftriaxone**
- **Chronic carrier status** in the **Gall bladder** - relapse rate ~10%.

#### 42. **Streptococcus viridians - Infective Endocarditis**

- Increasing PR interval suggestive of **aortic root abscess** - uncontrolled infection
- Aortic root abscess - high mortality even with surgery
- Surgery also indicated for those at high risk of cardiac failure or embolism; cerebral or coronary embolism associated with highest mortality
- Failure of fever to resolve after 1 week - suggestive of intra-cardiac abscess that will require surgery

#### 43. **Meningitis - organism**

1. Streptococcus gallolyticus - cause of endocarditis in patients with colon cancer or abnormality of biliary tree
2. Staphylococcus aureus - IV drug user, skin laceration, indwelling central line
3. Listeria - elderly, immunosuppressed, chemotherapy, patients with malignancies, transplant patients
4. Pseudomonas aeruginosa - meningitis following intracranial manipulation including neurosurgery

**44.** CD4 count >350, start Anti retroviral therapy after finishing 6 months of ATT

CD4 100-350 : wait until 2 months of anti-tubercular therapy is over to start ARR

CD4 <100 - start ART immediately ; associated with increased risk of immune reconstitution syndrome (IRIS)

CD4 < 50 - consider maybe delayed ART to prevent IRIS

#### 45. **Brucellosis**

- Gram negative coccobacilli - intracellular bacteria
- Zoonotic disease
- Transmission is from infected animals - unpasteurised milk, ingestion of raw/uncooked meat
- C/F - acute fever, malaise, hepatosplenomegaly
- Complications include - pneumonia, infective endocarditis, CNS infection
- Non specific flu like symptoms - sweating, tiredness, myalgia
- Joint involvement - arthritis, arthralgia, sarcro-ilitis
- Lymphadenopathy, hepatosplenomegaly
- Rare C/F - jaundice, skin rashes, septic arthritis
- INV - Brucella in blood cultures or CSF sample
- MX : notifiable disease in UK
- Long course of dual or triple antibiotic therapy
- Doxycycline PO + Streptomycin IM  
OR
- PO Quinolone + PO Rifampicin  
OR
- PO Doxycycline + PO Rifampicin +/- Gentamicin/Cotrimoxazole

#### 46. **Epstein Barr Virus - Gastric Cancer**

#### 47. **Clostridium difficile infection - increase in risk with concomitant use of Omeprazole along with antibiotics**

48. Rx cryptococcal meningitis - IV Amphotericin B + Flucytosine/Fluconazole

49. Plasmodium vivax - sub Saharan Africa, Central America and Indian subcontinent

Plasmodium ovale - sub Saharan Africa

50. Co-Amoxiclav : Amoxicillin + Clavulinic acid - excellent cover against beta lactase producing Gram positive organisms; and activity against anaerobes.

#### 51. **Cutaneous leishmaniasis** -

- Leishmania parasite - transmitted by phlebotomine sandflies

- Incubation period - few days to several months
- Erythematous nodules develops at the site of infected sandfly bite
- Golden crust forms - sore reaches its final size - usually 1-5 cm in diameter; over weeks or months
- Crust may fall away leaving a ulcer with raised edge; satellite papules are common
- After months or years, lesion starts to heal; leaving behind a depressed, mottled scar.

**52. Chromoblastomycosis** - chronic fungal infection that progresses very slowly, ~2mm per year. Presents as a single bump that can gradually turn into a plaque - complications include elephantiasis and squamous cell carcinoma.

**53. Mycobacterium marinum infection** - seen in people exposed to contaminated freshwater or saltwater. Single lump or pustule that breaks down and spread occurs along the lines of lymphatic drainage.

**54. Gonorrhoea**

- Bacteria - *Neisseria gonorrhoeae*
- Uncomplicated - localised to mucous membrane of urethra, endocervix, rectum, pharynx, conjunctiva
- Disseminated disease - joint involvement
- Men - asymptomatic with urethral discharge and dysuria
- Women - vaginal discharge, abdominal pain, dysuria
- Dx - NAAT + cultures; women - endocervical/vulvovaginal swab; men - first pass urine
- Test of cure 1 week after treatment
- Complications in men - infertility, epididymo-orchitis, prostatitis, urethral stricture
- Complications women - PID, pregnancy complications, Fitz Hugh Curtis syndrome
- C/F : purulent urethral discharge, dysuria, epididymal tenderness/swelling
- Rectal infection - asymptomatic, anal discharge, anal pruritic, perineal pain, tenesmus, rectal bleeding
- Women - increased purulent discharge, lower abdominal pain, dysuria

- Mx - **Ceftriaxone 1g IM injection**

**OR**

**Oral Ceftriaxone + Azithromycin**

**OR**

**Pregnant - Ceftriaxone 1g IM single dose [avoid fluroquinolones]**

55. **Diffuse infiltrative lymphocytic syndrome (DILS)** - weakness due to peripheral motor neuropathy; ascetic meningitis and cranial palsies can occur too

Other C/F : HIV positive patients most commonly seen, fever, xerophthalmia, xerostomia, abdominal pain, weakness, exertion dyspnoea.

B/L parotid gland enlargement, hepatomegaly

56. **Bacillary angiomatosis** - caused by *Bartonella henselae* or *Bartonella quintana* ; occurs primarily in individuals with severe immunocompression. Cutaneous disease presents numerous pinpoint purple papules and nodules.  
biopsy needed to differentiate from Kaposi's sarcoma.

57. **Quinine** - stimulates insulin release and due to extreme catabolism associated with burden of malaria infection - glycogen stores are rapidly depleted.

Test blood glucose - administer IV glucose replacement if necessary.

58. Culture negative infective endocarditis - *Coxiella*, *Brucella*, *Bartonella*

Non infective cause - malignancy, SLE (Libman Sacks endocarditis)

59. HPV 16 & 18 - cervical cancer, anal cancer, some types of oropharyngeal cancer

60. **Anti retro viral drugs - adverse effects :**

- **Indinavir** - renal stones, asymptomatic hyperbilirubinemia
- **Ritonavir** - P450 inhibitor

Protease inhibitors - Indinavir, Ritonavir

- **Tenofovir** - renal impairment, osteoporosis
- **Zidovudine** - anaemia, black nails, myopathy, significant reduction in white cell count
- **Didanosine** - pancreatitis
- **Abacavir** - idiosyncratic hypersensitivity ass. With rash and fever; associated with HLA B5701 type
- **Lamivudine** - skin rashes, arthralgia, peripheral neuropathy

NRTIs - Zidovudine, Lamivudine, Stavudine, Tenofovir, Zalcitabine, Emtricitabine, Didanosine, Abacavir

#### 61. Cyclospora cayentanensis

- Protozoan infection - endemic in tropical areas
- Chronic cause of diarrhoea which doesn't resolve with multiple antibiotics
- Incubation period - week
- Initially - flu like symptoms

62. Entacavir - 1st line treatment for chronic hepatitis B infection with decompensated liver disease

63. Orf - member of Poxvirus family, transmitted by close contact with sheep or goat.

Presentation - nodular lesion - usually solitary - on the fingers or hand which can ulcerate later.

Associated with mild systemic symptoms - fever, localised lymphadenopathy.

#### 64. Subacute bacterial endocarditis

- C/F - fever, generalised symptoms such as weight loss & malaise

- R/F - pre exposing heart valvular lesion; h/o dental abscess treatment

65. Malaria prophylaxis in patient with Epilepsy - Contraindicated drugs are - 1) Chloroquine 2) Mefloquine

Drugs **used** are -

1) **Proguanil hydrochloride with Atovaquone**

66. Lupus vulgaris

- Chronic progressive, irregular plaque like lesion with central scarring
- Most common manifestation of cutaneous Tuberculosis
- Lesion - can persist for several years, leads to chronic scarring and sometimes skin cancer
- Mx - ATT [ Rifampicin, Isoniazid, Pyrazinamide, Ethambutol ]

67. RMSF - Oral Chloramphenicol; Rickettsia rickettsii

C/F - non generalised headaches and fever, erythematous macular rash on palms and soles; can become petechial later on.

68. **Factors causing poor response to Hep. B vaccine -**

- 1) HIV positivity
- 2) Increasing age
- 3) Decreasing CD4 count
- 4) Increased HIV viral load

69. Jock itch / Tinea curries

- Caused by dermatophyte - Trichophyton rubric
- Scaly, erythematous border that gradually spreads down inner thigh
- Extremely rich
- Tx - topical anti fungal - Clotrimazole

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## RESPIRATORY SYSTEM

1. Bronchiectasis - organism



- The patient presents with a productive cough along with crackles that clear on coughing with radiographic evidence of dilated bronchi and thickened walls in the lower zones ('tram-track sign').
- On a background of rheumatoid arthritis, this suggests the patient has underlying bronchiectasis and is experiencing an exacerbation.
- The most common organism found in infective exacerbations of bronchiectasis is *Haemophilus influenzae* .

## 2. Transudate - Hypothyroidism

- Hypothyroidism can cause a pleural effusion due to an increase in capillary permeability and reduced lymphatic clearance, leading to fluid accumulation.
- This results in a transudative effusion, which is characterised by low protein and LDH levels.

## 3. Yellow Nail Syndrome - Exudate Pleural Effusion

- **Yellow nail syndrome**, while associated with pleural effusions, does typically result in an exudate.
- In yellow nail syndrome, there is often lymphatic dysfunction causing leakage of lymph into the pleural space resulting in a chylothorax which has characteristics distinct from both transudates and exudates.
- Pancreatitis typically causes an exudative pleural effusion. This occurs because of inflammation of the pancreas leading to increased vascular permeability and leakage of high-protein fluid into the pleural space.
- Pneumonia typically causes an exudative pleural effusion. This occurs because of inflammation of the pancreas leading to increased vascular permeability and leakage of high-protein fluid into the pleural space.
- Dressler's syndrome, a form of post-myocardial infarction syndrome, leads to pericarditis rather than typical pleural effusion. When it does cause pleural effusion, it is usually exudative due to concurrent inflammation.

- 4. ABPA - Type II
- EAA (Acute) - Type III
- EAA (Chronic) - Type IV

## 5. Occupational Asthma

- **Isocyanates** are a group of low molecular weight aromatic and aliphatic compounds. They are widely used in the production of flexible and rigid foams, elastomers, and paints. Exposure to isocyanates can cause sensitization leading to occupational asthma.
- **Soldering flux resin** contains colophony (pine resin) which when heated during soldering process releases fumes that can be inhaled causing respiratory sensitisation leading to occupational asthma.
- Exposure to **flour**, particularly in bakeries and mills, is a well-recognised cause of occupational asthma due to its high allergenic potential.
- **Platinum salts** have been linked with occupational asthma especially among workers involved in refining processes where they could inhale these salts.

## 6. Cadmium - Emphysema

- **Cadmium**, a heavy metal commonly found in industrial workplaces particularly in battery manufacturing, electroplating and some types of welding does not typically cause occupational asthma.
- It is associated with lung disease but this is usually chronic obstructive pulmonary disease (COPD) rather than asthma.
- Cadmium inhalation can lead to an acute syndrome called 'metal fume fever' or long-term damage like emphysema but it has not been definitively linked with causing occupational asthma.

## 7. Lung Function Tests - Interpretation

- Obstructive Lung Disease -
  - A. FEV1 - significantly reduced
  - B. FVC - reduced or normal
  - C. FEV1 / FVC - reduced
  - D. Conditions - Asthma, COPD, Bronchiectasis, Bronchiolitis obliterates
- Restrictive Lung Disease -
  - 1. FEV1 - reduced
  - 2. FVC - significantly reduced
  - 3. FEV1 / FVC - normal or increased

4. Conditions - Pulmonary fibrosis, Asbestosis, Sarcoidosis, ARDS, Kyphoscoliosis, Ankylosing spondylitis, Neuromuscular disorders, Severe obesity, Interstitial Lung Disease

- Raised TLCO conditions -
  - Asthma
  - Pulmonary Hemorrhages - Goodpastures, Granulomatosis with microscopic polyangitis
  - Left to right cardiac shunts
  - Polycythemia
  - Hyperkinetic states
  - Male gender, exercise
- Reduced TLCO conditions -
  - Pulmonary fibrosis
  - Pulmonary emboli
  - Pulmonary edema
  - Pneumonia
  - Emphysema
  - Anaemia
  - Low Cardiac output

## 8. **Mesothelioma**

- Loss of material from chromosome 22 is the abnormally commonly seen in mesothelioma
- This contains code for tumor suppressor genes
- MX : Pleurectomy or pneumonectomy can provide symptomatic relief
- Risk factors - cigarette smoking, asbestos exposure
- Drainage of pleural effusion NOT recommended - can cause tumor seeding
- SV40 - possible co-carcinogen in mesothelioma

## 9. **Venturi Mask**

- Venturi mask uses one of a number of different Venturi connectors.
- Each connector provides different percentages of oxygen
- Each connector will have a different diameter through which oxygen passes.

- This creates a negative pressure - causing room air to be sucked in, entrained, and mixed with oxygen flow from the source.
- Less entrainment = less ambient room air sucked in = higher FiO<sub>2</sub> being delivered.

#### 10. Lung involvement in SLE -

- Pleuropericarditis
- Atelectasis
- Pneumonitis
- Raised Hemidiaphragms
- Pulmonary fibrosis

#### 11. Alpha-1 Antitrypsin deficiency

- Cigarette smoking - risk factor for emphysema
- Hereditary cases - occurs in ~2% of patients
- ~15% patients will have associated cirrhosis
- Heterozygotes - increased risk if they smoke
- Homozygotes - predisposed to early presentation with early emphysema

#### 12. Cystic Fibrosis

- **Delayed puberty** can occur in patients with cystic fibrosis due to malnutrition and decreased fat absorption which can affect sex hormone production. In females, delayed menarche may be observed.
- **Nasal polyps** are a common finding in patients with cystic fibrosis. This occurs due to chronic inflammation and infection in the nasal passage and sinuses, leading to growths known as polyps.
- **Diabetes mellitus**, specifically Cystic Fibrosis-Related Diabetes (CFRD), is a unique type of diabetes that occurs in people with CF. The thick mucus seen in CF can block the ducts of the pancreas, preventing insulin from reaching the gut to regulate blood sugar.
- **Rectal prolapse**, where part or all of the wall of the rectum slides out of place, sometimes sticking out of the anus, can occur in children with cystic fibrosis due to frequent coughing and high stool burden secondary to pancreatic insufficiency causing increased intra-abdominal pressure.

### 13. Occupational Asthma

- **Isocyanates** are the most frequently associated substance with occupational asthma in this scenario.
- Occupational asthma is a type of asthma that occurs due to exposure to specific substances in the workplace.
- These substances can cause sensitisation, leading to inflammation and constriction of the airways, resulting in symptoms such as cough, wheezing, and reduced peak flow measurements.
- Isocyanates are commonly used in various industries, including automotive, paint manufacturing, and furniture production.
- They are known to be potent respiratory sensitizers and have been identified as one of the most common causes of occupational asthma.

### 14. TLCO

- Stable asthma - transfer factor unaffected
- Acute asthma - transfer factor **increased**
- Diffusion of Carbon Monoxide from the alveoli to pulmonary blood : governed by integrity of alveolar membrane, capillary blood volume or both [ **air - blood barrier** ]
- Reduction in diffusion capacity of CO is affected by conditions that affect the **capillary bed size** (e.g. - pulmonary emboli, pulmonary vasculitis) **or** conditions that causes **changes in characteristic of alveolar membrane** [e.g. - intra-alveolar filling process] **or** air-blood diffusion pathway is lengthened [ e.g. pneumonia, pulmonary edema, alveolar proteinosis ]
- Also - **reduced transfer factor** is seen in conditions that are infiltrative disorders of the lung - which affects both the capillary bed size and alveolar membrane integrity : sarcoidosis, interstitial lung disease, collagen vascular disease
- **Low TLCO** - removal or destruction of lung tissue - Surgical emphysema, post surgery —> decreases both membrane and blood volume components
- **Increase TLCO** - increase in capillary blood volume secondary to hemodynamic changes, increase in pulmonary arterial or left atrial pressures [congestive heart failure] or increase in pulmonary blood flow [ left to right cardiac shunts]

- **Alveolar haemorrhage** - false increase in TLCO despite presence of an underlying diffusion defect.

### 15. **Mycoplasma pneumoniae**

- Acute, cold, autoimmune haemolytic anaemia - most commonly seen in adolescents and young adults : due to Mycoplasma infection
- **Hemoptysis** occurs 1-2 weeks following infection; most commonly associated with a **rise in polyclonal anti-I IgM antibodies** in Mycoplasma pneumonia.
- Respiratory tract infection, headache, myalgia, cough, fever; CXR s/o bronchopneumonia.
- Cough - non productive
- Sputum if obtained - predominantly mononuclear cells
- Extra pulmonary complications such as :
  1. Rash
  2. Neurological syndromes - aseptic meningitis, encephalitis, neuropathies
  3. Myocarditis
  4. Pericarditis
  5. Haemolytic anaemia
- Mycoplasma - **lacks cell wall** - cannot use Penicillins / Cephalosporins
- Rx - **Macrolides** : Azithromycin, Erythromycin, Clarithromycin or Doxycycline

### 16. **Clubbing - Pulmonary causes :**

- Suppurative disease
- Long standing bronchiectasis
- Acute lung abscess
- Empyema
- Malignancy - carcinoma of bronchus and pleural malignancy
- Hypertrophic pulmonary osteoarthropathy - painful osteitis of distal ends of long bones of lower arms and legs
- Fibrosing alveolitis
- Asbestosis

### 17. **Pneumothorax**

- Primary spontaneous pneumothorax - at rest; men >> women

- Secondary spontaneous pneumothorax : associated with underlying lung condition
- **Aetiology** -
  - Anatomical abnormalities - sub pleural blebs
  - Smoking increased the risk of developing pneumothorax
  - PSP - taller, slim build patients
  - Tension pneumothorax - ventilated on ICU, trauma patients
  - Acute COPD
  - Chest drains - blocked, clamped or displaced
  - NIV
- C/F : shortness of breath; chest pain; diminished breath sounds; reduced lung expansion; hyper-resonance of lung sounds; auscultatory clicks at cardiac apex; trachea shift in tension pneumothorax
- Tension pneumothorax clinical signs : severe breathlessness, distended neck veins, hypotension, mediastinal shift, cardiac arrest
- MX :
  - No clinical distress, small < 2cm pneumothorax -
    - No specific therapy
    - Supplementary oxygen
    - Follow up Chest X-ray
  - Breathless or large > 2cm pneumothorax
    - (1)Supplemental oxygen
    - (2)Percutaneous needle aspiration : IV cannula into pleural space - intersection of mid-clavicular line and 2nd/3rd IC space
  - Secondary pneumothorax :
    1. Small < 1cm rim & no breathlessness - no oxygen, observation in hospital
    2. Moderate 1-2 cm & no breathlessness - supplemental oxygen, observation in hospital, Percutaneous needle aspiration, chest tube, suction
  - Pleurodesis for large > 2cm or breathless.

## 18. Interstitial lung disease - Systemic Sclerosis

- Fine crackles heard at lung bases
- 'Velcro' crepitations are heard
- Lung fibrosis more commonly in patients with **Scl 70, anti-DNA topoisomerase autoantibody**

- CXR - diffuse lung disease
- Oesophageal dilatation almost always present on HRCT

### 19. **Obstructive Sleep Apnoea**

- Excessive daytime sleepiness with irregular breathing at night
- C/F :
  - Poor concentration
  - Irritability and personality changes
  - Tiredness
  - Sleeping during the day
- Diagnosed using sleep study
- Risk factors :
  - Male >> female
  - Obesity
  - Neck circumference > 43cm
  - Middle and older age
  - Smoking
  - Acromegaly

Apnoea - Hypopnea Index -

**Mild** : 5-14 per hour

**Moderate** : 15-30 per hour

**Severe** : >30 per hour

- MX : lifestyle advice - weight loss, sleep routine, intra-oral devices : mandibular advancement device
- CPAP - reduced daytime sleepiness and nocturnal blood pressure
- Untreated sleep apnoea - associated with increased risk of arrhythmia, stroke, & CAD
- OSA - independent risk factor for type II diabetes.

### 20. **Right heart strain - findings**

- Retrograde flow of contrast during CT Pulmonary angiography - suggestive of raised right ventricular pressure due to obstructive shock secondary to pulmonary embolus.
- Normal CTPA - no contrast in IVC
- ECG of right heart strain - ST segment depression and T wave inversion in V1-V4, and inferior leads leads II, III aVF.
- C/F of Pulmonary embolism :
  - Dyspnoea



- Tachypnea
- Tachycardia
- Atrial flutter, atrial fibrillation and premature beats
- Fever - 34-50% of patients

21. Malignant pleural effusion - associated with poor outcome to radical radiotherapy in lung cancer

## 22. **Chest tube insertion with infected pleural effusion** -

### **Indications** :

- A. Patients with frankly purulent or turbid/cloudy pleural fluid on sampling
- B. Pleural fluid pH < 7.2 with suspected pleural infection
- C. Poor clinical progress despite antibiotic treatment
- D. Presence of organisms identified by Gram stain and/or culture from a non-purulent pleural fluid sample

## 23. **BODE Index** - developed by MRC - index of mortality in COPD

BODE Index contains :

- I. Body Mass Index
- II. Dyspnoea
- III. Exercise capacity - 6 minute walk test
- IV. FEV1 - strongest predictor of mortality

## 24. **Churg Strauss Syndrome - Eosinophilic Granulomatosis with Polyangitis**

- Small and medium-vessel vasculitis
- Eosinophilia + necrotising granulomatous inflammation
- Involves respiratory tract, renal system, skin and peripheral nerves
- Typically presents with history of asthma, with atopy, recurrent nasal polyps
- 7 out of 10 patients - have mono neuritis multiplex
- Renal involvement - hematuria, proteinuria, hypertension, raised creatinine levels.
- Diagnostic investigation of choice - **skin biopsy** : granuloma formation with small vessel arteriopathy.
- Clinical features :
  - a) Asthma

- b) Sensory neuropathy
- c) Lung abnormalities
- d) Sinusitis, nasal polyps
- e) Vasculitis phase can be preceded by weight loss, fever, lethargy
- f) Respiratory : asthma, allergic rhinitis, paranasal sinusitis, nasal polyps, cough, hemoptysis
- g) Cardiac : pericarditis/myocarditis, myocardial infarction (due to coronary vasculitis), heart failure
- h) Renal : hypertension, glomerulonephritis, chronic kidney disease
- i) GIT : bowel ischemia, perforation, PR bleeding, appendicitis
- j) Skin : purpura, lived reticularis, urticaria, necrotic bullae, digital ischemia
- k) Neurological : periphebral neuropathy, mononeuritis multiplex, stroke
- Diagnosed clinically - 4 out of 6 features :
  - 1. Asthma
  - 2. Blood eosinophilia >10 %
  - 3. Vasculitis neuropathy
  - 4. Pulmonary infiltrates
  - 5. Sinus disease
  - 6. Extravascular eosinophils on biopsy findings
- Mx : Corticosteroids

## 25. **Respiratory Failure**

- Type I - hyperaemia - < 8 kPa
- Type II - Hyperaemia + hypercapnia high PCO<sub>2</sub> > 6.5 kPa
- C/F : breathlessness, cardiac dysfunction, confusion, cardiac arrest
- Causes :
  - A. Reduced ventilatory drive - sedatives like opiates, alcohol
  - B. Brainstem disorders - encephalitis, tumour, CVA
  - C. Metabolic alkalosis
  - D. Mechanical problems - chest trauma, kyphoscoliosis, obesity
  - E. Neurological : GBS, polio, MND, Spinal muscular atrophy
  - F. Myopathies - muscular atrophy, myotonic dystrophy, hypothyroidism

G.V-Q mismatch - pulmonary embolus, cardiac shunt

H.Upper airway obstruction - laryngeal tumour, OSA

- MX : Type I correction with increasing inspired oxygen concentration
- Type II correction maybe requires ventilatory support
- Invasive ventilation -
  - Type II respiratory failure
  - Respiratory muscle paralysis
  - MODS
  - Trauma cases
  - Reduced GCS

26. Idiopathic pulmonary fibrosis - FEV1/FVC both are reduced proportionately - ratio remains normal.

27. ATT induced hepatitis - stop all therapy if ALT crosses 5 times the upper normal limit as there is increased risk of drug induced liver injury.

## 28. **Pulmonary Hypertension**

- Group I - Pulmonary arterial hypertension
  - A. Idiopathic
  - B. Familial - associated with gene mutation - **BMPR2** - bone morphogenic protein receptor type 2
  - C. Associated with pulmonary venous or capillary disease
  - D. Associated with systemic disease - collagen vascular disease, HIV, SLE, Cirrhosis
  - E. Drugs/toxins
  - F. Portal hypertension
  - G. Congenital heart disease - left to right shunts
  - H. Persistent pulmonary hypertension of newborn babies
- Group 2 - Pulmonary hypertension associated with Left heart disease
  - Atrial or ventricular disease - dilated cardiomyopathy, hypertrophic cardiomyopathy, ischaemic heart disease
  - Valvular heart disease - mitre stenosis, aortic stenosis
  - Extrinsic compression of central pulmonary veins
- Group 3 : Pulmonary Hypertension associated with lung disease and/or hyperaemia
  - COPD

- OSA
- Interstitial lung disease
- Chronic high altitude
- Alveolar hypoventilation disorders
- Chronic hypoxia - polio, myasthenia
- Group 4 - Pulmonary Hypertension due to Chronic Thrombotic/ Embolic Disease
  - Pulmonary emboli of proximal arteries
  - Obstruction of distal pulmonary arteries
  - Embolisation of thrombus, tumour, parasites or foreign material
  - Sickle cell disease
- Group 5 - Pulmonary Hypertension caused by disorders directly affecting pulmonary vasculature
  - A. Inflammatory - schistosomiasis, sarcoidosis
  - B. Pulmonary capillary hemangiomatosis
  - C. Glycogen storage disease
- C/F :
  - (a) exertion dyspnoea
  - (b) Fatigue
  - (c) Dry cough
  - (d) Hemoptysis
  - (e) Central cyanosis
  - (f) Right ventricular heave
  - (g) Loud P2
  - (h) Tricuspid regurgitation
  - (i) Peripheral edema/ascites
  - (j) Chest pain/angina
- ECG may show P pulmonate, right axis deviation, RV hypertrophy, RV strain, RBBB, ITC prolongation
- MX : Prostacyclin - PGI<sub>2</sub> : pulmonary and systemic vasodilator - to bridge patients to transplantation
- Endothelin receptor antagonists - Bosentan
- PDE-5 inhibitors - slows progression
- CCBs - to decrease pulmonary and systemic pressure

## 29. **COPD Management**

- Step 1 - Inhalational SABA or Inhalational SAMA
- Step 2 -

A. Step 2a - no asthmatic or steroid responsiveness features - LABA + LAMA

B. Step 2b - yes asthmatic or steroid responsive features - LABA + ICS 30.

- Triple therapy - ICS + 2a (or) LAMA + 2b
- Acute exacerbation of COPD -
  - (a) Oxygen therapy
  - (b) Antibiotics - Amoxicillin/doxycycline/clarithromycin
  - (c) Corticosteroids - oral prednisolone
  - (d) Beta-2 agonists
  - (e) Nebulised anticholinergics
  - (f) Physiotherapy
- Transplantations may be considered in patients < 65 years :
  - FEV1 and DLCO <20% predicted
  - History of hospitalisation with an exacerbation associated with acute hypercapnia
  - Pulmonary hypertension, and/or cor pulmonale despite oxygen therapy

30. **Yellow Nail syndrome** - abnormality of lymphatic drainage associated with -

- Recurrent bronchiectasis
- Small bilateral pleural effusions
- Lymphoedema
- Grossly thickened, yellow nails
- Mx - antibiotics to treat acute infection, regular follow ups

31. **Radiation pneumonitis** - seen in ~10% of patients receiving high-dose external beam radiotherapy. Symptoms begin 1-6 months after completion of treatment.

Rx - Systemic corticosteroids with addition of Azathioprine or Cyclosporine.

Good prognosis with early intervention.

32. **Occupational Asthma**

- Immunologic asthma / Occupational asthma - two categories :
  - A. High molecular weight - flour, laboratory animal proteins

B. Low molecular weight - di-isocyanates, formaldehyde, trimethylol ether anhydride

- Low molecular weight chemicals : incomplete antigens (=haptens) that combine with protein to produce sensitising neoantigen.
- High ,molecular weight agents are completely sensitising antigens.
- Isocyanates - most common agent causing occupational asthma followed by flour, grain.
- Specific IgE testing available for majority of pathogens.

33. **Bronchiolitis obliterans** - development of granulation tissue in small airways.

Presents with breathlessness and is rapidly progressive in patients with rheumatoid arthritis.

Lung function - irreversible airway obstruction.

Transfer factor - low

Transfer coefficient - normal

34. COPD - Pulmonary Rehabilitation - improved functional exercise capacity.

35. **Carcinoid tumour of lung**

- Tumor is normally vascular.
  - Histology - small polygonal cells with finely granular eosinophilic staining of cytoplasm and nuclei are small and round.
  - Bronchial carcinoid - derives from stem cells of bronchial epithelium - **Kulchitsky cells**.
  - 80-90% of them develop in bronchus of sub segmental size - patients often present with bronchial obstruction that has led to a lower respiratory tract infection.
  - Total surgical excision should be attempted if there is no evidence of metastasis.
- 
- **Adenocarcinoma** : forms a gland and produced mucin.
  - Bronchoalveolar cell carcinoma : arises from type 2 pneumocytes and spreads rapidly.
  - Small cell carcinoma of bronchus : arises from neuroendocrine Kulchitsky cells - composed of sheets of small, round to spindle cells with dark nuclei, scanty cytoplasm, fine granular nuclear chromatin with indistinct nucleoli. 'Salt and pepper appearance'

- Squamous cell carcinoma : well differentiated contains keratin pearls. Poorly differentiated may stain positive for keratin, with large irregular nuclei and coarse nuclear chromatin with large nucleoli.

Presence of intercellular bridging is diagnostic of squamous cell carcinoma.

36. Langerhans cell histiocytosis -proliferaton of langerhans cells in bronchiolar and bronchial epithelium, forming granulomas.

upper zone pulmonary fibrosis

C/F - cough, SOB on exertion, fever, fibrosis in mid to upper zones

CXR - bilaterally symmetrical reticulonodular pattern

Dx - incidentally on CXR

Spirometry - restrictive pattern

37. MacLeod Syndrome

- MacLeod Syndrome - unilateral emphysema following childhood bronchiolitis.
- Emphysema most commonly associated with smoking or alpha-1 antitrypsin deficiency.

38. **Empyema - pleural fluid analysis**

- Empyema - complicated parapneumonic effusion.
- Macroscopic pus
- pH < 7.2
- Glucose < 3.3 mol/L
- LDH > 1000

39. **Hemoptysis**

- Massive hemoptysis + stable hemodynamics —> angiography + embolisation (step 1) later if needed —> lobar resection
- Poor prognostic factors for hemoptysis -
  - Increasing age
  - Pre existing lung or cardiac disease
  - Repiratory compromise
  - Hypoxia
  - Ongoing hemoptysis
  - Shock
- Causes of hemoptysis - Respiratory causes :

1. Bronchial carcinoma
  2. Bronchiectasis
  3. Infections - Aspergillus, TB
  4. Trauma
  5. Vasculitis
  6. AV malformation
- Systemic vasculitides -
    - SLE
    - Granulomatosis with polyangitis
    - Goodpasture's syndrome
    - PAN
  - Cardiovascular disease
    - Pulmonary embolus
    - Mitral stenosis
    - Left ventricular failure

#### 40. **Childhood whooping cough - Bronchiectasis**

##### **Childhood bronchiolitis - unilateral emphysema**

41. Long term Oxygen therapy - **only** treatment shown to **prolong** life in COPD patients.

Relieving hypoxia - reduction in pulmonary arterial pressures and leads to prolongations of life.

Suitable patients - NOT smoking, FEV1 < 1.5 L, PaO2 < 7.3 KPa, PaO2 7.3 to 7.8 with signs of right heart failure / pulmonary hypertension/ pitting oedema

42. **Legionella pneumonia** in patients with **severe penicillin allergy** - Treatment is with **LEVOFLOXACIN**

#### 43. **Asbestosis**

Five forms of the disease -

- Pleural plaques : occurs >20 years after exposure; found on parietal pleura of chest wall, diaphragm, pericardium & mediastinum; asymptomatic; calcifies and presents as whitening of diaphragm on CXR



- **Diffuse pleural thickening** : can extend continuously over variable proportion of thoracic cavity, most marked at lung bases; exertion dyspnoea +/- chest pain
  - **Pleural effusions** : can occur in asbestos related disease, within 15 years of exposure; small and unilateral; resolves spontaneously
  - **Asbestosis** : causes fibrotic changes to lung, presents as worsening exertion dyspnoea, fine inspiratory crackles in lower zones and clubbing, untreatable disease
  - **Lung cancer** : mesothelioma most commonly associated
- 
- Associated with occupations such as - carpenters, plumbers, electricians, asbestos miners, painters, builders
  - Clinical features : worsening exertion dyspnoea
  - **Diffuse pleural thickening** - exertion dyspnoea, chest pain
  - **Asbestos related pleural effusion** - asymptomatic
  - **Asbestos** - coughing, dyspnea, chest pain, finger clubbing
  - **Mesothelioma** - lower back/chest pain, dyspnea, sweating, fever, weight loss, difficulty swallowing, hoarse voice
  - Asbestosis - Spirometry —> restrictive pattern; KCO - reduced
  - Mesothelioma - immunohistochemistry recommended in both biopsy and cytology specimens
  - **Hard lung metal disease = Giant Cell Interstitial Pneumonia**
  - Hard metal lung disease - describes lung damage caused by fine cobalt dust particles
  - Patients are typically exposed when cutting tools or jet engine parts using hard metals
  - Fibrosis develops after prolonged exposure
  - Lung biopsy - multi nucleated giant cells in the alveoli with granulomas present.

44. ARDS - low compliance, high elastic recoil, reduced transfer factor, low pulmonary artery wedge pressure

45. Primary Pulmonary Hypertension

- Presents with breathlessness, fatigue, angina (due to right ventricular ischaemia), pre syncope, syncope.
- **Autosomal dominant pattern with incomplete penetrance** of inheritance in familial cases

- Physical signs include -
  - (1) elevated JVP
  - (2) Left parasternal heave
  - (3) Pansystolic murmur - tricuspid regurgitation
  - (4) Right ventricular S4
  - (5) peripheral edema

46. Left hilar mass clinical sign - **whispering pectoriloquy**  
Likely because of the tumour and locally trapped secretions.

#### 47. **Progressive Massive Fibrosis**

- Associated with fibrotic masses in the apices.
- Also present are emphysematous changes.
- Mixed obstructive and restrictive lung defect with reduced transfer factor.
- Rheumatoid factor and ANA - **positive**
- History of coal dust inhalation
- Category 2 Coal workers Pneumoconioses - can progress to PMF in ~7% of cases

#### 48. **Narcolepsy**

- Chronic condition - characterised by disruption of sleep-wake cycle, and disturbance of REM sleep.
- Classical **tetrad** of symptoms/signs - excessive daytime sleepiness, cataplexy, sleep paralysis and hypnagogic/hypnopompic hallucinations
- Onset - **adolescence**

#### **Pathophysiology**

- Associated with syndromes - **Niemann Pick disease, Prader Willi syndrome, Norrie's disease**
- Genetic predisposition - **HLADQ B1 0602 allele**
- Cholinergic hypersensitivity
- Serotonin / Norad / Dopamine / Hypocretin pathway dysfunction
- CNS histamine deficiency

#### **Clinical Features**

- Excessive daytime sleepiness - improves after naps
- Cataplexy - loss of muscle tone triggered by emotional stimuli
- Sleep paralysis

- Hypnagogic / hypnopompic hallucinations
- Chronic fatigue
- Poor concentration
- Slurred speech
- Blurred vision
- Obesity
- Fragmented nocturnal sleep

#### Diagnosis / Investigation

- Sleep diary & Actigraphy
- Overnight polysomnography - may show snoring, frequent awakening, periods of REM sleep within first 15 minutes
- Multiple sleep latency test - sleep latency < 8 minutes +  $\geq 2$  sleep onset REM periods.
- CSF Hypocretin levels

#### Management

- CNS Stimulants - First line - **Modafinil**, Armodafinil
- Second line - Methylphenidate, Dexamfetamine
- **Patients with cataplexy :**
  - 1) first line - **sodium oxybate**
  - 2) second line - Fluoxetine, Paroxetine, Venlafaxine

49. PEFR predicts mortality in COPD patients.

#### 50. Hepatopulmonary syndrome

- Hepatic disease can result in right-to-left shunting, secondary to intrapulmonary vasodilation mainly in lower lobes.
- This is similar to Pulmonary AV malformations seen in hereditary hemorrhagic telangiectasia.
- There is increase blood flow through the lower lobes when patient moves from supine to standing position.
- This results in blood from the lower lobes which is poorly oxygenated, entering the left side of heart, leads to oxygen desaturation in the erect position.
- This phenomenon is called **orthodeoxia**.

#### 51. PEFR

- Sensitive measurement of airway obstruction

- Related to height than age
- IV Magnesium can be used in acute asthma if PEFR <50 %
- PEFR is effort dependent regardless of whether you have done the test before or not.

## 52. **Transfer coefficient (KCO)** - TLCO / Effective alveolar volume Va

Increase in KCO -

- Increase in RBS in lungs due to greater blood flow - haemorrhage, polycythemia
- Increased at full inflation when the density of pulmonary capillaries per unit alveolar volume is greater than normal - occurs when patients have extra-pulmonary volume restriction

Acute asthma - reduced KCO

ILD - reduced KCO

Pneumonia - reduced KCO

Pulmonary embolus - reduced KCO

## 53. Chronic Thromboembolic Pulmonary Hypertension - widening of alveolar - arterial gradient on exercise (A - a )

## 54. Pneumocystis pneumonia - normal X ray or b/l interstitial shadowing - perihilar in distribution

Pulmonary Tuberculosis - consolidation, cavitation, fibrosis, calcification on CXR

## 55. Upper airway obstruction - flow volume loops - shows typical flattening

## 56. Radiation pneumonitis

- CXR - area of hazy consolidation demarcated by a sharp margin due to crossing anatomical pulmonary planes
- CT - best method of early identification
- Ground glass attenuation and inter alveolar septal thickening
- Dense local fibrosis can develop 1-2 years after radiation

57. Hypoxia in primary pulmonary hypertension - factors causing : intra-pulmonary shunting, reduced diffusion capacity due to arterial fibromuscular hyperplasia.

### 58. **Hypogammaglobulinemia in ataxia telangiectasia**

- Inherited in autosomal recessive fashion
- Ataxic from an early age
- Oculomotor apraxia and choreathetosis later in life
- Alpha-fetoprotein can be raised.
- Cell defects and deficiencies in humeral immunity with defective DNA repair and IgA and IgE deficiencies result in recurrent infections and tumour susceptibility.

**Hereditary spinocerebellar degeneration** - autosomal dominant or recessive. Associated with slowly progressive cerebellar syndromes, tremors and ataxic gait.

Extrapyramidal features can be presents pyramidal signs, cortical symptoms such as behavioural disturbance, epilepsy, cognitive disturbances. NOT associated with bronchiectasis.

**Mounier-Kuhn syndrome** - congenital deficiency of bronchial cartilage; tracheal and bronchial dilation and associated with recurrent LRTIs.

**Williams-Campbell syndrome** - deficiency of bronchial cartilage particularly in sub segmental bronchi. Leads to bronchiectasis distal to the affected bronchi.

59. **Idiopathic pulmonary hemosiderosis** - occurs in younger people and characterised by pallor, weakness, lethargy, dry cough and occasional hemoptysis. No abnormal immunological features. Gas transfer factor is elevated because of hemoptysis blood is already in alveoli.

60. **Bronchial breathing** - consolidation, atelectasis, dense fibrosis Resembles sounds to normal trace as compared to normal breath sound.

Bronchial breathing is higher in pitch and blowing in quality. Heard throughout both inspiration and expiration.

61. Bronchiectasis - postural drainage daily is the most important in treatment

62. Alveolar-arterial (A-a) gradient

- Affected primarily by V/Q mismatch and shunting
- Changes in alveolar-arterial gradient occur with ventilatory disorders - pneumonia or disorders of vasculature - pulmonary embolus.
- A-a gradient =  $PAO_2 - (PaO_2 + PaCO_2/0.8)$
- $PAO_2$  - alveolar oxygen,  $PaO_2$  - arterial  $O_2$ ,  $PaCO_2$  - arterial  $CO_2$
- $PAO_2 = (100 - 7)/100 \times \% \text{ inspired oxygen}$

63. **Pneumonia - chronic complication** - Bronchiectasis : diagnosis can only be made after the illness because temporary or reversible bronchial dilatation is sometimes seen during acute illness.

Acute complications of pneumonia -

- Organising pneumonia
- Bronchopleural fistula
- Empyema
- Lung abscess

64. **Bronchiectasis**

- HRCT - signet ring sign
- Airways seen on longitudinal section on CT and there is a failure of tapering as the bronchus crosses towards the periphery.
- HRCT would show both dilation and thickening of affected bronchi, dilatation being present if internal diameter of bronchus is greater than diameter of its accompanying pulmonary artery.

65. **Eosinophilic granulomatosis with polyangitis**

Diagnosed if four of the following are present -

- Asthma
- Blood eosinophilia
- Vasculitis neuropathy
- Pulmonary infiltrates

- Sinus disease
- Extra vascular eosinophils on biopsy

#### 66. Scleroderma - pulmonary manifestations

- **Non specific interstitial pneumonia (NSIP)** is most common pattern of fibrotic lung disease seen in scleroderma
- Treatment - **Cyclophosphamide** and **Mycophenolate mofetil**
- PDE-5 inhibitors and endothelial receptor antagonists can be used for treating pulmonary hypertension.

67. Spiral CT or CT Angiography - low sensitivity for detecting pulmonary emboli in sub segmental pulmonary arteries

Accurate investigation for pulmonary emboli in main, lobar, segmental pulmonary arteries.

#### 68. Birt-Hogg-Dube syndrome - **BHD Syndrome**

Pneumothorax + lung cysts + fibrofolliculoma of skin + renal cancer

Due to mutant of follicular gene

Family history of pneumothorax and renal cancer.

#### 69. Acute severe asthma

- low PO<sub>2</sub>
- Low PCO<sub>2</sub>
- Normal CXR
- Low PEFR

Signs of severe attack -

- PEFR < 50% of predicted
- Pulse > 100 bpm
- RR > 25/min
- Inability to complete sentences

Life threatening asthma attack -

- PEFR < 33% of predicted
- Silent chest
- Hypotension
- Confusion, Exhaustion, coma

- Normal or raised PCO<sub>2</sub>, PO<sub>2</sub> <8, pH < 7.35

70. **Bronchial carcinoid** - recurrent hemoptysis with segmental collapse

71. **Mycobacterium malmoense**

- Mycobacterium malmoense is a non-tuberculous mycobacterium and a low-grade environmental pathogen in humans.
- This organism most commonly causes pulmonary infection in middle-aged and older adults with pre-existing lung disease or immunodeficiency.
- M. malmoense can also cause local invasion from a skin lesion. It causes non-specific symptoms, such as malaise and weight loss, or chest symptoms that take an atypical course.
- Chest X-ray appearances can be indistinguishable from those seen in patients with Mycobacterium tuberculosis infection, with upper-zone fibrosis and cavitation.
- A single isolate from a non-sterile site might not be significant and can just represent contamination. More than two isolates from a non-sterile site are required to establish disease.

72. **Pneumonia** - Risk factors for **increased mortality** :

- Age > 60 years
- RR > 30 / min
- Underlying disease
- Confusion
- Multilobular involvement
- Serum album < 35 g/L
- Hypoxia PO<sub>2</sub> < 8 KPa
- Leucocytosis > 20,000
- Leucopenia <4000
- Bacteraemia
- Atrial Fibrillation with fast ventricular rate

73. **Upper lobe fibrosis** -

C - Coal Wokers Pneumoconioses

H - Histioplasmosis, Hypersensitivity pneumonitis

A - Ankylosing spondylitis, Allergic Bronchopummonary Aspergillosis

R - Radiation therapy



T - Tuberculosis

S - Sarcoidosis, Silicosis

74. Subclavian line insertion - pneumothorax

75. Cystic fibrosis - neutrophil infiltration; neutrophil derived factors such as elastase increase damage to respiratory epithelium

76. Allergic Bronchopulmonary Aspergillosis - Proximal Bronchiectasis - diagnosed with Skin prick test

**77. Pleural effusion - exudate**

Exudates - high in protein content; commonly caused by inflammation and leakage of extravascular fluid.

Causes of exudative pleural effusion -

- Infections - pneumonia, Tuberculosis
- Malignancy - primary carcinoma of bronchus, metastatic carcinoma
- Pulmonary embolism
- Connective tissue disorders - SLE, Rheumatoid arthritis
- Subdiaphragmatic - pancreatitis, subphrenic abscess
- Trauma - hemothorax, chylothorax.

Uncommon causes -

- Infections - fungal, viral, parasitis
- Malignancy - lymphoma, pleural tumors
- Connective tissue - Sjogren's, granulomatosis with polyangiitis, immunoblastic lymphadenopathy
- Hepatic abscess
- Trauma - ruptured esophagus

78. Silicosis - mixed obstructive/restrictive picture

79. Hypersensitivity pneumonitis / Extrinsic Allergic Alveolitis - Restrictive picture on lung spirometry

**80. Hospital Acquired Pneumonia**

- Aetiology - Staph aureus, Gram negative bacteria common such as Klebsiella, E.coli, Pseudomonas, Proteus

## PATHOPHYSIOLOGY

- Result of oro-pharyngeal pathogens introduced into alveoli due to micro aspirations
- Also can be due to inhalation, IV cannulas, thoracocentesis

## CLINICAL FEATURES

- Breathlessness
- Reduced oxygen saturations
- Tachycardia
- Cough +/- productive
- Poor appetite
- Hospital admission **at least two days**
- Raised temperature
- Chest pain
- Decreased air entry

## INVESTIGATION

- Pulse oximetry
- Chest X ray
- ABG
- FBC
- CRP
- PFT
- Sputum sample

## MANAGEMENT

- Start antibiotics within four hours of establishing diagnosis
- Local guideines
- Recommendation - **third generation Cephalosporin + Aminoglycoside**

## 81. Forced Expiratory Flow between 25-75%

- Reflects the status of small airways
- Effort independent
- Impaired in smokers and in patients with graft v/s host disease with associated lung pathology
- Impaired in bronchiolitis obliterans
- Not useful for identifying large airway disease

## 82. **Military TB**

- Diffusely, widely disseminated spread of tubercle bacilli via bloodstream
- Can present with gradual onset of vague ill health, loss of weight and fever
- Can also present as tubercular meningitis
- **Hepatosplenomegaly** - advanced disease
- **Choroidal tubercles** - advanced disease
- CXR - initially Normal, later can show 1-2 mm lesions
- CT - lung parenchyma abnormality
- Mantoux test can be negative
- Transbronchial biopsy - positive at an early stage.

## 83. **Elevated unilateral hemidiaphragm - do Fluoroscopy to confirm**

During a forced inspiratory manoeuvre - unaffected hemidiaphragm descends forcefully, increasing the intra abdominal pressure and pushing the paralysed/affected hemidiaphragm upwards.

## FLUOROSCOPY - ONLY UNILATERAL PARALYSIS

84. Non small cell cancer - cough(47%) followed by breathlessness (37%) most common presentation.

~15% of patients with non small cell lung cancer are asymptomatic

85. OSA clinical features -

- Memory impairment
- Daytime somnolence
- Grossly disrupted sleep pattern
- Decreased libido
- Systemic hypertension

86. Isolated pulmonary carcinoid - thoracic surgeon for tumor resection

## 87. **Cryptogenic pulmonary eosinophilia**

C/F -

- Malaise
- Weight loss

- Fever
- Raised ESR
- Asthma in ~50% of patients

Rx : steroids - upto 1 year

88. **Caplan Syndrome** = Rheumatoid Arthritis + Pneumoconioses

89. **Idiopathic pulmonary fibrosis - poor compliance & increased lung elastic recoil**

90. **Tension Pneumothorax**

- Occurs when intrapleural pressure exceeds the atmospheric pressure
- It draws air into the pleural space during inspiration and not letting it out during expiration
- Patients become rapidly distressed with rapid laboured respiration, cyanosis, sweating and tachycardia.
- Cannula of adequate length - insert into 2nd Intercostal space in mid clavicular line
- Provide high concentration oxygen

91. Acute asthma - because of gas trapping there is an increase in residual volume and an increase in total lung capacity.

$TLC = VC + RV$

92. Pancoast tumor - pupil constriction, ptosis, facial anhidrosis, C7 C8 T1 involvement

93. **Mendelson syndrome** - acute pneumonia caused by regurgitation of stomach contents and aspiration of chemical material, usually gastric juices.

Can cause severe bronchospasm.

Pneumonia develops rapidly and within hours, patients become tachypnoeic, hypoxic, and febrile.

Minimal sputum production.

Commonly seen after anaesthesia when the gag reflex is depressed.

94. Neck size - best predictor of OSA.

- >43 cm or 17 inches - increased risk in men
- >16 inches in women - increased risk of OSA

## GASTROENTEROLOGY & HEPATOLOGY PASSMEDICINE

### 1. Whipple's disease

- Chronic multi system, condition - **infection with gram-positive Actinobacteria - Tropheryma whipplei** + abnormal response of cell mediated immunity
- Associated with HLA B27 antigen
- Jejunal biopsy - deposition of macrophages containing PAS positive granules within villi.

### CLINICAL FEATURES

- Abdominal pain
- Abdominal distension
- diarrhoea
- steatorrhea
- anorexia
- weight loss
- Other associated symptoms - generalised lymphadenopathy, arthropathy, cough, intermittent pyrexia
- Chronic cough
- Hyperpigmentation
- Endocarditis
- Disease progression can cause - anaemia, pleural effusion, cardiac valve disease, pericarditis
- CNS - cognitive function abnormalities
- Oculomasticatory and oculofascioskeletal myorhythmia

### INVESTIGATIONS

- Gastroscopy - small bowel biopsies
- PAS positive macrophages on histology
- PCR to identify bacterial DNA

### MANAGEMENT

- 14 days of Ceftriaxone or Benzylpenicillin
- Followed by a year of maintenance therapy with Trimethoprim/Sulfamethoxazole

## 2. **Gastrin hormone** -

- Secreted by G cells in antrum of stomach & duodenum
- Stimulated by : distension of stomach, vagus nerve, luminal peptides, luminal amino acids, hypercalcemia
- Inhibited by : Low astral pH, Somatostatin
- Actions :
  1. increased acid secretion by gastric parietal cells,
  2. Increases secretion of Pepsinogen
  3. Increased IF secretion
  4. Increased gastric motility
  5. Stimulates parietal cell maturation

## 3. **Cholecystokinin**

- Secreted by - I cells in upper small intestine
- Stimulated by - partially digested proteins and triglycerides
- Actions :
  - Increases secretion of enzyme rich fluid from pancreas
  - Contraction of gallbladder and relaxation of sphincter of Oddi
  - Decreases gastric emptying
  - Trophic effect on pancreatic acing cells
  - Induces satiety

4. Pancreas and Left suprarenal gland - make direct contact with left kidney

## 5. **Achalasia**

- Presents with progressive dysphagia and regurgitation
- Degeneration of ganglion cells in the myenteric plexus of the oesophagus
- Characterised by abnormal oesophageal peristalsis and lack of relaxation of lower oesophageal sphincter

## **CLINICAL PRESENTATION**

- Progressive onset of dysphagia to solids and/or liquids with regurgitation of undigested food
- Feeling of retrosternal fullness or pain
- Aspiration can occur if regurgitation occurs while lying down

## **INVESTIGATION**

- CXR - widened mediastinum due to dilated oesophagus
- Barium swallow - dilated oesophagus with narrow oesophageal gastric junction - bird beak appearance
- Oesophageal manometry - lack of peristalsis in distal esophagus with incomplete relaxation of lower oesophageal sphincter
- Oesophageal gastric duodenoscopy may be required if there are features suggestive of malignancy - rapid weight loss

## MANAGEMENT

- Symptoms control
- Short acting nitrates before meals - sublingual isosorbide dinitrate
- CCBs
- Botulinum toxin injection via endoscopy
- Surgical : Laparoscopic Heller myotomy, Peroral endoscopic myotomy

## 6. **Acute Pancreatitis**

- Etiology - GET SMASHED
  - a) G - gallstones
  - b) E - ethanol
  - c) T - trauma
  - d) S - steroids
  - e) M - mumps, coxsackie B virus
  - f) A - autoimmune
  - g) S - scorpion sting
  - h) H - hyperlipidemia, hypercalcemia, hypertriglyceridemia
  - i) E - ERCP
  - j) D - Drugs : Azathioprine, OCP, steroids, anti-retrovirals, Fibrates, Thiazides.

## Clinical Presentation

- Severe epigastric pain - radiating to back
- Pain worse after meals, improves on leaning forwards
- Nausea, vomiting
- Tachycardia, hypotension and oliguria
- Epigastric tenderness
- Abdominal distension, guarding
- Ileus, reduced bowel sounds
- Ascites
- Cullen's sign - discolouration around umbilicus

- Grey Turner's sign - discolouration in flanks

### Investigation

- Elevated pancreatic enzymes
- High risk patients - identified by scoring systems such as APACHE II, Ranson or Glasgow criteria - factors such as : age, hypoxia, WCC
- Serum amylase and lipase
- CT

### Management

- Analgesia - morphine sulphate or fentanyl
- Supplemental oxygen
- Anti emetics : Ondansetron
- Calcium gluconate in patients with hypocalcemia
- IV Antibiotics in severe infection
- Early ERCP - patients with pancreatitis secondary to gallstones to achieve duct compression

## 7. **Chronic pancreatitis**

- Aetiology :
  - Alcohol
  - Cystic fibrosis
  - Smoking
  - Hereditary causes
  - Idiopathic
  - Metabolic causes - hypercalcemia, hyperlipidemia
  - Autoimmune casues
  - Drugs - **thiazides, azathioprine, tetracyclines**

### **Clinical features**

- Malabsorption
- Steatorrhoea
- Abdominal pain
- Diabetes mellitus
- **Erythema ab igne** - skin changes due to constant use of hot water to help with pain

### Investigations

- X-ray - calcification



- CT - most sensitive, detects pancreatic calcification
- ERCP - irregular dilatation and structuring of pancreatic ducts
- MRCP - choice for diagnosis
- Exocrine insufficiency - assessment by Pancreolauryl and serum para-amino benzoic acid (PABA) testing
- Exocrine function - fecal elastase

#### Chronic Pancreatitis complications

- Pancreatic duct obstruction
- Pseudocysts
- Neuropathic pain
- Pancreatic ascites and pleural effusion
- Diabetes
- Exocrine insufficiency
- Increased risk of pancreatic cancer

**Pancreatic Pseudocysts** : collection of necrotic/hemorrhagic material and pancreatic enzymes within or near pancreas without epithelial lining

**Pancreatic divisum** - congenital abnormality where the dorsal and ventral ducts do not connect and drainage of dorsal duct is disrupted. Can experience recurrent pancreatitis; drainage occurs through minor papilla

### 8. Wedged hepatic venous pressure - hepatic sinusoids

Elevated wedged hepatic venous pressure is seen in sinusoidal and post-sinusoidal portal hypertension.

Wedged hepatic venous pressure - normal in : pre sinusoidal portal hypertension.

Hepatic venous pressure gradient - difference between WHVP and free hepatic venous pressures.

HVPG  $\geq$  5 mmHg : induced portal hypertension.

### 9. Wilson's disease

#### Overview

- Inherited in autosomal recessive fashion
- Mutation of ATP7B gene on Chromosome 13 : which impairs copper incorporation into ceruloplasmin and copper excretion
- High levels of free copper - via oxidant damage : causes inflammation and cell injury resulting in hepatitis
- Continued exposure to high copper levels causes fibrosis.
- CNS - basal ganglia.

### Clinical Features

- Liver features : hepatitis, cirrhosis, liver failure
- Adults present with CNS signs -
  - Tremors
  - Dysarthria
  - Dysphagia
  - Dementia
  - Parkinsonism
  - Ataxia/clumsiness
  - Mood disturbances - depression, mania, loss of libido
  - Cognition defects - decreased memory, decreased IQ
  - Eye : Kayser-Fleischer rings : green brown pigmentation

### Investigation

- Liver function tests
- 24 hour urinary copper - increased
- Reduced serum ceruloplasmin
- Reduced total serum copper
- Increased free/non-bound serum copper
- Slit lamp examination : KF rings, sunflower cataracts
- Low serum uric acid - due to increased urinary excretion

### Management

- Copper chelating agents - Penicillamine
- Alternative chelating agents : Tridentine hydrochloride
- Severe hepatic disease : liver transplantation

## 10. **Coeliac Disease**

### Overview

- Autoimmune condition - gluten activated abnormal mucosal response causing characteristic damage and chronic inflammation to lining of small intestine.

- Coeliac disease - also known as : Gluten sensitive enteropathy/ coeliac sprue/ non tropical sprue
- Refractory coeliac disease : recurrence of malabsorption clinical signs and symptoms associated with villous atrophy in coeliac patients who have adhered to a gluten-free diet for >12 months.
- Associated with HLA-DQ2 in 95%, rest associated with HLA-DQ8.
- Associated with other autoimmune conditions - T1DM, autoimmune thyroids, Pernicious anaemia

### Pathophysiology

- Immunological response to gluten peptide antigens which are derived Fromm wheat, rye, barley.
- In coeliac disease : these gluten peptides are resistant to human proteases, enabling them to persist in small intestinal lumen
- These peptides trigger immune activation in the intestinal mucosa - mediated by T helper cells.
- Tissue transglutaminase is release in response of gluten consumption
- Small intestine epithelium is damaged : loss of brush border, villous atrophy, crypt hyperplasia.

### Clinical features

- Diarrhoea
- Bloating
- Abdominal discomfort / pain
- Failure to thrive in children
- Weight loss
- Fatigue
- IDA - microcytic anaemia
- Vit B12/folate deficiency - microcytic anemia
- Osteopenia / osteoporosis
- Associated with conditions such as :
  - 1) dermatitis herpetiformis
  - 2) Down's syndrome
  - 3) Selective IgA deficiency
  - 4) T1DM
  - 5) Thyroid disease
  - 6) Liver disease

### Investigations

- Blood tests - FBC, Iron, Fit B12, Folate, Calcium
- IgA-tTG levels
- Endomysial antibody
- Small intestine endoscopy is indicated if serological tests are positive for confirmation of diagnosis
- Duodenal biopsy : intra-epithelial lymphocytes, villous atrophy, crypt hyperplasia

### Complications

- Osteoporosis / osteopenia
- Osteomalacia
- Abnormal LFTs
- Hyposplenism
- Dermatitis herpetiformis
- Malignancies : T-cell lymphoma, carcinomas of upper digestive tract
- Infertility
- Increased risk of vaccine failure : may need additional doses to invoke immunity

## 11. Cryoglobulinemia

### Overview

- Associated with Hepatitis C virus, Monoclonal gammopathy, connective tissue disease
- Presence of cryoglobulin that precipitate at lower temperatures than 37 Degree Celsius and dissolves on rewarming

### Classification - Brouet Classification

- Type I : made of IgG or IgM : associated with monoclonal gammopathies such as MG of unknown significance (MGUS), Waldenstrom macroglobulinemia, chronic lymphocytic leukaemia, Multiple myeloma
- Type II : mixture of polyclonal immunoglobulin with rheumatoid factor. Associated with Hepatitis C, Sjogrens, SLE. **Positive rheumatoid factor**
- Type III : polyclonal; associated with HCV or autoimmune disease
  - Rheumatoid arthritis, Sjogren's ; **positive Rheumatoid factor.**

### Clinical Features

- Constitutional symptoms - arthralgia, fatigue, myalgias
- **Meltzer's triad** - purpura, arthralgia, weakness seen in **types II and III**.
- Cutaneous - digital ischemia, lived reticularis, Raynauds phenomenon (type I), palpable purpura, skin necrosis
- Renal - Membranoproliferative glomerulonephritis
- Neurology - peripheral neuropathy, mononeuritis multiplex, mononeuropathies

12. Intestinal pseudo-obstruction : seen in advanced Parkinson's disease

Causes symptoms of intermittent abdominal bloating and vomiting.

Rx - pro kinetics; **avoid Metoclopramide**

### 13. Gallstones risk factors :

- Female sex
- Multiparity
- OCP use
- Terminal Ileal Crohn's disease - due to excessive production of lithogenic bile
- High dietary animal fat intake
- Rapid weight loss
- Diabetes mellitus

14. HLA DQ2 and HLA DQ8 - Coeliac disease

HLA B27 - IBD, Psoriasis, Ankylosing spondylitis, reactive arthritis

NOD2 gene mutation - Crohn's disease

HLA DR3 and DR4 - Type 1 Diabetes

HFE gene mutations - Hereditary haemochromatosis

### 15. Vitamin C - Collagen synthesis

- Vitamin C - essential for collagen formation
- Helps maintain integrity of substances of mesenchymal origin - connective tissue, osteoid tissue, dentin.
- Vitamin C- wound healing and promotes recovery from burns

- Severe deficiency - scurvy : haematological manifestations and abnormal osteoid and dentin formation
- Radiology - generalised bone rarefaction, metaphyseal deformity of fractures and subperiosteal hepatomas.
- Vitamin C - co-factor required for hydroxylation of selected proline and Lysine amino acids in the pro collagen protein - to form hydroxyproline and hydroxylysine.
- These pro collagen proteins form a helical structure
- Vitamin C deficiency - decreased formation of pro collagen protein - resulting in weak collagen molecule.

## 16. **Autoimmune Hepatitis**

### Overview

- Associated with other autoimmune conditions like :
  - (a) Pernicious anaemia
  - (b) Ulcerative colitis
  - (c) Glomerulonephritis
  - (d) Autoimmune thyroiditis
  - (e) Autoimmune hemolysis
  - (f) Diabetes mellitus
  - (g) Primary sclerosing cholangitis
  - (h) Coeliac disease
  - (i) Rheumatoid arthritis
- Type I autoimmune hepatitis : associated with HLA DR3 and HLA-DR4
- Type II associated with HLA-DQB1 and HLA-DRB
- Environmental triggers : CMV, Hepatitis A/C/D, EBV
- Drugs - Nitrofurantoin, Diclofenac, Atorvastatin, Herbal agents

### Classification

- Type 1 : most common; presence of anti-smooth muscle Ab (ASMA) and Anti nuclear antibodies (ANA); Increased IgG
- Type 2 : children, presence of antibodies to liver/kidney microsomes (ALKM-1) and liver cytosol antigen (ALC-1)
- ANA and ASMA negative in type 2 autoimmune hepatitis.

### **Clinical Features**

- Fever
- Malaise
- Myalgia

- Urticarial rash
  - Pleurisy
  - Polyarthrititis
  - Pulmonary infiltration
  - Glomerulonephritis
  - Nausea
  - Upper abdominal pain
  - Hepatomegaly
  - Mild pruritic
  - Gradual jaundice
- 
- Liver Biopsy : piecemeal necrosis and mononuclear infiltration of portal and peri portal areas

### **Diagnostic Criteria**

- No genetic liver disease : normal ceruloplasmin, normal Alpha-1 antitrypsin, normal iron and ferritin levels
- No markers or current active infection - hepatitis A/B/C
- No toxic liver injury to alcohol or drugs
- Increased auto-antibodies
- Bloods show —> increased AST and IgG levels

### **Management**

- Moderate/severe inflammation : serum AST > 5 times upper limit, serum globulin > 22 times upper limit, liver biopsy showing confluent necrosis
- Prednisolone - gradual tapering over 4 weeks
- Prednisolone + Azathioprine
- Long term Azathioprine use : extra hepatic malignancy, increased infections, bone marrow suppression

### **17. Lynch syndrome - Aspirin**

- AKA hereditary non-polyposis colon cancer syndrome
- Underlying mechanism is due to DNA mismatch repair variants defect
- Aspirin - reduction in progression to colon cancer

### **18. Protein losing enteropathy**

- measurement of alpha 1 anti-trypsin levels are useful for confirming diagnosis

- Albumin degraded by proteases in the gut
- Alpha 1 antitrypsin is a plasma protein resistant to proteases degradation
- Measurement of Alpha 1 antitrypsin levels can indicate plasma leakage of proteins in gut

19. Moderate ileal resection - bile salt malabsorption : can be confirmed with SEHCAT scan.

Rx : Cholestyramine - works by acting as bile acid sequestrate.

**20. Colorectal cancer - increased risk with Staphylococcal Boris endocarditis.**

Colonoscopy is mandatory

21. Systemic mastocytosis - increased mast cells and increased histamine production —> increased gastric acid secretion

Resection of small bowel —> loss of inhibition in small bowel by hormones —> increased gastric acid secretion

22. Coeliac disease : recurrent mouth ulcers, diarrhoea, failure to thrive - clinical manifestations of coeliac disease in young people.

Mouth ulcers and intensely pruritic rash - also associated with dermatitis herpetiformis

**23. Protein losing enteropathy - causes :**

- Sarcoidosis
- IBD
- Pseudomembranous colitis
- CMV colitis
- Tuberculosis
- Connective tissue disease

**24. Imatinib uses :**

- Chronic Myeloid Leukaemia
- Gastrointestinal stromal tumor
- Systemic macrocytosis
- Some sarcomas



## 25. **Hereditary Hemochromatosis**

### Overview

- Inherited liver condition : causes iron overload —> chronic liver disease
- Autosomal recessive pattern with variable penetrance
- Mutation : HFE gene —> increased intestinal iron absorption —> iron deposition in joints, liver, pancreas, pituitary, adrenals, skin
- 2 most common HFE mutations : C282Y and H63D

### Pathophysiology

- Hepatic hepcidin gene expression - low
- Low hepcidin expression : macrophages continuously releases iron
- Iron stored as ferrite - deposited in organs as hemosiderin

### Clinical Features

- Tiredness
- Arthralgia
- Loss of Libido
- Hypogonadism
- Skin pigmentation - bronzing of skin
- Signs of CLD
- Hepatomegaly

### Investigations

- Serum transferrin saturation : **increased**
- Serum ferritin : **increased**
- HFE genotyping
- Liver biopsy
- Ferritin > 500
- Serum iron > 30
- Transferrin saturation >60%
- TIBC <20

### Management

- Venesection
- Iron chelating therapy
- Complications - cirrhosis, hepatocellular carcinoma, cardiomyopathy, diabetes, cardiac failure

## 26. Primary Sclerosing Cholangitis

- Progressive bile duct inflammation, structuring and cholestasis
- Causes scarring of bile ducts and accumulation of toxins.
- ALP raised due to damage of cells of biliary tree and bile ducts
- Diagnosed with MRCP
- Auto immune
- Clinical features : fatigue, pruritic, obstructive jaundice, cirrhosis, hepatic failure
- INV : MRCP, raised ALP, Anti-smooth muscle Abs and ANA may be present
- MX : Cholestyramine - can resolve pruritic
- Ursodeoxycholic acid
- Abx - for associated cholangitis

## 27. Drugs causing hepatitis :

- Isoniazid
- Rifampicin
- Methyldopa
- Atenolol
- Enalapril
- Verapamil
- Nifedipine
- Amiodarone
- Ketoconazole
- Cytotoxics
- Halothane

## 28. Drugs causing Cholestasis :

- OCP
- Clotrimazole
- Azathioprine
- Chloramphenicol
- Cimetidine
- Ranitidine
- Erythromycin
- Nitrofurantoin
- Imipramine
- Ibuprofen
- Hypoglycaemics

### 29. **Menetrier's disease**

- Rare condition associated with giant gastric folds, mainly in fundus and body of stomach
- M/C - hyperplasia of gastric pits, gland atrophy, and increase in mucosal thickness
- Hypochlorhydria present - almost nil gastric production
- C/F : epigastric pain
- Protein loss from gastric mucosa - hypoalbuminemia
- Rx : PPI for symptomatic relief.

### 30. **Biguanides - Metformin can cause bile acid malabsorption.**

- Bile salts cause diarrhoea by reducing water absorption and electrolytes in the colon and stimulates colonic motility
- Mx : substitute Metformin

Other causes of bile acid malabsorption diarrhoea : ileal resection, terminal ileal disease, cholecystectomy.

### 31. **Primary Biliary Cholangitis**

- Causes small duct obliteration and build up of toxins
- ALP is raised
- AMA antibodies hallmark of PBC.
- Strongly associated with - rheumatoid arthritis, Sjogren's syndrome, CREST syndrome
- Progressive inflammation and destruction of small intrahepatic ducts

#### Clinical Features

- Raised Alp as incidental finding
- Cholestatic jaundice
- Diarrhoea
- Lethargy
- Xanthelasma due to hypercholesterolemia
- Skin pigmentation
- Clubbing
- Hepatosplenomegaly
- Portal hypertension varices
- Osteoporosis & osteomalacia

#### Investigation

- Anti-mitochondrial body M2 antibody present in 95% of cases

- Raised IgM

Mx: **Cholestyramine** for pruritis

**Obeticholic acid** for reducing circulating bile acid

### **32. Poor prognosis markers in acute pancreatitis : Glasgow Criteria**

- 1) age > 55
- 2) WCC > 15,000
- 3) Blood glucose > 10
- 4) Serum urea >16
- 5) Albumin <32
- 6) AST and ALT >200
- 7) Serum LDH >600
- 8) Serum calcium <2
- 9) PaO<sub>2</sub> <8

### **33. Vascular lesions of colon -**

- Two types - 1) angiodysplasia 2) hemangiomas
- Angiodysplasia - colonic angiodysplasia consists of small, submucosal arteriovenous malformations of unknown etiology
- Occur sporadically, or in association with hereditary telangiectasia of skin and mouth in Osler-Weber-Rendu syndrome; presents normally with rectal bleeding
- Hemangiomas - cavernous or giant hemangiomas and involves the whole thickness of bowel wall; commonly occur in rectum and present with bleeding per rectum.

#### **Clinical Features**

- Painless per rectum bleeding
- Positive fecal occult blood test
- Recurrent small bowel lower GIT bleeding causing anaemia
- Diagnosis : Colonoscopy - showing spider naevi like lesions or hemangiomas.
- Mx : Angiodysplasia : coagulation via colonoscopy may be curative
- Mx : Hemangiomas - electrocoagulation or sclerotherapy

Angiodysplasia investigation : 2 colonoscopies —> capsule endoscopy

**34. Barrett's oesophagus - surveillance**

- No dysplasia - endoscopy every 2-5 years
- Low grade dysplasia - endoscopy every 6 month; repeat endoscopy with quadrantic biopsies every 1cm
- High grade dysplasia - endoscopy every 3 months; visible lesion present — consider endoscopic ablation with mucosal resection or radio frequency ablation
- Barrett's oesophagus with dysplasia —> endoscopy to be repeated as soon as feasible if four quadrant biopsy specimens were not obtained at 1 cm intervals or if there were any mucosal irregularities that were not removed with endoscopic resection.
- Endoscopic resection of mucosal irregularities is required to assess the grade of dysplasia accurately.
- Repeat endoscopy shows poorly differentiated cell - highly suggestive of oesophageal malignancy and evaluation of esophagectomy needs to be done.

**35. Lactulose**

- Synthetic sugar broken down only by gut bacteria in the colon.
- The acidic metabolites produced in the process have an osmotic effect which increases the water content and volume of stools.
- Acidic metabolites also have an effect in increased ionisation of freely diffusible ammonia into ammonium which cannot diffuse back into blood - used in hepatic encephalopathy.

36. Capecitabine - oral administration - metabolised to 5-Fluorouracil.

5-Fluorouracil - IV administration

37. Gallstones - black pigment stones - hereditary spherocytosis, sickle cell disease, thalassemia, cirrhosis

Black pigment stones - small, friable, irregular and radiolucent, largely composed of bile pigments

**38. Zinc deficiency - dermatitis, alopecia**

IBD patients prone to zinc deficiency due to loss of absorption of zinc.

39. Bleeding duodenal ulcer - posterior aspect of duodenum —> **posterior superior pancreaticoduodenal artery**

Anterior duodenum + head of pancreas —> **anterior superior pancreaticoduodenal artery**

Pylorus and primal duodenum —> **proximal duodenal artery**

Stomach —> **gastroepiploic artery**

40. Acute hepatitis B infection - IgM anti-abc

41. Crohn's disease - 2 exacerbations within 12 months —> **Azathioprine**

Before starting Azathioprine —> check TPMT activity

Complications - myelosuppression, abnormal liver enzymes, pancreatitis

Persistent active Crohn's disease despite using Azathioprine —> anti tTNF therapy = Infliximab or Adalimumab

Fistulating Crohn's disease —> anti TNF therapy is first line

42. Acute Fulminant Hepatitis - Hepatitis A and Hepatitis E

43. **Immune Reconstitution Inflammatory Syndrome** - few weeks after starting treatment with Whipple's disease.

Symptoms : diarrhoea, joint pain, fever.

Mx : **Corticosteroid** therapy

**Whipple's disease relapse** —> **Penicillin zG 4 MU IV Q4H**

or

Ceftriaxone 2g IV BD for 4 weeks

f/b Doxycycline 100mg BD +  
Hydroxychloroquine 200mg TID

#### 44. **Gardner Syndrome**

- **Autosomal dominant mode of inheritance**
- C/F : multiple adenomatous intestinal polyps, osteomas, soft tissue tumors including lipomas, fibromas, epidermoid cysts
- Congenital hypertrophy of retinal pigment epithelium is also a feature.
- Mutation of APC gene on Chromosome 5q21
- Colonic carcinoma develops in ~7% of individuals by 21 years; ~50% by 39 years; ~90% by 45 years
- Total colectomy is the treatment of choice
- **Juvenile Polyposis** : autosomal dominant condition, presents first in childhood and characterised by multiple hamartomatous polyps throughout GI tract
- **Peutz Jeghers syndrome** : autosomal dominant associated with intestinal hamartomas + peri-oral pigmented macules

45. *Entamoeba histolytica* - frequent low volume stools + mucus, associate with large number of leukocytes in stool.

Diagnosis confirmed by microscopic stool examination or examination of colonic exudates obtained at sigmoidoscopy.

Mx : high dose Metronidazole

#### 46. **Pharyngeal Pouch**

- Caused by protrusion of mucosa through the muscle layers of wall of pharynx
- Diverticulum occurs through Killian's dehiscence between the thyropharyngeus and cricopharynxgeus parts of inferior constrictor muscle

Clinical Features

- Dysphagia
- Regurgitation

- Weight loss
- Hoarseness
- Aspiration pneumonia
- Swelling on left side of cheek which gurgles on palpation -

**Boyce's sign**

- Halitosis
- Recurrent sore throat
- Lung abscess

**Management**

- Pouches can be excised endoscopically or externally
- Open excision of pharyngeal pouch
- Endoscopic stapling or diathermy
- Mendelson syndrome : beware of inhalation during induction of general anaesthesia

47. Hemochromatosis - C282Y mutation - reduced expression of hepcidin gene —> excessive iron accumulation

C282Y —> part of genetic code for HFE protein and this mutation impairs the ability of HFE to bind beta-2 microglobulin. Impaired binding to beta-2 microglobulin causes HFE to aggregate in intracellular space.

48. Primary Biliary Cholangitis - raised ALT, raised ALP, raised high density Lipoprotein HDP; associated with Sjogren's syndrome

49. **Obstetric Cholestasis** : 30-36 weeks of pregnancy; presents with pruritic of plasma and soles; associated with UTIs; risk of foetus prematurity and still birth; Labs - raised transaminases and bile acids; ALP is raised in pregnancy so not significant lab finding.

50. Absolute contraindications to liver transplant -

- 1) untreated HIV
- 2) Irreversible pulmonary disease
- 3) Ongoing alcohol abuse
- 4) Extra-hepatic malignancy

51. **Pancreatic carcinoma**



- Predominantly adenocarcinoma - highest incidence between ages 65 and 75 years
- Diabetes - associated with increased risk of pancreatic cancer
- Associated with these hereditary cancer syndromes :
  - A. Hereditary pancreatitis
  - B. Peutz-Jeghers syndrome
  - C. Familial atypical multiple mole melanoma
  - D. Familial breast cancer syndrome
  - E. Hereditary non polyposis colorectal cancer syndrome

### Clinical Features

- Abdominal pain radiating to back
- Weight loss
- Loss of appetite
- Epigastric mass
- Obstructive jaundice
- New onset diabetes - polydipsia, polyuria, nocturia, weight loss

### Investigations

- USG and CT pancreas protocol
- CT chest, abdomen and pelvis to stage cancer
- ERCP - microscopic diagnosis
- CA 19-9
- NICE Recommendations :
  - (1) Age > 40 years with jaundice → 2 week referral
  - (2) Urgent CT/USG if patients >60 years old with weight loss + —
    - (a) Diarrhoea
    - (b) Back pain
    - (c) Nausea
    - (d) Vomiting
    - (e) Constipation
    - (f) New onset diabetes

### Management

- Pain management
- Enteric coated pancreatin
- Locally advanced - combination chemotherapy

- Curative surgery - pancreatoduodenectomy - Whipple's operation

## 52. Ribavirin

- Adverse effects :
  1. Haemolytic anaemia
  2. Nausea
  3. Vomiting
  4. Dry mouth
  5. Stomatitis
- Caution with its use :
  - A. Pregnancy - avoid getting pregnant for 6 months
  - B. Cardiac disease
  - C. Hemoglobinopathies
  - D. Severe liver dysfunction
  - E. Autoimmune disease
  - F. Previous psychiatric history
- Extensive monitoring - RFT, LFT, FBC at 2 weeks and 4 weeks of treatment

53. Mycophenolate Mofetil - adverse effect : Crohn's like enterocolitis has been reported in a number of renal transplant patients. Investigations will reveal - mucosal ulceration and skip lesions ordinarily seen in Crohn's disease.

## 54. Liver Biopsy - Contraindications :

- Increased INR >1.5
- Thrombocytopenia <50,000
- Severe ascites
- Difficult body habits
- Suspected hemangiomas
- Suspected echinococcal infection

55. **Menkes disease** - X linked recessive disorder - mutation of ATP7A gene; associated with marked copper deficiency. Manifests in early childhood with failure to thrive, seizures, hypotonia, and neurological dysfunction. Liver involvement is rare.

## 56. **Dubin Johnson syndrome**

- Autosomal recessive

- Defective hepatic secretion of conjugated bilirubin
- High direct bilirubinemia
- Liver biopsy - dark granular pigments on biopsy
- Rotor syndrome - similar features BUT biopsy would be normal

#### 57. **Crigler Najar syndrome**

- Familial unconjugated hyperbilirubinemia
- Type 1 - presents at birth with severe chronic unconjugated hyperbilirubinemia with development of neurological symptoms later
- Type 2 - less severe with 50% in the first year of life; sometimes can present at 30 years of age as well.

58. GIT polyps associated with highest malignancy potential - adenomas, serrated polyps, polyps with villous architecture,

59. Gastric Antral Valvular Ectasia GAVE - watermelon stomach - endoscopic appearance of columns of red tortuous ectatic vessels along longitudinal folds of antrum. Frequently bleed leading to occult GI loss.

Rx — radio frequency ablation at endoscopy

60. Ulcerative Colitis - Colectomy - Indications :

- Stool frequency > 8 times
- Colon diameter > 5.5 cm
- CRP > 45

Hemoglobin & WCC —> not correlated with progression to colectomy

61. Bile duct obstruction - MRCP

62. Transudate Protein <30- hepatic cirrhosis, right heart failure, hypoalbuminemia, acute nephritis, Budd Chiari syndrome

Exudate Protein >30 - infections like TB, Pneumonia, SBP, Inflammation - vasculitis, pancreatitis, Malignancy

63. Gastric reflux due to - parasympathetic stimulation of lower circular smooth muscle fibers of oesophagus  
Vagal excitatory fibres stimulation - muscle fibres contract

64. Homozygosity for HLA DQ2 - increased risk of celiac disease and enteropathy associated T cell lymphoma.

65. Coeliac disease - partial villous atrophy and intraepithelial lymphocytes

66. Severe malnutrition - steatohepatitis and hypercholesterolemia

**67. Systemic sclerosis - diarrhoea**

- Patients with systemic sclerosis have strictures, dilatation and diverticulum formation within small bowel.
- These changes + slow GIT motility → vulnerable to problems with SIBO
- Common organisms - E.coli and Bacteroides spp - both are capable of unconjugating and hydrolysis bile salts.
- These bacteria can also caused vit. B12 deficiency as they interfere with vit. B12 and intrinsic factor binding.
- SIBO treatment - rotating antibiotics (Metronidazole & Ciprofloxacin)

68. Prolonged APTT which does not correct in a 50:50 study suggests the presence of a clotting factor inhibitor rather than deficiency of clotting factor.

**Isolated prolonged APTT** - factor VIII deficiency or presence of factor VIII inhibitor or Anti phospholipid antibody syndrome.

**Acquired antibodies** to factor VIII can occur with drugs - **Phenytoin, penicillin, sulfa drugs.**

Other causes of acquired factor VIII deficiency -

- 1) pregnancy
- 2) Diabetes
- 3) Psoriasis
- 4) SLE, Myasthenia gravis, Multiple sclerosis

69. **Drugs causing chronic hepatitis** - Ketoconazole, Methyldopa, Nitrofurantoin, Isoniazid

70. Lactose intolerance can happen after Giardiasis infection.

71. No surveillance colonoscopy for patients >75 years or life expectancy less than 10 years (e.g. - Child Pugh C scoring)

72. Peutz Jeghers syndrome - autosomal dominant - STK11/LKB1 gene - on chromosome 19

73. Hepatitis C response to antiviral treatment —> viral genotyping  
Hepatitis C divided into 6 genotypes - genotype 3 most difficult to treat

74. Mucosal associated lymphoid tissue

- Complications - paraprotein formation and pseudohypoproteinemia are common
- Originate from B cells
- ~80% are eradicated with H pylori treatment
- Metastasis is rare
- Can arise from any mucosal surface

75. Primary Sclerosing CHolangitis - HLA A1, B8 DR3

~20% have cholangiocarcinoma at post mortem

~75% of cases associated with UC  
IBD

76. **Sulfasalazine - adverse effects**

- Pancytopenia
- Hypersensitivity reactions
- Periorbital edema
- Stomatitis
- Parotitis

77. Drugs - liver side effects

- 1) Cholestasis liver injury - Chlorpromazine, Azathioprine, Captopril, Cyclosporine, Penicillamine, Erythromycin, COCP, Flucloxacillin
- 2) Hepatitis picture : Paracetamol, Phenytoin, Ethanol, Rifampicin, Allopurinol, Isoniazid

3) Mixed cholestasis / hepatitis : Co-Amoxiclav, Sulphonamides, Sulfasalazine, Carbamazepine

78. Aspirin reduces risk of oesophageal, gastric, colorectal cancers.

79. Hepatitis E - Marked Cholestasis

80. Systemic sclerosis - GIT involvement :

- 1) oesophageal strictures
- 2) Malabsorption
- 3) Small intestinal bacterial overgrowth
- 4) Endoscopy - mass in stomach
- 5) Intestinal pseudo obstruction
- 6) Anal incontinence

80. Diabetic gastroparesis - Domperidone

81. Mutations in APC gene - commonly associated with FAP and **Medulloblastoma**.

This is one of the forms of **Turcot syndrome** - polyps + primary brain tumor

**Glioblastoma** associated with **HNPCC**

82. Hepatitis C - Direct acting antivirals - **Simeprevir & Sofosbuvir**

**83. Pregnancy Related Cholestasis :**

- Elevated serum bile acids
- Normal urate
- Fat soluble vitamin malabsorption —> prolonged Prothrombin time
- AFLP : pre eclampsia and high rate levels
- Hyperemesis gravidarum - abnormal liver enzymes
- HELLP - hemolysis, elevated liver enzymes, low platelets; microangiopathic process associated with HTN with risk of haemorrhage and stroke

84. Chronic alcoholism referring - risk of encephalopathy with high protein diet due to accumulation of ammonia in brain

## 85. Small bowel Active Crohn;s disease - finger clubbing

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### CLINICAL HEMATOLOGY/ ONCOLOGY PASSMEDICINE & PASSTETS

#### 1. Blood films - pathological forms

- Target cells : Sickle cell, thalassemia, IDA, Hyposplenism, Liver disease
- Tear drop poikilocytes : Myelofibrosis
- Spherocytes : Hereditary Spherocytosis, AIHA
- Basophilic Stippling : Lead poisoning, Thalassemia, Sideroblastic Anaemia, Myelodysplasia
- Howel Jolly bodies : Hyposplenism
- Schistocytes (helmet cells) : Intravascular hemolysis (Cold AIHA), Mechanical heart valve, DIC
- Pencil poikilocytes : IDA
- Burr cells (Echinocytes) : Uraemia, pyruvate kinase deficiency
- Acanthocytes : Abetalipoproteinemia
- Hypersegmented neutrophils : Megaloblastic anaemia

#### 2. CMV - transmitted in leucocytes.

3. Irradiated blood products - depleted of T-lymphocytes and used avoid transfusion-associated graft versus host disease (TA-GVHD) caused by engraftment of viable donor T lymphocytes.

#### 4. Breast Cancer - Risk factors :

- BRCA1, BRCA2 - 40% lifetime risk of breast/ ovarian cancer
- 1st degree relative, premenopausal relative with breast cancer
- Nulliparity, 1st pregnancy > 30 years
- Early menarche, late menopause
- Combined HRT, COCP use
- Past great cancer

- Not breast feeding
- P53 gene mutations
- Obesity
- Previous surgery for benign disease

## 5. Burkitt Lymphoma

- Endemic - African form - maxilla or mandible
- Sporadic form - abdominal tumor (commonly ileo-caecal region); common in HIV
- c-MYC gene translocation t (8:14)
- EBV - African form
- M/C : Starry sky appearance - lymphocytes sheets interspersed with macrophages containing dead apoptotic tumor cells
- Mx : chemotherapy - high risk of tumor lysis syndrome.
- Rasburicase - recombinant variant of xanthine oxidase : given to reduce risk of tumor lysis syndrome
- Complications of tumor lysis syndrome :
  1. Hyperkalemia
  2. Hyperphosphotemia
  3. Hypocalcemia
  4. Hyperuricemia
  5. Acute renal failure

## 6. Cancers in UK : Breast > lung > Colorectal > Prostate > Bladder

## 7. Chronic Lymphocytic Leukaemia - Management :

Indications for treatment :

- Progressive marrow failure - development or worsening of anaemia and/or thrombocytopenia
- Massive >10 cm or progressive lymphadenopathy
- Massive > 6 cm or progressive splenomegaly
- Progressive lymphocytosis : >50 % increase over 2 months or lymphocyte doubling time < 6 months
- Systemic symptoms - weight loss >10 % in last 6 months, extreme fatigue, fever > 38 degree for > 2 weeks, night sweat
- Autoimmune cytopenia - ITP

Management :

- Fludarabine, Cyclophosphamide, Rituximab (FCR)



- Ibrutinib - use for patients who have failed previous therapy

#### 8. CLL : Poor prognosis :

- Age > 60 years
- Male sex
- Lymphocyte count > 50,000
- Prolymphocytes > 10% of total blood lymphocytes
- Lymphocytes doubling time < 12 months
- Raised LDH
- CD38 expression positive
- TP53 mutation

#### Chromosomal changes :

- Deletion of one arm of chromosome 12 (del13q) - most common abnormality —> GOOD PROGNOSIS
- Deletion of short arm of chromosome 17 (del 17p) —> **POOR PROGNOSIS**

#### 9. Cytotoxic Agents

##### 1) **Alkylating agents -**

- **Cyclophosphamide** - MOA : causes cross linking in DNA  
Adverse effects : hemorrhagic cystitis, myelosuppression, transitional cell carcinoma

Hemorrhagic cystitis - treated with Mesna and hydration;  
cyclophosphamide toxic metabolite —> Acrolein which can cause damage to urothelium; treatment with Mesna removes the Acrolein

##### 2) **Cytotoxic antibiotics :**

- **Bleomycin** - degrades preformed DNA - lung fibrosis (lower zone)
- Anthracyclines Doxorubicin - stabilises DNA-topoisomerase II complex which inhibits DNA & RNA synthesis  
Adverse : Cardiomyopathy

##### 3) **Anti metabolites**

- **Methotrexate** : inhibits dihydrofolate reductase and thymidylate synthesis; **Adverse** - myelosuppression, mucositis, liver fibrosis, lung fibrosis lower zones
- **5-Fluorouracil** : Pyrimidine analogues inducing cell cycle arrest and apoptosis by blocking thymidylate synthase (works during S phase) ; **adverse** - myelosuppression, mucositis, dermatitis
- 6-Mercaptopurine : purine analogue activated by HGPRTase decreasing purine synthesis; adverse - myelosuppression
- Cytarabine : Pyrimidine antagonist - interferes with DNA synthesis at S phase and inhibits DNA polymerase  
Adverse - myelosuppression, ataxia

#### 4) Acts on Microtubules

- **Vincristine, Vinblastine** : inhibits formation of microtubules;  
Adverse - Vincristine → Peripheral neuropathy ( reversible ), paralytic ileus  
Adverse - Vinblastine →. Myelosuppression
- Docetaxel - prevents microtubule depolymerisation & disassembly decrease free tubulin; adverse - neutropenia

#### 5) Topoisomerase inhibitors :

- **Irinotecan** : inhibits topoisomerase I which prevents relaxation of supercoiled DNA - adverse : myelosuppression

#### 6) Other cytotoxic drugs

- **Cisplatin** - causes cross linking of DNA (MOA similar to cyclophosphamide); adverse - ototoxicity, peripheral neuropathy, hypomagnesemia
- **Hydroxyura (hydroxycarbamide)** - inhibits ribonucleotide reductase, decreasing DNA synthesis; adverse - myelosuppression

#### 10. Drug induced pancytopenia :

- a) Cytotoxic
- b) Antibiotics - trimethoprim, chloramphenicol
- c) Anti rheumatoid - gold, penicillamine
- d) Carbimazole - agranulocytosis & pancytopenia

- e) Anti epileptics - carbamazepine
- f) Sulphonylureas - Tolbutamide

### 11. **Fanconi Anaemia :**

- Autosomal recessive
- Haematological - aplastic anaemia, increased risk of AML
- Neurological
- Skeletal : short stature, thumb/radius abnormalities
- Cafe au lait spots

### 12. **Genetics & Surgical disease -**

#### **—> Li-Fraumeni syndrome**

- Autosomal dominant
- Germline mutations to p53 tumor suppressor gene
- Malignancies - sarcomas, leukemias
- Diagnosed when patients develop sarcoma < 45 years, first degree relative diagnosed with any cancer < 45 years or sarcomas at any age

#### **—> BRCA 1 & 2 :**

- Chromosome 17 - BRCA 1
- Chromosome 13 - BRCA 2
- 60% breast cancer risk
- Ovarian cancer risk : 55% BRCA1 and 25% BRCA2
- BRCA 2 : Associated with prostate cancer risk in men

#### **—> Lynch Syndrome**

- Autosomal dominant
- Colonic cancer and endometrial cancer at young age
- 80% of individuals will develop cancer
- High risk patients - evaluation using Amsterdam criteria

#### **Amsterdam Criteria -**

- 1) three or more family members with confirmed diagnosis of Colon Ca. - one of whom is a first degree relative
- 2) Two successive affected generations
- 3) FAP has to be excluded
- 4) One or more colon cancers diagnosed under < 50 years

—> Gardners Syndrome :

- Autosomal dominant
- Familial colorectal polyposis
- Multiple colonic polyps
- Extra colonic disease - skull osteomas, thyroid cancer, epidermoid cysts
- Desmoid tumors ~15% of cases
- Mutation of APC gene on Chromosome 5

### 13. **Haematological Malignancies - Genetics :**

- t(9;22) - Philadelphia Chromosome
  - >95% of patients with CML
  - ABL proto-oncogene fusion with BCR gene on chromosome 22
  - BCR-ABL fusion gene - fusion protein which has excessive tyrosine kinase activity
  - Poor prognostic factor in ALL
- t (15 ; 17)
  - Seen in acute promyelocytic leukaemia AML-M3 subtype
  - Fusion of PML and RAR-alpha genes
- t ( 8 ; 14 )
  - Burkitt's lymphoma
  - MYC oncogene translocated into an immunoglobulin gene
- t ( 11 ; 14 )
  - Mantle cell lymphoma
  - Deregulation of cyclin D1 (BCL-1) gene
- t (14 ; 18)
  - Follicular lymphoma
  - Increased BCL-2 transcription

### 14. **Hereditary Angioedema**

- Autosomal dominant
- Low plasma levels of C1 inhibitor protein
- C1-INH protein : multifunctional serine protease inhibitor

- Uncontrolled release of bradykinin during attacks causing edema of tissues

INV - low C1-INH levels during attack

Low C2 and C4 levels during and between attacks

Serum C4 - screening tool

Symptoms :

- Painful macular rash
- Painless, non-pruritic swelling of subcutaneous / submucosal tissues
- Upper airways, skin or abdominal organs deemed
- URTICARIA NOT PRESENT

Management :

- Acute - IV C1-inhibitor concentrate, FFP
- Prophylaxis - anabolic steroid Danazol
- DOES NOT respond to Adrenaline, anti-histamines, or glucocorticoids

## 15. Hodgkin's Lymphoma :

- Malignant proliferation of lymphocytes characterised by presence of Reed-Sternberg cells
- Third and seventh decades

Histological classification :

- **Nodular sclerosing** : most common ~70%, good prognosis; associated with lacunar cells, F > M
- Mixed cellularity : ~20%, good prognosis, associated with high number of RS cells
- Lymphocyte predominant : ~5% of total cases, BEST prognosis
- Lymphocyte depleted - rare, WORST prognosis

B symptoms indicative of poor prognosis :

- 1) weight loss of >10% in last 6 months
- 2) Fever > 38
- 3) Night sweats

Other factors indicative of poor prognosis :

- 1) age > 45 years
- 2) Stage IV disease
- 3) Hemoglobin < 10.5
- 4) Lymphocyte count < 600
- 5) Male sex
- 6) Albumin < 40
- 7) WBC > 15,000

Risk factors : HIV, EBV

Clinical Features :

- 1) lymphadenopathy - neck (cervical/ supra clavicular) > axillary > inguinal
- 2) Painless, non tender, asymmetrical lymphadenopathy
- 3) Alcohol induced lymph node pain is characteristic of Hodgkin's lymphoma
- 4) Systemic - B symptoms -
  - A. Weight loss
  - B. Pruritic
  - C. Night sweats
  - D. Fever (Pel - Ebstein)

Investigations :

- NC anaemia
- eosinophilia ( due to increased production of cytokines IL-5)
- Raised LDH
- Lymph node biopsy : RS cells are diagnostic - multi nucleated or bilobed nucleus with prominent eosinophilic inclusion like nucleoli (owl's eye appearance)

Ann-Arbor Staging :

- Stage I : single lymph node
- Stage II : 2 or more lymph nodes / regions on same side of diaphragm
- Stage III : nodes on both sides of diaphragm
- Stage IV : spread beyond lymph nodes

- Each stage divided into A or B -
  - A = no systemic symptoms other than pruritus
  - B = weight loss > 10% in 6 months / night sweats / fever > 38

### **Lugano Classification :**

- Stage I : single lymph node region or single extra lymphatic organ or site
- Stage II : two or more lymph node regions on same side of diaphragms or localised involvement of extra-lymphatic tissue and one or more lymph nodes on same side of diaphragm
- Stage III : involvement of lymph node regions on both sides of diaphragm, also accompanied by localised involvement of extra lymphatic organ or site (IIIE), involvement of spleen (IIIS) or both (IIIE + IIIS)
- Stage IV : diffuse involvement of one or more extra lymphatic organs with or without associated lymph node involvement.

Chemotherapy regimens :

- 1) **ABVD** - Doxorubicin, Bleomycin, Vinblastine, Dacarbazine
- 2) **BEACOPP** - Bleomycin, Etoposide, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine, Prednisone

Complications - increased risk of secondary malignancy in particular solid tumors - breast and lung

## **16. Methaemoglobinemia**

Congenital causes -

- 1) hemoglobin variants - HbH, HbM
- 2) NADH Methaemoglobin reductase deficiency

Acquired causes -

- 1) Drugs - Sulphonamides, Nitrates, Dapsone, Sodium nitroprusside, Primaquine
- 2) Chemicals - aniline dyes

Aniline dyes - bladder cancer

Primaquine - G6PD

### Features of Methaemoglobinemia -

- 1) chocolate cyanosis
- 2) Dyspnoea
- 3) Headache
- 4) Anxiety
- 5) Severe forms - acidosis, arrhythmia, seizures, coma
- 6) Normal pO<sub>2</sub> but decreased oxygen saturations

### Management :

- Enzyme deficiency of NADH Methaemoglobin reductase —> **ascorbic acid**
- **IV Methylthionium chloride (Methylene blue)** for acquired causes

## 17. Multiple Myeloma

### CRABBI

#### • Calcium -

- Hypercalcemia
- Due to increased osteoclastic bone resorption caused by local cytokines (e.g., IL-1, TNF) released by myeloma cells
- Other contributing factors - impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels
- Causes constipation, nausea, anorexia, confusion

#### • Renal -

- Monoclonal proliferation of immunoglobulins results in light chain deposition within renal tubules
- Causes renal damage which presents as dehydration and increasing thirst
- Other causes of renal impairment : amyloidosis, nephrocalcinosis, nephrolithiasis

#### • Anaemia

- Bone marrow crowding suppresses erythropoiesis leading to anaemia
- Causes fatigue and pallor

#### • Bones

- Bone marrow infiltration by plasma cells and cytokine mediated osteoclast overactivity causes lytic bone lesions



- Presents as pain in back and increased risk of pathological fractures
- Bleeding
  - Bone marrow crowding - thrombocytopenia - increased risk of bleeding and bruising
- Infection
  - Reduction in production of normal Immunoglobulin results in increased susceptibility to infections

Other features :

- amyloidosis - macroglossia
- Carpal tunnel syndrome
- Neuropathy
- Hyper viscosity

Labs :

- FBC - anaemia
- Peripheral blood film - Rouleaux formation due to hyperviscosity
- U & E - renal failure
- Bone profile - hypercalcemia

BM Aspiration - dry tap - diagnosis confirmation if number of plasma cells are increased

Imaging : Whole body MRI

- X - rays —> rain drop skull

## **Diagnostic Criteria -**

### **Major criteria :**

- 1) Plasmacytoma - evidenced by biopsy specimen
- 2) 30% plasma cells in a bone marrow sample
- 3) Elevated levels of M protein in blood or urine

Minor criteria -

- 1) 10% - 30% plasma cells in bone marrow sample
- 2) Minor elevations in M protein levels in blood or urine
- 3) Osteolytic lesions
- 4) Low levels of antibodies in the blood

Stage I - B2 micro globulin < 3.5; Albumin > 35 → 62 months survival

Stage III - B2 micro globulin > 5.5 → 29 months survival

Stage II - neither I or III → 45 months

#### 18. **Neutropenia - causes :**

- Viral - HIV, EBV, Hepatitis
- Drugs - Cytotoxics, Carbimazole, Clozapine
- Benign ethnic neutropenia - common in African / Afro - Caribbean; no treatment needed
- Haematological malignancy - myelodysplastic malignancies, aplastic anaemia
- Rheumatological conditions
- SLE - due to circulating Anti neutrophil antibodies
- Rheumatoid arthritis - due to hypersplenism seen in Felty's syndrome
- Severe sepsis
- Hemodialysis

#### 19. **Normocytic Anaemia - causes**

- 1) Anaemia of chronic disease
- 2) Chronic kidney disease
- 3) Aplastic anaemia
- 4) Haemolytic anaemia
- 5) Acute blood loss

#### 20. **Oral Allergy Syndrome -**

- Birch pollen allergy - carrot, parsley, spinach
- Rye grass pollen allergy
- Rubber latex allergy
- OAS caused by cross sensitisation to a structurally similar allergen present in pollen
- Non plant foods do not cause OAS as no structurally similar allergen present in meat

#### **Clinical features**

- OAS - season allergy symptoms - conjunctivitis, rhinitis, asthma - presents minutes after eating specific raw food

- Itching and tingling of lips, tongue, mouth - most common symptoms
- Mild swelling and redness of lips, tongue and throat may occur
- Severe cases - nausea and vomiting
- Anaphylaxis - RARE

## 21. **Platelet transfusion - contra indications :**

- Chronic bone marrow failure
- Autoimmune thrombocytopenia
- Heparin induced thrombocytopenia
- Thrombotic thrombocytopenic purpura

## 22. **Polycythemia Rubra Vera**

- Myeloproliferative disorder caused by clonal proliferation of marrow stem cell → leading to increase in red cell volume and also causes over production of neutrophils and platelets
- Mutation of JAK2 - most common
- Other mutations : TET2 and ASXL1

### Clinical features :

- Pruritus - after hot bath - Aquagenic pruritus
- Increased blood viscosity - hypertension, headache
- Erythromelalgia - burning cyanosis in hands/feet
- Transient visual disturbances
- Thrombosis features → stroke, MI, PE, DVT
- Increased RBC turnover → gouty arthritis
- Splenomegaly
- Hypertension
- Hyper viscosity - arterial and venous thrombosis
- Haemorrhage due to abnormal platelet function
- Low ESR

### Labs to be done in patients suspected of Polycythemia rubra vera -

- FBC - raised hematocrits, neutrophils and platelets can be raised
- JAK2 mutation
- Serum ferritin
- RFT and LFT
- Low ESR
- Raised Leukocyte Alkaline Phosphatase

## **Management**

- Aspirin - reduced risk of thrombotic events
- Venesection - 1st line treatment to keep Hb in normal range
- Chemotherapy - hydxyurea & Phosphorous-32 therapy
- Ruxolitinib - JAK 1/2 inhibitor - used if severe pruritus, symptomatic splenomegaly

## **23. Porphyria**

### Acute Intermittent Porphyria

- Autosomal dominant
- Defect in Porphobilinogen deaminase
- Female >> males; 20-40 years age group
- C/F ; abdominal symptoms, neuropsychiatric symptoms
- Hypertension and tachycardia common
- Urine turns deep red on standing

### Porphyria cutanea tarda

- Most common hepatic porphyria
- Defect in uroporphyrinogen decarboxylase
- Caused by hepatocyte damage - alcohol, oestrogens
- C/F : Photo sensitive rash with bullae, skin fragility on face and dorsal aspect of hands
- Urine - elevated porphyrinogen levels and pink fluorescence of urine under Wood's lamp
- Mx - Chloroquine

### Variegate porphyria

- Autosomal dominant
- Defect in porphyrinogen oxidase
- Photosensitive blistering rash, abdominal and neurological symptoms
- Common in south africans

## **24. Primary Immunodeficiency**

### **—> Neutrophil Disorders**

#### 1) Chronic granulomatous disease

- lack of NADPH oxidase reduces ability of phagocytes to produce ROS

- Causes recurrent **pneumonias** and **abscess** - particularly Staph aureus and fungi
- Negative nitroblue-tetrazolium test
- **Abnormal dihydrorhodamine flow cytometry test**

## 2) **Chediak Higashi Syndrome**

- microtubule polymerisation effect - leads to a decrease in phagocytosis
- Affected children : partial albinism and peripheral neuropathy
- Recurrent bacterial infections
- Giant granules in neutrophils and platelets

## 3) **Leukocyte adhesion deficiency**

- defect of LFA-1 integrin (CD18) protein on neutrophils
- Recurrent bacterial infections
- Delay in umbilical cord sloughing may be seen
- Absence of neutrophils/pus at sites of infection

—> B cell disorders

### 1) **Common variable immunodeficiency**

- low antibody levels - IgG, IgM, IgA
- Recurrent chest infections
- Can predispose to autoimmune disorders and lymphoma

### 2) **Bruton's Congenital agammaglobulinemia**

- X-linked recessive
- Defect in Burton's tyrosine kinase (BTK) gene that causes severe block in B cell development
- Recurrent chest infections
- Absence of B cells with reduced immunoglobulins of all classes

### 3) **Selective Immunoglobulin A deficiency**

- maturation defect in B cells
- Most common primary antibody deficiency
- Recurrent sinus and throat infections
- A/W coeliac disease and may cause false negative coeliac antibody screen
- Severe transfusion reactions may occur due to anti-IgA antibodies  
—> anaphylaxis

—> T cell disorders

### 1) **DiGeorge Syndrome**

- 22q11.2 deletion
- Failure to develop 3rd and 4th pharyngeal pouches
- C/F : congenital heart disease (TOF), learning difficulties, hypocalcemia, recurrent viral/fungal diseases, cleft palate

—> Combined B cell & T cell disorders

### 1) **Severe combined immunodeficiency**

- X-linked defect due to defect in common gamma chain
- Common gamma chain : protein used in the receptor for IL-2 and other interleukins
- Other causes : adenosine deaminase deficiency
- Recurrent bacterial, viral and fungal infections
- Reduced T cell receptor excision circle

### 2) **Ataxic telangiectasia**

- defect in DNA repair enzymes
- **Autosomal recessive**
- **C/F** : cerebellar ataxia, telangiectasia, recurrent chest infections
- 10% risk of developing leukaemia or lymphoma

### 3) **Wiskott-Aldrich syndromes**

- defect in WASP gene
- X linked recessive
- C/F : recurrent bacterial infections, eczema, thrombocytopenia
- Low IgM levels
- Increased risk of autoimmune disorders and malignancy

### 4) **Hyper IgM syndromes**

- mutations in CD40 gene
- Infections - Pneumocystic pneumonia
- Hepatitis
- Diarrhoea

25. Protein C deficiency : autosomal co-dominant condition; venous thromboembolism, skin necrosis following Warfarin therapy due to thrombosis of venues leading to skin necrosis

Concomitant start of heparin can reduce the risk

26. HNPCC - colon cancer, endometrial cancer in women.

Risk of these cancers which are high - small intestine, ureter, stomach, ovary, kidney

## 27. **Acute Myeloid leukaemia**

- Causes bone marrow failure and subsequent thrombocytopenia
- AML - results from accumulation or rapid proliferation of poorly differentiated myeloblasts in blood which can infiltrate liver and spleen

### **Risk factors -**

- Previous chemotherapy
- Previous haematological dyspoiesis - myelodysplastic syndrome, aplastic anaemia
- Congenital disorders - Down's, Fanconi anaemia, neurofibromatosis
- Familial syndromes - germline mutations of AML1

### **Clinical Features -**

- Anaemia - pallor, fatigue, dyspnoea, palpitations
- Decreased WBC - infections, fever, lymphadenopathy
- Thrombocytopenia - ecchymoses, frequent bleeding, petechiae
- Hepatosplenomegaly
- Organ infiltration - spleen = early satiety, LUQ fullness, gingivitis, respiratory distress

### **Labs**

- FBC - anaemia, macrocytosis, leukocytosis, neutropenia, thrombocytopenia
- Peripheral smear - Auer rods, blasts
- Increased uric acid, increased LDH
- BM - hyper cellular bone marrow

### **Management**

- Chemotherapy - Cytarabine, Idarubicin, Daunorubicin

- Hydroxyucarbamide + Allopurinol + Rasburicase

### Complications

- Tumor lysis syndrome
- Leukostasis - respiratory distress
- Neutropenia, pancytopenia
- Infections
- DIC

### 28. Oesophageal Tumors

- Two main types - adenocarcinoma and squamous cell carcinoma
- Risk factors - GORD, smoking, alcohol intake, obesity
- Adenocarcinoma - Barrett's oesophagus, obesity, GORD
- SCC - smoking, high alcohol intake

### **Clinical features**

- Asymptomatic patients until late stage
- Pain on swallowing - odynophagia
- Dysphagia
- Dyspepsia
- Weight loss
- Hoarseness
- Vomiting
- Anorexia

### Investigation

- Endoscopy
- Barium swallow - stricture with irregular shouldering
- CT - staging and checking for metastases
- Endoscopic USG for local staging

T2 - chemotherapy then surgery

29. Transfusion graft v/s host disease - pancytopenia, liver dysfunction, diarrhoea, rash

Cytotoxic agents affecting T cell function - Fludarabine - prone to opportunistic infections like Pneumocystis infection.

Patients should be co-administered Co-trimoxazole to prevent this.



30. **Hairy cell leukaemia** - **activating point mutation of BRAF** isoform of RAF (**BRAF V600E**) has been implicated in the pathogenesis.

Hairy cell leukaemia expresses **CD103**.

HCL - can also express range of B cell markers - CD19, CD20, CD22, CD25.

31. Phase I trial - pharmacokinetics, human toxicity of the drug

Phase II - to study optimal dosing, common adverse effects, activity of drug, efficacy of drug against disease

Phase III - to compare new drug with conventional therapy

Phase IV - determines long term toxicity of the drug

32. Amyloidosis - AL and AA subtypes

AL - lambda light chains - secondary to Multiple Myeloma and MGUS

AKA as primary amyloidosis - more common in men > 50 years, and has poor prognosis.

Rx - Melphalam and Prednisolone

Elderly patients - Pulsed dexamethasone, alkylating agents and interferon.

33. Painless crevical lymphadenopathy —> excision biopsy lymph node

34. Von Willebrand's disease

- Most common inherited bleeding disorder
- **Autosomal dominant**
- **vWF** - large glycoprotein which forms massive multimer; promotes platelet adhesion to damaged endothelium and carries molecule for factor VIII

Types -

- Type 1 - partial reduction in vWF
- Type 2 - abnormal form of vWF
- Type 3 - total lack of vWF (**autosomal recessive**)

Labs

- Prolonged bleeding time
- APTT prolonged
- Factor VIII levels moderately reduced
- Defective platelet aggregation with Ristocetin

Management

- Tranexamic acid for mild bleeding
- Desmopressin (DDAVP) - raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- Factor VIII concentrate

35. 5-15% of Polycythemia Rubra Vera → progress to myelofibrosis or Acute Myeloid Leukaemia

### 36. Sickle cell crisis -

**Treatment** : fluids and high dose folic acid for increased erythropoiesis

4 types :

#### 1) **Thrombotic / vaso-occlusive / painful crises**

- Precipitated by infection, dehydration, deoxygenation
- Infarcts occur in various organs including the bones (e.g. avascular necrosis of hip, hand-foot syndrome in children, lungs, spleen, brain).

#### 2) **Acute Chest syndrome**

- Vase-occlusion within the pulmonary vasculature → infarction in lung parenchyma
- **C/F** : dyspnea, chest pain, pulmonary infiltrates on CXR, low PO<sub>2</sub>
- Mx - pain relief, oxygen therapy, antibiotics, transfusion which improves oxygenation

- Most common cause of death after childhood

### 3) **Aplastic crises**

- Caused by sudden infection with Parvovirus B19
- Sudden fall in Hemoglobin
- Bone marrow suppression - reduced reticulocyte count

### 4) **Sequestration crises**

- Sickling within organs like spleen or lungs causes pooling of blood and worsening of anaemia
- Increased reticulocyte count

### 37. **Thymoma**

- Commonest tumor in the anterior mediastinum
- Associated with :
  - A. Myasthenia grass (30-40% of patients with thymoma)
  - B. Red cell aplasia
  - C. Dermatomyositis
  - D. SLE
  - E. SIADH
- Causes of death - compression of airway, cardiac tamponade

### 38. **Wiskott-Aldrich syndrome**

- Combined B-cell and T-cell dysfunction
- X-linked recessive
- Mutation of WASP gene
- Recurrent bacterial infections
- Eczema
- Thrombocytopenia
- Low IgM levels

### 39. **Waldenstrom's Macroglobulinemia**

- Lymphoplasmacytoid malignancy characterised by secretion of monoclonal IgM paraprotein
- C/F -
  - (1) Systemic upset - weight loss, lethargy
  - (2) Hyperviscosity syndrome - visual disturbance - pentameric configuration of IgM increases serum viscosity
  - (3) Hepatosplenomegaly

(4)Lymphadenopathy

(5)Cryoglobulinemia - Raynaud's

- Investigations - Monoclonal IgM paraproteinemia
- BM biopsy → **diagnostic** : infiltration of BM with lymphoplasmacytoid lymphoid cells

- Mx : **rituximab-based combination chemotherapy**

40. Methaemoglobinemia - elevated levels of Methaemoglobin - increased presence of Meth-Hb can lead to tissue hypoxia.

It has **normal PO2 but decreased oxygen saturations**.

**Meth-Hb** - Acidosis - metabolic acidosis due to lactic acid build up because of tissue hypoxia.

Chocolate cyanosis - brownish discolouration of skin and mucous membranes seen in Meth-Hb as it imparts a chocolate-brown colour in the blood.

#### 41. **Thrombotic thrombocytopenic purpura**

- Abnormally large and sticky multimers of vWF causes platelets clumping in blood vessels
- TTP - **deficiency** of **ADAMTS13** which breakdown the large vWF
- C/F :
  1. Typically adult females
  2. Fever
  3. Fluctuating neurological signs due to micro emboli
  4. Microangiopathic haemolytic anaemia
  5. Thrombocytopenia
  6. Renal failure
- Causes -
  - (a)Post infection - urinary, gastrointestinal
  - (b)Pregnancy
  - (c)Drugs - cyclosporin, Cop, clopidogrel, aciclovir
  - (d)Tumour
  - (e)SLE
  - (f) HIV

#### 42. **Latex fruit syndrome**

- Cross reactivity between latex proteins and certain fruits like banana.
- Because of proteins found in natural rubber latex share structural similarities with plant proteins
- Apple can cause oral allergy syndrome due to cross reactivity with birch pollen.

#### 43. **Autoimmune haemolytic anaemia**

- Warm AIHA - antibody titre is usually **IgG** - **extravascular hemolysis**
- **Causes of Warm AIHA** -
  - 1) idiopathic
  - 2) autoimmune disease - SLE
  - 3) neoplasia - lymphoma, CLL
  - 4) drugs - methyldopa
- Cold AIHA - IgM - hemolysis at 4 degree; **intravascular hemolysis**; can have symptoms of Raynaud's and acrocyanosis.
- **Causes :**
  - Neoplasia : lymphoma
  - Infections, Mycoplasma, EBV
- SLE and lymphoma : mixed warm-cold hemolytic anaemia

#### 44. Acute intermittent porphyria - porphobilinogen deaminase

Porphobilinogen deaminase = hydroxymethylbilane synthase

#### 45. G6PD - blister cells, polychromatic

#### 46. Neutropaenic sepsis : gram positive, coagulase negative Staph epidermis

#### 47. **Filgrastim : G-CSF**

Selected for use in high risk patients at a high risk of neutropenia -

- 1) elderly
- 2) Specific malignancies - NHL, ALL

3) Previous neutropenic episodes

4) Those receiving combination chemotherapy and radiation therapy

- It seems that G-CSF tends to be used mostly in scenarios where a large benefit is expected.
- The *largest* benefit of G-CSF is expected with chemotherapy regimes that are given particularly with the intent to cure or prolong remission, or when there is a risk of febrile neutropenia >40%.
- Examples of this include chemotherapy regimens for patients with non-Hodgkin's lymphoma (as seen with the patient above), relapsed Hodgkin's lymphoma, germ cell tumours and acute lymphoblastic leukaemia (ALL).
- G-CSF can also be considered for patients undergoing myeloablative therapy followed by bone marrow transplantation, or in patients with a severe congenital, cyclic, or idiopathic neutropenia.
- G-CSF common side effect - bone pain

**48. Initial management of acute chest syndrome -**

- Oxygen therapy to maintain saturations >95%
- IV fluids to ensure euvolaemia
- Adequate pain relief
- Incentive spirometry in all patients
- Antibiotics with cover for atypical microorganisms
- Early consultation with critical care team and hepatology

49. Therapeutic plasmapheresis - most effective for haemolytic anaemia associated with *Mycoplasma pneumoniae*

50. Duffy blood group antigen alleles - Fya and Fay - entry for *Plasmodium vivax*

51. Long term hormone replacement therapy associated with increase risk of breast cancer, cardiovascular disease and thromboembolism

52. Leucocyte Alkaline Phosphatase

Raised in -

- Myelofibrosis
- Leukaemia reactions
- Polycythemia rubra vera
- Infections
- Steroids
- Cushing's syndrome
- Pregnancy, OCP

Lowered in -

- CML
- Pernicious anaemia
- PNH
- Infectious mononucleosis

53. Acute intermittent porphyry - abdominal, neurological and psychiatric symptoms

Porphyria cutanea tarda - photosensitive bullae

54. CLL - increased risk of warm autoimmune haemolytic anaemia

55. Beta thalassemia trait - microcytic anaemia with disproportionate MCH and MCV. Also associated with increased iron and increased ferritin and increased TIBC.

56. Prolonged APTT = factor VIII deficiency → intrinsic pathway

Factor VII deficiency = prolonged PT → extrinsic pathway

Factor X deficiency = prolonged PT and APTT.

57. **Superior vena cava obstruction**

- Oncological emergency caused by compression of SVC; commonly associated with lung cancer.

Clinical Features :

A. Dyspnoea most common

B. Swelling of face, neck and arms - conjunctival and periorbital oedema

C. Headache - worse in morning

D. Visual disturbance

E. Pulsatile jugular venous distension

Causes :

I. Common malignancies - small cell lung cancer, lymphoma

II. Other tumors - metastatic seminoma, Kaposi's sarcoma, breast cancer

III. Aortic aneurysm

IV. Mediastinal fibrosis

V. Goitre

VI. SVC thrombosis

Management :

- Endovascular stenting

- Radiotherapy / Chemotherapy

- Dexamethasone : to reduce papilloedema which is a sign of raised ICP and Pemberton sign

58. Blood films - typical pictures :

1) hyposplenism - post splenectomy, coeliac disease

- a) Target cells

- b) Howell Jolly bodies

- c) Pappenheimer bodies

- d) Sideritic granules

- e) Acanthocytes

2) Iron deficiency Anaemia

- A. Target cells

- B. Pencil poikilocytes

- C. Combined with B12 / folate —> mixed microcytic + microcytic picture

3) Myelofibrosis - tear drop poikilocytes

4) intra vascular hemolysis - schistocytes

59. Haematological malignancies & infections -



- 1) EBV - Hodgkin's lymphoma, Burkitt's lymphoma, Nasopharyngeal carcinoma
- 2) HTLV-1 : Adult T cell leukaemia/lymphoma
- 3) HIV-1 : High grade B cell lymphoma
- 4) H.pylori : MALT
- 5) Malaria : Burkitt's lymphoma

60. Leukaemia reaction features -

- high leukocyte alkaline phosphatase score
- Dohle bodies - toxic granulations in white cells
- Left shift of neutrophils = three or fewer segments of nucleus

61. TA circulatory overload —> hypertension

TA acute lung injury —> hypotension

62. Drugs causing pancytopenia -

- 1) Cytotoxic
- 2) Antibiotics - trimethoprim, chloramphenicol
- 3) Anti rheumatoid - gold, penicillamine
- 4) Carbimazole
- 5) Anti - epileptics - carbamazepine
- 6) Sulphonylureas - tolbutamide

63. Alteplase - tissue plasminogen activator - activates plasminogen to plasmin which degrades fibrin

Reversal of alteplase —> FFP + IV Tranexamic acid

64. Serum tryptase levels are elevated within 1 hour of anaphylaxis

65. Essential thrombocytosis treatment : Hydroxyurea / Hydroxycarbamide, IFN - alpha for younger patients, low dose aspirin to reduce thrombotic risk

66. CLL - Fludarabine, cyclophosphamide and rituximab (FCR) is correct. For fit patients with intact TP53 and with mutated IGHV, chemoimmunotherapy with FCR remains an acceptable initial therapy. Mutations of TP53 are associated with a poor response to

chemo-immunotherapy (e.g. FCR) and warrant the use of novel agents such as Bruton tyrosine kinase inhibitors (e.g. ibrutinib), or BCL2 inhibitors (e.g. venetoclax). Several recent trials have shown that mutated IGHV cases have a prolonged progression-free survival (PFS) after treatment with FCR.

**Active surveillance** is incorrect. Indications for treatment include progressive marrow failure, massive (>10 cm) lymphadenopathy, massive (>6 cm) splenomegaly, progressive lymphocytosis (> 50% increase over 2 months or lymphocyte doubling time < 6 months) or systemic symptoms. The patient, in this case, has a lymphocyte doubling rate < 6 months and has the development of cytopenias suggestive of significant bone marrow infiltration. The patient in this case, therefore, requires treatment.

67. Philadelphia translocation, t(9;22) - good prognosis in CML, poor prognosis in AML + ALL

The Philadelphia chromosome is a specific genetic abnormality in chromosome 22 of leukaemia cancer cells. It results from a reciprocal translocation between chromosome 9 and 22, which leads to the formation of BCR-ABL fusion gene that encodes for a tyrosine kinase protein with unregulated activity. This protein plays a crucial role in cell proliferation and survival, contributing to the pathogenesis of leukaemia. The presence of this Philadelphia chromosome is associated with a worse prognosis in acute lymphoblastic leukaemia (ALL), as it often leads to resistance against traditional chemotherapy agents.

68. Factor V Leiden is a mutation of one of the clotting factors in the blood called factor V. This specific mutation makes it harder for activated protein C, an anticoagulant, to inactivate factor V. As a result, clotting continues for a longer period than usual, increasing the risk of developing abnormal and potentially harmful clots - venous thromboembolism.

69. Antithrombin III deficiency

- Autosomal dominant inheritance

- Inhibits several clotting factors - thrombin, factor X, factor IX.
- It mediates the effect of heparin
- Heparin works by binding to antithrombin III - enhancing anticoagulant effect of heparin by inhibiting formation of thrombin and other clotting factors.
- C/F - recurrent venous thromboses
- Mx - lifelong warfarin, heparin during pregnancy, antithrombin III concentrates during surgery or childbirth

70. Hydroxycarbamide reduces the frequency of painful episodes and the risk of life-threatening illness or death. However, it can also increase your risk of infections. It is advised not to be taken in pregnancy.

Hydroxycarbamide essentially makes your red blood cells bigger, stay rounder and more flexible. Therefore, less likely to turn into a sickle shape. This is achieved by increasing a special kind of haemoglobin called haemoglobin F.

71. BRCA2 mutation - prostate cancer, breast cancer, pancreatic cancer

BRCA2 gene - located on long arm of chromosome 13

ALK gene mutation - adenocarcinoma of lung; found on chromosome 2

C-KIT mutation - GIST and AML; chromosome 4

EFGR mutation - renal cell carcinoma, non small cell lung carcinoma; EFGR gene on chromosome 7

KRAS mutation - pancreatic cancer  
Found on chromosome 12

72. Essential thrombocythosis - JAK2 mutation negative → CALR  
Calreticulin mutation is positive in 20% of patients with ET

73. This patient is having transfusion-associated graft versus host disease (TA-GvHD), which is a rare but lethal transfusion complication. The pathology of this condition is the failure of the

recipient to eliminate donor-derived T-cells, which then recognize HLA class II in recipient and cause excessive release of cytokines.

There are three major risk factors for this condition.

1. Volume and age of transfused blood.
2. Depressed immune function especially, that involving T-cells and cell-mediated immunity. Hodgkin's disease is a risk factor which this patient has.
3. Similar HLA haplotype sharing.

TA-GvHD is a delayed reaction that occurs 2-6 weeks after transfusion. The patient presents with diarrhoea, liver damage, and rash. Laboratory studies show pancytopenia. A biopsy of skin or bone marrow can be diagnostic. A biopsy specimen of the skin will show abundant necrotic keratinocytes. Bone marrow shows marked hypocellularity with macrophage infiltration.

There is no treatment, so prevention by using gamma-irradiated blood products in high-risk patients is the key.

74. Universal donor of FFP - AB Rhesus negative

75. Skin Prick Test:

- 1- Easy to perform
- 2- Inexpensive
- 3- Use control (Histamine '+' and Sterile water '-')
- 4- Read after 15 min
- 5- Useful for food allergy and pollen
- 6- Use diluted antigen and pierce the skin
- 7- +Ve test is formation of wheal

RAST:

- 1- Check amount of IgE to specific Ag
- 2- Result from 0 '-' to 6 '+'
- 3- Useful in food allergy, inhaled pollen, bee/wasp
- 4- Used if skin prick can not be used

Skin Patch Test:

- 1- Useful for contact dermatitis
- 2- need dermatologist
- 3- Read after (48+48)hours
- 4- Test allergen and irritant

76. IFN alpha treatment in :

- 1) hepatitis B
- 2) hepatitis C
- 3) Kaposi's sarcoma
- 4) hairy cell leukaemia
- 5) metastatic renal cell cancer

77. CA 1125 - primary peritoneal cancer, ovarian cancer

78. Sideroblastic anaemia

- Delta aminolevulinate synthase 2 deficiency
- Acquired causes -
  - A. Myelodysplasia
  - B. Alcohol
  - C. Lead
  - D. Anti TB medications
- Investigations :
  - (1)FBC - hypo chromic microcytic anaemia
  - (2)Iron studies - high ferritin, high iron, high transferrin saturation
  - (3)Blood film - basophilic stippling of red cells
  - (4)Bone marrow - Prussian blue stain will show ringed sideroblasts
- Management - supportive, Pyridoxine may help

79. Waldenstrom's macroglobulinaemia - Organomegaly with no bone lesions

Multiple myeloma - Bone lesions with no organomegaly

80. Hereditary angioedema (HAE) is pathophysiologically separate from anaphylaxis and is treated differently. Therapeutic options are:

intravenous infusion of human C1-esterase inhibitor or  
subcutaneous injection of the bradykinin receptor inhibitor icatibant

81. Aprepitant is an anti-emetic which blocks the neurokinin 1 (NK1) receptor. It is a substance P antagonists (SPA). It is licensed for chemotherapy-induced nausea and vomiting (CINV) and for prevention of postoperative nausea and vomiting. It is also been shown to be effective in treating clinical depression.

82. Bladder carcinoma - aromatic amines - Benzidine and beta naphthylamine

83. Sideroblastic anaemia - **Perl's stain - ring sideroblasts**

84. Hodgkin's lymphoma - most common type = nodular sclerosing

85. **Acute Lymphoblastic Leukaemia**

Good Prognosis -

- 1) FAB L1 type
- 2) Common ALL
- 3) pre-B phenotype
- 4) Low initial WBC
- 5) Del (9p)
- 6) Trisomy 4, 7 and 10
- 7) Hyper diploidy
- 8) t(12;21) - also known as TEL-AML1 fusion protein
- 9) Translocation (1;19)

**Poor prognosis** -

1. Hypodiploidy
2. FAB L3 type
3. T or B cell surface markers
4. Philadelphia translocation t(9;22)
5. Age < 2 years or > 10 years
6. Male sex
7. CNS involvement
8. High initial WBC >100,000

9. non-Caucasian

86. Testicular teratomas - AFP and beta-HCG tumor markers

87. Gastric cancer - least likely to be inherited

88. **Hereditary Angioedema** - uncontrolled release of **Bradykinin** causes tissue edema

89. 1 dose of IM adrenaline → discharge after 2 hours

2 doses of IM adrenaline → discharge after 6 hours

90. **Hereditary angioedema** (HAE) is a rare genetic disorder characterised by episodes of severe swelling in various body parts including the hands, face, airway and intestinal tract. It's caused by low levels or improper function of a protein called C1 inhibitor which helps regulate inflammation. **Anabolic steroids like Danazol** are used as long-term **prophylaxis** in HAE because they increase the production of C1 inhibitor, thus reducing the frequency and severity of attacks.

91. Burkitt's lymphoma, a type of non-Hodgkin's lymphoma, is associated with translocations involving the MYC oncogene. The most common translocation in this malignancy is t(8;14), which results in the juxtaposition of the MYC gene from chromosome 8 to the immunoglobulin heavy chain locus on chromosome 14. This leads to overexpression of the MYC protein, a transcription factor that promotes cell proliferation and growth.

92. Most common bleeding disorder - vWF disease

Most common hyper coagulable state - Factor V Leiden / activated Protein C resistance

93. **Exposure to aflatoxin is a risk factor for hepatocellular carcinoma.**

Exposure to nitrosamine is a risk factor for gastric and oesophageal carcinoma.

Exposure to aniline dye is a risk factor for transitional cell carcinoma.

Exposure to arsenic is a risk factor for lung malignancy and liver angiosarcoma.

Exposure to benzene is a risk factor for leukaemia.

#### 94. **Bleeding disorders and prevalence**

The most common inherited cause of thrombophilia is activated protein C resistance (Factor V Leiden) which has a prevalence of 5%. The prevalence of other inherited causes thrombophilia are listed below.

Antithrombin III deficiency has a prevalence of 0.02%.

Protein C deficiency has a prevalence of 0.3%.

Protein S deficiency is also a rare cause and has a prevalence of 0.1%.

Prothrombin gene mutation is the second most common inherited cause of thrombophilia with a prevalence of 1.5% however this is still more rare than Factor V Leiden.

95. AML - less time, less platelets —> blasts

CML - more time, more platelets —> bands

96. AML poor prognosis -

1) > 60 years

2) >20% blasts after first course of chemo

3) Deletion of chromosome 5 or 7

97. **Hypogammaglobulinaemia** refers to a deficiency of immunoglobulins (IgA, IgG, and/or IgM) in the blood. In the case of this patient with **chronic lymphocytic leukaemia** (CLL), hypogammaglobulinaemia is a common complication due to impaired production of immunoglobulins by the malignant B cells.



This leads to an **increased susceptibility to infections**, such as pneumonia. The fact that the patient has had four admissions for pneumonia in the past six months suggests that his immune system is compromised, making hypogammaglobulinaemia the most likely factor responsible.

## 98. Chromosomes & diseases

- chromosome 4 = Huntington's disease, PKD
- Chromosome 8 = gamma globin genes in foetal HB synthesis
- Chromosome 12 = Rett syndrome, bladder cancer
- Chromosome 16 = alpha thalassemia, alpha globulin genes
- Chromosome 20 = Creutzfeldt Jacob disease, Niemann Pick disease type C.

## 99. **Tumor markers**

- CA 125 → ovarian cancer
- CA 19-9 → pancreatic cancer
- CA 15-3 → breast cancer
- PSA → prostate cancer
- AFP → HCC, teratoma testicular
- CEA → colorectal cancer
- S-100 → melanoma, schwannoma
- Bombesin → Small cell lung carcinoma, gastric carcinoma, neuroblastoma

## 100. **Venous thromboembolism :**

### **General risk factors -**

- increased risk with advancing age
- Obesity
- Family history of VTE
- Pregnancy
- Immobility
- Hospitalisation
- Anaesthesia
- Central venous catheter - femoral >> subclavian

### **Underlying conditions :**

- Malignancy
- Thrombophilia e.g.: activated protein C resistance, protein C and protein S deficiency
- Heart failure
- APLA
- Polycythaemia
- Behcet's disease
- Nephrotic syndrome
- Sickle cell disease
- Homocystinuria
- PNH
- Hyper viscosity syndrome

Drugs :

- OCP
- HRT
- Tamoxifene, Raloxifen
- Antipsychotics = Olanzapine

## 101. Multiple Myeloma

- Bone disease - result of cytokines released by plasma cells that activate osteoclasts and suppresses osteoblasts —> osteolytic lesions and pathological fractures
- Kidney disease - deposition of Bence Jones proteins in distal tubules of kidney and hypercalcemia secondary to bone destruction

Clinical features

- C R A B
- C - hyperCalcemia; R - renal impairment; A - anaemia & thrombocytopenia; B - bone pain
- Bone pain
- Anaemia and fatigue
- Recurrent infections
- Hypercalcemia
- Renal failure

Investigations/Labs

- Serum protein electrophoresis

- Skeletal survey
- Urine - Bence Jones protein
- BM Aspiration - plasma cell infiltration > 10 %
- Staging and prognosis - **beta 2 microglobulin**

#### Management

- Corticosteroids
- Bisphosphonates
- Thromboprophylaxis

#### Complications

- Anaemia
- Renal failure
- Amyloidosis
- Pathological features
- Infections

102. Rasburicase - uric acid oxidation - it is an enzyme that breaks down uric acid.

Urine testing for patients on Rasburicase - falsely elevated uric acid levels - transport sample on ice cube to freeze action of Rasburicase

103. TRALI - donor antibodies

Febrile reactions - donor neutrophils

Graft v/s host disease - donor T lymphocytes

Haemolytic transfusion reaction - host T lymphocytes to mismatched blood products

#### 104. **Heparin induced thrombocytopenia**

- Caused by IgG antibodies that recognise multi molecular complexes of platelet factor 4 and heparin.
- Received heparin within 100 days - at risk of fall in platelets.
- DVT, PE, Major limb artery thrombosis, Stroke, MI, B/L adrenal hemorrhagic necrosis can occur

105. Tyrosine kinase inhibitor - Imatinib; adverse effects —> edema, rash, nausea & musculoskeletal pain.

EGFR inhibitor - Cetuximab —> colorectal cancer

Dihydro folate reductase inhibitor —> MTX

VEGF receptor inhibitor —> Sunitinib — Renal cell carcinoma

106. **Cabot rings** - megaloblastic anaemia, haemolytic anaemia, lead poisoning

**Heinz bodies** - haemolytic anaemia

**Pappenheimer bodies** - haemolytic anemia, sideroblastic anaemia, sickle cell disease

**Russell bodies** - Ig containing inclusion bodies found in plasma cells

Howell Jolly bodies - basophilic nuclear remnants in circulating RBCs

107. Alteplase reversal - Tranexamic acid

108. BETA THALASSEMIA TRAIT —> HbA2 level is raised

109. Acanthosis nigricans associated with gastric cancer

110. **S phase drug : MTX, 5-FU**

G2 phase : Bleomycin

M phase : Docetaxel

G1 phase : Etoposide

111. Relative risk for developing small cell and squamous cell lung cancer is higher in smokers.

## 112. Aplastic anemia

If a suitable HLA donor i.e., sibling present → anti-thymocyte globulin is preferred treatment

If no mention of suitable donor → haematopoietic stem cell transplant

113. Dermatomyositis associated with ovarian cancer, breast, pancreatic, lung cancer.

Mention of bloating and weight loss in history or any cancer features.

114. Fat embolism syndrome - multiple petechiae rash over axilla and skin folds of upper body

115. **Positive acute phase reactants** - TNF-alpha, IL-6, ferritin

Negative acute phase reactant - albumin

## 116. Protein C deficiency

- Acts to inactivate forms of pro-coagulant factors Va and VIIIa
- Deficiency of protein C causes increased risk of venous thromboses.
- Protein C → vitamin K dependent serine protease
- Thrombin activate protein C when bound to thrombomodulin.
- Skin necrosis on administration of warfarin occurs
- Autosomal codominant condition

117. Desmopressin (DDAVP) releases preformed vWF and vWF complexes with factor VIII to prolong factor VIII survival.

118. Acute promyelocytic leukaemia - poor prognosis : older age, poor cytogenetics, multi drug resistance, co-existing medical conditions.

## 119. **Mycosis fungoides**

- Indolent lymphoma of mature T-cells predominantly involving skin
- Patient has circulating abnormal T cells called **Sezary cells**
- Sezary cells + erythroderma = Sezary syndrome

- Sezary syndrome —> severe pruritic, psoriasis like lesions.
- Mx : Chemo

120. Fully HLA matched, CMV matched **male** donors >>>>>>  
fully HLA matched CMV matched **female** donors

121. Nephrotic syndrome —> **Protein S deficiency**

122. Desmopressin (DDAVP) used in conjunction with Tranexamic acid in patients with von Willebrand disease for dental procedures.

123. CLL - defective B cell disorder - hypogammaglobulinemia

124. Gross splenomegaly = CML & Myelofibrosis.

In CML —> white cell count > 100,000.

Myelofibrosis —> WCC mildly raised

Myelofibrosis - leucoerythroblastic blood picture with teardrop cells typical of diagnosis of myelofibrosis.

125. Neurofibromatosis type 2 chromosome 22q12.2 —> Bilateral acoustic neuroma

Another feature is occurrence of Juvenile posterior sub capsular lenticular opacities

126. **Sideroblastic Anaemia**

- Red cells fail to completely form haem
- Leads to deposits of iron in the mitochondria that form a tin around the nucleus called ring sideroblasts.
- Congenital - delta aminolevulinate synthase 2 deficiency
- Acquired - myelodysplasia, alcohol, lead, anti TB medications
- INV - FBC : hypo chromic microcytic anaemia
- High ferritin, High iron, High transferrin saturation
- Blood film - basophilic stippling
- BM - Prussian blue staining —> ring sideroblasts
- Mx : Pyridoxine may help

127. **Acute Myeloid Leukaemia** - most important prognostic marker is bone marrow karyotype.

Cytogenetic analysis of blast cells.

Low risk of relapse - t(8;21) or chromosome 16 inversion

High risk of relapse - deletion of chromosome 5 or 7

128. Invasive aspergillosis —> Galactoman test

### 129. **Methaemoglobinemia**

Mx - methylene blue or ascorbic acid

Causes -

Congenital causes :

- 1) cytochrome b5 reductase deficiency
- 2) Pyruvate kinase deficiency - reduced NADH production
- 3) Hemoglobinopathy HbM disease - which alters the structure of globin units —> tyrosine replaces histidine which changed Fe<sup>2+</sup> to Fe<sup>3+</sup>

Drug causes :

- 1) local anaesthetics
- 2) Aniline dyes
- 3) Benzene derivatives
- 4) Chloroquine
- 5) Nitrites
- 6) Metoclopramide
- 7) Antibiotics - dapsone
- 8) Sulphonamide
- 9) Smoke

130. Malignant acanthosis nigricans —> hyper pigmented velvety skin and thicker skin over palms and soles

Highly suggestive of GI malignancy —> urgent UGI Endoscopy

131. RBC 120 days

Neutrophils 5.4 days

Platelets 8-9 days

### 132. **Thalassemia**

- Alpha thalassemia — gene deletions on chromosome 16
- Alpha + haotype - low risk

- Alpha 0 halotype —> high risk

#### Clinical Presentation

- Pallor
  - Jaundice
  - Haemolytic anaemia
  - Hepatosplenomegaly
  - Frontal bossing of skull
  - Dysrhythmias
  - Cardiac failure - myocardial siderosis
- 
- Beta thalassemia — HbA2 > 3.5%

### 133. **Antibodies and paraneoplastic syndrome**

- 1) Anti Yo antibodies - ovarian and breast Paraneoplastic cerebellar degeneration

Paraneoplastic cerebellar degeneration occurs when tumor cells express proteins that are normally expressed in cerebellum triggering autoimmune reaction : dysarthria, ataxia, nystagmus.

- 2) Anti Hu antibodies - small cell lung cancer

- 3) Anti Ro antibodies - associated with SLE and neonatal heart block

- 4) Anti-Tr antibodies - Hodgkins lymphoma

- 5) Anti-Zic4 - small cell lung cancer

### 134. Milan criteria for liver transplant -

Single Tumor size  $\leq 5$  cm

Upto three tumors,  $\leq 3$  cm

No extra hepatic or major vessel involvement

135. FOLFOX - Folinic Acid, Flurouracil & Oxiplatin - used for colorectal carcinoma

136. Multiple myeloma - lytic lesions :



**Low intensity on T1 weighted fission MRI**  
**High intensity on T2 weighted diffusion MRI**

**137. Triose phosphate isomerase deficiency**

- rare autosomal recessive disorder
- C/F : neonatal haemolytic anaemia, cardiomyopathy, splenomegaly, susceptibility to infection, severe neurological dysfunction in wasting, weakness and spasticity

**138. Hypernephroma**

- clear cell or renal adenocarcinoma
- Hematogenous spread to bone causes lytic lesions and hypercalcemia
- Classic triad : hematuria + loin pain + abdominal mass
- Other C/F : night sweats, left varicocele due to compression of renal vein

**139. Eculizumab**

- Urine dipstick positive for blood, not for RBC blood cells.
- Classical description of PNH due to intra vascular hemolysis
- Monoclonal antibody that inhibits terminal complement protein C5
- Diagnosis of investigation - flow cytometry to detect low levels of CD59 and CD55.
- C/F of PNH - haemolytic anemia, pancytopenia +/- , hemoglobinuria, thrombosis ( Budd Chiari syndrome), aplastic anaemia can develop.

140. Urticaria, tachycardia, back pain after starting blood transfusion —> ABO incompatibility

141. Protein C and protein S are vitamin K dependent —> to obtain their meaningful result repeat thrombophilia screen one month after the patient is off Warfarin

142. **Cisplatin side effects** - Ototoxicity, Nephrotoxicity, Neurotoxicity, Hypomagnesemia, Hypokalemia, Hypocalcemia.

Cisplatin MOA : promotes cross-linking to form DNA adducts —> leads to promotion of intra-cellular signalling via pathways such as p53, p73, and MAP kinase leading to increased cellular apoptosis.

#### 143. CML Treatment

1st line - **Imatinib** - common side effect **Nausea, diarrhoea**, can cause **Gynecomastia**

2nd line - **Dasatinib**

2nd line - resistant to Imatinib or intolerant of Imatinib —> **Nilotinib**

Last option after trial with all Tyrosine Kinase inhibitors —>

**Ponatinib** or used for those patients who carry T315KD mutation

144. **Reticulocyte count** most useful when there is a suspected plastic crises v/s acute haemolytic anaemia.

Low reticulocyte count —> points towards aplastic crisis.

High reticulocyte count —> points towards hemolysis occurs.

#### 145. Heparin induced thrombocytopenia - deep vein

**thrombosis** most common complication of HIT.

- HIT is caused by IgG antibodies that recognise complexes of PF-4 and heparin.
- Thrombosis then results.
- Platelet count falls typically between day 5 and 10 after starting heparin treatment.
- Mx - unfractionated heparin and alternative anticoagulants such as Fondaparinux or Argatroban.

#### 146. Few important syndrome

- 1) **Felty's syndrome** - neutropenia + chronic arthritis + splenomegaly
- 2) Curran syndrome - association of kidney, hand and foot abnormalities
- 3) Di George syndrome - genetic disorder - heart defects, learning difficulties, cleft palate and thymus anomalies
- 4) Kostmann syndrome - severe congenital neutropenia
- 5) De Grouchy syndrome - 18q deletion syndrome, problems from childbirth

147. Acute anaemia —> reticulocytes increased

Increased reticulocytosis —> either 1) hemolysis or, 2) bleeding

Raised bilirubin —> hemolysis

Normal bilirubin. —> bleeding

Low haptoglobin -> hemolysis

Raised LDH —> hemolysis

Blood film spherocytes & reticulocytes —> hemolysis

148. Imatinib for GIST —> inhibition of c-kit

Imatinib for CML —> inhibition of tyrosine kinase

B-raf inhibitor —> malignant melanoma - Vemurafenib

PDGFR alpha inhibitor —> also tyrosine kinase inhibitor of imatinib

149. Carcinoma colon - Duke stage C and stage D —> chemotherapy with 5-FU and colonic acid improves mortality

### 150. **Aplastic Anaemia**

- Pancytopenia with hypo cellular bone marrow in the absence of an abnormal infiltrate or marrow fibrosis.
- Idiopathic pancytopenia with hypo cellular bone marrow and no abnormalities.

Causes :

- Congenital causes - Fanconi anaemia, Dyskeratosis congenita, Reticular dysgenesis
- Acquired causes :
  1. Cytotoxic drugs and cancer treatment
  2. Drugs - anti epileptics ( Carbamazepine, Phenytoin), antibiotics ( Sulphonamides, Chloramphenicol), NSAID, Gold
  3. Virus - Parvovirus B19, HIV, Hepatitis
  4. PNH, Myelodysplastic syndrome

Inherited marrow failure syndromes -

- **Fanconi anaemia** : **autosomal recessive** or **X-linked**; mutations in genes that code for nuclear complex involved in DNA damage response
- **GATA2 deficiency** : dysfunction in zinc finger transcription factors involved in hematopoiesis; cytopenia, myelodysplastic syndromes, acute leukaemia, infection, immunodeficiency, lymphoedema.

#### Clinical Features

- recurrent infections
- Fatigue
- Pallor
- Bleeding
- Easy bruising
- Tachycardia
- Dyspnoea
- Fanconi anaemia : hearing loss, pigmentation abnormalities, urogenital abnormalities

151. Right leg DVT followed by a stroke —> perform ECHO as it can lead to a paradoxical embolus through patent foramen ovale causing the stroke.

#### 152. RET proto-oncogene

- Found on chromosome 10
- Codes for receptor Tyrosine kinase
- Loss of function mutations associated with Hirschsprung's disease
- Gain of function mutations associated with MEN-2 and medullary thyroid carcinoma.
- **MEN2a** - Medullary thyroid cancer + pheochromocytoma + primary hyperparathyroidism
- **MEN2b** = Medullary thyroid cancer + Pheochromocytoma + Marfanoid habitus + mucosal/digestive neurofibromatosis.

153. Sick cell trait - cause of nephrogenic diabetes insipidus - asymptomatic from typical sickle cell symptoms such as anaemia, painful sickle cell crises and frequent infections.

Nephrogenic diabetes insipidus - sickle cell disease or trait

SIADH - acute intermittent porphyria

154. Unfractionated heparin contamination = elevated thrombin time & normal reptilase time

155. Gross splenomegaly - 1) CML or 2) Myelofibrosis

CML - white count is significantly raised, raised platelet counts, neutrophil predominant, metamyelocytes ++, myelocytes ++,

CML patients can have acute attack of gout —> due to auto destruction of very high white cell count which will cause significant DNA breakdown and causes acute gout.

Myelofibrosis - pancytopenia significant.

Anaemia due to reduced erythropoiesis, splenic destruction of circulating RBCs, autoimmune hemolysis.

156. Severe ITP —> platelets less than 30,000 : treat with IV Immunoglobulins IVIG

IVIG >> Methylprednisolone — if patient is diabetic and has uncontrolled blood sugars

No IVIG in options —> choose Methylprednisolone

157. Irradiated blood cells - depletes donor lymphocytes

158. **Anaplastic thyroid cancer**

- Rarest of all thyroid tumours
- Cervical lymph node metastases present in 90% of patients at the time of diagnosis.
- Lung metastases 50%
- Upper airway obstruction and trachea invasion - 25%
- Poor prognosis
- Median survival of 4-5 months
- Bone, liver and cervical LN metastases are common.

159. **Tumour classification R system**

- RX - presence of residual tumour, cannot be assessed
- R0 - no residual tumour
- R1 - microscopic residual tumor
- R2 - macroscopic residual tumor

160. Squamous cell cancer of skin

- Spreads by lymphatics
- Rarely seen under age of 45 years
- Related to UV exposure and occurs in sun exposed areas such as face and lower lips
- Excision biopsy for accurate diagnosis.
- Chronic immunosuppression - risk factor.
- Radical surgery and radiotherapy - treatment of choice
- Spreads to distant sites by lymphatic channels

161. Protein C deficiency test - Copperhead snake venom test —> which converts inactive protein C to active form of Protein C

162. **Upper GI Tract** - most common site of primary extra nodal malignant lymphoma

163. **Radiotherapy** - secondary cancers are the most likely long-term risk of radiotherapy.

Radiotherapy of chest area —> breast cancer

164. UF Heparin v/s LMWH

- LMWH less risk of HIT thrombocytopenia
- Bioavailability is higher for LMWH than for UF Heparin
- LMWH has longer half life (3-6 hours) than UF Heparin which has half life about 1.5-3 hours
- LMWH has lesser risk of bleeding

165. Standard chemotherapy for small cell lung cancer —> Cisplatin + Etoposide

Carboplatin used if patients cannot tolerate Cisplatin.

166.

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## NEUROLOGY

### PASSMEDICINE & PASSTEST

#### 1. **Absence seizures**

- EEG - bilateral, symmetrical 3Hz spike and wave pattern
- Mx - **sodium valproate, Ethosuximide** - first line
- Good prognosis - 90-95% seizure free in adolescence.

#### 2. **Causes of absent ankle jerk + absent extensor plantar**

- Subacute combined degeneration of spinal cord
- Motor neuron disease
- Friedrich's ataxia
- Syringomyelia
- Taboparesis - Syphilis
- Conus medullaris lesion

Lesions producing both UMN (extensor plantar) & LMN (absent ankle jerk) signs.

#### 3. **Ataxia Telangiectasia**

- Autosomal recessive disorder
- Caused by defect in **ATM gene** which encodes for DNA repair enzymes
- Most common inherited combined immunodeficiency disorders.
- Presents in early childhood with abnormal movements
- Onset at 1-5 years

#### Features

- Cerebellar ataxia
- Telangiectasia - spider angiomas
- IgA deficiency resulting in recurrent chest infections
- 10% risk of developing malignancy, lymphoma or leukaemia

#### 4. **Autonomic Neuropathy**

##### Features:

- Impotence

- Inability to sweat
- Postural hypotension
- Loss of decrease in heart rate following deep breathing
- Pupils dilate after adrenaline administrations

Causes :

- Diabetes
- GBS
- Multisystem atrophy (MSA)
- Shy Drager syndrome
- Parkinson's
- Infections - HIV, Chagas disease, neurosyphilis
- Drugs - anti hypertensives, TCA
- Craniopharyngioma

## 5. **Benign Rolandic Epilepsy**

- Form of childhood epilepsy that typically occurs between 4-12 years

Features :

- Seizures occur mostly at nights
- Typically partial seizures [paraesthesia affecting face]
- Secondary generalisation of seizures may occur
- EEG - centretemporal spikes
- Seizures stop by adolescence

## 6. **Brain Lesions**

Parietal Lobe lesions -

- Sensory inattention
- Apraxia [ unable to perform tasks ]
- Astereognosis - tactile agnosia [ inability to discriminate shape and size by touch ]
- Inferior homonymous quadrantanopia
- Gerstmann's syndrome - lesion of dominant parietal = Alexia, acalculia, finger agnosia, and right-left disorientation

Alexia = inability to read or comprehend written language; CAN spell and write words



### Occipital Lobe Lesions :

- Homonyms hemianopia with macular sparing
- Cortical blindness
- Visual agnosia

### Temporal lobe lesions :

- Wernicke's aphasia - word substitution, neologism, speech fluent
- Superior homonymous quadrantanopia
- Auditory agnosia
- Prosopagnosia = difficulty recognising faces

### Frontal lobe lesions :

- Broca's aphasia
- Disinhibits
- Perseveration = repetition of articulatory process such as word, phrase regardless of absence or cessation of stimulus
- Anosmia
- Inability to generate list

### Cerebellum lesions :

- Midline lesions - gait and truncal ataxia
- Hemisphere lesion - intention tremor, past pointing, dysdiadochokinesis, nystagmus

- Medial thalamus & Mammillary bodies of hypothalamus : Wernicke & Korsakoff syndrome

- Sub-thalamic nuclei of basal ganglia : Hemiballismus

- Striate (caudate nucleus) of basal ganglia : Huntington chorea

- Amygdala : Kluver-Bucy syndrome [ hyper sexuality, hyperorality, hyperphagia, visual agnosia ]

## 7. **CADASIL**

- Cerebral Autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy
- Autosomal dominant
- NOTCH3 mutation on chromosome 19

- Presenting features - migraines, multiple strokes, dementia.

### **8. Carbamazepine adverse effects :**

- P450 inducer
- Dizziness
- Ataxia
- drowsiness
- Headache
- Visual disturbances - diplopia
- Steven Johnson syndrome
- Leucopenia & agranulocytosis
- Hyponatremia due to SIADH

### **9. Normal CSF values -**

- Pressure : 60-150
- Protein : 0.2-0.4 g/L
- Glucose : >2/3 blood glucose
- Cells : RBC - 0, WBC - <5/mm<sup>3</sup>

### **Conditions causing increased lymphocytes in CSF :**

- viral meningitis/encephalitis
- TB meningitis
- Lyme disease
- Behcets disease
- SLE
- Lymphoma
- Leukaemia

### **Conditions causing raised protein levels :**

- GBS
- TB meningitis
- Bacterial meningitis
- Viral meningitis
- Groin's syndrome - increase CSF protein below a spinal canal blockage like tumor, disc, infection

### **10. Cervical spondylitic myelopathy**

Clinical features :

- variety of motor weakness, sensory loss and bowel/bladder dysfunction
- Neck pain
- Wide based, ataxic or spastic gait
- UMN weakness in lower legs - increased reflexes, increased tone and upping plantar
- Bladder dysfunction e.g., urgency, retention

### **11. Drugs causing peripheral neuropathy**

- Amiodarone
- Isoniazid
- Vincristine
- Nitrofurantoin
- Metronidazole

### **12. DVLA - Neurological disorders**

1) Epilepsy / Seizures - all patients must not drive and must inform the DVLA

- first unprovoked/isolated seizure - 6 months off if there are no structural abnormalities on brain imaging and no EEG epileptic activity
- Established epilepsy or multiple unprovoked seizures : may qualify for driving license if free from seizure for 12 months
- No seizures for 5 years +/- medication —> TIL 70 license is usually restored
- NO driving during withdrawal of epileptic medications for 6 months after last dose

2) Syncope

- simple faint : no restriction
- Single episode, explained and treated : 4 weeks off
- Single episode, unexplained : 6 months off
- Two or more episodes : 12 months off

3) Other conditions

- stroke / TIA : 1 month off driving, no need to inform DVLA if no residual effect

- Multiple TIAs : 3 months off, **inform** DVLA
- Craniotomy - 1 year off driving
- Pituitary tumor craniotomy : 6 months
- Chronic neurological disorders : **Inform** DVLA, complete PK1 form

### 13. **Dystrophinopathies**

- X - linked recessive
- Mutation in gene encoding dystrophin on Xp21
- Dystrophin - protein which connects muscle membrane to actin
- DMD - frameshift mutation causing one or both binding sites to be lost
- Becker's : non-frameshift mutation in dystrophin gene resulting in both binding sites to be preserved leading to a milder form

#### Duchenne Muscular Dystrophy

- progressive muscle weakness from 5 years of age
- Calf pseudo hypertrophy
- Gower's sign

#### Becker muscle dystrophy

- develops after the age of 10 years
- Intellectual impairment more common

### 14. **Epilepsy in Children : Syndromes**

#### 1) **Infantile spasms / West's syndrome**

- brief spasms beginning in the first few months of life
- Flexion of head, trunk and limbs —> extension of arms
- Progressive mental handicap
- Rx : Vigabatrin and steroids
- Poor prognosis

#### 2) **Typical (petit mal) absence seizures**

- onset : 4-8 years
- EEG : 3 Hz generalised, symmetrical
- Mx : Sodium valproate, Ethosuximide

#### 3) **Lennox-Gastaut syndrome**

- extension of infantile spasms
- Atypical absences, falls, seizures
- EEG : slow spike
- Mx : Ketogenic diet may help

#### 4) **Juvenile myoclonic epilepsy / Janz syndrome**

- onset teenage years, G >> boys
- Infrequent generalised seizures, often in morning / following sleep deprivation
- Sudden shock-like myoclonic seizure
- Mx : Sodium valproate

—> Epilepsy and pregnancy :

- aim for monotherapy
- Sodium valproate : associated with neural tube defects
- Phenytoin : associated with cleft palate
- Lamotrigine : dose may be increased in pregnancy

Pregnant women taking Phenytoin are given vitamin K in the last month of pregnancy to prevent clotting disorders in the newborn.

#### 15. Epilepsy : Treatment

- Start anti-epileptic after first seizure if any of the following :
  1. Patient has a neurological deficit
  2. Brain has structural abnormality
  3. EEG s/o unequivocal epileptic activity
  4. Patient or their family consider another seizure attack unacceptable

- Maternal use of sodium valproate is highly contraindicated - increased risk of neurodevelopment delay in children

- GTCS —> Males : Sodium Valproate, Females : Lamotrigine / Levetiracetam

- Focal seizures : 1st line - Lamotrigine, 2nd line - Carbamazepine / Oxcarbamazepine

- Absence seizures : Ethosuximide, 2nd line - Lamotrigine / Levetiracetam
- Carbamazepine exacerbates absence seizures

- Ethosuximide MOA = blocks T type Calcium channels in thalamic neurons

#### 16. Causes of b/l facial nerve palsy :

- sarcoidosis
- GBS
- Lyme disease
- B/l acoustic neuromas

Causes of unilateral facial palsy -

LMN - Bell's palsy, Ramsay hunt syndrome, Acoustic neuroma, HIV, Parotid tumor, MS, DM

UMN u/l facial palsy - Stroke.

LMN - affects all facial muscles

UMN lesion - - spares upper face

#### 17. Common perineal nerve injury - at neck of fibula - when leg crossing, squatting, or kneeling.

Other precipitating factors : prolonged immobility, recent weight loss, Baker's cysts, plaster casts

Foot drop weakness of hip abduction = L5 radiculopathy

#### 18. Friedrich's Ataxia

- Most common cause of early onset hereditary ataxias
- **Autosomal recessive** - trinucleotide repeat disorder characterised by GAA repeat in **X25** gene on **Chromosome 9** {**frataxin**}
- Does not demonstrate phenomenon of anticipation

**Clinical features :**

- Absent ankle jerks / extensor planters
- Cerebellar ataxia
- Optic atrophy
- Spinocerebellar tract degeneration
- **HOCM - most common cause of death**
- High arched palate
- Diabetes mellitus
- Kyphoscoliosis

**19. Guillian Barre syndrome**

- Cross reaction of antibodies with Gangliosides in the PNS
- Correlation between anti-ganglioside antibody (anti-GM1) and clinical features

**Clinical Features :**

- ~65% of patients experience back pain/leg pain in the initial stages of illness
- Ascending paralysis
- Reflexes are reduced or absent
- History of Respiratory illness / gastrointestinal illness
- Cranial nerve involvement - diplopia, b/l facial nerve palsy
- Autonomic involvement - urinary retention, diarrhoea

Lumbar puncture - albumino cytological dissociation (increase in protein with normal WBC)

Nerve conduction studies - decreased velocity, prolonged distal motor latency, increased F wave latency

**Miller Fish syndrome**

- variant of GBS
- Ass. With - ophthalmoplegia, areflexia, and ataxia
- Descending paralysis
- anti-GQ1b antibodies are present in 90% of cases

Management : IVIG or plasma exchange  
1st line - IVIG

FVC to regularly monitor respiratory muscle function.

Poor prognosis factors :

- age > 40 years
- Poor upper extremity muscle strength
- Previous history of diarrhoea illness
- High anti-GM1 titre
- Need for ventilatory support

## 20. **Brain injury**

### 1. Extradural / Epidural hematoma

- bleeding into space between dura mater and skull
- Temporal region where a rupture of middle meningeal artery occurs
- C/F : Raised ICT, lucid interval

### 2. **Subdural hematoma**

- bleeding into the outermost meningeal layer
- Commonly around the frontal and parietal lobes
- R/F - old age, alcoholism, anticoagulation
- Fluctuating confusion/consciousness levels

### 3. **Subarachnoid haemorrhage**

- sudden occipital headache
- Rupture of cerebral aneurysm

### 4. **Intra cerebral hematoma**

- collection of blood within the substance of brain
- R/F - hypertension, vascular lesion (aneurysm, AV malformation), Cerebral amyloid antipathy, trauma, brain tumor
- CT imaging - hyperdensity lesion

## 21. **Hereditary Sensorimotor Neuropathy type I -**

- autosomal dominant
- Defect in **PMP-22** gene which codes for **Myelin**
- Motor symptoms predominate
- Distal muscles - wasting, pes cavus, clawed toes
- Foot drop, leg weakness



## 22. Huntington's disease

- **autosomal dominant**
- **Trinucleotide repeat disorder** - repeat of **CAG**
- Phenomenon of anticipations present —> where disease presents at an earlier age in successive generations.
- Degeneration of cholinergic and GABAergic neurone in striatum of basal ganglia.
- Defect in Huntington gene on Chromosome 4

### **Clinical features :**

- chorea
- Personality changes - irritability, apathy, depression, intellectual impairment
- Dystonia
- Saccadic eye movements

## 23. Lateral Medullary Syndrome

- Also known as **Wallenberg syndrome**
- Occlusion of PICA posterior inferior cerebellar artery
- C/F :
  - Cerebellar features : ataxia, nystagmus
  - Brainstem features : **Ipsilateral** —> dysphagia, facial numbness ,cranial nerve palsy
  - Brainstem - **Contralateral** —> limb sensory loss

## 24. Lacunar stroke

- Small deep infarcts
- mainly occurring in basal ganglia, lenticular nucleus and white matter of internal capsule, pons, and centrum semiovale.

Five classic forms -

1. Pure motor hemiparesis
2. Pure sensory stroke
3. Sensorimotor stroke
4. Ataxic hemiparesis
5. Clumsy hand dysarthria

## 25. Atypical aura symptoms

- motor weakness

- Double vision
- Visual symptoms affecting only one eye
- Poor balance
- Decreased level of consciousness

## **Migraine - Management :**

**Acute treatment** : 5-HT receptor agonists

Oral triptan + NSAID

**or**

Oral triptan + PCM

Ages 12-17 years → nasal triptan.

Migraine prophylaxis :

- 1) Propranolol
- 2) Topiramate - CI in women of childbearing age - **teratogenic**
- 3) **Amitriptyline**

**Menstrual Migraine** - Frovatriptan / Zolmitriptan

Monoclonal antibody against Calcitonin gene related peptide receptor - **ERENUMAB**

## **26. Motor Neuron Disease**

Management :

- Riluzole - prevents stimulation of glutamate receptors, main use in ALS, prolongs life by about 3 months
- Respiratory care - BiPAP - prolongs life around 7 months
- Nutrition - Percutaneous gastrostomy tube

Amyotrophic Lateral Sclerosis - LMN signs in arms, UMN signs in legs

Familial ALS - chromosome 21, codes for superoxide dismutase

## **27. Multiple Sclerosis - Management :**

Acute Relapse : high dose steroids (oral or IV Methylprednisolone) for 5 days.

Disease Modifying drugs :

1. Natalizumab - recombinant monoclonal antibody;
  - antagonist to alpha -4 beta - 1 integrin found on surface of leucocytes
  - Inhibits migration of leucocytes across the endothelium and into the BBB
  - Given IV
2. Ocrelizumab - humanised anti CD20 monoclonal antibody, given IV
3. Fingolimod : Sphingosine 1 phosphate receptor modulator, ORAL administration; MOA : prevents lymphocytes from leaving lymph nodes
4. Beta interferon : given SC / IM
5. Glatiramer acetate : acts as immune decoy, given SC,

Multiple Sclerosis : Good Prognosis features

- female sex
- Young patient 20s or 30s
- Relapsing - remitting disease
- Sensory symptoms only
- Long interval between first two relapses
- Complete recovery between relapses

28. Drugs exacerbating Myasthenia gravis:

- penicillamine
- Quinidine
- Procaiamide
- Beta blockers
- Lithium
- Phenytoin
- Antibiotics - gentamicin, macrocodes, quinolones, tetracycline

## 29. **Myotonic dystrophy / Dystrophica Myotonica**

- Autosomal dominant, trinucleotide repeat disorder
- Two main types - DM1 and DM2
- DM1 : CTG repeat at end of DMPK gene - chromosome 19; distal weakness more prominent
- DM2 : repeat expansion of ZNF9 gene on chromosome 3; proximal weakness more prominent

General features :

- myotonic facies : long haggard appearance
- Frontal balding
- Bilateral ptosis
- Cataracts
- Dysarthria

Other features :

- myotonia - tonic spasm of muscle
- Weakness of arms and legs
- Mild mental impairment
- Diabetes mellitus
- Testicular atrophy
- Cardiac - heart block, cardiomyopathy
- Dysphagia

## 30. **Normal Pressure Hydrocephalus**

- Reversible cause of dementia
- Secondary to reduced CSF absorption at the arachnoid villi
- classical triad : urinary incontinence + dementia and bradyphasia + gait abnormality
- CT scan : hydrocephalus with ventriculomegaly +/- sulcal enlargement

## 31. **Otosclerosis**

- replacement of normal bone by vascular spongy bone
- Progressive conductive deafness due to fixation of the stapes at the oval window
- Autosomal dominant
- Clinical features : conductive deafness, tinnitus, +ve family history

- Mx : hearing aid, stapedectomy

### 32. Paraneoplastic affecting CNS :

#### 1. **Lambert Eaton Syndrome**

- associated with small cell lung cancer
- Antibodies against pre-synaptic voltage gated calcium channels

#### 2. Anti-Hu

- Associated with small cell lung carcinoma & neuroblastomas
- Cerebellar syndrome
- Sensory neuropathy
- Encephalomyelitis

#### 3. Anti-yo

- associated with ovarian and breast cancer
- Cerebellar syndrome

#### 4. Anti-GAD antibody

- associated with breast, colorectal and small cell lung cancer
- Stiff persons's syndrome or diffuse hypertonia

#### 5. Anti-Ri

- associated with breast and small cell lung cancer
- Ocular opsoclonus-myoclonus

#### 6. Purkinje cell antibody

- peripheral neuropathy; associated with breast cancer

Small cell lung cancer - Paraneoplastic associations :

1. Lambert Eaton syndrome
2. SIADH
3. Cushing's syndrome
4. Anti-Hu cerebellar syndrome
5. Anti-GAD : diffuse hypertonia
6. Anti-Ri : ocular opsoclonus-myoclonus

### 33. Parkinsons's disease

Features :

- Bradykinesia - difficulty initiating movement, short shuffling steps, with reduced arm swing
- Tremor : 3-5 Hz, marked at rest, worse when stressed or tired, pill rolling tremors
- Rigidity : lead pipe
- Mask like facies
- Flexed posture
- Micrographic
- Drooling of saliva
- Psychiatric - depression, dementia, psychosis, sleep disturbances
- Impaired olfaction
- Fatigue
- Autonomic dysfunction - postural hypotension

Test to differentiate between essential tremors v/s Parkinson's disease —> 123 Iodine-FP-CIT single photon emission CT (SPECT) scan.

Drooling of saliva - Glycopyrronium bromide

Adverse effects : Levodopa -

- dry mouth
- Anorexia
- Palpitations
- Postural hypotension
- Psychosis
- Dyskinesia at peak dose : dystonia, chorea, athetosis

Dopamine receptor agonists

- associated with increased risk of hallucinations
- High risk of impulse control disorders and excessive daytime somnolence

Ergot derived - Bromocriptine, Cabergoline

- associated with higher risk of retroperitoneal, pulmonary and cardiac fibrosis

- labs before starting treatment : ECHO, ESR, Creatinine, CXR

Non ergot derived : Ropinirole, Apomorphine

- Excessive daytime somnolence : stop driving, adjust medications to reduce effect of sleepiness, Modafinil can be given
- Orthostatic hypotension develops —> medication review; persistence of symptoms —> midodrine

MAO-B inhibitors :

- Selegiline
- Inhibits breakdown of dopamine secreted by dopaminergic neurone

Amantadine :

- adverse : ataxia, slurred speech, confusion, dizziness, lived reticularis.

COMT inhibitors :

- Entacapone, Tolcapone

### **Antimuscarinics**

- blocks the cholinergic receptors
- **Used in drug-induced Parkinsonism**
- **Procyclidine, Benztropine, Trihexyphenidyl (benzhexol)**

### 34. Phenytoin

MOA : binds to sodium channels increasing their refractory period

Adverse effects -

1) Acute :

- Initially : dizziness, diplopia, nystagmus, slurred speech, ataxia
- Later : confusion, seizures

2) chronic

- gingival hyperplasia : due to increased expression of PDGF
- Hirsutism
- Coarsening of facial features
- Drowsiness
- Megaloblastic anaemia due to altered folate metabolism
- Peripheral neuropathy
- Osteomalacia due to increased vit D metabolism
- Lymphadenopathy
- Dyskinesia

### 3) idiosyncratic

- Fever
- Rashes
- Toxic epidermal necrolysis
- Hepatitis
- Dupuytren's contracture
- Aplastic anaemia
- Drug induced lupus

### 4) teratogenic

- cleft palate
- Congenital heart disease

Trough levels, immediately before next dose is to be checked

## 35. Restless Leg Syndrome : Management

- simple measures - walking, stretching
- Treat IDA - measure ferritin to rule out IDA
- 1st line : dopamine agonists - **Pramipexole, Ropinirole**
- **Benzodiazepines**
- **Gabapentin**

## 36. Hearing tests : Rinne's and Weber's

- Rinne's normal : AC > BC bilateral
- Conductive hearing loss :
  - Rinne's - **BC > AC - affected ear**
  - **Weber's : lateralises to affected ear**
- Sensorineural hearing loss



- Rinne's = AC > BC both ears
- Weber's = lateralises to unaffected ear

### 37. Sodium Valproate - adverse effects

- teratogenic : neural tube defects, increased risk of neurodevelopment delay
- P450 inhibitor
- Nausea
- Increased appetite, weight gain
- **Alopecia**
- Ataxia
- Tremor
- **Hepatotoxicity**
- **Pancreatitis**
- Thrombocytopenia
- **Hyponatremia**
- Hyperammonemic encephalopathy - **L-carnitine** for treatment

### 38. Spinal Cord Lesions

Mixed motor + Sensory Lesions -

1) Brown Squared syndrome : spinal cord hemisection

Tracts affected -

- Lateral corticospinal tract
- Lateral spinothalamic tract
- Dorsal columns

Clinical features :

- I/L spastic paresis below level of lesion
- I/L loss of proprioception and vibration sense
- C/L loss of pain and temperature

2) Subacute Combined Degeneration of Spinal Cord (vit B12 & vit E deficiency )

Tracts affected :

- Lateral corticospinal
- Dorsal column
- Spinocerebellar tracts

Clinical Features :

- B/L spastic paresis
- B/L loss of proprioception and vibration sensation
- B/L limb ataxia

### 3) Friedrich's ataxia

Tracts affected :

- Lateral corticospinal
- Dorsal column
- Spinocerebellar tracts

Clinical Features :

- B/L spastic paresis
- B/L loss of proprioception and vibration sense
- B/L limb ataxia
- Cerebellar ataxia —> intention tremor

### 4) Anterior spinal artery occlusion

Tracts affected :

- Lateral corticospinal
- Lateral spinothalamic

Clinical Features :

- B/L spastic paresis
- B/L loss of pain and temperature

### 5) Syringomyelia

Tracts affected :

- ventral horns
- Lateral spinothalamic tract

Clinical Features :

- flaccid paresis - affects mainly the intrinsic hand muscles
- Loss of pain and temperature

6) multiple sclerosis

Tracts affected :

- asymmetrical, varying spinal tracts involved

Clinical features

- Combination of Motor + sensory + ataxia symptoms

39. Cerebellum —> oscillopsia - alternating nystagmus, jerk nystagmus, direction of fast and slow components changes every 2 minutes

lesion : cerebellum [ flocculus and nodulus ]

Optic chiasma —> see saw nystagmus

40. Stroke - disability assessment : **Barthel index**

Used to assess functional status of patient post stroke and to monitor their improvement with ongoing rehabilitation to regain independence after the event

**41. Aneurysmal SAH - complications**

- re-bleeding : arrange repeat CT; associated with high mortality
- Hydrocephalus
- Vasospasm
- Hyponatremia - SIADH
- Seizures

Predictive factors of SAH -

- 1) consciousness level on admission
- 2) Age
- 3) Amount of blood visible on CT

42. **Syringomyelia**

- cape like features - neck, shoulders and arms

- Loss of sensation to temperature
- **Preservation** of light touch, proprioception and vibration
- Spastic weakness - lower limbs mainly
- Neuropathic pain
- Upgoing planters
- Autonomic features
- Horner's syndrome - due to compression of sympathetic chain

INV - full spine MRI to detect tumor or tethered cord

#### 43. **3rd nerve palsy**

- Eye is down and out
- Ptosis
- Dilated pupils - surgical third nerve palsy

Causes :

- Diabete mellitus
- Vasculitis - temporal arteritis, SLE
- False localising sign due to uncle herniation
- Posterior communicating artery aneurysm - pupil dilated, pain present
- Cavernous sinus thrombosis

#### 44. **Topiramate**

- MOA : blocks voltage gated Na channels; increases GABA action, Carbonic anhydrase inhibition - decreases urinary citrate excretion and formation of alkaline urine that favours the creation of calcium phosphate stone
- **inducer** of P450 enzyme CYP3A4
- COCP - UKMEC 3; implant - UKMEC 2
- Depo-provera and IUS - safe for use with Topiramate

Adverse effects :

- reduced appetite & weight loss
- Dizziness
- Paraesthesia
- Lethargy
- Poor concentration
- Acute myopia & secondary angle closure glaucoma

- Teratogenic - Increased risk of fetal malformations

#### 45. Von Hippel Lindau syndrome

- Autosomal dominant
- Predisposes to neoplasia
- VHL gene - short arm of chromosome 3

Features :

- cerebellar hemangiomas - can cause SAH
- Retinal hemangiomas - can cause vitreous hemorrhage
- Renal cysts - premalignant cysts
- Pheochromocytoma
- Extra renal cysts : epididymal cyst, pancreatic cyst, hepatic cyst
- Endolymphatic sac tumor
- Clear cell renal cell carcinoma

#### 46. **Foster Kennedy Syndrome**

- This syndrome reflects a **frontal lobe tumour** - usually a meningioma in this age group - leading to **ipsilateral optic atrophy and papilloedema of the contralateral optic nerve.**
- The reason for the optic atrophy is as a result of direct damage from the space occupying lesion.
- Other causes are AVMs and juvenile nasopharyngeal angiofibroma.

#### 47. Multiple Sclerosis

- The patient has presented with spastic paraparesis, characterised by **hypertonia, hyperreflexia, clonus** and a **pyramidal pattern of weakness (with flexors affected more than extensors in the lower limbs).**
- The history of similar neurological symptoms resolving without intervention points to the relapsing-remitting pattern often seen in multiple sclerosis.
- While all of the listed conditions could cause spastic paraparesis, the absence of sensory symptoms, the specific distribution of signs and the relapsing-remitting pattern make **multiple sclerosis** the most likely diagnosis.
- Multiple sclerosis can manifest with a diverse range of neurological symptoms, and not all patients will present as described here.

- Nevertheless, the alternative diagnoses are less probable for this clinical picture for the reasons delineated below.

48. In **status epilepticus**, **IV levetiracetam, phenytoin or sodium valproate** should be given if not responding to benzodiazepines.

49. **Internuclear Ophthalmoplegia**

- **Caused by Multiple sclerosis, vascular disease**
- Can cause of horizontal disconjugate eye movement
- Due to a lesion in the **medial longitudinal fascicles - located in the paramedian area of midbrain and pons.**
- **MLF** - controls the horizontal eye movement by interconnecting the III, IV, VI cranial nerves
- C/F : impaired adduction on **same side of lesion**
- Horizontal nystagmus of abducting eye on opposite side

49. **Right superior homonymous quadrantanopia.** This is because the left temporal lobe, where the meningioma was located, contains Meyer's loop of the optic radiation. Damage to this area during surgery can result in a visual field defect known as '**pie in the sky**', which is formally called the right superior homonymous quadrantanopia. This condition manifests as a loss of vision in the upper-right quadrant of both eyes.

50. **Neuromyelitis optica** which is also known as **Devic's disease** is an **autoimmune** disorder in which immune system cells and antibodies attack the optic nerves and the spinal cord.

- The pathophysiology is still however completely unclear.
- The diagnosis of neuromyelitis optica is determined as follows:

**Absolute** criteria:

- Optic neuritis
- Acute myelitis

**Supportive** criteria:

- Brain MRI not meeting criteria for MS at disease onset

- Spinal cord MRI with contiguous T2-weighted signal abnormality extending over three or more vertebral segments
- **NMO-IgG seropositive status** (The NMO-IgG test checks the existence of antibodies against the aquaporin 4 antigen.)

Compared to multiple sclerosis, the acute episodes are not understood to be triggered by the immune system's T cells, but rather by **antibodies** called **NMO-IgG**.

51. Cluster headache triggers : alcohol, nocturnal sleep  
Prophylaxis - Verapamil

52. Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

53. **CADASIL**

- Cerebral Autosomal Dominant Arteriopathy with Subcortical infarcts and leukoencephalopathy
- Mutation in NOTCH3 gene
- Multi infarct dementia
- Recurrent TIAs and strokes
- Neuro-cognitive decline : depression, low mood,
- Presents with migraine and depression
- Family history ++
- MRI - multiple widespread hyper intense lesion in white matter, basal ganglia, thalamus and pons

54. **Absence seizures** - **Carbamazepine** - Contra indicated.

55. **Chlorpromazine**, a typical antipsychotic medication, has been associated with **drug-induced Parkinsonism**.

- This is due to its dopamine D2 receptor antagonism in the nigrostriatal pathway of the brain.
- Dopamine is an essential neurotransmitter involved in motor control and its deficiency in this pathway leads to the

characteristic symptoms of Parkinsonism such as bradykinesia, rigidity, and tremor.

- It's important to note that this is a reversible form of Parkinsonism and symptoms usually resolve upon discontinuation of the offending drug.
- However, if discontinuation is not possible due to psychiatric reasons, symptoms can be managed using anticholinergic drugs or amantadine under UK guidelines.

56. The arcuate fasciculus is a bundle of axons that generally connects Broca's area and the Wernicke's area.

- Lesions in this area result in conduction aphasia. Conduction aphasia is characterised by fluent speech, relatively intact comprehension and poor repetition.
- The main deficit in this scenario is impaired repetition. The patient is unable to repeat short sentences with high frequency words, such as, 'he did it' and 'this is it' and low-frequency complex phrases, such as, 'baby hippopotamus' and 'British constitution'.
- Over-learned sequences, such as, 'one, two, three' are not tested in this scenario and are usually only impaired in severe cases.
- This patient has relatively intact comprehension as she is able to complete 3 step commands. More complex comprehension questions, such as, 'If a seal was killed by a polar bear which one is still alive?' may cause difficulty for the patient.
- The animal naming test (ANT1) used in this scenario is a semantic fluency test that consists of naming as many animals as possible in 1 minute.
- A normal ANT1 score is typically considered to be >14.

57. Intravenous phenytoin can cause hypotension and bradyarrhythmias. Phenytoin is believed to protect against seizures by causing voltage-dependent block of voltage gated sodium channels. Phenytoin is also a class IB antiarrhythmic drugs which blocks sodium channels in the heart resulting in shortening of repolarization.

58. The phenomenon being described is **astereognosis**.

- This is the inability to identify an object by active touch of the hands without other sensory input, such as visual or sensory information.



- Despite often being able to identify shapes and unique features of an object, there is a disruption in the processing of these tactile stimuli into the object's learned functions.
- This is the case in this question, where the patient cannot name objects in the absence of visual input.
- **Hemisphere dominance for stereognosis determines laterality of astereognosis: dominant-sided lesions cause bilateral astereognosis (as in this case) whereas non-dominant-sided lesions cause contralateral astereognosis.**

**59. Antibodies to RNA-binding protein Nova-1** are not responsible for this patient's findings. Nova-1 antibodies are associated with paraneoplastic opsoclonus-myoclonus-ataxia syndrome (POMAS), which presents with involuntary eye movements (opsoclonus), jerking movements of the limbs (myoclonus), and unsteady gait (ataxia). POMAS is also linked to small cell lung carcinoma but has a distinct clinical presentation from LEMS.

**Antibodies to NMDA-receptors** are associated with anti-NMDA receptor encephalitis, an autoimmune encephalitis that typically affects young women and may be associated with ovarian teratomas. Clinical features include memory deficits, psychiatric symptoms, seizures, movement disorders, dysautonomia, and decreased level of consciousness. This clinical presentation does not match the patient's findings.

**60. Holmes Adies pupils**

- Post viral degeneration in the ciliary ganglion
- Pupil is initially dilated with a tonic reaction to light and sectorial vermiform movements
- Pupil sphincter is impaired by accommodative spasm → Miosis (constricted)
- Holmes-Adie = Adie's pupil + hyporeflexia

**61. Myasthenia Gravis**

- Antibodies against post synaptic NMJ receptors - Nicotinic ACh receptors of Muscle specific tyrosine Kinase receptor (MuSK)
- Painless fatiguable, skeletal muscle weakness

Associations :

- Other autoimmune conditions - SLE, Rheumatoid arthritis
- HLA B8 & HLA DR3 gene
- Ocular myasthenia - HLA DR1
- 75% of cases associated with thymus abnormalities

Clinical Features :

- ophthalmoplegia
- Ptosis
- Diplopia
- Weakness of eyelid closure
- Muscle weakness - shoulder girdle, face, neck, limbs and trunk
- Loss of facial expression - myasthenia snarl
- Dysarthria
- Dysphagia
- Slurred speech
- Dysphonia - voice fading after continuous talking
- Breathing difficulty

Myasthenia crisis :

- precipitated by acute infection and medications such as Aminoglycosides ( gentamicin) and corticosteroids.
- Increasing muscle weakness
- Increasing double vision
- Hemodynamic instability

Investigations :

- ACh receptor and MuSK antibodies test
- TFT
- Gold standard - single fibre EMG

Management :

- Cholinesterase inhibitor - Pyridostigmine
- MMF, Azathioprine, Cyclophosphamide can be used
- Plasmapheresis & IVIG
- Rituximab

62. Multiple sclerosis - Polygenic inheritance

**63. Anterior Spinal Artery Occlusion :** supplies the anterior 2/3rds of the spinal cord.

- segments of the core in watershed areas : T2-T4 are at high risk of ischaemia.
- Sudden pain in back and distribution of the affected segment associated with b/l flaccid weakness and dissociated sensory loss
- Impaired pinprick sensation and temperature sensation below the level of lesion.
- Intact joint position and vibration sense.

**64. Carbon Monoxide poisoning- Roth spots :** white centred haemorrhages consisting of perivascular collection of lymphocytes.

Other causes of Roth spots are :

- Myeloma
- Trauma
- Hypoxia
- Anaesthesia
- Pre-eclampsia
- HIV retinopathy

Severe CO poisoning - cardiac arrhythmia, confusion, seizures, decreased consciousness levels, respiratory depression, death.

**65. Parietal lobe lesion :**

Unilateral parietal lobe signs :

- C/L hemisensory loss and sensory inattention
- Homonymous hemianopia inferior quadrantanopia
- Mild hemiparesis
- Abolition of optokinetic nystagmus

Unilateral - dominant parietal lobe (left parietal) -

- disorders of language : Alexia
- Agnosia
- Gerstmann syndrome : right left confusion, acalculia, agraphia, finger agnosia
- Ideomotor and ideational apraxia

Unilateral non-dominant parietal - right parietal lobe

- visuospatial dysfunction
- Constructional apraxia : cannot draw a circle or copy drawing
- Dressing apraxia
- Anosognosia

66. This is a case of variant Creutzfeldt-Jakob disease (vCJD).

- The typical presentation is that of a younger patient with progressive dementia (less rapid than the sporadic CJD) with myoclonus and, in the later stages, mutism and vertical upgaze palsy (found in 50%).
- An MRI brain reveals a characteristic 'hockey stick sign' where the pulvinar region and dorsomedial thalamus are hyperintense on T2-weighted imaging (or pulvinar sign where the pulvinar region is hyperintense only).
- CSF protein for 14-3-3 and periodic sharp wave complexes on the EEG are more commonly seen in sporadic CJD.

67. Paroxysmal hemicrania - type of trigeminal autonomic cephalgia - characterised by trigonal distribution of pain with cranial autonomic features.

MX : Indomethacin

68. Check IgA levels - before starting Immunoglobulin therapy for the likely diagnosis of Miller-Fish syndrome

Miller Fish syndrome : ophthalmoplegia + areflexia + ataxia

Anaphylaxis risk is very high in those patients with IgA deficiency.

69. Secondary causes of restless legs syndrome :

- IDA
- Folate deficiency
- Magnesium deficiency
- Amyloidosis
- Diabetes mellitus
- Pregnancy

Rx : Dopamine agonist - Ropinirole, Pramipexole,  
BZD - Clonazepam

#### 70. Pituitary apoplexy secondary to acute haemorrhage

- combination of sudden onset severe headache + bitemporal hemianopia —> pituitary apoplexy
- Often occurs with pituitary adenomas
- Elevated prolactin : indication that the normal hypothalamic inhibitory pathways which affects anterior pituitary prolactin secretion are damaged due to haemorrhage
- Hyponatremia - due to low ACTH secondary to direct corticotrophin producing cells - low cortisol —> low sodium levels;
- Hyponatremia can also be due to SIADH - preferential retention of water dilutes serum Na concentrations
- Low TSH —> direct damage by thyrotrophs due to haemorrhage
- Imaging : MRI Brain

71. Riluzole is a glutamate antagonist which has been shown to slow the progression of amyotrophic lateral sclerosis (ALS) and confer a survival benefit. The NICE guideline NG42 recommends offering riluzole to people with ALS to slow disease progression. It works by decreasing the release of glutamate, thereby reducing neuronal excitotoxicity, which is thought to play a role in the pathogenesis of ALS.

72. Ergot derivative dopamine agonists : Bromocriptine, Cabergoline, Pergolide, Lisuride - all causes **fibrosis due to their mechanism on 5-HT<sub>2B</sub> receptors**

Pergolide —> heart valvular disease

73. Stopping anti epileptic drugs (AED) can be considered if seizure free for >2 years and stopping drugs over 2-3 months

74. **Brachial neuritis** is characterized by acute onset unilateral severe pain followed by shoulder and scapular weakness several days later

75. Betahistine is a histamine analogue that works by improving the microcirculation and pressure of the inner ear, which helps to relieve symptoms associated with Meniere's disease such as vertigo, tinnitus, hearing loss and aural fullness. It is commonly used in the UK for the prophylaxis of this condition due to its effectiveness and relatively low side effect profile.

76. **Ondansetron** is a selective 5-HT<sub>3</sub> receptor antagonist. It works by blocking serotonin, both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone (CTZ) located in the area postrema of the medulla oblongata. The CTZ is outside of the blood-brain barrier, so it can respond to changes in blood chemistry as well as direct neural input from other parts of the brain. This makes it an important site for antiemetic drugs like ondansetron.

77. occlusion of the **right posterior inferior cerebellar artery**, causing lateral medullary syndrome (also known as Wallenberg syndrome). Symptoms of this syndrome include cerebellar signs (ataxia and dysarthria), contralateral paraesthesia, and ipsilateral Horner's syndrome due to the involvement of sympathetic pathways in the lateral medulla. Given that Horner's syndrome is on the right side, the patient has an occlusion of the right posterior inferior cerebellar artery.

78. NOD2/CARD15 mutations are associated with Crohn's  
**FXN** mutations are associated with **Friedreich's** ataxia  
**GLA** mutations with **Fabry** disease  
**SCN5a** mutations are associated with **Brugada** Syndrome.

79. Patients with degenerative cervical myelopathy can present with a number of problems [2]:

- Pain/stiffness: affecting the neck, upper and/or lower limbs. Lhermitte's sign is a sharp pain radiating down the spine on flexion of the neck, which is classically associated with multiple sclerosis, though it can occur in cervical myelopathy.
- Loss of function: Clumsiness (e.g. cant do shirt buttons, hold cup), leg weakness leading to impaired gait, imbalance and falls.

- Sphincter disturbance: this can range from frequency and urgency to incontinence.

Neurological examination can reveal lower motor neuron signs at the level of the lesion and upper motor neuron signs below. Note that neurological signs can be subtle and a high degree of suspicion is needed

80. A useful mnemonic to remember the features of Wernicke's encephalopathy is **CAN OPEN**

**C**onfusion

**A**taxia

**N**ystagmus

**O**phthalmoplegia

**P**eripheral

**N**europathy

81. GBS

Poor prognostic features

- age > 40 years
- poor upper extremity muscle strength
- previous history of a diarrhoeal illness (specifically *Campylobacter jejuni*)
- high anti-GM1 antibody titre
- need for ventilatory support

82. Hemiballistic chorea - sub thalamic nucleus

Dentate nucleus - ataxia

Red nucleus - tremor

Hippocampus - memory impairment

83. **Poliomyelitis**

- Caused by Poliovirus - enterovirus through feco-oral route
- Three countries have not eliminated polio - Nigeria, Pakistan, Afghanistan
- Naked ss RNA type of enterovirus

Clinical Features :

- Acute flaccid weakness
- Reduced motor function and tone of affected limb
- Reduced tendon reflexes of affected limb
- Atrophy of affected limb
- GIT - nausea, vomiting, abdominal pain, constipation, diarrhoea
- Bulbar paralytic poliomyelitis - respiratory muscle atrophy
- Aseptic viral meningitis - fever, headache, vomiting

Investigations :

- viral culture from CSF, stool and pharynx
- CSF - lymphocytosis & increased protein
- Antibodies to poliovirus

Management :

- prevention through vaccines : OPV and IPV - injection form
- Supportive management

**84. Frontotemporal dementia / Pick's disease / Frontal lobe dementia**

- two genes identified : both on chromosome 17
  - 1) microtubule associated protein tau (MAPT)
  - 2) progranulin (GRN)
- most common cause of genetic FTD → hexanucleotide repeat expansion in C9orf72
- Half of FTD cases are caused by tau pathology - Pick's bodies

Clinical features :

- alterations of behaviour, personality and social conduct
- Three variations :

Behavioural variant :

1. Loss of inhibition
2. Inappropriate social behaviour
3. Loss of motivation
4. Loss of empathy
5. Loss of sympathy
6. Repetitive or compulsive behaviours



7. Loss of control over eating and drinking
8. Lack of insight

O/E - no neurological signs

Semantic dementia :

1. Loss of vocabulary
2. Fluency of speech maintained
3. Asks for meaning of familiar words
4. Loss of recognition of familiar faces

Progressive non fluent aphasia :

1. Slow hesitant, difficult speech
2. Grammatical errors in speech
3. Loss of literacy skills

## 85. CNS tumors

- Glioblastoma - M/C : regional heterogeneity within a single lesion, highly anaplastic glial cells, vascular proliferation and thrombosis, necrosis.
- Glioblastoma - macroscopic : greyish ill defined mass, areas of necrosis & haemorrhage

Anaplastic Astrocytoma :

- Microscopic : astrocytes, nuclear atypic
- Macroscopic : white ill defined mass, extending into gyri

Meningioma :

- M/C : psammoma, psammoma bodies, sheets of spindle shaped cells
- Gross : rubbery, round lobulated mass, firmly attached to dura

Clinical Features :

- raised ICP due to mass effect
- Seizures

Pituitary tumors :

- acromegaly
- Cushing's disease due to excess ACTH

- Galactorrhea
- Hyperthyroidism due to increased TSH
- Visual field defects - bitemporal hemianopia - optic chiasma
- Headache
- Microadenomas < 10mm
- Macroadenomas > 10mm

#### 86. Parinaud syndrome

- vertical eye movements : bilateral control of cortex and upper brainstem
- Dorsal midbrain —> associated with failure of vertical gaze
- Parinaud syndrome - also associated with convergent nystagmus + mydriasis + impaired pupillary reflexes
- Upgaze affected more >>> than downsize

#### 87. Friedrich's ataxia

- autosomal recessive
- GAA repeat expansion of Frataxin gene - FXN gene which codes for Frataxin protein
- Spinocerebellar tracts, dorsal columns, pyramidal tracts, cerebellum, medulla

#### Clinical features :

- progressive ataxia - early sign
- Absence of deep tendon reflexes
- Spasticity
- Peripheral sensory neuropathy
- Dysarthria - early sign of disease
- Difficulty swallowing
- Muscle weakness
- Progressive kyphoscoliosis
- Pes cavus
- Hammer toes
- Heart - hypertrophic cardiomyopathy, myocardial fibrosis, CHF and cardiac arrhythmia - most common cause of death
- Pancreas - diabetes mellitus, impaired glucose tolerance
- Eyes - optic atrophy
- Hearing loss - later stages of disease

Mx : coenzyme Q10 and vitamin E - can slow progression

88. Juvenile myoclonic epilepsy - Levetiracetam in ages <55

89. Posterior Inferior Cerebellar artery supplies :

- 1) vestibular nucleus : nystagmus, vomiting
- 2) Inferior cerebellar peduncle : I/L limb ataxia
- 3) Spinothalamic tract : C/L loss of pain and temperature sensation in limb and torso
- 4) Spinal nucleus and tract of trigeminal nerve : I/L loss of pain and temperature sensations in face
- 5) Nucleus ambiguus - I/L laryngeal, pharyngeal and palatal paralysis - allows uvula to be pulled away from the side of lesion
- 6) Descending sympathetic fibers - I/L Horner syndrome

90. Lesion in medial medulla - **Dejerine syndrome**

- hypoglossal nucleus is damaged
- I/L deviation of tongue
- C/L weakness of limbs due to disruption of descending corticospinal fibers

91. Lesions which cause mixture of UMN + LMN signs -

- 1) Vitamin B12 deficiency
- 2) SCD
- 3) Tertiary syphilis - tabes dorsalis
- 4) Motor neuron disease
- 5) Friedrich's ataxia
- 6) Conus medullaris lesion
- 7) Diabetes mellitus

92. Mild to moderate liver disease - 2nd line anti epileptic :  
Levetiracetam - dose need not be changed

Severe liver disease - Levetiracetam dose is halved.

Lamotrigine - dose needs to be **severely reduced** in patients with liver disease - mild or moderate or severe.

Phenytoin & Sodium valproate - Contra indicated in liver disease

93. Asymmetrical tremors - suggestive of Idiopathic Parkinson's disease

Progressive supra nuclear palsy PSP - axial rigidity, falling backwards

Turning en bloc - feature of both idiopathic Parkinson's and PSP

#### 94. Peripheral neuropathy - predominantly motor

- GBS
- Porphyria
- Lead poisoning
- HSMN - Charcot Marie Tooth
- CIDP
- Diphtheria

Peripheral neuropathy - predominantly sensory

- diabetes
- Uraemia
- Leprosy
- Alcoholism
- Vitamin B12 deficiency
- Amyloidosis

Autonomic Neuropathy causes :

- diabetes
- GBS
- Multiple system atrophy, Shy Drager syndrome
- Parkinson's
- Infections - Chagas, HIV, Neurosyphilis
- Drugs : Anti hypertensives, tricyclics
- Craniopharyngioma
- Amyloidosis

95. Vestibulo-ocular reflex —> brainstem reflex to declare brainstem death

96. Transcortical motor aphasia - effortful, non fluent spontaneous speech

Preserved repetition

Preserved comprehension

Dominant inferior frontal region - Broca's area is although spared.

Right handed persons - left brain dominant

97. GBS - vital capacity measurement

98. **Visual field defects**

- bitemporal hemianopia : optic chiasma due to pituitary tumor / craniopharyngioma
- Central scotoma : effects of macular degeneration
- Inferior homonymous quadrantanopia : Parietal lobe
- Superior homonymous quadrantanopia : Temporal lobe

99. Lewy bodies - Parkinson's disease

Mallory bodies - alcoholic liver disease

Negri bodies - Rabies

Neurofibrillary tangles - Alzheimer's disease

Pick's bodies - neuronal tangles found in Pick's disease

100. Optic disc swelling —> enlarged blind spot  
Usually seen in Intracranial Hypertension

101. **Essential Tremors**

- postural, symmetrical tremor - affecting upper limbs, legs, jaw and head
- Autosomal dominant

Rest tremors - Parkinson's disease, drug induced Parkinson's

Postural tremor - occurs when limb is raised against gravity;  
physiological tremor, anxiety, alcohol, Wilson's disease

Action/Intention tremor - occurs during voluntary active movements; cerebellar disease

Mx : beta blocker - Propranolol

Alternative - Primidone - barbiturate

#### 102. Spinal Bulbar muscular atrophy - Kennedy Syndrome

- proximal weakness and cramps
- Wasting
- Fasciculations
- Weakness
- Hyporeflexia
- Perioral fasciculations \*\*\*
- **Androgen insensitivity** - gynecomastia , infertility
- X-linked recessive : CAG trinucleotide repeat

103. Creutzfeldt Jakob disease —> **diagnostic scan** —> Lumbar puncture - RT-QuIC peptide assay 95.8% sensitivity and 100% specificity for sporadic CJD diagnosis

104. Hypnagogic hallucinations - going to sleep.

Hypnopompic hallucinations - on waking up

Hallucinations - can be visual / tactile / auditory  
Feeling of levitations or out of body experience

105. Simvastatin - peripheral neuropathy

106. SCD of spinal cord - vit B12 deficiency - increased T2 weighted signal in posterior columns = dorsal columns

107. Verapamil & lithium - prophylaxis in cluster headache

### 108. Features of Lateral Medullary syndrome -

- vestibular nuclei : vomiting, vertigo, nystagmus
- Inferior cerebellar peduncle : I/L Cerebellar signs - ataxia, dysmetria, dysidiadochokinesia
- Central tegmental tract : palatal myoclonus
- Lateral spinothalamic : C/L loss of pain and temperature in body
- Spinal trigeminal nucleus & tract : I/I loss of pain and temperature from face
- Nucleus ambiguus - supplying vagus and glossopharyngeal nerve : I/L laryngeal, pharyngeal, and palatal hemiparalysis, dysphagia, hoarseness, diminished gag reflex
- Descending sympathetic fibers : I/L Horner syndrome

109. Topiramate - acute myopia and secondary angle closure glaucoma

**110. Optic Neuritis Treatment Trial - 50% will progress to MS if they have at least one MRI T2 lesion**

**Normal baseline MRI —> 25% chances of having MS**

### 111. Holmes Adie Syndrome

- neurological condition that causes pupil abnormalities - Holmes Adie pupil and absent deep tendon reflexes.
- Holmes Adie pupil : slow response to light but Normal accommodation reflex
- Causes : Trauma, auto immune, ciliary ganglion damage due to syphilis
- C/F : unilateral dilated pupil which constricts very slowly in response to light and loss of deep tendon reflexes.
- **Ross syndrome** : variant of Holmes-Adie pupil - triad of Holmes Adie pupil + loss of DTR - hypohidrosis.

**112. Inclusion body myositis** - muscle weakness of quadriceps and long finger flexors

Asymmetry of signs

Presents with falls

Serum CK normal

IBM most common in >50 years age

113. Cervical myelopathy - extrinsic cord compression - result of bony injury during a fall.

Bladder or bowel dysfunction commonly seen due to B/L UMN lesions.

114. **Multifocal Motor neuropathy - anti-GM1 antibodies**

Conduction block present

Causes progressive, asymmetrical and distal upper limb weakness

anti-GM1 can be seen in - GBS, multifocal Motor neuropathy MMN

115. Vasculitis neuropathies can occur secondary to -

- 1) cryoglobulinemia
- 2) Rheumatoid arthritis
- 3) Polyarteritis nodosa
- 4) Eosinophilic granulomatosis with polyangitis - Churg Strauss
- 5) SLE
- 6) Granulomatosis with Polyangitis

116. **Botulism**

Clinical features :

- blurred vision, diplopia, and ptosis secondary to CN III, IV and VI palsies
- Dysarthria and dysphagia due to oculobulbar weakness - cranial nerves IX, X and XII
- Symmetric descending paralysis
- Absent deep tendon reflexes
- Infants - hypotonia, weak cry, feeding difficulties
- Autonomic dysfunction - urinary retention, postural hypotension, dry mouth

117. **Ornithine Aminotransferase** - trophic of choroid and retina

Begins as a small yellowish spot and increases to a circular lesion edged with a pigment.



C/F - children —> myopia, decreased night vision, tunnel vision, and progresses to blindness

Decrease of this enzyme —> increased plasma levels of Ornithine

118. REM sleep disorder in Parkinsons's disease —> **Melatonin**

### **119. Syringomyelia**

Post-traumatic syringomyelia is a well-recognised long-term complication of extensive spinal cord injury.

Classically it causes sensory disturbance with a loss of pain and temperature sensation, out preservation of light touch (as seen here). The syrinx is a fluid-filled cyst existing in the central spinal cord, and compresses the anterior horn (lower motor neurones) and spinothalamic tract (pain and temperature sensation); this causes weakness (not evident here, as there was pre-existing weakness from the accident) and sensory disturbance.

Usually the dorsal columns (light touch and proprioception) are spared, but as the syrinx expands it may involve these tracts. It is not clear exactly why the syrinx develops, but possible causes include: liquefaction of intraparenchymal haematoma; ischaemia due to tethering; arterial or venous obstruction; release of intracellular lysosomal enzymes; and mechanical damage from cord compression. MRI is indicated to confirm the diagnosis, followed by a neurosurgical opinion to inform management.

### **120. Syringomyelia associated with Type 1 Chiari malformation**

Elongated cerebellar tonsils - displaced into upper cervical canal through the foramen magnum

121. Essential tremors —> Propranolol, Primodine, Topiramate

Propranolol - CI in asthma

Topiramate - CI in women of child bearing age

Primodine - Barbiturate - P450 inducer

122. Bell's palsy - hyperacusis and loss of lacrimation - when lesion occurs before geniculate ganglion

123. Cervical Dystonia - Botulinum toxin

Involuntary neck movements and episodic right torticollis  
Rx - 1st line —> Botulinum toxin injection

#### 124. **Multifocal motor neuropathy**

- Motor conduction block (MCB) diagnostic of MMN
- MCB : failure of nerve action potential to propagate across a segment of intact myelinated nerve fibre
- MCB —> reduction in amplitude and area of Compound muscle action potential after stimulation
- CMAP is normal distal to the affected segment
- MCB ==> ulnar and median nerves

#### 125. **Drugs for reducing relapse in Multiple Sclerosis :**

##### 1) **Natalizumab**

- recombinant monoclonal antibody
- Antagonist to alpha 4 - beta 1 integrin found on surface of leucocytes
- Inhibits migration of leucocytes across endothelium across the BBB
- IV administration

##### 2) **Ocrelizumab**

- anti CD20 monoclonal antibody
- IV administration

##### 3) **Fingolimod**

- sphingosine 1 phosphate receptor modulator
- Prevents lymphocytes from leaving the lymph nodes
- Oral formula available

##### 4) **Beta interferon**

- sub-Q / IM administration

##### 5) **Glatiramer acetate**

- immunomodulating drug
- Sub-Q administration

#### 126. **Cysticercosis**

- **larvae of pork tapeworm - Tania sodium**
- Contracted by ingestion of tapeworm eggs - usually contact with faces of human tapeworm carrier
- Once inside bowel —> eggs hatch and invasion into blood stream occurs with hematogenous spread to brain —> can cause seizures
- Cysts present in muscles can cause hard nodules
- X-ray of cysts —> radio-opaque lesions

### 127. **Spontaneous intracranial hypotension (SIH)**

- postural nature of headache —> lying flat relieves the headache
- Low CSF pressure headache —> commonly seen following lumbar puncture
- Lower limit of CSF pressure —> 10 cm H<sub>2</sub>O

Mechanism of SIH - insidious CSF leak that leads to low CSF pressure —> expressed clinically as orthostatic headache in association with one or more

#### **C/F of SIH :**

- nausea
- vomiting
- horizontal diplopia
- unsteadiness
- Vertigo
- Altered hearing
- Neck pain
- Stiffness of neck

Dx - confirm by measuring opening pressure of CSF

MRI - diffuse pachymeningeal enhancement, sagging of brain, tonsils descent, posterior fossa crowding

### 128. GBS - segmental demyelination

Occurs due to focal degeneration of the susceptible myelin sheath, leaving the underlying axon intact.

129. CADASIL - NOTCH3 gene on Chromosome 19q12

130. Global wasting of hand muscles - damage to T1 nerve root

131. Causes of unilateral ptosis -

- disinsertion of aponeurosis of elevator palpebrae superioris
- Horner syndrome
- Third nerve palsy

132. Bilateral internuclear ophthalmoplegia —> multiple sclerosis

133. Risk factors of Alzheimer's disease :

- Hypertension
- Obesity
- Family history \*\*\* most important
- Vascular risk factors - insulin resistance, dyslipidemia, obesity
- APOE4 genotype
- Traumatic brain injury
- Down's syndrome

134. **Phenytoin** - half life of 22 hours

Takes 5-14 days to reach steady state concentrations

Wait for 2 weeks after dose change to check serum Phenytoin levels

Clinically effective dose -> 3-4 mg/kg

135. **Binswanger's disease : cerebral white matter disorder**

- occurring in those with a multitude of vascular problems
- MRI : diffuse small occlusive vessel disease
- C/F : multiple TIAs or lacunar strokes
- Complications : dementia, pseudobulbar palsy and gait apraxia

Millard-Gubler syndrome : pontine brainstem syndrome

I/L CN VI palsy —> localises the lesion

Moya Moya disease : occlusive vasculopathy

Occlusion of terminal segments of intra cranial internal carotid arteries and extensive collateral vascularisation gives a typical hazy appearance on cerebral angiograms.

C/F : recurrent headache, recurrent TIA and seizures

### 136. Horner syndrome :

1st order neuron causes / central causes - anhidrosis of face, arm and trunk

- 1) syringomyelia
- 2) Multiple sclerosis
- 3) Encephalitis
- 4) Brain tumors
- 5) Lateral medullary syndrome

2nd order neuron / preganglionin - anhidrosis of face

- 1) cervical rib
- 2) Thyroid carcinoma
- 3) Thyroidectomy
- 4) Bronchogenic carcinoma
- 5) Trauma
- 6) Thoracic artery aneurysm

3rd order - no anhidrosis

- 1) cluster headache
- 2) Carotid artery dissection
- 3) Cavernous sinus thrombosis
- 4) Middle ear infection

### 137. Tourette syndrome - Risperidone

138. Downbeat nystagmus - lesion at foramen magnum —> Arnold Chiari malformation- downward gaze — oscillopsia of vision

Upbeat nystagmus —> brainstem lesion - lesion between midbrain and medulla

Brun's nystagmus : mild horizontal nystagmus in one direction of gaze and coarse horizontal nystagmus in opposite direction  
Brainstem compression —> cerebello pontine angle tumors

Convergence retraction nystagmus : Parinaud syndrome - dorsal midbrain lesions

Pendular nystagmus —> multiple sclerosis

139. Myasthenia gravis - 30mg QID for 2-4 days

140. Horizontal diplopia —> same side abducens palsy

141. Topiramate adverse effects- weight loss, renal stones, cognitive & behavioral changes

142. Middle Cerebral artery occlusion :

Superior division :

- dominant hemisphere : expressive aphasia
- C/L hemiparesis of face, hand, arm, relative sparing of leg
- C/L hemisensory loss in same distribution
- No homonymous hemianopia

Inferior division of MCA -

- C/L homonymous hemianopia
- Astereognosis and agraphesthesia on C/L side
- Lack of awareness - anosognosia
- Neglect and failure to recognise C/L side
- Neglect of C/L external space
- Dressing apraxia
- Constructional apraxia

143. Drugs worsening Myasthenia gravis :

- 1) D-penicillamine
- 2) Succinylcholine
- 3) Aminoglycosides
- 4) Fluoroquinolones
- 5) Quinidine, Procainamide
- 6) Propranolol
- 7) Lithium
- 8) Macrolides, Tetracyclines, Gentamicin, Quinolones

144. Variant CJD - Increased signal in pulvinar of thalamus

145. Myotonic dystrophy. This is a multisystem disorder, characterised by progressive muscle wasting and weakness. It is typically associated with myotonia (delayed relaxation of muscles after voluntary contraction), cataracts (which may explain the loss of red-reflex), heart conduction defects, endocrine changes such as insulin resistance leading to glycosuria, and central nervous system effects. The presentation of this patient with bilateral ptosis, loss of red reflex in both eyes, and glycosuria strongly suggests myotonic dystrophy.

146. Unilateral cerebellar lesions cause ipsilateral signs.

Useful and well-known mnemonic to remember symptoms of cerebellar disease is DANISH:

- D - Dysdiadochokinesia, Dysmetria (past-pointing), patients may appear 'Drunk'
- A - Ataxia (limb, truncal)
- N - Nystagmus (horizontal = ipsilateral hemisphere)
- I - Intention tremour
- S - Slurred staccato speech, Scanning dysarthria
- H - Hypotonia

### Causes

- Friedreich's ataxia, ataxic telangiectasia
- neoplastic: cerebellar haemangioma
- stroke
- alcohol
- multiple sclerosis
- hypothyroidism
- drugs: phenytoin, lead poisoning
- paraneoplastic e.g. secondary to lung cancer

## PASSTEST & PASSMEDICINE

### 1. **ADP inhibitors - drug interactions :**

- ADP inhibitors - Clopidogrel, Prasugrel, Ticagrelor, Ticlodipine
- MOA : Adenosine Diphosphate inhibitors - P2Y1 and P2Y12 inhibitors
- Aspirin 75 mg + Clopidogrel (75mg) / Prasugrel (10mg) / Ticagrelor (90mg) for 12 months followed by aspirin alone
- Ticagrelor - dyspnoea : due to reduced Adenosine clearance
- Clopidogrel x PPI - Omeprazole, Esmoprazole —> reduced anti platelet effect
- Absolute CI to Prasugrel use :
  1. Patients with prior stroke or TIA
  2. High risk of bleeding
  3. Prasugrel hypersensitivity
- Ticagrelor **contraindicated** in :
  - (a) patients with high risk of bleeding
  - (b) History of intracranial haemorrhage
  - (c) Severe hepatic dysfunction
  - (d) Caution in patients with Asthma/COPD - due to higher risk of dyspnea

### 2. **Adult ALS**

- compressions ratio to ventilation - 30 : 2
- Defibrillation :
  - A. Single shock —> pulseless VT / VF followed by 2 minutes CPR
  - B. Three successive shocks if in a monitored care unit
- Adrenaline 1mg - IM - non shockable rhythm
- Non shockable rhythms - asystole, PEA
- Shockable rhythms - adrenaline 1mg to be given after third shock
- Repeat adrenaline every 3-5 minutes
- Amiodarone 300mg : VF or pulseless VT after 3 shocks have been administered
- Amiodarone 150mg —> after 5 shocks



### 3. **Amiodarone**

- Class III anti-arrhythmic drug
- Treatment of atrial, nodal and ventricular tachycardias
- MOA : Blocks K channel —> inhibits repolarisation and prolongs action potential.
- Can also block sodium channels class Ia activity

#### Limitations :

- very long half life ; loading doses frequently used
- Central vein —> thrombophlebitis
- Prolongs QT interval — proarrhythmic drug
- P450 inhibitor

#### Adverse effects :

- thyroid dysfunction - hypothyroidism and hyperthyroidism
- Corneal deposit
- Pulmonary fibrosis, pneumonitis
- Liver fibrosis, hepatitis
- Peripheral neuropathy, myopathy
- Photosensitivity
- Slate grey appearance
- Thrombophlebitis and injection site reactions
- Bradycardia
- QT prolongation

### 4. **Antiplatelets : Guidelines**

- Acute coronary syndrome : Aspirin (lifelong) + Ticagrelor (12 months) ; Aspirin CI —> Clopidogrel lifelong
- PCI : Aspirin (lifelong) + Prasugrel / Ticagrelor ( 12 months)
- TIA : Clopidogrel (lifelong); 2nd line - Aspirin + Dipyridamole (both lifelong)
- Peripheral arterial disease : Clopidogrel (lifelong); 2nd line : Aspirin (lifelong)

### 5. **Aortic dissection - Complications**

- backward tear : Aortic regurgitation, aortic incompetence
- Backward tear can give rise to inferior MI - right coronary artery involvement

- Forward tear will give rise to unequal BP in arms, stroke, renal failure

## **6. Aortic Regurgitation**

- leaking of aortic valve in reverse direction during diastole
- Caused by either 1) disease of aortic valve; 2) dilation of aortic root and ascend aorta

AR due to valve disease :

- acute presentation —> infective endocarditis
- Chronic presentation :
  1. Rheumatic fever
  2. Calcific aortic valve disease
  3. Cognitive tissue disease - SLE, Rh arthritis
  4. Bicuspid aortic valve

**AR due to aortic root disease :**

- acute presentation - aortic dissection
- chronic presentation :
  - A. Bicuspid aortic valve
  - B. Spondyloarthropathies
  - C. Hypertension
  - D. Syphilis
  - E. Collagen : Marfan's, Ehler-Danlos

Clinical Features :

- 1) early diastolic murmur - increased intensity with handgrip manoeuvre
- 2) Collapsing pulse
- 3) Wide pulse pressure
- 4) Quincke's sign - nailbed pulsation
- 5) De Musset's sign - head bobbing
- 6) Austin flint murmur - severe AR - mid diastolic murmur : due to partial closure of anterior mitral valve cusps caused by regurgitation streams

MX : Surgery of aortic valve if patient is symptomatic with severe AR (or) symptomatic with severe AR + LV systolic dysfunction

## 7. Aortic Stenosis

Clinical Features :

- chest pain
- Dyspnoea
- Pre syncope
- Syncope
- Murmur - ESM; radiates to carotid
  
- narrow pulse pressure
- Slow rising pulse
- Delayed ESM
- Absent S2
- S4 present
- Thrill
- LVH can be LV failure
  
- <65 years : degenerative calcification
- > 65 years : bicuspid aortic valve
- William's syndrome - supraaortic stenosis
- Post rheumatic disease
- Subaortic - HOCM

## 8. Arrhythmogenic Right Ventricular Cardiomyopathy

- autosomal dominant
- Right ventricular myocardium replaced by fibrofatty tissue
- Mutation of gene encoding desmosome protein

C/F : palpitations, syncope, sudden cardiac death

- INV : ECG abnormalities in V1-V3 : T wave inversions.
- Epsilon wave in 50% of patients - terminal notch in QRS complex
- ECHO - enlarged, hypokinetic right ventricle with thin free wall
  
- Mx : Sotalol, Catheter ablation to prevent V-tac; implantable cardioverter-defibrillator

NAXOS DISEASE : Autosomal recessive variant of ARVC  
ARVC + Palmoplantar keratosis + woolly hair

## 9. Atrial Fibrillation

- **Rate control** : beta blocker (or) rate limiting calcium channel blocker
- Beta-blocker / Diltiazem / Digoxin
- Rhythm control : pharmacological or cardioversion
- Cardioversion - highest risk of embolus formation at time of converting into sinus rhythm
- Used only in patients with short duration of symptoms <48 hours or be anti coagulated for a period of time before attempting cardioversion.
- CHA2 DS2 - VASc scoring

|                                                                   |
|-------------------------------------------------------------------|
| C - congestive heart failure : 1 point                            |
| H - hypertension : 1 point                                        |
| A2 - age $\geq$ 75 years : 2 points<br>age 65-74 years. : 1 point |
| D - Diabetes : 1 point                                            |
| S2 - prior stroke / TIA / thromboembolism : 2 points              |
| V - vascular disease - IHD and PAD : 1 point                      |
| S - female : 1 point                                              |

- score 0 = no treatment
- Score 1 = males : consider anticoagulation; females - no treatment
- Score 2 or  $> 2$  : anticoagulation
- patient in atrial fibrillation for  $> 48$  hours  $\rightarrow$  anticoagulation for 3 weeks before cardio version.
- Perform TOE transesophageal echo to r/o Left atrial appendage thrombus (LAA thrombus)
- A-fib  $> 48$  hours  $\rightarrow$  electrical DC cardio version

- High risk of cardio version failure (previous failure or AF recurrence) —> 4 weeks of **Amiodarone** / **Sotalol** before going for DC cardio version
- anticoagulation for 4 weeks after cardioversion.
- Pharmacological cardio version of A-fib :
  - A. Amiodarone
  - B. Flecainide
  - C. Other less used : Quinidine, Ibutilide, Propafenone

## 10. **Atrial Myxoma**

- most common primary cardiac tumor
- 75% occurs in left atrium - attached to fossa ovalis
- Females >>> males

Clinical features :

- dyspnoea
- Fatigue
- Weight loss
- PUO
- Clubbing
- Emboli
- Atrial fibrillation
- MDM - tumor plop
- ECHO : pedunculate heterogenous mass attached to fossa ovalis region of interatrial septum

11. **Ostium secundum** - associated with **Holt-Oram syndrome** : tri-phalangeal thumbs  
ECG - RBBB with Right axis deviation

**Ostium primum** - presents earlier than ostium secundum;  
associated with abnormal AV valves  
ECG : RBBB with LAD, prolonged PR interval

## 12. **AV block**

- 1) 1st degree heart block : prolong PR > 0.2 sec
- 2) 2nd degree heart block :

A. Type 1 - Mobitz type I - Wenkebach : progressive prolongation of PR interval until a dropped beat

B. Type 2 - Mobitz type II : PR interval constant, P wave not followed by QRS

3) 3rd degree heart block : no association between P wave and QRS complex

## 12. **Beta blockers**

### **Indications :**

- Angina
- Post MI
- Heart failure
- Arrhythmia
- Hypertension
- Thyrotoxicosis
- Migraine prophylaxis
- Anxiety

### **Adverse effects :**

- Bronchospasm
- fatigue
- Cold peripheries
- Sleep disturbances - nightmares
- Erectile dysfunction
- Cannot use while patient is on Verapamil - can give rise to complete heart block

13. Bicuspid aortic valve - associated with Left dominant circulation ( posterior descending arises from LCX and not RCA) and Turner's syndrome

Complications - AR, AS

High risk of aortic dissection and aneurysm formation of ascending aorta

14. Bivalirudin - reversible direct thrombin inhibitor

15. Features suggestive of VT and **not** SVT

1) AV dissociation

- 2) Fusion or capture beats
- 3) Positive QRS concordance in chest leads
- 4) Marked LAD
- 5) History of IHD
- 6) QRS > 160 ms
- 7) No response to adenosine or vagal manoeuvres

#### 16. **Brugada syndrome**

- autosomal dominant
- Cause of SCD
- SCN5A gene - encodes for myocardial sodium ion channel
- ECG : convex **ST segment elevation > 2mm** in >1 out of V1 - V3 chest leads followed by a **negative T wave inversion**
- Partial RBBB
- ECG changes more apparent after giving Flecainide or Ajmaline

#### 17. **Cardiac catheterisation & oxygen saturation levels**

- 70% oxygen saturations - RA, RV and PA
- LA, LV, aorta - 98-100%

Atrial Septal Defect :

- RA, RV, PA - 85% oxygen
- LA, LV, Aorta - 100 % oxygen

Ventricular septal defect : oxygenated blood mixed in RV and RV onwards increased saturation

- RA : 70% oxygen
- RV, PA - 85% oxygen
- LA, LV, Aorta - 100% oxygen

Patent Ductus arteriosus : higher pressure aorta with lower pressure PA

- RA, RV : 70%
- PA - 85%
- LA, LV, Aorta 100%

VSD with Eisenmenger's :

- RA, RV, PA : 70%

- LA : 100%
- LV, Aorta - 85%

PDA with Eisenmenger's :

- RA, RV, PA - 70%
- LA, LV - 100%
- Aorta - 85%

ASD with Eisenmenger's :

- RA, RV, PA - 70%
- LA, LV, Aorta - 85%

### 18. **Cardiac Tamponade**

- Beck's triad : hypotension + raised JVP + muffled heart sounds
- Other C/F : dyspnea, tachycardia, absent Y wave on JVP due to limited RV filling, pulses paradoxus, Kussmaul's sign
- ECG - electrical alternans
- Mx ; urgent pericardiocentesis

### 19. **Cardiomyopathies:**

1) Hypertrophic Obstructive cardiomyopathy HOCM

- SCD in young athletes
- Mutation in gene encoding **Beta-myosin heavy chain**
- ECHO - MR, Systolic anterior motion (SAM) of anterior mitral valve
- Asymmetric septal hypertrophy

2) **Arrhythmogenic right ventricular dysplasia**

- RV myocardium replaced by fibrofatty tissue
- Mutation in gene encoding for **desmosome**
- ECG : T wave inversion in V1 - V3
- Epsilon wave - terminal notch in QRS complex

Dilated Cardiomyopathy - causes :

- 1) Alcohol
- 2) Coxsackie B virus
- 3) Wet beri beri
- 4) Doxorubicin



Restrictive cardiomyopathy - causes :

- 1) amyloidosis
- 2) Post radiotherapy
- 3) Loeffler's endocarditis

Acquired Cardiomyopathy :

- 1) Peripartum cardiomyopathy —> late month of pregnancy to 5 months postpartum; common with multiple pregnancies
- 2) Takotsubo cardiomyopathy —> stress induced cardiomyopathy; patient develops chest pain and heart failure. Apical ballooning of myocardium.

Secondary cardiomyopathies :

1. Infective : Coxsackie B virus, Chagas disease
2. Infiltrative - amyloidosis
3. Storage : Hemochromatosis
4. Toxicity - Doxorubicin, Alcoholic
5. Endocrine - DM, Thyrotoxicosis, Acromegaly
6. Inflammatory - Sarcoidosis
7. Neuromuscular - Friedrich's ataxia, DMD, Myotonic dystrophy
8. Nutritional deficiencies : Wet beri beri
9. Autoimmune - SLE

20. Catecholaminergic polymorphic VT - autosomal dominant, causes SCD.

Autosomal dominant —> Defect in Ryanodine receptor RYR2 in the myocardial sarcoplasmic reticulum

Autosomal recessive forms may be present which involves mutation of calsequestrin 2 gene

C/F - exercise or emotion induced Polymorphic VT causing syncope, SCD

Mx - Beta blockers, Implantable cardioverter-defibrillator

21. Central acting anti-hypertensives :

- methyldopa - pregnancy hypertension

- Monoxidine - essential hypertension resistant to conventional treatment
- Conidine - alpha-2 receptors in the vasomotor centre.

## 22. Chest pain - evaluation

- Current chest pain / chest pain < 12 hours + abnormal ECG = emergency admission
- Chest pain 12-72 hours = same day hospital admission
- Chest pain > 72 hours = ECG and troponin measurement before deciding action

## 23. Cholesterol embolism : eosinophilia, purpura, renal failure, livedo reticularis

## 24. Chronic heart failure - Management :

### First line therapy -

- Beta blocker + ACE inhibitor
- Beta blockers - Carvedilol, Bisoprolol, Nebivolol
- Both have **no effect on mortality with Preserved EF**

### Second line therapy -

- Aldosterone antagonist
- Spironolactone, Eplerenone
- ACE inhibitors and Aldosterone antagonists → hyperkalemia - monitor K

### SGLT-2 inhibitors -

- reduce glucose reabsorption, increases glucose excretion urinary
- Canagliflozin, Dapagliflozin, Empagliflozin
- Reduces hospitalisation secondary to heart failure and CV death

### Third Line therapy -

- Ivabradine, Sacubitril-valsartan, hydralazine in combination with nitrate, digoxin, and cardiac resynchronisation therapy
- Ivabradine - used if PR > 75 bpm & LVEF < 35 %;
- Sacubitril-Valsartan : LVEF < 35%, initiated following ACEi or ARB wash-out period
- Digoxin : indicated only if co-existent atrial fibrillation present

- Hydralazine + nitrate → Afro-Caribbean patients

Cardiac resynchronisation therapy : for patients with heart failure and wide QRS; biventricular pacing,.  
Reduces hospitalisation in NYHA Class III patients.

## 25. Congenital Heart Disease - types

Acyanotic heart disease

- VSD
- ASD
- PDA
- Coarctation of aorta
- Aortic valve stenosis

Cyanotic :

- TOF
- Transposition of great arteries
- Tricuspid atresia

## 26. Dabigatran

- licensed for use for prevention of stroke in patients with **non-valvular a-fib** with the following R/F -
  - A. Previous stroke / TIA / systemic embolism
  - B. LVEF < 40 %
  - C. NYHA class 2 or above
  - D. Age > 75 years
  - E. Age > 65 years + DM / HTN/ CAD

Dabigatran major adverse effect - **haemorrhage**

**Reversal** of Dabigatran : **Idarucizumab** - rapid reversal

## 27. Diabetes & Hypertension

- T1DM : 135/85 is target BP

- T1DM + albuminuria or 2 or more than 2 features of metabolic disorder - 130/80
- ACEi and ARBs → renoprotective function
- ARBs - preferred for Afro-Caribbean individuals
- Beta blockers not used in uncontrolled hypertension as when beta blockers + thiazides (not preferred) → **insulin resistance, impairs insulin secretion & alters autonomic response to hypoglycaemia**

**28. Dipyridamole** - inhibits Phosphodiesterase → elevates cAMP levels → reduced intracellular Ca levels  
Also reduced cellular uptake of adenosine and inhibition of thromboxane synthesis

### 29. DVLA & Cardiology disease

- Hypertension - SBP >180 or DBP >100 - disqualified from driving Group 2 vehicles
- Angioplasty - 1 week
- ACS - 4 weeks
- Pacemaker - 1 week
- ICD insertion - for ventricular arrhythmia : 6 months; prophylactic ICD → 1 month
- ICD - permanent ban for Group 2 drives
- Catheter ablation for arrhythmia - 2 days
- Aortic aneurysm ≥6cm → notify DVLA
- Aortic aneurysm ≥6.5 cm disqualified from driving
- Heart transplant - no driving for 6 weeks, no need to notify DVLA

### 30. ECG - Axis deviation

Left axis deviation :

- left anterior hemiblock
- LBBB
- Inferior MI
- WPW syndrome - right sided accessory pathway
- Hyperkalemia
- Ostium primum ASD, Tricuspid atresia
- Minor LAD in obese people

Right axis deviation :

- right ventricular hypertrophy
- Left posterior hemiblock
- Lateral MI
- CLD - cor pulmonale
- Pulmonary embolism
- Osmium secundum ASD
- WPW - left accessory pathway
- Minor RAD in tall people

### ECG - Coronary arteries :

| Portion of heart | ECG changes         | Coronary artery          |
|------------------|---------------------|--------------------------|
| Anteroseptal     | V1 - V4             | Left anterior descending |
| Anterolateral    | II, III, aVF        | Right coronary           |
| Lateral          | I, aVL, +/- V5 - V6 | Left circumflex          |
| Posterior        | V1 - V3 changes     | LCX / RCA                |

Reciprocal changes of STEMI are seen - Posterior MI:

- horizontal ST depression
- Tall broad R waves
- Upright T waves
- Dominant R wave in V2

Posterior infarct confirmed by ST elevation and Q waves in posterior leads (V7 - V9)

### ECG - Digoxin

- down sloping of ST segment - never tick sign or scooped out sign
- Flattened / inverted T waves
- Short QT interval
- AV block, bradycardia
- LBBB

### ECG - Hypokalaemia

- U waves
- Small or absent T waves
- Prolonged PR interval
- ST depression
- Long QT

ECG - hypothermia

- bradycardia
- J wave - Osborne waves - small hump at the end of QRS
- 1st degree heart block - PR prolongation
- Long QT
- Atrial and ventricular arrhythmia

ECG : Prolonged PR interval

- IHD
- Digoxin toxicity
- Hypokalaemia
- Rheumatic fever
- Aortic root pathology - abscess secondary to IE
- Lyme disease
- Sarcoidosis
- Myotonic dystrophy

Short PR interval —> WPW syndrome

31. Eisenmenger's syndrome

- Reversal of L—>R shunt in congenital heart defect due to pulmonary hypertension.
- Uncorrected L—>R shunt causes remodelling of pulmonary vasculature —> obstruction to pulmonary blood and pulmonary hypertension
- Ass. With - 1) VSD 2) ASD 3) PDA
- C/F : cyanosis, clubbing, RVF, hemoptysis, embolism, disappearance of original murmur

## 32. **Heart Failure**

Systolic dysfunction :

1. Ischaemic heart disease
2. Dilated cardiomyopathy
3. Myocarditis

#### 4. Arrhythmias

Diastolic dysfunction :

1. HOCM
2. Restrictive cardiomyopathy
3. Cardiac tamponade
4. Constrictive pericarditis

High output cardiac failure :

- anaemia
- AV malformation
- Paget's disease
- Pregnancy
- Thyrotoxicosis
- Wet beri beri

### 33. Heart Sounds

S1

- closure of mitral and tricuspid valves
- **Soft S1** : prolonged PR, MR
- **Loud S1** : MS, Left to right shunt, short PR interval, atrial premature beats, hyper dynamic states

S2

- Closure of aortic and pulmonary valves
- Soft S2 : aortic stenosis
- Splitting of S2 during inspiration is normal

S3

- due to diastolic filling of ventricle
- Heard in LVF (dilated cardiomyopathy), constrictive pericarditis (pericardial knock) and mitral regurgitation.

S4

- aortic stenosis, HOCM, Hypertension
- Atrial contraction against stiff ventricle - coincides with P wave on ECG
- HOCM - double apical impulse due to a palpable S4

S2 characteristics :

S2 is caused by closure of aortic valve followed by pulmonary valve

- splitting of S2 increased by deep inspiration - normal finding.

- Soft S2 - **aortic stenosis**
- Loud S2 -
  1. **Hypertension**
  2. **hyper dynamic states**
  3. **ASD w/o pulmonary hypertension**
- Fixed split in the middle : **Atrial septal defect**
- **Widely split S2 :**
  - Deep inspiration
  - Pulmonary stenosis
  - Severe MR
  - RBBB
- Reversed / Paradoxical split { P2 occurs before A2 }
  - LBBB
  - Severe AS
  - Right ventricular pacing
  - WPW - type B — causes early P2
  - PDA

34. **Hydralazine** : increased cGMP causing smooth muscle cell contraction.

Contraindicated in SLE, CVA, IHD

Adverse effects :

- tachycardia
- Palpitations
- Flushing
- Fluid retention



- Headache
- Drug induced lupus

### 35. **Xanthomas** :

- 1) Palmar xanthoma —> remnant hyperlipidemia
- 2) Eruptive Xanthoma : familial hypertriglyceridemia, Lipoprotein lipase deficiency
- 3) tendon xanthoma, tuberous xanthoma, xanthelasma - familial hypercholesterolemia, remnant hyperlipidemia

Xanthelasma - yellowish papule and plaques caused by localised accumulation of lipid deposits on the eyelid.

Mx : surgical excision / topical trichloroacetic acid / laser therapy / electrodesiccation

### 36. Infective ENDocarditis :

Poor prognostic factors :

- Staph aureus infection
- Prosthetic valve - especially early, infection acquired during surgery
- Culture negative endocarditis
- Low complement levels

Staphylococci - 30% mortality

Bowel organism - 15%

Streptococci - 5%

Management - Antibiotics :

- 1) Initial blind therapy
  - native valve : Amoxicillin + low dose Gentamicin
  - Penicilin allergic / MRSA / severe sepsis : Vancomycin + low dose gentamicin
  - Prosthetic valve : Vancomycin + Rifampicin + low dose gentamicin

2) Native valve endocarditis caused by Staphylococci :

Flucloxacillin

Penicillin allergic / MRSA : Vancomycin + Rifampicin

3) Prosthetic valve endocarditis caused by Staphylococci :

Benzylpenicillin

Penicillin allergic / MRSA : Vancomycin + Rifampicin + Low dose gentamicin

4) Endocarditis by sensitive species of Strep. Viridian :

**Benzylpenicillin**

Penicillin allergic : Vancomycin + Low dose Gentamicin

5) Endocarditis by less sensitive Streptococci : **Benzylpenicillin + low dose gentamicin**

Penicillin allergic : **Vancomycin + Low dose Gentamicin**

### **Surgery - indications :**

1. Severe valvular incompetence
2. Aortic abscess - indicated by a lengthened PR interval
3. Infections resistant to Abx and anti-fungals
4. Cardiac failure refractory to standard medical treatment
5. Recurrent emboli after antibiotic therapy

### **37. Jugular Venous Pressure**

- non pulsatile JVP : **SVC obstruction**
- Kussmaul's sign - paradoxical rise of JVP - **Constrictive pericarditis**
- **A wave** : atrial contraction
- Large a wave : increased atrial pressure -> tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- Cannon a wave : due to atrial contractions against closed tricuspid valve; seen in : Complete heart block, V-tac, ventricular ectopics, nodal rhythm, single chamber ventricular pacing
- C wave : closure of tricuspid valve
- V wave : passive filling of blood in right atrium against a closed tricuspid valve

- Tricuspid regurgitation - large v waves
- x descent : fall in atrial pressure during ventricular systole
- Y descent : opening of tricuspid valve

### 38. Kawasaki Disease :

- Type of vasculitis seen in children

Clinical features :

- high grade fever > 5 days; resistant to antipyretics
- Conjunctival injection
- Bright red, cracked lips
- Strawberry tongue
- Cervical lymphadenopathy
- Red palms and soles - which later peel

Mx : High dose aspirin, IVIG

Screening - ECHO for coronary artery aneurysm

39. **Long QT syndrome** - inherited conditions associated with delayed repolarization of ventricles.

- common defects are LQT1 and LQT2 gene mutations - affects the slow delayed rectifier potassium channels
- LQT1 : Exertional syncope - swimming
- LQT2 : emotion / exercise / auditory stimuli
- LQT3 : at rest or at night

Causes :

- Congenital :
  1. Jervell-Lange-Nielsen syndrome : includes deafness
  2. Romano Ward syndrome - no deafness
- Drugs
  - Amiodarone, Sotalol
  - Class Ia anti arrhythmic
  - TCA, SSRI - Citalopram
  - Methadone
  - Chloroquine

- Terfenadine (nasal decongestant)
- Erythromycin
- Anti psychotics - Haloperidol
- Ondansetron

- Hypocalcemia, Hypokalaemia, Hypomagnesemia
- Acute MI
- Myocarditis
- Hypothermia
- SAH

Mx : Beta blockers, Implantable CD

#### 40. **Loop diuretics - Adverse effects :**

- 1) Hypotension
- 2) Hyponatremia
- 3) Hypokalaemia
- 4) Hyomagnesemia
- 5) Hypocalcemia
- 6) Hypochloraemic alkalosis
- 7) Ototoxicity
- 8) Renal impairment - dehydration + direct toxic effect
- 9) Hyperglycaemia
- 10) Gout

#### 41. Ebstein's anomaly abnormalities -

- adherence of septal and posterior leaflets of tricuspid valve to underlying myocardium
- Downward (apical) displacement of functional annulus of tricuspid valve
- Dilation of atrialised right ventricle with varying degree of hypertrophy and thinning of wall
- Redundancy, fenestration and tethering of anterior leaflet of tricuspid valve
- Dilation of right atrioventricular junction

#### 42. **Pericarditis**

Four temporal stages of ECG in pericarditis -

- 1) Stage I : diffuse concave upward ST segment elevation with concordance of T waves
- 2) ST segment depression in aVR or V1, PR depression, low voltage, absence of reciprocal ST segment changes
- 3) Stage II : ST segments returns to baseline, T wave flattening
- 4) Stage III : T wave inversion
- 5) Stage IV : gradual resolution of T wave inversion

43. **Clopidogrel** is a **prodrug** which requires conversion into its active form by the liver enzyme **CYP2C19**. **Omeprazole**, a proton pump inhibitor (PPI), **inhibits** this enzyme and therefore can reduce the effectiveness of clopidogrel. This interaction has been associated with an increased risk of adverse cardiovascular events. UK guidelines recommend that patients requiring both clopidogrel and a PPI should be prescribed **pantoprazole** or **lansoprazole** instead, as these do not interact.

44. **Moxonidine** is a centrally acting antihypertensive drug, which works by stimulating imidazoline receptors in the brain. This stimulation results in reduced sympathetic outflow from the central nervous system, leading to decreased vascular resistance and lower blood pressure. It's mainly used for treating essential hypertension when other treatments are not sufficient or are contraindicated.

45. The key diagnostic tests used to identify patients likely to benefit from cardiac resynchronization therapy is the **transthoracic echocardiogram** and **ECG**.

Those with left ventricular ejection fractions of <35% and a LBBB (QRS duration greater than 120 ms) on ECG are excellent candidates for CRT (biventricular pacing). The echo will show asynchronous contraction of the LV and RV and subsequently reduced ejection fraction.

Biventricular pacing improves quality of life and exercise tolerance amongst other endpoints, and does so by ensuring that the ventricles contract at the same time (resynchronization) due to asynchronous stimulation (LBBB causing asynchronous activation) via the conduction system.

A transoesophageal echo is **not** required.

46. Prinzmetal angina - treatment = dihydropyridine calcium channel blocker FELODIPINE

#### 47. **Murmurs**

Systolic murmurs -

Ejection systolic -

Louder on inspiration : Pulmonary stenosis, Atrial septal defect

Louder on expiration : Aortic stenosis, HOCM

Ejection systolic murmur - Tetralogy of Fallot

Pansystolic - MR, TR, VSD

MR - high pitched, blowing in quality

TR - increases on inspiration

VSD - harsh in character

Late systolic murmurs : MVP, Coarctation of aorta

Diastolic murmurs -

Early diastolic : Aortic regurgitation, Graham Steel murmur

AR murmur - high pitched, blowing

Graham steel murmur - pulmonary regurgitation - high pitches, blowing

Mid-Late Diastolic murmur : Mitral stenosis, Austin flint murmur

Mitral stenosis - rumbling character

Austin FLint murmur - severe AR , rumbling

Conitnous machinery like - PDA

48. Myocardial infarction - complications :

- Cardiac arrest - due to ventricular fibrillation; most common cause of death following MI
- Cardiogenic shock : large part of ventricular myocardium damaged, left ventricular free wall rupture

- Chronic Heart Failure : Loop diuretics - Furosemide will decrease fluid overload. ARBs and Beta-blockers —> improve prognosis of patients with CHF
- Bradyarrhythmias - AV block following Inferior wall MI
- Pericarditis : first 48 hours following transmural MI is common.
- Dressler's syndrome - 2-6 weeks after MI; autoimmune reaction against antigenic proteins as the myocardium recovers. C/F : fever + pleuritic pain + pericardial effusion and raised ESR. Mx - NSAIDs
- Left ventricular aneurysm : associated with persistent ST elevation and left ventricular failure. Thrombus may form within the aneurysm increasing the risk of stroke.
- Left ventricular free wall rupture - 1-2 weeks afterwards; presents with acute heart failure secondary to cardiac tamponade - based JVP, pulses paradoxus, diminished heart sounds. Mx - urgent pericardiocentesis and thoracotomy
- Ventricular septal defect : rupture of inter ventricular septum occurs in the first week; C/F : acute heart failure associated with PSM.
- Acute MR - infero-posterior infarction; due to ischaemia or rupture of papillary muscle. C/F - acute hypotension, pulmonary edema. Early to mid systolic murmur.

49. MI secondary prevention : Dual antiplatelet therapy + ACEi + Beta blocker + statin

Sexual activity -> after 4 weeks

Avoid PDE5 inhibitors with Nitrates or Nicorandil.

Post acute coronary syndrome and is medically managed :  
Ticagrelor + Aspirin —> stop Ticagrelor after 12 months.

Post PCI : Prasugrel / Ticagrelor + Aspirin, stop second antiplatelet after 12 months

Patients who had acute MI + symptoms and/or signs of heart failure and reduced LV systolic function —> Add aldosterone antagonist (Eplerenone)

Start Eplerenone : 3-14 days after MI , after starting ACEi therapy

STEMI - no access to higher centre —> thrombolysis

STEMI access to higher centre —> PCI

Thrombolysis - tissue plasminogen activator (tPA) >>>  
streptokinase  
Tenecteplase and Alteplase

Perform ECG within 90 minutes of thrombolysis to assess if there has been a > 50% reduction in the ST elevation

No adequate resolution of ST elevation —> go for rescue PCI

Dose adjusted insulin infusion with regular monitoring of glucose levels to below 11 mmol/ L

#### 50. Pacemaker

- LBBB —> ventricular dis-synchrony
- Ventricular dis-synchrony can impair ventricular function and heart failure
- Cardiac Resynchronisation therapy : involves simultaneous pacing of both ventricles (biventricular or BiV pacing) using a biventricular pacemaker.
- Leads are placed in right atrium, left atrium, and left ventricle.
- CRT can help improve pump performance, reduce functional mitral regurgitation, reverse the deleterious process of ventricular remodelling in patients with heart failure.

#### 51. Atrial Fibrillation

- A-fib is supra ventricular tachycardia - ass. With irregular disorganised electrical atrial activity, ineffective contraction of atria, and chaotic firing of AV node causing irregular contraction of ventricles.
- **Paroxysmal AF** - recurrent episodes lasting longer than 30 seconds, self termination, duration less than 7 days
- Persistent AF - episodes lasting longer than 7 days or less than 7 days requiring drugs / cardioversion
- Permanent AF - fails to terminate using cardioversion or relapses after termination within 24 hours



### Clinical Features :

- SOB
- Palpitations
- Tachycardia / bradycardia
- Syncope
- Dizziness
- Chest pain
- Irregularly irregular pulse
- ECG - loss of p wave s/o irregular ventricular rhythm

### Mx guidelines for A-fib :

- patients with A-fib for < 48 hours and hemodynamically unstable :
  1. Hemodynamically unstable signs include : SBP < 90, HR > 150, breathlessness, LOC, chest pain, palpitations, syncope
  2. Vagal manoeuvre can be tried initially - Valsalva manoeuvre, carotid sis massage
  3. Pharmacological conversion - Amiodarone, Flecainide
  4. **Flecainide** - used if no structural heart disease
  5. Urgent rate control - beta blocker (**not stall**) & Verapamil may be used IV
- patients with symptoms of A-fib for > 48 hours
  - A. Rate control is preferred
  - B. Beta blockers ( not sotalol ) , diltiazem , verapamil - 1st line
  - C. Two drug therapy can be used if monotherapy fails
  - D. Electrical cardioversion preferred
  - E. Rhythm control - beta blocker - 1st line
  - F. Rhythm control - 2nd line - AMiodarone / Dronaderone - these become 1st line in patients with heart failure or left ventricular impairment
  - G. Pill in pocket approach (PRN Rx) - for paroxysmal AF
- Anticoagulation : CHA2 DS2 VASc score
- Risk of bleeding - ORBIT score

\*\* oral Amiodarone - long half time and takes a long time to achieve loading —> cant be used for PRN approach pocket in pill

\*\* Flecainide - contra indicated in patients with impaired ventricles after MI

52. **Fondaparinux** - activates **antithrombin III**, inhibition of coagulation factors Xa; Sub-Q administration

Bivalirudin - direct thrombin inhibitor - IV administration

Dabigatran - direct thrombin inhibitor - taken orally

### 53. **Patent Ductus arteriosus**

- Abnormal connection between aorta and pulmonary trunk
- Commonly seen in babies of high altitude and maternal rubella infection in 1st trimester
- Acyanotic heart disease
- Later can become cyanotic - differential cyanosis of peripheral extremities

Clinical features :

- left subclavicular thrill
- Continuous machinery murmur
- Large volume, bounding, collapsing pulse
- Wide pulse pressure
- Heaving apex beat

Mx : Indomethacin / Ibuprofen - inhibits the PG synthesis and closes the connection.

Prostaglandin E1 can be used to keep the connection open when associated with other heart defects for surgery later date.

### 54. Bradycardia

- Atropine - 500 mcg IV
- Repeat Atropine upto 3mg
- Transcutaneous pacing
- Isoprenaline / Adrenaline infusion as alternatives
- Isoprenaline 5mcg / min IV
- Adrenaline 2-10 mcg /min IV
- Seek specialist advice

- Arrange transvenous pacing

Risk factors for asystole :

- complete heart block with broad complex QRS
- Recent asystole
- Mobitz type II AV block
- Ventricular pause > 3 seconds

Tachycardia

Broad complex tachycardia -

Regular Broad complex : assume ventricular tachycardia unless previously confirmed SVT with Bundle branch block

Mx - loading dose Amiodarone 300mg f/b 24 hour infusion

Irregular broad complex : seek expert help

Possibilities include - A-fib with Bundle branch block, a-fib with ventricular pre-excitation, torsades de pointes

Torsades de pointes —> 2g Magnesium over 10 minutes

Narrow Complex tachycardia :

Regular : Vagal manoeuvre followed by Adenosine.

Adenosine : 6 —> 12 —> 18

If ineffective - alternatives include Verapamil / beta blockers.

Unsuccessful - consider Atrial flutter and rate control with beta-blockers

Irregular : onset < 48 hours —> electrical or chemical cardioversion

Rate control : beta blockers are first line

55. Peripheral arterial disease - uncommon drugs used

- 1) Naftidrofuryl oxalate - vasodilator used in patients with poor quality of life

2) Cilostazol : PDE III inhibitor - both antiplatelet and vasodilator effects - not recommended by NICE

## 56. Pulmonary Arterial Hypertension

- Progressive exertion dyspnoea is the classical presentation
- Exertion syncope
- Exertion chest pain
- Peripheral edema
- Cyanosis

Mx :

- acute vasodilator testing should be done first to decide on appropriate management strategy
- Positive response to acute vasodilator testing : **Oral CCBs.**
- Negative response to acute vasodilator testing :
  - A. Prostacycline analogues : **Treprostinil, Iloprost**
  - B. Endothelial receptor antagonist : **Bosentan** (non selective)
  - C. Selective Endothelial receptor A antagonist : **Ambrisentan**
  - D. **Phosphodiesterase inhibitor** : Sildenafil

## 57. Pulses

Pulsus paradoxus : greater than normal ( $>10\text{mm Hg}$ ) fall in BP during inspiration

Faint or absent pulse on inspiration

Dx - severe asthma, cardiac tamponade

Slow rising pulse / plateau pulse : aortic stenosis

Collapsing pulse : aortic regurgitation, PDA, Hyperkinetic state - anaemia, thyroid excess, fever, exercise ,pregnancy

Pulsus alterans : regular alteration of the force of arterial pulse  
Seen in severe LVF

Bisferiens pulse : double pulse two peaks in systole  
Seen in mixed aortic valve disease  
Can also be seen in HOCM

## Jerky pulse - HOCM

58. Nitrates adverse effects : prolonged erection, headache, heart burn, flushed skin, sudden onset hearing loss

Nicorandil - anti anginal medication - dual properties of nitrate and potassium channel activator.

Arterial and venous dilator

Promotes K efflux

NOT to be used with Sildenafil.

59. Cardiac enzyme affected early on in myonecrosis : specific to cardiac muscle —> glycogen phosphorylase isoenzyme BB, increased 1-3 hours after myocardial event.

## 60. **Anterior infarction complications :**

- late VT / VF
- Left ventricular aneurysm
- Left ventricular thrombus and systemic embolism
- Complete heart block
- Ischaemic MR
- CCF
- VSD with septal rupture

Inferior infarction complications :

- higher re-infarction rate
- Inferior aneurysm with MR
- Pulmonary embolism
- CHB and types of heart block : The atrioventricular (AV) node is supplied by the AV nodal artery, which is a branch of the right coronary artery in 90% of people. The other 10% come from the left circumflex artery. It manifests itself as a second or third-degree heart block with moderate bradycardia and a junctional escape rhythm on the ECG.
- 
- Papillary muscle dysfunction

## 61. **Mechanical valves - valve hemolysis**

Haemolytic anaemia seen more commonly with mechanical heart valves than bioprosthetic valves.

Bioprosthetic valves —> hemolysis associated with paravalvular regurgitation or bio-prosthetic structural degeneration.

C/F : anaemia, heart failure, jaundice, dark urine, high LDH

Peripheral smear - schistocytes, small RBC fragments s/o microangiopathi anaemia.

62. African individuals have CK levels upto 4 times normal.

63. Statins inhibit HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Decreases intrinsic cholesterol synthesis

64. **Sacubitril-valsartan** would therefore be the most appropriate agent to commence as the patient has an LVEF <35%, is symptomatic and already established on an ACE-inhibitor (ACE-i) and beta-blocker. This drug combines the neprilysin-inhibitor sacubitril with the angiotensin receptor blocker (ARB) valsartan and is recommended for third-line use in the 2018 NICE heart failure management guidelines. As sacubitril-valsartan contains an ARB it should only be commenced following a wash-out period of any ACEi or ARB a patient is already established on (in this case the patient's ramipril should be stopped).

65. Complete heart block following an inferior MI is **NOT** an indication for pacing, **unlike with an anterior MI**

**66.** In mitral stenosis, an opening snap indicates the leaflets still have some mobility

67. Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur

- left ventricular hypertrophy or failure

68. Bivalirudin works by directly inhibiting thrombin, an enzyme that plays a central role in the coagulation cascade. Thrombin is responsible for converting fibrinogen into fibrin, which forms the structural basis of a blood clot. By inhibiting thrombin, bivalirudin prevents this conversion and thus the formation of clots. Importantly, this action is reversible, meaning that once bivalirudin is metabolised and removed from the body, thrombin can resume its normal function.

69. atorvastatin is contra-indicated in pregnancy. The British National Formulary (BNF) states that statins should be avoided in pregnancy and also 3 months before attempting pregnancy. This is because congenital anomalies have been reported and it is thought that the reduced synthesis of cholesterol possibly affects fetal development.

70. Prosthetic heart valves - antithrombotic therapy:

- bioprosthetic: aspirin
- mechanical: warfarin + aspirin

Prosthetic valves : warfarin for first 3 month. Aspirin - life long

Mechanical valves : bileaflet valve / ball and cage valves

Aspirin + Warfarin >>> DOACs

Aspirin is added if history of IHD present.

INR aortic - 3, moral 3.5

71. Selenium deficiency is known to cause Keshan disease, a type of dilated cardiomyopathy. This condition is named after the region in China where it was first identified and there, it was linked to low selenium levels in the soil. Selenium is an essential trace element that plays a critical role in protecting cells from oxidative damage and infection. It's incorporated into selenoproteins which have various functions including antioxidant defence and thyroid hormone metabolism.

72. Aortic stenosis - most common cause:

- younger patients < 65 years: bicuspid aortic valve
- older patients > 65 years: calcification

73. Restrictive cardiomyopathy: amyloid (most common), haemochromatosis, Loffler's syndrome, sarcoidosis, scleroderma

74. ANP & BNP are inactivated by a membrane bound endopeptidase, neprilysin, which is found in a number of tissues but in especially high concentrations in the kidney. This led to the development of the neprilysin inhibitor, sacubitril.

75. Concurrent inhibition of **ACE** and **neprilysin (Sacubitril)** significantly increases the risk of **angioedema**. This risk arises because both ACE inhibitors and neprilysin inhibitors increase levels of bradykinin, a peptide that promotes inflammation and vascular permeability, which can lead to angioedema.

## 76. **Hyperlipoproteinaemia**

- **type I hyperlipoproteinaemia** : hyper chylomicronaemia - associated with eruptive xanthomas. Complications include occlusion of retinal vein, acute pancreatitis, steatosis, organomegaly and lipaemia retinalis.
- Type II hyperlipoproteinaemia : associated with xanthoma tendinosum - nodular swellings on tendons. Type II hyperliproteinaemia classified further into types IIa and IIb : whether increase in triglyceride occurs in addition to increase in LDL-cholesterol.
- Type III hyperlipoproteinaemia : tuberoeruptive xanthomas - due to high numbers of chylomicron and high levels of intermediate-density lipoprotein.
- Most common cause : apolipoprotein E2/E2 genotype.
- Type III is due to cholesterol rich VLDL.
- Associated with hypercholesterolaemia and hypertriglyceridemia, normal concentration of apolipoprotein B
- Two types of skin signs - 1) palmar xanthomata or orange discolouration of skin palmar creases 2) tuberoeruptive xanthomata on elbows and knees.



- Type III associated with early onset CVD and peripheral vascular disease.

- type IV hyperlipoproteinaemia : associated with eruptive xanthomas
- Type V hyperlipoproteinaemia : mixed hyperlipoproteinaemia familiar or mixed hyperlipidemia. High levels of VLDL + high chylomicron. Associated with glucose intolerance and hyperuricemia.

77. A third heart sound, or S3, is often associated with conditions that lead to rapid filling of the ventricles. This can happen in dilated cardiomyopathy, a condition characterised by dilation and impaired contraction of the left or both ventricles. The increased volume load leads to rapid early diastolic filling, causing an audible S3. In addition to this, the patient's age and symptoms of exertional dyspnoea are consistent with dilated cardiomyopathy.

78. Amiodarone has a long half-life - it is highly lipophilic and widely absorbed by tissue, which reduces its bioavailability in serum. Therefore, a prolonged loading regime is required to achieve stable therapeutic levels

79. Sick Sinus syndrome -

- periods of sinus bradycardia
- Sinus arrest
- Combination of sinoatrial or atrioventricular conduction defects
- Supra ventricular tachycardia - causing regular fast heart rates.

Cause - fibrosis or fatty infiltration of sinus node, AV node, His bundle or its branches.

Mx : permanent pacemaker

80. Pulmonary hypertension -

Mean Pulmonary artery pressure > 25 mmHg at rest  
> 30 mmHg on exercise.

81. This patient has hyperthyroidism based on a suppressed TSH. The two common causes are Graves' disease (cross-reaction of antibodies with the TSH receptor) and a toxic multi-nodular goiter (excess production from functionally autonomous thyroid nodules). A dose of non-radioactive iodine (as is contained in contrast) will, as the question alludes to, have varying effects on their production of the thyroid hormones.

In patients with Graves' disease the Wolff-Chaikoff effect will dominate. This is the suppression of thyroid hormone production in part due to a transient inhibition of thyroid peroxidase with rising intrathyroidal iodine.

In patients with autonomous thyroid nodules, however, hyperthyroidism will dominate since the nodules do not respond to normal hormonal autoregulatory mechanisms. They will continue to produce excessive thyroid hormone.

Out of all the options, a thyroid radionuclide isotope scan will differentiate between these two diseases.

Graves' disease will show uniformly elevated iodine uptake. Toxic multinodular goiter will show multiple foci of variably increased iodine uptake.

Hyperthyroidism and cardiac catheterisation:

- Cardiac catheterisation requires the use of an iodine-containing contrast.
- This may worsen hyperthyroidism caused by toxic multinodular goitre, whereas it may improve the symptoms in patients with Grave's disease (Wolff-Chaikoff effect).
- The most reliable diagnostic method is a radionuclide ( $^{99}\text{Tc}$ ,  $^{123}\text{I}$  or  $^{131}\text{I}$ ) scan of the thyroid, which will distinguish the diffuse, high uptake of Grave's disease from nodular thyroid disease.
- If a toxic multinodular goitre or toxic adenoma is detected, the patient should receive an antithyroid drug before undergoing catheterisation.
- The antithyroid medication must be continued for at least 2 weeks after the procedure.

### 83. Coronary artery disease and DVLA regulations

Knowledge of the DVLA regulations for coronary artery disease is essential for all parts of the MRCP examination. Ensure you are

familiar with the latest up-to-date guidelines available from the DVLA website.

This man holds a group 2 licence, and hence he should be advised to inform the DVLA of his recent presentation with unstable angina (a type of acute coronary syndrome) and stop work until re-licensing can be performed.

For group 2 licence holders, all acute coronary syndromes are considered relevant and this disqualifies the individual from driving for at least 6 weeks. In this man, although his troponin is negative, the pain at rest counts as part of the acute coronary syndrome.

Re-licensing may be permitted if a suitable exercise test is achieved (need to complete three stages of the Bruce protocol (typically at least 8 minutes of the Bruce protocol), without significant symptoms, ECG or haemodynamic abnormalities) and there are no other disqualifying conditions.

Note that anti-anginal medicines include nitrates, beta blockers, calcium-channel blockers, nicorandil, ivabradine and ranolazine prescribed for anti-anginal purposes or for other reasons, e.g. cardio-protection.

84. To answer this question correctly requires you to recognise that the patient has pericarditis. The patient is young and unlikely to have ischaemic heart disease. The history of recent influenza is a predisposing factor for pericarditis.

The presence of concave ST-segment change in multiple coronary territories is also strongly suggestive of pericarditis.

Interpreting an ECG:

- The ECG changes in acute pericarditis consist of ST elevation with concavity upward in all leads facing the epicardial surface, ie anterior, inferior and lateral is the correct answer
- Only cavity' leads aVR, V1 and, rarely, V2 show ST depression
- This is followed by the return of ST segments to baseline and flat or inverted T waves
- Without the loss of R waves or development of Q waves
- As the illness improves, T waves become normal but may occasionally persist in patients with chronic pericarditis
- Rhythm and conduction abnormalities are not typical in pericarditis unless the myocardium is involved
- If troponin levels are significantly elevated, this can suggest myocardial involvement; patients should have BNP levels

measured and magnetic resonance imaging to quantify myocardial inflammation.

Causes of acute idiopathic pericarditis:

- Infections (viral infections (eg coxsackie B virus), tuberculosis, other bacteria, fungi)
- Inflammatory; post-myocardial infarction/cardiomyopathy (autoimmune rheumatic disorder)
- Others (neoplasia, uraemia, trauma, aortic dissection, hypothyroidism, irradiation, drugs eg hydralazine).

85. Epsilon waves on ECG - right ventricular conduction delay.

- appears as a sharp deflection after termination of QRS complex during the ST segment or upstroke of T wave.
- Seen in right ventricular leads - V1 and V2
- Right ventricular dysplasia characterised by displacement of myocytes by fat
- This delays the excitation and depolarisation of viable myocytes enveloped by fatty tissue and leads to epsilon potentials

86. Coarctation of aorta- commonest site of obstruction of aortic lumen is just distal to the origin of Left subclavian artery.

Systolic pressures in arms >>> SBP of legs

If — SBP of right arm higher than 30mmHg than SBP of left arm —  
> Left subclavian is involved in the coarctation.

87. Long QT 1 syndrome -

- LQT1 gene = KCNQ1 on chromosome 11
- KCNQ1 codes for voltage gated potassium channel KvLQT1 and is highly expressed in heart
- This is a slow delayed rectifier potassium channel

LQT2 - rapid delayed rectifier potassium channel  
Mutation is KCNH2 on chromosome 7

88. In practice, a number of these interventions would be commenced together, but as the question asks specifically for one intervention, the correct answer is as stated ramipril.

After a patient has had a myocardial infarction (MI), it is imperative to consider all modifiable risk factors to lower the risk of further vascular events.

Non-pharmacological interventions

The most important intervention is to stop smoking; after just 1 year there is a significant drop in the risk of MI.

Weight loss in an obese individual will reduce co-morbidity but has not been shown to prolong survival.

It would be ethically impossible to arrange randomised trials of smoking cessation or weight loss, so such interventions have to rely on epidemiological evidence to judge the outcome.

Pharmacological interventions

In the other interventions trial evidence has given a number of patients needed to treat in order to prevent one fatality (NNT), and this is one way of judging which intervention has the most likelihood of prolonging survival.

For B blockers the NNT is 143 (ISIS 1 study).

For aspirin the NNT is 42 (ISIS 2 study).

For angiotensin-converting enzyme (ACE) inhibitors the NNT is 22 (SOLVD).

For statins the NNT is 33 (CARE).

Lowest NNT - better the drug.

### 89. Patent Foramen Ovale - paradoxical embolus

PFOs - when right atrial pressure exceeds left atrial pressure - this shunt will open and allow Venous blood to enter the arterial circulation.

PFO - requires Valsalva during anECHO with agitated saline to visualise them the best.

### 90. Indications of Referral to Electrophysiologist :

| Condition | When to Refer | Potential Treatment |
|-----------|---------------|---------------------|
|-----------|---------------|---------------------|

|                                        |                                                            |                         |
|----------------------------------------|------------------------------------------------------------|-------------------------|
| SVT                                    | > 1 episode                                                | Radiofrequency ablation |
| Atrial Flutter                         | > 1 episode                                                | Radiofrequency ablation |
| Atrial fibrillation                    | High symptomatic, refractory or intolerant to drug therapy | Radiofrequency ablation |
| Ventricular fibrillation               | Refer only if there is NO obvious cause                    | ICD insertion           |
| Ventricular tachycardia                | Refer if unless there is an obvious reversible cause       | RFA or ICD              |
| Ischaemic Cardiomyopathy               | EF > 30% on optimal medical therapy                        | Primary prevention ICD  |
| NYHA III or IV, QRS > 130 ms, EF < 35% | On optimal medical therapy                                 | Heart failure pacing    |

## Pacemaker Nomenclature - five position code

Position 1 : A for atrium, V for ventricle, D for dual

Position 2 : chambers sensed; A / V / D / O  
O = absence sensing

Position 3 : how pacemaker responds to a sensed event

“ I “ - indicated that a sensed event inhibits the output pulse and causes pacemaker to recycle for one or more timing cycles

“T” - indicates output pulse is triggered in response to a sensed event

“D” - indicates that there are dual modes of response. Event sensed in the atrium inhibits the atrial output but triggers a ventricular output. Programmable delay between the sensed atrial event and triggered ventricular output to mimic normal PR interval. If ventricular lead senses a native ventricular signal during the programmed delay - it will inhibit ventricular output.

“O” - indicates no response to sensed output.

Position 4 : reflects rate modulation , also known as rate responsive or rate adaptive pacing.

“R” - in the 4th position indicates pacemaker has rate modulation.

Position 5 - rarely used, specifies location or absence of multisite pacing - defined as stimulation sites in both Atria , both ventricles, more than one stimulation site in any chamber, or a combination of these.

## 91. **Ventricular Tachycardia**

- Monomorphic VT - caused by myocardial infarction
- Polymorphic V - due to prolonged QT interval
- MX : any sin of SBP < 90, heart failure, chest pain —> Immediate Cardioversion
- Drug therapy - Amiodarone - only through **central line**
- Lidocaine - use in caution with LV impairment
- NO VERAPAMIL

Torsades de Pointes : Polymorphic VT with QRS complexes of varying amplitudes.

IV Magnesium - first line therapy.

## 92. **Heart Sounds :**

First Heart Sound :

- closure of mitral valves and tricuspid valves
- Heard at the end of diastole and start of ventricular systole
- Corresponds to R wave on ECG
- Quiet S1 : MR, Long PR interval, Obesity, 1st degree heart block, LBBB
- Loud S1 : MS, Hyperdynamic states, Tachycardia, low BMI, Atrial Myxoma
- Widely split S1 - RBBB, Ebstein's anomaly, Ventricular tachycardia

Second Heart Sound :

- closure of aortic and pulmonary valves

- Loud S2 - hypertension
- Quiet S2 - aortic stenosis
- Wide split S2 - RBBB, Pulmonary stenosis, VSD, MR
- Fixed split S2 - ASD
- Paradoxical split S2 - LBBB, PDA, Aortic stenosis. HOCM

#### Third Heart Sound :

- rapid ventricular filling
- Occurs in early diastole
- Ventricular dysfunction - IHD with ventricular dysfunction, cardiomyopathy, myocarditis, cor pulmonate
- Increased volume load on ventricle - Valve regurgitation, L to R cardiac shunts, volume overload

#### Fourth heart sound :

- heard in late diastole, just after first heart sounds
- Late diastolic filling associated with atrial contraction
- Sign of stiff or hypertrophic ventricle
- Left sided S4 : HTN, hypertrophic cardiomyopathy, aortic stenosis
- Right sided S4 : pulmonary stenosis, Pulmonary HTN

#### 93. Automatic supraventricular tachycardia - **normal P wave morphology**

#### AV nodal reentry SVT - **abnormal P wave**

94. Thiazide diuretic in pregnancy - neonatal thrombocytopenia, bone marrow suppression, jaundice, electrolyte disturbances, hypoglycaemia

Also can causes : reduced placental perfusion, uterine inertia, situation of labor

#### 95. ECHO Modern transthoracic mode -> LVEF



Continuous wave imaging mode is of ECHO -> valvular regurgitation and aortic stenosis severity

Pulsed wave - by emission from a Doppler signal - to provide information on velocity and direction of flow

#### **96. Eisenmenger syndrome - complications**

- polycythemia
- bleeding disorder
- cerebral embolism or abscess
- Avoid pregnancy
- Syncopal episodes can precede death

#### **97. ECG features suggestive of Ventricular Tachycardia :**

- broad complexes > 160 ms
- Absence of LBBB or RBBB
- AV dissociation in any of the 12 leads
- Capture beats - SA node transiently captures the ventricles while AV dissociation happens giving rise to a normal QRS
- Fusion beats : sinus + ventricular beat coincide to produce a hybrid complex of intermediate morphology
- Positive or negative concordance throughout chest leads - entirely positive (R) or entirely negative (QS) complexes - NO RS complexes
- RS duration of > 100 ms

#### **98. Restrictive Cardiomyopathy**

- secondary to Amyloidosis with immunocyte dyscrasia
- Right heart failure, raised JVP, deep Y descent
- Heart size commonly is normal
- Apex frequently non palpable due to thick pericardium
- CXR : pericardial calcifications
- ECG : diffusely diminished voltages
- ECHO - small, thick ventricles, and thick intertribal septum due to amyloid deposit which leaves a granular sparkling appearance

**99. \*\*\* LUTEMBACHER SYNDROME - Ostium secundum (ass. With RBBB with RAD) in combination with Rheumatic mitral stenosis.**

100. Primary pulmonary hypertension is an absolute contra indication to pregnancy.

101. Early graft occlusions after CABG occur in 5-10% of patients within the first 30 days.

Usually thrombotic and are related to technical problems with the anastomosis, injury to vein related to manipulation during harvesting.

Aspirin : reduced early graft occlusion

102. Primary Pulmonary Hypertension - familial types - **defect in genes most common BMPR2**

**Other genes : ALK3, ENG, SMAD9, CAV1, KCNK3**

103. CCBs - act on SA node and AV node

104. Multifocal atrial tachycardia in patients with pulmonary hypertension —> treatment is with **Verapamil / Diltiazem**

**No pulmonary hypertension 0—> beta blockers**

105. Tricuspid regurgitation - loss of 'x' descent in JVP - causing fusion of fusion c and v waves - to form giant v waves

106. Defibrillation - **Monophasic 360 J; Biphasic 150-200 J**

107. Severe Pulmonary Edema : Mx -

- sitting patient up
- Administering high flow oxygen
- Diuretics
- Powerful vasodilators - diamorphine & glyceryl trinitrate
- Oral ACEi

108. HOCM - septal wall thickness > 3 cm —> associated with increased risk of sudden cardiac death

109. Permanent Pacemaker indications :

- persistent symptomatic bradycardia
- Trifasicular block
- Mobitz Type 2 AV block
- Sinus pause > 3 seconds

### 110. Atrial Myxoma

- R/F : family history, female sex, Carney syndrome
- Carney syndrome / Carney complex : rare genetic tumbral disorder associated with MEN, or associated with primary pigmented nodular adrenal dysplasia (PPNAD).  
Carney syndrome: can cause - cardiac myxomas, abnormal pigmentation and myxomas of skin, breast myxomatosis, melanotic schwannoma, testicular and ovarian tumors.  
Mx : B/L adrenalectomy
- C/F : fever, weight loss, transient mitral stenosis, early diastolic plop, finger clubbing, pulmonary hypertension, SOB
- Diagnostic INV - ECHO
- Mx : surgical resection

111. Stabbing in the chest —> pulmonary valve involved  
It is the anterior most valve of the human heart

112. Absolute contraindications to carotid sinus massage -

- myocardial infarction
- TIA in the last 3 months
- Cerebrovascular accident in last 3 months
- Carotid artery occlusion
- Previous ventricular arrhythmia

113. Complete heart block - **large volume pulse** due to compensatory increase in stroke volume, and **systolic flow murmurs , irregular cannon “a” waves on JVP**

### 114. Paroxysmal Atrial Fibrillation

- both A-fib and atrial flutter can occur with alcoholic binges
- A-fib : irregular

- Flutter : regular, rates are more typically 150 bpm, (2:1) or 100 bpm ( 3:1 )

Paroxysmal A-fib :

- treatment : < 48 hours —> heparin + synchronised DCCV direct current cardioversion
- > 48 hours —> 4-6 weeks of full anticoagulation INR > 2 if using warfarin before synchronised DCCV
- Earlier DCCV can be done if transoesophageal ECHO can be done to rule out left atrial appendage
- Chemical cardioversion : IV Flecainide in absence of IHD
- Else —> IV Amiodarone
- Long term prophylaxis —> Sotalol

115. Chemotherapy associated with cardiovascular complications :

Doxorubicin, Daunorubicin, Idarubicin, Mitoxantrone

116. SVT in pregnancy - **Metoprolol**

117. Risk factors for sudden death in HOCM :

- history of previous cardiac arrest
- Sustained ventricular tachycardia
- Recurrent syncope
- Adverse genotype and family history
- Multiple episodes of non sustained ventricular tachycardia on ambulatory ECG
- Marked increases in the thickness of left ventricular wall

118. Right bundle branch block with left axis deviation - distinct entity of Ventricular tachycardia - typical QRS configuration and responsiveness to Verapamil.

119. **Adenosine** : purine nucleoside - rapid IV injection - slows conduction through AV node by acting as a G protein-coupled receptor agonist of Adenosine A1 receptor on AV node

- inhibition of adenylate cyclase —> reduction cAMP

- Adenosine by activating A1 receptor also leads to cardiac potassium channel activation and calcium channel inhibition

### 120. **Pericarditis : ECG changes -**

- **stage I** : diffuse concave upward ST segment elevation with concordance of T waves, ST segment depression in aVR or V1, PR segment depression, low voltage, absence of reciprocal ST segment changes
- Stage II : ST segment return to baseline, T wave flattening
- Stage III : T wave inversion
- Stage IV : gradual resolution of T wave inversion

### 121. Chronic Angina : Beta blockers

Reduces the frequency and duration of anginal episodes and improves exercise tolerance.

Acts by competitively inhibiting the catecholamine effect on beta receptor → reduced heart rate and improves coronary perfusion. Associated with positive outcome benefit

### 122. **Sub Clavian steal syndrome**

- occlusion or stenosis of proximal SCA - leading to decreased antegrade or retrograde flow in the I/L vertebral artery
- C/F : upper extremity symptoms - fatigue, aching, coolness of affected arm and numbness
- Neurological : diplopia, vertigo, decreased vision, nystagmus, gait unsteadiness
- Symptoms can be precipitated by extreme exercise on the affected side

### Pathophysiology:

- Subclavian steal produces symptoms by flow-related phenomena rather than embolic.

When an atherosclerotic lesion in the proximal subclavian artery progresses to cause haemodynamically significant stenosis, collateral vessels from the subclavian artery gradually enlarge.

The upper extremity becomes dependent on these large collateral blood vessels that originate from the subclavian artery distal to the obstruction.

The collateral vessels serve as points of re-entry for blood flowing retrograde into the arm from the head, shoulder and neck, thereby providing the extremity with adequate perfusion.

When the arm is exercised, the blood vessels dilate to enhance perfusion to the ischaemic muscle, thus lowering the resistance in the outflow vessels.

Blood is siphoned from the head, neck and shoulder through collateral vessels to supply this low-resistance vascular bed, satisfying increased oxygen demand by the exercising muscles of the upper extremity.

This results in posterior cerebral circulation neurological symptoms.

123. Supraventricular tachycardia with bundle-branch block may resemble ventricular tachycardia on the ECG

- Eighty percent of all broad complex tachycardias are secondary to ventricular tachycardia and the proportion is even higher in patients with structural heart disease.
- Be very wary of diagnosing an SVT with aberrancy in a patient with a history of ischaemic heart disease.
- In all cases of doubt, the rhythm should be treated as a ventricular tachycardia.
- If the patient is unstable, eg. Blood pressure is low, emergent electrical cardioversion should be performed.

ECG diagnosis of VT:

The ECG shows a rapid ventricular rhythm with broad (often 0.16 s or more) abnormal QRS complexes

AV dissociation may result in visible P waves

Capture beats (intermittent narrow QRS complex owing to normal ventricular activation via the AV node and conducting system) and fusion beats (intermediate between ventricular tachycardia beat and capture beat) are seen

Ventricular tachycardia is more likely than supraventricular tachycardia with bundle-branch block when there is:

a very broad QRS ( $> 0.14$  seconds)

atrioventricular dissociation

a bifid upright QRS with a taller first peak in V1

a deep S wave in V6

a concordant (same polarity) QRS direction in all chest leads (V1 - V6).

#### 124. Drug-induced Torsades de Pointes

- Drugs are a common cause of acquired LQTS and TdP.
- Many drugs have been implicated including:
  - Antiarrhythmic drugs (e.g. sotalol, quinidine, disopyramide, procainamide, flecainide)
  - Certain non-sedating antihistamines (e.g. terfenadine and astemizole)
  - Antibiotics - Erythromycin, clarithromycin, azithromycin, levofloxacin, moxifloxacin, gatifloxacin, trimethoprim-sulfamethoxazole, clindamycin, pentamidine, chloroquine
  - Antifungals - Ketoconazole, itraconazole
  - Certain psychotropic medications (e.g. risperidone, haloperidol, phenothiazines, thioridazine, trifluoperazine, sertindole, zimeldine, ziprasidone)
  - Tricyclic and tetracyclic antidepressants
  - Certain gastric motility agents (e.g. cisapride)
  - Lithium.

125. **Sotalol** : has both Class II and Class III anti-arrhythmic properties

Class III agents : blocks cardiac potassium channels

Class II - beta blockers

126. Structurally normal heart with broad complex irregular tachycardia —> **Procainamide**

127. Atrial fibrillation - radio frequency ablation - circumferential ablation around the area where pulmonary veins joins the atrium.

AV nodal re entry tachycardia ablation at entry of coronary sinus

128. The aim of endothelin receptor antagonist therapy is to reduce pulmonary vascular resistance and hence reduce the strain on the right ventricle. Right ventricular failure is the most common cause of death in patients with primary pulmonary hypertension.

129. BNP - actions:

- vasodilator: can decrease cardiac afterload

- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

130. First heart sound - R wave

Pathological S4 - P wave

S wave - occurs between S1 and S2

T wave - occurs between S2 and S3

U wave - depolarisation of Purkinje fibers

131. Thiazides - adverse effects :

- 1) Dehydration
- 2) Postural hypotension
- 3) Hypokalaemia - due to increased Na delivery to distal part of DCT → increased Na reabsorption in exchange for potassium and hydrogen ions
- 4) Hyponatremia
- 5) Hypercalcemia
- 6) Gout
- 7) Paired glucose tolerance
- 8) Impotence

Rare adverse :

- thrombocytopenia
- Agranulocytosis
- Photosensitivity rash
- Pancreatitis

132. Patent ductus arteriosus (PDA) is a non-cyanotic congenital heart disorder. It is a type of left-right shunt in which blood passes from the aorta to the pulmonary vessel via the patent ductus arteriosus. Newborns may have a normal presentation, but on auscultation, a **continuous machine-like murmur** is characteristic. **Indomethacin** is the drug of choice for treating the



patent ductus arteriosus in a newborn. It acts by inhibiting prostaglandin E2.

PDA is commonly found in premature babies. It is observed for spontaneous closure in asymptomatic patients. Symptomatic babies undergo an echocardiogram a few days after birth. Depending on the echocardiogram findings, the PDA is managed medically or surgically. Medical management involves giving indomethacin or ibuprofen to the newborn. Giving these medicines to the mother has no role in the closure of the PDA. Prophylactically treating a newborn right after delivery is also not recommended.

133. Statins : liver impairment: the 2014 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

3 times upper normal after 3 months of use - then stop and switch drug

134. Acute Coronary Syndrome - Poor prognostic  
Poor prognostic factors

- age
- development (or history) of heart failure
- peripheral vascular disease
- reduced systolic blood pressure
- Killip class\*
- initial serum creatinine concentration
- elevated initial cardiac markers
- cardiac arrest on admission
- ST segment deviation

135. Hydralazine - increases cGMP leading to smooth muscle relaxation more in arterioles than veins

136. The following are risk factors for asystole. Even if there is a satisfactory response to atropine specialist help is indicated to consider the need for transvenous pacing:

- complete heart block with broad complex QRS
- recent asystole
- Mobitz type II AV block
- ventricular pause > 3 seconds

137. The key point to this question is that whilst tetralogy of Fallot is more common than transposition of the great arteries (TGA), Fallot's doesn't usually present until 1-2 months following the identification of a murmur or cyanosis. In the neonate, TGA is the most common presenting cause of cyanotic congenital heart disease

138. Patients on warfarin undergoing emergency surgery - give four-factor prothrombin complex concentrate

**139. Patients with very poor dental hygiene may develop endocarditis secondary to Viridans streptococci e.g. *Streptococcus sanguini***

140. Atrial flutter is typically caused by a re-entrant circuit in the right atrium. The 'tricuspid valve isthmus' is a critical part of this circuit and its ablation can interrupt this re-entry, thereby restoring sinus rhythm. This procedure has high success rates and low complication rates, making it the treatment of choice for atrial flutter.

141. Simvastatin, a commonly prescribed statin for the management of hyperlipidaemia, has potential drug interactions with grapefruit juice. This is due to the fact that grapefruit juice contains certain chemicals that can interfere with the enzymes responsible for metabolising simvastatin in the body (specifically CYP3A4 enzymes). The inhibition of these enzymes can lead to an increased concentration of simvastatin in the bloodstream, which may increase the risk of side effects such as myopathy and rhabdomyolysis.

142.

Other causes of an absent radial pulse include: aortic dissection with subclavian involvement and peripheral arterial embolus (as

mentioned above), trauma and iatrogenic (post-cath and Takayasu arteritis)

143. For patients in whom stable angina cannot be excluded by clinical assessment alone NICE recommend the following (e.g. symptoms consistent with typical/atypical angina OR ECG changes):

- 1st line: CT coronary angiography
- 2nd line: non-invasive functional imaging (looking for reversible myocardial ischaemia)
- 3rd line: invasive coronary angiography

Examples of non-invasive functional imaging:

- myocardial perfusion scintigraphy with single photon emission computed tomography (MPS with SPECT) or
- stress echocardiography or
- first-pass contrast-enhanced magnetic resonance (MR) perfusion or
- MR imaging for stress-induced wall motion abnormalities

144. **Serum Creatine Kinase** activity in **Afro-Caribbean** people is often upto three times the upper limit of normal for White populations.

Underlying genetic basis for raised CK is slowly being outdates It is due to polymorphisms in the CKM and LILRB5 genes associated with higher baseline's levels. It would seem these patients baseline CK is around 400 U/L.

145. Transthoracic ECHO - patients with documents IHD with reduced functional capacity, unexplained SOB and clinical signs of heart failure.

Dobutamine Stress ECHO only for pre-operative testing prior to high risk vascular procedures with reduced functional capacity.

146. Torsades de pointes : Maroilles - Erythromycin, Clarithromycin,

Quinolones : Ciprofloxacin, Ofloxacin

Torsades de pointes is exacerbated by co-administration with CYP-P450 inhibitors such as Ketoconazole

147. Autonomic manieres like Valsalva or Carotid sinus massage helps to localise the site of block in heart block

- AV node : has good autonomic nervation and responds to increase in vagal tone
- Carotid sinus massage and valsalva increases vagal tone that worsens an AV block, NOT infra nodal block
- Atropine - improves the AV nodal block and worsens the His-Purkinje system

148. Factors which predicts best long-term maintenance of sinus rhythm in atrial fibrillation following DCCV :

- AF duration less than 6 months
- Left atrial size - A-fib persists if LA size > 5 cm

149. Right ventricle MI - association with inferior wall ventricular infarction

RCA involvement

C/F : low cardiac output, JVP distension

No pulmonary congestion

Kussmaul's sign increased jugular venous distension with inspiration may be evident

### 150. Heyde syndrome

- High shear stress and increased velocity across the stenotic aortic valve leads to unfolding and activation of vWF
- This prevents vWF from binding to collagen - which is useful for attachment of platelets
- Increasingly important in patients with angiodysplasia within the GIT as associated with aortic stenosis and Heyde syndrome \

Heyde syndrome = aortic stenosis + GI bleeding angiodysplasia + acquired vWF syndrome

### 151. Trypanosomiasis

- American trypanosomiasis or Chagas disease - South America

- Transmission by scratching infected faces of the bug into skin abrasion
- Acute form - fever, myalgia, hepatosplenomegaly and myocarditis
- Rare cases - delayed ventricular dilation with heart failure
- Enlarges oesophagus and colon
- Unilateral periorbital edema and swelling of eyelids can occur -  
**Romana's sign - classical of Trypanosmiasis**

152. Valsalva increases murmur in HOCM and MVP

Valsalva makes murmurs quieter in AS, PS, and TR

Squatting increases murmurs of VSD, AS, aortic insufficiency and mitral insufficiency

Squatting causes quiet murmurs in HOCM

153. Drugs causing pulmonary hypertension - **Methamphetamine** and **Fenfluramine**

154. Elevated direct and indirect bilirubin levels after CABG can indicate hemolysis on bypass

155. Amyloidosis - commonest cause of restrictive cardiomyopathy in UK

156. Carcinoid heart disease - accumulation of fibrous tissue in the heart, especially under surface of tricuspid valve. Carcinoid heart disease can hold the tricuspid valve in a semi-closed position —> tricuspid stenosis and regurgitation can occur.

Liver metastasis of carcinoid syndrome —> releases serotonin and kallikrein which travels through liver sinusoids —> central vein of each lobule —> hepatic veins —> IVC and right heart

Increased serotonin and kallikrein — bronchospasm, diarrhoea, flushing

157. HOCM —> MYH7 = encodes beta myosin heavy chain

MYBPC3 = enodes myosin-binding protein C

158. Ejection Fraction =  $EDV - ESV / EDV$

159. Management of cold water drowning

- Re-warming should be done in hospital that has extracorporeal re-warming facilities
- Head out upright immersion in water at body temperature results in 32-66% increase in cardiac output due to pressure of surrounding water
- Resistance to circulation is suddenly removed as patient leaves the water which leads to venous pooling and can cause circulatory collapse
- This is the cause of death
- Patients have to be lifted out of water in prone position
- Continuous chest compression should be applied during transport

160. **Allergic myocarditis** - rare adverse event of Co-trimoxazole therapy.

161. Type A aortic dissection - hypotension, syncope

Type B aortic dissection - hypertension

162. Trans thoracic ECHO —> left ventricular apex, structure and function of ventricles

Trans esophageal ECHO —> posterior cardiac structures - atria, left atrial appendage, valves and pulmonary veins

163.

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## NEPHROLOGY

### PASSMEDICINE & PASSTEST

1. Acute Interstitial Nephritis :

- Drugs - Penicillin, Rifampicin, NSAIDs, Furosemide, Allopurinol
- Marked interstitial edema and interstitial infiltrates in connective tissue between renal tubules

- C/F : fever, rash, arthralgia, eosinophilia, mild renal impairment, hypertension
- Tubulointerstitial nephritis with uveitis : young females; fever, weight loss, painful red eyes. CUE : +ve for leukocytes and protein.

## 2. Acute kidney Injury

- Pre-renal causes : hypovolemia due to ischaemia / diarrhoea / vomiting, renal artery stenosis
- Renal / Intrinsic causes : glomerulonephritis, ATN, AIN, rhabdomyolysis, tumor lysis syndrome
- Post renal causes : kidney stone in ureter / bladder, benign prostatic hyperplasia, external compression of ureter

|                             | Pre renal Azotemia      | Acute Tubular Necrosis |
|-----------------------------|-------------------------|------------------------|
| Urine sodium                | < 20 mmol/L             | >40 mmol/L             |
| Urine osmolality            | >500 mOsm / kg          | < 350 mOsm / kg        |
| Response to fluid challenge | Good                    | Poor                   |
| Fractional Na excretion     | <1 %                    | > 1 %                  |
| Serum Urea : Creatinine     | Raised                  | Normal                 |
| Fe Urea                     | < 35 %                  | > 35 %                 |
| Urine : Plasma osmolality   | > 1.5                   | < 1.1                  |
| Urine : Plasma urea         | > 10 : 1                | < 8 : 1                |
| Specific gravity            | > 1020                  | < 1010                 |
| Urine                       | Normal / bland sediment | Brown granular casts   |

Pre renal azotemia : Kidneys hold on to sodium to reserve volume

## 3. ADPKD

- ADPKD type 1 - chromosome 16, presents with renal failure earlier
- ADPKD type 2 : chromosome 4
- Screening INV - USG abdomen
- USG criteria in patients with positive family history -
  - A. Two cysts, unilateral or bilateral if aged < 30 years

B. Two cysts in both kidneys if aged 30-59 years

C. Four cysts in both kidneys > 60 years

- Tolvaptan - Vasopressin receptor 2 antagonist : to slow progression of cyst development and renal insufficiency if they have CKD Stage 2 / 3, rapidly progressing disease.

Clinical features :

- hypertension
- Recurrent UTIs
- Flank pain
- Hematuria
- Palpable kidneys
- Renal impairment
- Renal stones
- Extra renal manifestations : liver cysts, berry aneurysms
- Cardiovascular - MVP, MR/TR, aortic root dilation, aortic dissection

#### 4. Alport's syndrome

- X linked dominant pattern
- Defect in gene coding for type IV collagen resulting in abnormal glomerular basement membrane
- Disease is more severe in males than females
- Question hint - failing renal transplant
- Clinical features :
  - A. Microscopic hematuria
  - B. Progressive renal failure
  - C. Bilateral sensorineural deafness
  - D. Lenticonus - protrusion of lens into anterior chamber
  - E. Retinitis pigmentosa
  - F. Renal biopsy : splitting of lamina densa on EM
- Diagnosis : Molecular genetic testing
- EM - GBM shows longitudinal splitting of lamina densa of GBM, causing basket-weave appearance.

#### 5. Amyloidosis

- extracellular deposition of insoluble fibrillar protein
- Non fibrillar protein : amyloid-P component —> derived from acute phase protein serum amyloid P



- Other non fibrillary components : apolipoprotein E, heparin sulphate proteoglycans
- Diagnosis : **Congo red staining - apple green birefringence**
- Serum amyloid precursor (SAP) scan
- AL amyloidosis : most common form; L = immunoglobulin light chain fragment
- Due to Myeloma, Waldenstrom's, MGUS
- C/F : nephrotic syndrome, cardiac and neurological involvement, macroglossia, periorbital ecchymoses

#### AA amyloid

- A = precursor serum amyloid A - acute phase reactant
- Chronic infection, chronic inflammation
- TB, bronchiectasis, rheumatoid arthritis
- Renal involvement most common

#### Beta - 2 microglobulin amyloidosis

- precursor protein - beta - 2 microglobulin - part of MHC
- Associated with patients on renal dialysis

#### 6. Normal anion gap metabolic acidosis :

- GI bicarbonate loss - diarrhoea, ureterosigmoidostomy, fistula
- RTA
- Drugs - Acetazolamide
- Ammonium chloride injection
- Addison's disease

#### 7. Raised anion gap metabolic acidosis :

- lactate - shock, hypoxia
- Ketones : DKA, alcohol
- Urate - renal failure
- Drugs - metformin
- Acid poisoning : salicylates, methanol
- Chronic paracetamol use : 5-oxoproline

#### 8. Goodpasture's syndrome

- small vessel vasculitis
- Pulmonary haemorrhage, RPGN
- anti-GBM antibodies against type IV collagen

- C/F- pulmonary hmghe, nephritis → proteinuria + hematuria
- Renal biopsy - linear IgG deposits along basement membrane
- Raised transfer factor secondary to pulmonary haemorrhage
- Mx : plasma exchange, steroids, cyclophosphamide

9. ARPKD - chromosome 6; encodes fibrocystic - protein important for normal renal tubule development

Dx : prenatal USG or in early infancy with abdominal masses and renal failure

Renal Bx : multiple cylindrical lesions at right angles to cortical surface

10. Transitional cell carcinoma of bladder R/F :

- smoking
- Exposure to aniline dyes - printing and textile industry; 2-naphthylamine and benzidine
- Rubber manufacture
- Cyclophosphamide

Squamous cell carcinoma of bladder R/F :

- Smoking
- Schistosomiasis

11. Calciphylaxis - deposition of calcium within arterioles causing microvascular occlusion and necrosis of tissue seen in end-stage renal failure

R/F : hypercalcemia, hyperphosphatemia, hyperparathyroidism

Warfarin - exacerbates risk of calciphylaxis

12. Elevate hepcidin levels leads to decreased iron absorption from gut and impaired release of stored iron from macrophages and hepatocytes

This causes reduced iron levels available for erythropoiesis

In CKD - metabolic acidosis inhibits the conversion of  $\text{Fe}^{3+}$  to  $\text{Fe}^{2+}$  in the duodenum leading to reduced iron absorption.

12. CKD - bone disease

- low vitamin D = due to low 1-alpha hydroxylation in kidneys

- High phosphate
- Low calcium due to lack of vitamin D and high phosphate
- Secondary hyperparathyroidism - due to low calcium high phosphate and low vitamin D

Osteitis fibrosis cystica - hyperparathyroid bone disease

Adynamic : reduced cellular activity of both osteoblasts and osteoclasts in bone

Osteomalacia : due to reduced vitamin D

Osteosclerosis & osteoporosis

CKD - bone disease management

- Reduced intake of phosphate
- Phosphate binders
- Vitamin D : alfacalcidol, calcitriol

Phosphate binders :

- calcium based binders : problems include hypercalcemia and vascular calcification
- Sevelamer : non calcium based binder, binds to dietary phosphate and prevents its absorption.
- Sevelamer can also reduce uric acid levels and improves lipid profiles of patients with CKD

- Patients who have proteinuric CKD - treat with SGLT-2 inhibitors
- Primarily act by blocking reabsorption of glucose in the proximal tubule —> lowers the renal threshold —> glycosuria
- By blocking SGLT2 —> reduces sodium reabsorption —> natriuresis reduces intravascular volume and blood pressure
- It also increases the delivery of sodium to macula densa —> normalises tubuloglomerular feedback and reduces intra-glomerular pressure

### ACR Thresholds for offering ACEi / ARB in CKD patients

- comorbid T1 or T2 DM:  $\geq 3\text{mg}/\text{mmol}$
- comorbid HTN:  $>30\text{mg}/\text{mmol}$
- no HTN or DM:  $>70\text{mg}/\text{mmol}$  (+refer to nephrology)

so basically yes the cut-off is  $>3$  for Diabetic CKD pts, but 30 for hypertensive CKD patients.

### 13. Chronic Pyelonephritis

Predisposing factors : VUR in children, obstruction - recurrent renal stones

- blunted calyx
- Corticomedullary scarring with atrophy of tubules
- Eosinophilic casts in tubules

### 14. Renal Transplant - complications :

- hyperacute : major HLA mismatch & ABO incompatibility
- Rejection occurs immediately and macroscopic features manifest following completion of vascular anastomosis and removal of clamps
- Removal of graft; or else graft in situ can cause abscess formation

Acute rejection -

- mononuclear cells predominate

Chronic rejection :

- HLA mismatch
- Previous acute rejection increases the risk
- Vascular changes most prominent with myointimal proliferation leading to organ ischaemia

- Renal artery thrombosis : sudden loss of urine output; immediate surgery, delays  $> 30$  minutes high rate of graft loss
- Renal artery stenosis : uncontrolled hypertension, allograft dysfunction and oedema; Mx - angioplasty

- Renal vein thrombosis : pain and swelling over graft site, hematuria and oliguria
- Urine leaks : diminished urine output, rising creatinine, fever, abdominal pain; USG - perigraft collection, necrosis of ureter tip and anastomosis revision is needed
- Lymphocyte : presents as a mass; drained with percutaneous technique and sclerotherapy

### 15. Cystinuria

- Autosomal recessive disorder
- Recurrent formation of renal stones
- Defect in membrane transport of cysteine, ornithine, lysine and arginine COLA
- Chromosome 2 - SLC3A1 gene
- Chromosome 19 - SLC7A9 gene
- Recurrent renal stones
- Yellow and crystalline, semi-opaque on X-ray
- Dx : Cyanide - nitroprusside test
- Mx : hydration, D-penicillamine, urinary alkalinisation

### 16. Nephrogenic Diabetes Insipidus

#### Causes :

- genetic : affecting the ADH (vasopressin) receptor
- Less commonly - mutations affecting aquaporin 2 channel
- Electrolytes : hypercalcemia, hypokalaemia
- Lithium - desensitises ability to respond to ADH in collecting ducts
- Demeclocycline
- Tubulo-interstitial disease : obstruction, sickle cell, pyelonephritis

High plasma osmolality

Low urine osmolality

Urine osmolality > 700 mOsm/kg — exclude DI

Mx : nephrogenic : thiazides, low salt/protein diet

Central DI —> Desmopressin

### 17. Erythropoietin

- stimulates the production of erythrocytes.
- Adverse effects of Erythropoietin :
  - accelerated hypertension —> encephalopathy & seizures
  - Bone aches
  - Flu-like symptoms
  - Skin rashes, urticaria
  - Pure red cell aplasia - **reduced risk with Darbepoietin**
  - Raised PCV increases risk of thrombosis
  - Iron deficiency secondary to increased erythropoiesis

### 18. Fanconi syndrome

- generalised reabsorptive disorders of renal tubular transport in PCT
- Type 2 RTA
- Polyuria
- Aminoaciduria
- Glucosuria
- Phosphaturia
- Osteomalacia

Causes :

1. Cystinosis - most common in children
2. Sjogren's syndrome
3. Multiple myeloma
4. Nephrotic syndrome
5. Wilson's disease

### 19. Focal Segmental Glomerulosclerosis

- Cause of nephrotic syndrome

Causes :

- secondary to renal pathology - IgA nephropathy, reflux nephropathy
- HIV
- Heroin
- Alports syndrome
- Sickle cell

Renal Bx : focal and segmental sclerosis and hyalinosis on light microscopy

Effacement of foot processes on EM

Mx : Steroids + / - immunosuppressants

High recurrence rate in renal transplant

<10% chance of spontaneous remission in untreated FSGS

20. Nephritic syndrome - haematuria, hypertension

- RPGN - presents as AKI; Goodpasture's syndrome, ANCA positive vasculitis
- IgA Nephropathy = Berger's disease / Mesangiocapillary GN : young adult with hematuria following URTI

Mixed Nephritic / Nephrotic presentation :

- diffuse proliferative glomerulonephritis - post streptococcal GN in children, most common form of renal disease in SLE
- MPGN = mesangiocapillary - type 1 → cryoglobulinemia, hepatitis C; type 2 : Partial lipodystrophy

Nephrotic syndrome -

- Minimal change disease : child with nephrotic syndrome, causes - Hodgkin's, NSAIDs; good response to steroids
- Membranous glomerulonephritis - proteinuria, nephrotic syndrome, chronic kidney disease; causes : infection, rheumatoid drugs, malignancy; 1/3 develop CKD, 1/3 resolve, 1/3 respond to cytotoxic
- Focal segmental glomerulosclerosis : secondary to HIV, heroin; presentation - proteinuria, nephrotic syndrome, chronic kidney disease

21. Haemolytic Uraemic Syndrome

Triad of :

- acute kidney injury
- Microangiopathic haemolytic anaemia
- Thrombocytopenia

- most cases are secondary to Shiga producing E.coli O157:H7
- Verotoxigenic, enterohemorrhagic
- Pneumococcal infections
- HIV
- Rare — SLE, drugs, cancer

Primary / Atypical HUS - due to complement dysregulation

- Mx : Eculizumab - C5 inhibitor monoclonal antibody

## 22. **Henoch Schonlein purpura**

- IgA mediated small vessel vasculitis

Clinical features :

- palpable purpuric rash with localised oedema over buttocks and extensor surfaces of arms and legs
- Abdominal pain
- Polyarthrititis

Mx : analgesia for arthralgia.

1/3 of patients have relapse

23. Anti retro viral drugs - Protease inhibitor - **Indinavir** - precipitates intratubular crystal obstruction

23. IgA nephropathy

Associated with -

- alcoholic cirrhosis
- Coeliac disease
- Dermatitis herpetiformis
- Henoch Schonlein purpura

- due to mesangial deposition of IgA immune complexes
- Mesangial hypercellularity, +ve IF for IgA & C3

- young male, recurrent macroscopic hematuria
- Associated with recent URTI

- 25% patients develop ESRF
- Good prognosis - frank hematuria



- Poor prognosis : male gender, proteinuria, HTN, smoking, hyperlipidemia, ACE genotype D

## 24. Lower Urinary Tract Symptoms

—> predominantly voiding symptoms :

- hesitancy
- Poor stream
- Straining
- Incomplete emptying
- Terminal dribbling

Mx : pelvic floor muscle training, bladder training

Moderate / severe —> alpha blocker

Enlarged prostate —> offer 5-alpha reductase inhibitor

—> predominantly overactive bladder

- moderating fluid intake
- Bladder retraining
- Antimuscarinic drugs : Oxybutynin IR / Tolterodine IR / Darifenacin OD
- Nocturia : Low dose Furosemide 40mg in afternoon; Desmopressin

## 25. Membranoproliferative GN / Mesangiocapillary GN

- nephrotic syndrome / hematuria / proteinuria
- Type 1 - cryoglobulinemia, hepatitis C
- Renal Bx : **tram track appearance** due to subendothelial and mesangial immune deposits
- Type 2 - dense deposit disease
- Caused by partial lipodystrophy, factor H deficiency
- Persistent activation of complement pathway - low circulating levels of C3
- C3b nephritic factor can also be found in 70% of cases
- C3b nephritic factor stabilises C3 converts

- Renal Bx : EM - intramembranous immune complex deposits with dense deposits
- type 3 : hepatitis B, hepatitis C

## 26. Membranous glomerulonephritis

- Sub epithelial deposits - spike and dome appearance
- Idiopathic - anti-phospholipase A2 antibodies
- Infections : hepatitis B, malaria, syphilis
- Malignancy
- Drugs - gold, penicillamine, NSAIDs
- SLE, thyroiditis

Good prognosis : female sex, young age, asymptomatic proteinuria at time of presentation

## 27. Peritoneal dialysis infections Rx :

Vancomycin / Teicoplanin + Ceftazidime

## 28. Plasma Exchange - Indications :

- Guillian Barre syndrome
- Myasthenia gravis
- Goodpasture's syndrome
- ANCA positive vasculitis (if rapidly worsening renal failure is present)
- TTP / HUS
- Cryoglobulinemia
- Hyperviscosity syndrome - secondary to myeloma

Complications of plasma exchange -

- Hypocalcemia
- Metabolic alkalosis
- Coagulation factor depletion
- Immunoglobulin depletion

## 29. **GnRH agonists - Goserelin**

**GnRH antagonist - Degarelix**

**Bicalmutide** - non steroidal anti-androgen, blocks androgen receptor

Cyproterone acetate - steroidal anti androgen, prevents DHT binding from intra -cytoplasmic protein complexes

Abiratone - androgen synthesis inhibitor

30. Risperidone - pollakiuria - frequent daytime urinary incontinence

31. Autosomal dominant polycystic kidney disease (ADPKD) type 1 is associated with a mutation in the PKD1 gene located on chromosome 16. This gene encodes for a protein called polycystin-1, which plays an important role in maintaining the structure and function of the kidneys. Mutations in this gene lead to the formation of multiple cysts in both kidneys, causing them to enlarge and lose function over time.

**32. Renal cell carcinoma - paraneoplastic effects :**

- erythropoietin = polycythemia
- PTH related peptide = hypercalcemia
- Renin
- Paraneoplastic hepatic dysfunction syndrome = cholestasis, hepatosplenomegaly
- Varicocele - left sided, due to tumor compressing veins
- Stauffer syndrome - cholestasis/hepatosplenomegaly, secondary to increased levels of IL-6
- Receptor tyrosine kinase inhibitors - Sorafenib, Sunitinib - better efficacy than IFN-alpha

33. Renal stones

Management plans for **Renal stones** :

- 1) < 5 mm —> watchful waiting
- 2) 5-10 mm —> shockwave lithotripsy
- 3) 10-20 mm —> shockwave lithotripsy OR ureteroscopy
- 4) >20 mm —> percutaneous nephrolithotomy

Ureteric stones :

- shockwave lithotripsy +/- alpha blockers < 10 mm
- 10-20 mm —> ureteroscopy

Ureteric stones causing obstruction + infection = surgical emergency

Nephrostomy tube placement / insertion of ureteric catheter / ureteric stent placement

Renal stones prevention -

- calcium stones : high fluid intake, thiazide diuretics
- Oxalate stones : CHolestyramine, pyridoxine
- Uric acid stone - allopurinol, urinary alkalinization

Urate stones R/F : **gout, ileostomy**

Drug causes of renal stones : **loop diuretics, steroids , Acetazolamide, Theophylline**

34. HLA matching - DR > B > A

Post renal transplant problems :

- ATN of graft
- Vascular thrombosis
- Urine leakage
- UTI

Hyperacute rejection - due to antibodies against ABO or HLA antigens ; **type II hypersensitivity reaction**

Acute graft rejection : mismatched HLA - cell mediated - cytotoxic T cells ; CMV can also cause acute graft rejection

35. **Gitelman's syndrome** -

**Genetics : loss of function mutation in SLC12A3 gene - codes for thiazide sensitive Na-Cl co-transporter in DCT**

- defect in thiazide sensitive sodium potassium co-transporter in DCT
- Normotension
- Hypokalaemia
- Hypocalciuria
- Hypomagnesemia
- Metabolic alkalosis

**36. Familial hypocalciuric hypercalcemia - rarely can have acute pancreatitis**

**37. Membranous nephropathy**(commonest type in adults) associated with SLE, **malignancies** of the bowel and Bronchus, penicillamine therapy, and hepatitis B infection. Can also be associated with plasmodium malaria infection in the tropics.

Strong association with HLA-DR3

Commonly seen in males

**38. Retroperitoneal fibrosis**

Associated with :

- Riedel's thyroiditis
- Previous radiotherapy
- Sarcoidosis
- Inflammatory abdominal aortic aneurysm
- Drugs - Methysergide

**39. Scrotal problems :**

Epididymal cyst

- posterior on testicle
- A/W : Polycystic kidney disease, Cystic fibrosis, von Hippel Lindau syndrome
- Dx : USG
- Mx : supportive

Hydrocele

- accumulation of fluid within tunica vaginalis
- Communicating : patency of processus vaginalis allowing peritoneal fluid to drain down into scrotum

- Non communicating : excessive fluid production within tunica vaginalis
- hydrocele can develop secondary to : epididymo-orchitis, testicular torsion, testicular tumors

Clinical features :

- soft, non tender swelling of semi scrotum
- Can get above the scrotum
- Dx : USG

Varicocele -

- abnormal enlargement of testicular veins
- Bag of worms
- Sub fertility
- Mx : USG with Doppler studies

#### 40. SLE - Lupus Nephritis

- Class I : normal kidney
- Class II : mesangial glomerulonephritis
- Class III : focal and segment proliferative glomerulonephritis
- Class IV : diffuse proliferative glomerulonephritis
- Class V : diffuse membranous glomerulonephritis
- Class VI : sclerosing glomerulonephritis

- class IV : diffuse proliferative type is most common and severe type

- Renal Bx of class IV will show :

1. Glomeruli showing endothelial and mesangial proliferation, wire loop appearance
2. Capillary wall thickened secondary to immune complex deposition
3. EM : sub endothelial immune complex deposits
4. Granular appearance on IF

#### 41. Scrotal tumors

- germ cell tumors produced hCG → increase in both estradiol and testosterone production → rise in estradiol is >>> than testosterone giving rise to gynecomastia
- Leydi cell tumors → directly secretes more estradiol and converts additional androgen precursors to oestrogen

Tumor markers :

- seminomas : hCG
- Non seminomas : AFP and/or hCG
- Germ cell tumors - LDH

- Seminomas 95% survival stage I
- Teratoma 85% survival stage I

42. First line investigations in patients with CKD → vit B12, folate and Iron studies

Second line → **serum iron profile**

Third line → **EPO**

43. Lithium toxicity - **avoid** - **Thiazide diuretics**, ACEi, ARBs, Metronidazole, NSAIDs

Most of the filtered lithium is reabsorbed at **proximal tubule**  
COLT Pee

C : Carbonic anhydrase - PCT

O : Osmotic diuretics - loop of Henle

L : Loop diuretics : ascending limb of loop of Henle

T : Thiazide diuretics - early DCT

P : Potassium sparing diuretics - distal section of DCT

44. Chemotherapy - rapid lysis of malignant cells → release of large amounts of nucleoprotein and increased uric acid production. Increased uric acid production → acute hyperuricaemic nephropathy - kidney disease and high uricaemia. Uric acid crystals may deposit in collecting ducts, pelvis and ureters → extra renal obstruction due to stone.

45. Type 2 mesangiocapillary glomerulonephritis : **idiopathic** or either after **measles** infection.

Type 2 - persistent activation of alternative complement pathway.

Low circulating levels of C3

Mesangial cell proliferation with electron-dense, linear intermembrane deposits that stain positive for C3. Also associated with partial lipodystrophy and factor H deficiency

Type 1 mesangiocapillary GN : Biopsy : **tramline appearance**

C/F : hematuria, proteinuria, nephrotic syndrome or frank kidney disease Low C3, C4. Infections with Hepatitis B, hepatitis C, cryoglobulinemia

46. Isolated hematuria - elderly patient —> possible Dx of transitional cell carcinoma of bladder

Gold standard is **cystoscopy + CTU**

47. IgA nephropathy - **mesangioproliferative GN**

Hematuria , Hypertension

Recurrent episodes of micro- or macro-hematuria.

IgA nephropathy - familial.

**Elevated IgA levels**

**Circulating IgA immune complexes and abnormal IgA glycosylation**

IgA deposition may occur in cirrhosis and gluten enteropathy.

48. **Sarcoidosis - renal disease** : high calcium level and hepatosplenomegaly

Presents with fatigue, weight loss, arthritis, dry eyes, and breathlessness.

Can lead to acute or chronic nephritis.

Classical feature : **non-caveating granuloma**

Can also present with glomerulonephritis : Membranous glomerulonephritis

49. **Acute tubular necrosis** - associated with :



- **acute pancreatitis**
- **hypotension**
- **shock**
- **haemorrhage**
- **burns**
- **diarrhoea**
- **vomiting**
- **myocardial infarction**

Other factors : Aminoglycosides, ACEi, Platinum based chemotherapy

Helpful pointers towards ATN :

- 1) urine osmolality < 350 mOsm / kg
- 2) Urinary sodium > 40 mmol/L
- 3) FeNa > 1%

50. Retroperitoneal fibrosis : **associated with abdominal aortic aneurysm**

- thought to be an auto allergic response from the leak of ceroid material out of atherosclerotic plaques
- Ureters become embedded in dense retroperitoneal fibrous tissue —> unilateral or bilateral ureteric obstruction.
- May extend from L2 to pelvic brim
- Excretion Urography - ureteric obstruction at level of pelvic brim
- Mx : corticosteroids and surgical stenting of ureteric obstruction

51. TB urinary tract - CT Urography —> cavating lesions in renal papillary areas commonly with calcification; evidence of ureteral obstruction with hydronephrosis

52. Cystinuria

- defective renal tubular reabsorption and jejunal absorption of cysteine and other dibasic amino acids - Ornithine, Lysine, Arginine
- SLC3A1 - chromosome 2
- SLC7A9 - chromosome 19
- Mx : hydration, Penicillamine, urinary alkalinization

Hartnup's disease : autosomal recessive metabolic disorder affecting absorption of non-polar amino acids { tryptophan, niacin, glutamate, valine, leucine, asparagine and Indian } by intestine and kidney.s

Affected gene - SLC6A19 - chromosome 5

C/F : FTT, photosensitivity, intermittent ataxia, nystagmus, tremor  
Triggers - sunlight, fever, drugs, stress

53. Hepatorenal syndorme - pre kidney disease - urinary sodium < 20 mOsm / L

Mx : volume challenge with low dose Dopamine or Vasopressin

54. ACR classification -

A1 - < 3 mg/mmol

A2 : 3 to 30 mg / mol

A3 : > 30 mg / mmil

#### 54. **Medullary sponge kidney**

- dilation of collecting ducts in the papillae, with accompanying for cystic changes
  - One or both, or part of one kidney, can be affected
  - Severe cases : **medullary area has sponge-like appearance**
  - Cyst formation - commonly associated with development of small calculi within the cyst
  - Diagnosis : excretion urography showing small calculi in papillary zones with surrounding increased density - dilated collecting ducts are filled with contrasting medium.
  - Increased risk of kidney stone formation
  - Associated hypercalciuria or renal tubular acidosis.
- pregnancy in patients with medullary sponge kidney : increased risk of stone formation symptomatic, asymptomatic bacteriuria, UTI

55. Reflux nephropathy - possibility of vesico-urethral reflex  
Possible in pregnancy  
Chronic renal scarring, renal impairment and proteinuria

BP control during pregnancy - labetaolol, methyldopa

56. Barter syndrome - hypokalaemia, normotension, metabolic alkalosis.

Increased renal loss of calcium magnesium

Gitelman syndrome - reduced calcium excretion

57. Peritoneal dialysis - complications :

- bacterial peritonitis : coagulase negative, staphylococci, Staph epidermis, and Staph aureus
- Ultrafiltration failure : high transporters of glucose which leads to dialysate fluid rapidly losing osmolar benefit —> less effective ultrafiltration
- Encapsulating peritoneal sclerosis : serious and rare complication of long term PD with risk factors including repeated peritonitis and duration of PD
- Hernias
- Fluid leak
- Malnutrition

Complications of hemodialysis :

- Hypotension
- Infection
- Venous stenosis or occlusion
- Air embolus
- Anaphylactic reaction to sterilisation agents

Long term -

1. Vascular disease - high risk of IHD
2. Dialysis related amyloid - beta 2 micro globulin present
3. Arthritis
4. Carpal tunnel syndrome due to beta-2 microglobulin deposition

Dysequilibrium syndrome : caused by cerebral oedema due to rapid shifts of uraemia toxins with too rapid hemodialysis in a severely uraemia patient.

58. Sickle cell disease - Chronic kidney disease

- manifested by falling Hb levels due to low EPO levels.
- Renal function of older patients with sickle cell disease should be monitored.
- CKD in sickle cell - insidious onset, low Hb levels, creatinine levels lower than normal in steady state sickle disease

59. Renal tract TB - refractory hypertension, sterile pyuria, hematuria, dysuria, renal tract calcification.

Refractory HTN due to : renin mediated, segmental renal ischaemia

Granulomas form in renal medulla, ureters, bladder and vas deferens.

60. **Aristolochic acid nephropathy** - Chinese herb nephropathy and Balkan endemic nephropathy

Anaemia, rapid renal atrophy and fibrosis, proteinuria and high incidence of genitourinary cancer.

61. The water deprivation test results, along with the clinical symptoms of polyuria and polydipsia, indicate that this patient has diabetes insipidus. As the patient is on lithium and has no clinical features suggesting a cranial cause of diabetes insipidus, he most likely has nephrogenic diabetes insipidus. The exact molecular mechanism by which lithium causes dysfunction at the collecting duct is still to be fully determined, but it is currently accepted that lithium desensitises the kidney's ability to respond to antidiuretic hormone (ADH).

62. **Positive cyanide nitroprusside test** : Cystinuria and Homocystinuria

63. Antiretroviral therapy is the treatment of choice for the disease. If a patient is already taking antiretroviral therapy (which should be all HIV-diagnosed patients) adherence should be checked.

There are five key features of HIVAN:

- massive proteinuria resulting in nephrotic syndrome
- normal or large kidneys
- focal segmental glomerulosclerosis with focal or global capillary collapse on renal biopsy
- elevated urea and creatinine
- normotension

64. Severe diarrhoea can cause excess bicarbonate loss. 0.9% Sodium chloride contains 154mmol/L of sodium and 154mmol/L chloride. Large volume resuscitation with normal saline leads to an overload of chloride ions into the blood. The increased chloride ions, force bicarbonate into the cells and in doing so reduce the available bicarbonate for the pH buffering system. The result is a **hyperchloraemic metabolic acidosis**.

65. Complications of plasma exchange

- hypocalcaemia: due to the presence of citrate used as an anticoagulant for the extracorporeal system
- metabolic alkalosis
- removal of systemic medications
- coagulation factor depletion
- immunoglobulin depletion

66. **Fabry disease**

- X linked lysosomal storage disorder
- Myelin deposits in tubular epithelium and vascular epithelium causing ischaemic nephropathy
- Defect in enzyme alpha glucosidase
- Dx : slit lamp examination of cornea
- M/C of urine sediment - Maltese cross lipid globules
- Skin angiokeratomas
- Decreased sweating
- Leg lymphoedema
- Peripheral neuropathy

- Cardiac - complete heart block, left ventricular hypertrophy, restrictive cardiomyopathy

#### 67. Gitelman's syndrome - distal tubule

Low magnesium, Sodium chloride channel inactivation

Loss of hydrogen ions —> alkalosis

Hypocalciuria

Excessive renin

Increased aldosterone

Metabolic alkalosis

Chondrocalcinosis due to CPPD deposition

- Autosomal recessive
- Disorder affecting the Na-Cl cotransporter in DCT
- Similar to over treatment of thiazides
- Metabolic alkalosis, hypocalciuria, hypomagnesemia
- Decreased sodium —> hypovolemia —> excessive renin secretion
- Excessive renin secretion -> increased aldosterone (**without hypertension**) —> hypokalaemia due to increased potassium secretion by Na/K ATPase pump

#### 68. Liddle's syndrome - collecting ducts

**LIDDLE**

**Low Hydrogen ions - metabolic acidosis**

**I - high BP**

**D - autosomal dominant**

**D - drugs - amiloride**

**L - low potassium**

**E - ENaC activation**

- Similar to pseudohyperaldosteronism
- Deficiency in ENaC channels in DCT used in reabsorbing sodium
- Normal people = aldosterone stimulates number of active ENaC channels
- Liddle's syndrome —> inhibition of degradation of ENaC channels similar to increased ENaC activity
- Increased Na levels, increased water retention, hypertension
- Low Potassium and low hydrogen ions

- Hypokalaemia, metabolic alkalosis, with HTN and volume overload

### 69. **RTA type 1 - distal RTA - Sjogren's, SLE**

- Failure to excrete Hydrogen ions
- Slightly acidic urinary pH 4.5-8
- When there is systemic acidosis, urine pH should decrease to maintain homeostasis → but if kidneys fails to lower urine pH < 5.3, it is suggestive of Distal RTA Type 1.
- Seen in autoimmune diseases, rejection of kidney transplant chronic pyelonephritis, Lithium , secondary to NSAID, lithium, amphotericin
- Decreased H ion secretion → excessive hydrogen ions → metabolic acidosis
- Metabolic acidosis → hyponatremia and hypovolemia
- Hypovolemia → increased RAAS → increased aldosteronism → hypokalaemia
- Other features : **low urinary citrate, hypercalciuria** → predisposes to renal stone, rickets, osteomalacia and nephrocalcinosis.
- Nephrocalcinosis, renal Stone formation
- Complete distal RTA - hyperchloremic acidosis
- Urine pH cannot be lowered > 5.5
- Hypokalaemia, hyperchloremic metabolic acidosis
- Conditions - hypercalciuria, hyperoxaluria, medullary sponge kidney, sickle cell disease, chronic urinary obstruction

### 70. **RTA type 2**

- Defect in resorption of bicarbonate ions from PCT
- Metabolic acidosis and increased urinary Na
- Decreased serum Na → increased aldosterone → hypokalaemia
- RTA type 2 → hypokalemia.
- Hypophosphatemia - RTA type 2 is seen in Wilson's disease
- Acidosis - hypokalaemia - hypophosphatemia
- Urine pH can be lowered below 5.3 with Ammonium chloride
- Hypokalaemia hyperchloremic metabolic acidosis
- HIGH URINE PH

## 71. RTA type 4

- **Deficiency of mineralocorticoids**
- **Hyporeninaemic hypoaldosteronism**
- Due to medications - NSAIDs reducing renin release, or ACEi
- Addison's disease
- Decreased aldosterone → less sodium resorption
- Decreased aldosterone → decrease K excretion
- Hyperkalemia
- Hyperkalemia hyperchloraemic metabolic acidosis
- NSAID decreased renin and aldosterone secretion →  
**hyporeninemic hypoaldosteronism**

## 72. Renal artery stenosis associated with fibromuscular dysplasia has a variable course and often does not progress.

**Angioplasty** - may improve hypertension in some patients.

Atherosclerotic renal disease - progressive in patients with >60% stenosis, 5% progress to total occlusion by 1 year, 11% by year 2

73. Cholesterol embolism is a common occurrence in patients with advanced atherosclerotic disease. Diabetes mellitus is associated with an increased risk of developing this condition.

Abnormal creatinine on admission increases the risk

## 74. Significant residual urine - intermittent catheterisation

Minimal residual urine - oxybutynin

2nd line → Toteridone and Solifenacin

## 75. MDRD - creatinine = muscle mass

76. Nephrotic syndrome - hypoalbuminemia, proteinuria and peripheral edema and hypercholesterolemia

Normal HDL levels

Raised LDL cholesterol.



77. Finasteride, a 5-alpha reductase inhibitor, is used in the treatment of benign prostatic hyperplasia (BPH) and its effectiveness can take up to six months. This is because finasteride works by inhibiting the conversion of testosterone into dihydrotestosterone (DHT), which contributes to prostate enlargement. The reduction in prostate size and associated symptom relief, therefore, takes some time.

78. Collecting an ACR sample

- by collecting a 'spot' sample it avoids the need to collect urine over a 24 hour period in order to detect or quantify proteinuria
- should be a first-pass morning urine specimen
- if the initial ACR is between 3 mg/mmol and 70 mg/mmol, this should be confirmed by a subsequent early morning sample. If the initial ACR is 70 mg/mmol or more, a repeat sample need not be tested.

Interpreting the ACR results

- the NICE guidelines state 'regard a confirmed ACR of 3 mg/mmol or more as clinically important proteinuria'

NICE recommendations for referral to a nephrologist:

- a urinary albumin:creatinine ratio (ACR) of 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated
- a urinary ACR of 30 mg/mmol or more, together with persistent haematuria (two out of three dipstick tests show 1+ or more of blood) after exclusion of a urinary tract infection
- consider referral to a nephrologist for people with an ACR between 3-29 mg/mmol who have persistent haematuria and other risk factors such as a declining eGFR, or cardiovascular disease

79. Erythropoietin treats CKD associated anaemia which in turn would improve exercise tolerance. It does not improve renal function.

80. This patient has presented with lower urinary tract symptoms (LUTS) which are very common in men over the age of 50 years. In

this case, the patient has predominately overactive bladder symptoms and therefore conservative measurements such as adjustments to fluid intake and bladder retraining should be trialled. If, however, these approaches fail an antimuscarinic should be offered as first-line medications. Common examples of these drugs include oxybutynin, tolterodine or darifenacin. These medications are thought to affect/block receptors located at the detrusor muscles that make up the bladder, reducing overactive symptoms. Second-line treatment includes the beta-3 agonist mirabegron which can be trialled if antimuscarinics do not improve symptoms.

81. IgA nephropathy, also known as Berger's disease, is the most common cause of glomerulonephritis worldwide. It is characterised by the deposition of immunoglobulin A (IgA) in the glomeruli leading to inflammation and damage. The classic presentation is episodic macroscopic haematuria, often following a mucosal infection such as an upper respiratory tract infection. However, it can also present with recurrent macroscopic haematuria without any precipitating factors. Coeliac disease has been linked with IgA nephropathy due to the shared pathophysiology of abnormal IgA immune responses.

82. This patient is suffering with **tremors** caused by **tacrolimus** which is his long term immunosuppression to maintain the preemptive renal transplant which he received due to his underlying adult polycystic kidney disease. Tremor is a common tacrolimus-associated side effect noticeable with outstretched hands.

Other side effects - impaired glucose tolerance, diabetes mellitus

83. A large body of evidence from the use of **azathioprine** in **pregnancy** for the treatment of both rheumatological conditions and inflammatory bowel disease, supports its use. Although it is less effective in the management of SLE with renal disease versus other options, balance of benefit risk makes it the preferred intervention.

84. Contrast-induced nephropathy contains large concentrations of iodine and due to this is a common cause of AKI in hospital. It is defined as a rise in creatinine within 72 hours (sometimes extended

to within 5 days) of contrast administration. Renal function typically resolves to normal levels after 7 to 10 days. Treatment includes hydration with isotonic saline or sodium bicarbonate. Some patients may require renal replacement therapy if severe.

**85. Renal Papillary Necrosis : CT findings :** Bilateral small kidneys, ring shadows in medulla, renal pelvis filling defects

**86.** Beckwith-Wiedemann syndrome is a inherited condition associated with organomegaly, macroglossia, abdominal wall defects, Wilm's tumour and neonatal hypoglycaemia.

**87.** *Cytomegalovirus* infection is one of the most important opportunist infections in transplant receptors. Usually happens between the first month after transplant and the sixth month. Clinically is characterized by fever, deranged transaminases, leukopenia and thrombocytopenia. It is diagnosed by polymerase chain reaction (pcr) and treated with Ganciclovir.

**88.** cutaneous **squamous cell carcinoma**. Patients who are immunosuppressed following a renal transplant are at particular risk of skin cancer. In contrast to the general population, squamous cell carcinoma (SCC) is more common than basal cell carcinoma (BCC). As described here, SCC typically presents as a quickly enlarging irregular crusted lesion that can ulcerate and produce pain or bleeding. It is commonly found in sun-exposed areas and can metastasise.

**89.** Goodpasture syndrome - pulmonary hemorrhage

One of the main complications is pulmonary haemorrhage. Factors that increase the likelihood of this include:

- smoking
- lower respiratory tract infection
- pulmonary oedema
- inhalation of hydrocarbons
- young males

**90.** HIV-associated nephropathy is seen in advanced HIV. In the absence of other potential causes (inherited or iatrogenic), HIV is

the most likely cause of this patient's renal impairment. It manifests as rapidly advancing nephrotic syndrome. Ultrasound shows large echogenic kidneys. Light microscopy most commonly shows a pattern of collapsing focal segmental glomerulosclerosis (FSGS) which often shows marked focal or global collapse of the basement membrane associated with hypertrophy and hyperplasia of the overlying podocytes. Therefore, **podocyte proliferation with marked focal collapse of the glomerular basement membrane** is correct.

91. In the context of renal transplantation, HLA-DR matching is considered the most important. This is because HLA-DR antigens are highly polymorphic and play a crucial role in immune response. The presence of anti-HLA-DR antibodies can lead to acute rejection of renal allografts, hence matching these antigens between donor and recipient can significantly reduce the risk of rejection.

92. **Abiraterone acetate** is a selective androgen synthesis inhibitor that works by **blocking cytochrome P450 17 alpha-hydroxylase**. It blocks androgen production in the testes and adrenal glands, and in prostatic tumour tissue. Abiraterone is administered orally in combination with prednisolone. In a phase III clinical trial in men with castrate refractory prostate cancer who had yet to receive chemotherapy, the combination of abiraterone and prednisolone resulted in a significant survival benefit compared to placebo and prednisolone (progression free survival 16.5 months vs. 8.3 months). It is indicated for treating metastatic castration resistant (hormone-relapsed) prostate cancer in adult men who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated. It is also indicated for treating metastatic castration resistant prostate cancer in men whose disease has progressed on or after a docetaxel-based chemotherapy regimen.

### 93. **Dialysis related Amyloidosis**

- Due to accumulation of beta-2 micro globulin
- Component of class 1 HLA and is normally filtered at the glomerulus, reabsorbed and metabolised in the PCT.

- Accumulation of beta-2 micro globulin in CKD patients occur in HD patients after at least 5 years.
- C/F : Carpal tunnel syndrome, chronic arthropathy of shoulders b/ l, followed by knees, wrists and small joints of hands; peri-articular soft-tissue swelling may be seen.

94. IgA nephropathy - diffuse mesangial proliferation and extracellular matrix expansion.

F = deposits of C3, IgA and +/- IgG.

95. Kidney transplant from CMV negative donor —> acute rejection  
T cell mediated alloimmune reaction.

Rx : Anti T-cell monoclonal antibodies and corticosteroids

96. **Nephrotic syndrome** - reduced total thyroxine levels : due to increased urinary excretion of thyroxine - binding globulin.

97. Nephrotic syndrome w/o hematuria in SLE patient suggest Class V Lupus nephritis - membranous nephropathy

- Presence of tubule-interstitial structure on EM, immune deposits along tubular basement membrane
- Presence of concurrent sub-endothelial and mesangial deposits
- Class V Lupin Nephritis : **only form** of renal disease in SLE where serological and C/F of disease may be absent.
- Complement levels - normal
- dsDNA antibodies - absent

98. **Renal transplant - immunosuppression**

- Cardiovascular disease : Tacrolimus and Ciclosporin can cause hypertension and hyperglycaemia.
- Tacrolimus - hyperlipidemia
- Monitor patients for accelerated cardiovascular disease
- Renal failure : nephrotoxic effects of Tacrolimus and Ciclosporin; graft rejection; recurrence of original disease in transplanted kidney
- Tacrolimus - hyperkalemia common side effect
- MMF - hyperkalemia is seen, lesser incidence than with Tacrolimus

- Valganciclovir - reduces renal function, not as common as hyperkalemia with Tacrolimus

Immunosuppression :

1. INITIAL : Ciclosporin / Tacrolimus + monoclonal antibody
2. MAINTENANCE : Ciclosporin / Tacrolimus + MMF
3. Add steroids if more than one steroid responsive acute rejection episode

Monoclonal antibody = selective IL-2 inhibitors —> Daclizumab, Basiliximab

99. Schistosoma mansoni - glomerulonephritis is common. Immunoglobulins, Complement components and Schistosome antigens are deposited in mesangial area —> nephrotic syndrome +/- hypertension

100. Drugs causing acute interstitial nephritis : beta lactams, sulfonamides, rifampicin, ethambutol, erythromycin

101. Neurogenic bladder

- Seen in diabetes mellitus, multiple sclerosis, cerebrovascular disease, advanced Parkinson's disease and spinal injuries
- Detrusor hyperreflexia

102. Hemodialysis - protein calorie malnutrition is most common

103. Erythropoietin - released by interstitial fibroblasts within the renal cortex.

Main extra renal site —> perisinusoidal cells in liver

104. Goodpasture's syndrome - lung biopsy =  **hemosiderin laden macrophages**

**105. Acetazolamide** - normal anion gap metabolic acidosis - chronic asymptomatic condition with partial respiratory compensation

106. Granulomatosis with polyangitis - **poor prognosis - AKI s/o renal involvement**

107. **Ganciclovir - synthetic guanine derivative**

108. Hemodialysis dialysate - **potassium concentration 2 mmol / L**

**Hyperkalemic patients —> low K dialysate to establish a concentration gradient**

109. **Hepatorenal syndrome** - splanchnic vasodilation, renal vasoconstriction.

Splanchnic vasodilation releases Nitric oxide which dilates the splanchnic and systemic due to portal hypertension. This causes arteriolar underselling, increasing bacterial translocation.

Ultimately, systemic vascular resistance falls and renal vasoconstriction occurs.

Medical management : Midodrine, Somatostatin, Dopamine

110. Diabetes - renal glomerulosclerosis

Also prone to papillary necrosis.

Thickening of GBM and glomerulosclerosis - **Kimmelsteil Wilson syndrome**

111. Diverticulitis / Diverticular perforation - if culture from patients on Peritoneal dialysis have mixed Gram negative and/or anaerobic organisms —> secondary peritonitis due to perforated large bowel or appendix.

112. **Nephrotic Syndrome** - **hypoalbuminaemia** - **intravascular volume depletion**

Due to decreased intra vascular oncotic pressure, leading to leakage of ECF from blood into interstitial.

Although there is ECF retention, intravascular contraction due to loss of oncotic pressure occurs.

Primary Na and water retention → edema

### **113. Emergency dialysis indications :**

- hyperkalemia
- Refractory pulmonary edema
- Refractory metabolic acidosis pH < 7.2
- Uraemic complications - pericarditis, encephalopathy

114. Diabetes insipidus - low urine osmolality, high serum osmolality, hypernatremia, dehydration.

Patients with lithium-related DI → may benefit from taking Amiloride 5-10mg / day

### **115. Transplant Rejection -**

Hyperacute reaction :

- due to recipient antibodies against donor kidney
- Occurs within minutes of revascularisation
- Kidney swells and becomes discoloured
- Clumping of RBCs and platelets, fibrin deposited and interstitial haemorrhage occurs
- Transplant nephrectomy required

Acute rejection

- acute deterioration in allograft function associated with specific pathological change in graft
- Acute cell mediated and acute antibody mediated
- Cell mediated rejection
- Common in first two weeks, can occur upto 6 months
- Mononuclear cell infiltrations occurs in the interstitial and subsequently in vessel walls
- Mx : high dose steroids

Antibody mediated rejection

- graft dysfunction
- Histological evidence of tissue injury
- Positive staining of C4d



- Presence of donor specific antibody

#### Chronic renal transplant rejection

- result of gradual decrease in kidney function - 3 months after surgery
- Hypertension, proteinuria —> commonly seen features
- Transplant vasculopathy —> single most important factor of chronic renal transplant rejection

116. Poor prognosis of granulomatosis with polyangitis —> presence and severity of renal function

117. Alpha blockers - Doxazosin - patients with spinal cord injury with autonomic neuropathy

118. Contrast induced nephropathy - Risk factors :

- diabetes
- Age > 75 years
- Uncontrolled hypertension
- Renal impairment
- Prior dehydration
- Non steroidal agents

119. Penicillamine - causes Nephrotic syndrome due to membranous nephropathy

120. Lupus nephritis - most common = diffuse proliferative GN

Proliferative GN > 50% glomeruli with crescents ++

Any type of lupus nephritis - consider RAAS blockade

Quick progression to CKD if untreated.

Mx : Prednisolone with Cyclophosphamide / Mycophenolate

Class I LN - abnormal urine sediment with normal light M/C

Class II LN : mesangioproliferative GN

Class IV : diffuse proliferative

Class V : membranous nephropathy

Class VI : advanced sclerosis

121. Patient with chronic alcohol and raised anion gap —> check Na and K

If normal —> points towards lactic acidosis

If abnormal —> **alcohol ketoacidosis - excessive vomiting would cause loss of Na, K and Cl**

**122. Diabetes** —> renal papillary necrosis due to untreated infection.

Linear breaks at papillary base, and ureteric obstruction results if papillae have been sloughed off.

**123. Retroperitoneal fibrosis** : malaise, back pain, NC NC anaemia, uraemia, raised ESR

- B/L ureteric obstruction beginning at the level of pelvic brim and peri aortic mass may be identified on CT / MRI
- **Surgery with ureteric stenting** is Mx
- Long term corticosteroid therapy may be beneficial
- Drugs involved in Retroperitoneal fibrosis : **methysergide** and **Practolol**

**124. Chronic interstitial nephritis** : hematuria, proteinuria, gradual increase in creatinine level and associated with use of NSAID

- most cases are seen in with use of chronic NSAID
- Presents with renal colic secondary to papillary necrosis.
- Mx : removal of causative agent and standard kidney care
- Other drugs causing this :
  1. Lithium
  2. Penicillin
  3. Acyclovir
  4. Mesalazine
  5. Phenytoin.

**125. Calcium Oxalate stone**

- patients who ingest excess amounts of food rich in oxalate ( spinach, tea)
- Calcium restricted diet

- GI disease - Crohn's —> Crohn's disease have increased colonic oxalate absorption
- Short bowel syndrome are at very high risk of oxalate stones.

126. Type 1 MPGN —> EM : sub endothelial immune complex deposition and splitting of capillary basement membrane —> **tram track appearance**

**127. Nephrotic syndrome - increase alpha - 1 globulin, increased alpha -2 globulin, decreased serum albumin**

Increase in globulin levels occurs due to increased synthesis in patients with renal protein low.

Monoclonal paraprotein band may be present if myeloma is the underlying cause.

Reduced IgA, IgG, IgM

Complications : sepsis due to Pseudomonas and other encapsulated organisms.

**128. Rhabdomyolysis** - tissue destruction or breakdown results in the release of intracellular potassium

129. IgA nephropathy - poor prognosis : **Hypertension**

130. Scleroderma renal crisis : rare complication of systemic sclerosis

- associated with presence of RNA polymerase antibodies
- Sever hypertensive hyper-reninaemic HTN occurs
- Mild MAHA can occurs
- Disease of small vessels resulting in obliterative vasculopathy and eventual onion-skin appearance.
- Mx : ACEi for control of BP
- DO NOT GIVE STEROIDS

131. Chronic reflux nephropathy - INV : **excretion urography**

**Excretion urography can show** : renal outline, calyces clubbing, cortical scarring

132. Causes of **large kidneys** :

- Amyloidosis
- Stage 1 diabetic nephropathy
- Hydronephrosis
- Acromegaly
- Renal vein Thrombosis
- Adult PKD

133. **Goodpasture's syndrome** : anti-GBM disease, HLA DR2

**HLA-DR1\*15:01** - restricted T cell epitope

134. Acute tubular necrosis - lab findings

Urinary Na > 40 & Urine osmolality < 350

135. CKD —> elevated LDL cholesterol and Triglycerides, **low** HDL cholesterol

T2DM —> hypertriglyceridemia, increased LDL and low HDL

136. **Acute Pyelonephritis** : Gram negative E.coli or Klebsiella

C/F : fever, rigours, flank pain, dysuria, polyuria, hematuria, nausea vomiting, headache, diarrhoea.

Abx : Oral Co-Amoxiclav / Ciprofloxacin

137. Hypokalaemia + HTN = Conn's syndrome

1st line investigation —> Renin : Aldosterone ratio

138. **HIV associated nephropathy**

- due to viral infection of glomerular endothelial, mesangial and epithelial cells
- R/F : long standing HIV, Afro-Caribbean origin
- Kidneys are large on USG

- Bx : FSGS with collapsed glomerular tuft, evidence of numerous tubuloreticular structure on EM
- Deposits of ribonucleoprotein and cell membrane that form under the influence of interferon alpha

138. CMV after renal transplant can present with interstitial pneumonia

139. **Retroperitoneal fibrosis** : mediastinal fibrosis, sclerosing cholangitis, **Riedel's thyroiditis**

Lower back pain, fever, myalgia, weight loss

Complications : thromboembolism and HTN

**Drugs** - Methysergide, Methyldopa, Beta blockers and Hydralazine

140. **Loin pain - hematuria syndrome** :

- poorly defined disorder characterised by loin / flank pain - severe nature + hematuria
- Co-existent thin basement membrane disease
- Bleeding into loin and obstruction causes the pain
- Dependency on narcotics is common

141. *Cystinuria - hexagon shaped crystals*

Recurrent urolithiasis with negative x-ray

Positive urine cyanide nitroprusside test

142. Renin secretion is stimulated by hypo-Na low blood volume

143. Hemodialysis - solute removal —> diffusion

Water and fluids removal —> ultrafiltration

144. CKD diminished activity of one alpha hydroxylase, which leads to failure of converting CholeCalciferol to its active metabolite 1,25 - dihydroxycholecalciferol

145. PCT - Sodium reabsorption

**146. Xanthogranulomatous pyelonephritis :**

- abnormal response causing increase in macrophages due to renal infection or urinary tract obstruction
- Related to **Malakoplakia** - rare inflammatory condition in immunocompromised patients and secondary to bactericidal defect in macrophages
- C/F : flank mass palpable, can mimic renal cancer.
- ALWAYS unilateral.
- C/F : anorexia, fevers, weight loss, flank pain
- CT scan : replacement of renal parenchyma with rounded, low density areas surrounded by ring of enhancement
- Can later have complication of AA amyloidosis → nephrotic syndrome
- Pigment laden macrophages

**147. Contrast induced nephropathy incidence - 25%**

Patients with pre-existing diabetes, + creatinine < 400 incidence - 60%

Patients with pre-existing diabetes + creatinine > 400 incidence = 100%

CCF incidence = 7-8%

Full renal recovery 68%

Partial recovery - 14%

Death / dialysis / transplantation 18%

148.

**ENDOCRINOLOGY**

**PASSMEDICINE & PASTETS**

**1. Acromegaly**

- Excessive GH secondary to pituitary adenoma

- Minority of cases : ectopic GHRH or GH production as paraneoplastic effect - e.g. - pancreas tumor

#### Clinical Features :

- coarse facial appearance
- Spade like hands
- Increase in shoe size
- Large tongue
- Prognathism
- Interdental spaces
- Excessive sweating and doily skin - due to sweat gland hypertrophy
- Other features of pituitary tumor : hypopituitarism, headaches, bitemporal hemianopia
- Raised prolactin —> galactorrhea
- 6% of patients have MEN-1
- Diabetes
- Arthropathy - pseudogout
- Sleep apnea
- Carpal tunnel syndrome
- Multinodular goitre
- Increased risk of colonic cancer
- Hypertension, increased risk of cardiovascular disease due to LVH
- Enlarged testes
- Renal stones due to hypercalciuria
- Raised phosphate
- Raised prolactin, galactorrhea, menstrual change
- Raised TGs

#### Other conditions associated with acromegaly :

- McCune Albright syndrome
- Neurofibromatosis
- MEN-1
- Familial case : familial isolated pituitary adenoma (FIPA) - mutation of aryl-hydrocarbon receptor interacting protein gene. AIP gene ; patients with AIP gene mutation tend to be younger and have larger, more invasive tumors.

INV : Raised IGF-1 levels - 1st line test  
OGTT to confirm the raised IGF-1 levels  
Serum IGF-1 to monitor disease  
MRI - to detect pituitary tumors  
Visual field and acuity testing.

Mx : 1st line = trans-sphenoidal surgery

Medical management :

- Somatostatin analogue : directly inhibits the release of GH - Octreotide
- Pegvisomant : GH Receptor antagonist : prevents dimerisation of GH - OD Sub-Q injection
- Dopamine agonists : Bromocriptine

## 2. Addison's disease

- Adrenal insufficiency - primary : due to adrenal cortex destruction = Addison's disease
- Secondary hypoadrenalism - due to exogenous steroid use
- Addison's disease : autoimmune destruction of adrenal glands —> failure to secrete mineralocorticoid

Clinical features :

- Weight loss
- Abdominal pain
- Psychosis
- Loss of pubic hair in women
- Postural hypotension
- Auricular cartilage calcification
- Increased pigmentation of gums
- High ACTH —> high MSH —> pigmented palmar creases, buccal mucosa
- Adrenal crisis = hypotension, tachycardia, hyperthermia, coma
- Pigmentation seen only in Primary adrenal insufficiency
- Hyponatremia, hyperkalemia.

Other causes of hypoadrenalism :

- Tuberculosis
- Metastases - bronchial carcinoma



- Meningococcal septicaemia - Waterhouse Friderichsen syndrome
- HIV
- Antiphospholipid syndrome

Labs - Low Na / glucose; High K / Ca<sup>++</sup>

- raised urea
- Hypoglycaemia
- Hyponatremia
- Hyperkalaemia
- Metabolic acidosis
- Raised TSH
- Hypercalcemia

Blood - eosinophilia, lymphocytosis, NC NC anaemia

Gold standard test : short Synacthen test - to check for hormonal deficiency

Failure of plasma cortisol to rise above 550 mol / L at 30 or 60 minutes after IM / IV injection of 250 mcg synthetic ACTH

Adrenal antibodies - anti-21-hydroxylase can also be seen.

### 3. Acute phase proteins

Negative acute phase proteins :

1. Albumin
2. Transthyretin
3. Transferrin
4. Retinol binding protein
5. Cortisol binding protein

Acute phase reactants - positive

1. CRP
2. Procalcitonin
3. Ferritin
4. Fibrinogen
5. Alpha - 1 antitrypsin
6. Ceruloplasmin
7. Serum Amyloid A
8. Serum Amyloid P
9. Haptoglobin
10. Complement

CRP - synthesised by liver and binds to Phosphocholine in bacterial cells and cells undergoing apoptosis.

CRP binds to these cells and activated the complement system.

#### 4. Amenorrhoea

Causes of primary amenorrhoea in those **with** secondary sexual characteristics -

- 1) physiological causes : constitutional delay - familial, pregnancy
- 2) Genito-urinary malformations : imperforate hymen, transverse septum, absent uterus / vagina
- 3) Endocrine disorders : hypothyroidism, hyperthyroidism, hyperprolactinemia, Cushing syndrome, PCOS

Causes of primary amenorrhoea **without** secondary sexual characteristics :

- 1) Primary Ovarian Insufficiency : Turner's syndrome (46XO) and gonadal agonises (46XX or 46XY)
- 2) Chemotherapy, pelvic radiation, autoimmune disease
- 3) Hypothalamic dysfunction due to -
  - Stress
  - Excessive exercise
  - Weight loss
  - Chronic systemic illness

| CONDITION                                            | FSH          | LH                        | PROLACTIN                   | TESTOSTERONE                                                   |
|------------------------------------------------------|--------------|---------------------------|-----------------------------|----------------------------------------------------------------|
| <b>Hyperprolactinemia</b>                            | Normal / Low | Normal / Low              | High                        | Normal                                                         |
| <b>PCOS</b>                                          | Normal       | Normal / increased by 40% | Normal / increased by 5-30% | Normal / moderately increased<br>Free androgen index increased |
| <b>Ovarian failure</b>                               | High         | High                      | Normal                      | Normal                                                         |
| <b>Hypothalamic (weight loss, stress, exercise )</b> | Low / normal | Low / normal              | Normal                      | Normal                                                         |

INV :

- exclude pregnancy
- FBC, U & Es, Coeliac screen, TFT
- Gonadotrophins : low level = hypothalamic causes, high level = ovarian failure
- Prolactin

- Androgens
- Oestradiol

Mx -

- Refer those with primary amenorrhoea to secondary care for specialist investigation and management
- Refer at an earlier age if :
  - A. Growth retardation
  - B. Symptoms and signs of androgen excess
  - C. Thyroid disease
  - D. Galactorrhea
  - E. Suspected genital tract malformation, intra cranial tumor, chromosomal anomaly
- Endocrinologist — hyperprolactinemia, thyroid disease, androgen excess

Complications of amenorrhoea :

- infertility
- Psychosocial distress
- Increased cardiovascular risk
- Osteoporosis

## 5. Androgen Insensitivity Syndrome

- **X-linked recessive**
- End organ resistance to testosterone in genotypical male children 46XY to have female phenotype
- Complete androgen insensitivity syndrome = testicular feminisation syndrome
- C/F : primary amenorrhoea, little or no pubic and axillary hair, undescended tests, breast development due to increased conversion of testosterone to estradiol

Dx : buccal smear / chromosomal analysis to reveal 46XY genotype

Mx : B/L orchidectomy, oestrogen therapy

## 6. Autoimmune polyendocrinopathy syndrome

- APS type 1 —> Multiple Endocrine Deficiency Autoimmune Candidiasis MEDAC

- **Autosomal recessive** —> mutation of AIRE1 gene on chromosome 21
- 2 out of 3 features needed : 1) chronic mucocutaneous candidiasis 2) Addison's disease 3) Primary hypoparathyroidism
- APS type 2 = **Schmidt's syndrome**
- **Polygenic inheritance**
- Linked to HLA DR3/DR4
- Addison's disease +
  1. T1DM
  2. Autoimmune thyroid disease

Vitiligo - can be present in both types.

#### 7. Bartter's syndrome

- Autosomal recessive
- Disorder of Na / K / Cl cotransporter NKCC2 in ascending limb of loop of Henle
- Defective Chloride absorption —> **severe hypokalaemia**
- Associated with **Normotension**
- Childhood - failure to thrive
- Polyuria, polydipsia
- Hypokalaemia
- Normotension
- Weakness

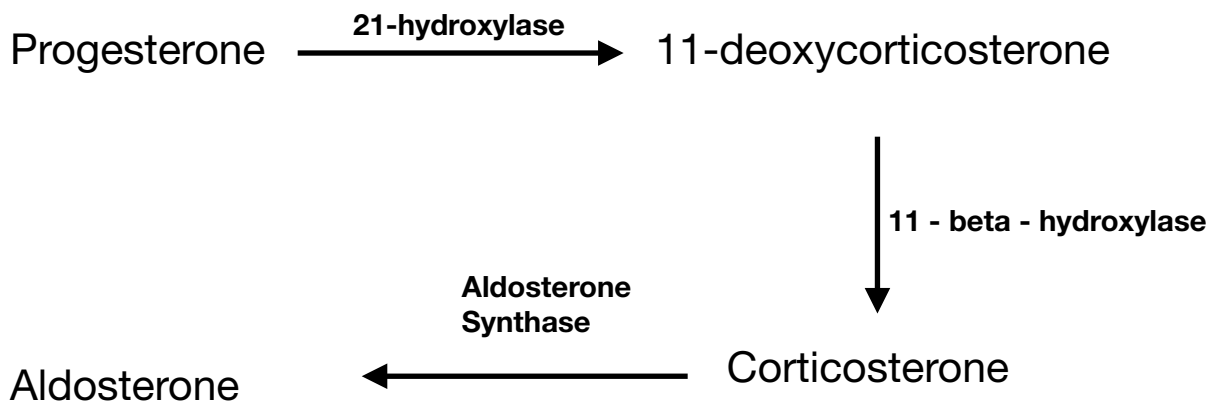
8. **Carbimazole** - blocks thyroid peroxidase from coupling and iodinating the tyrosine residues in thyroglobulin —> reducing thyroid hormone production.

Adverse effects - **agranulocytosis, can cross placenta - use in low doses during pregnancy**

#### 9. Congenital Adrenal Hyperplasia

- Autosomal recessive
- 21 - hydroxylase deficiency ~90% of cases = cortisol deficiency. +/- aldosterone deficiency and androgen excess

- Classic form = severe form, salt losing type or non salt losing type
- Non classic form = mild form, later onset



- 21-hydroxylase deficiency —> decreased production of Corticosterone, Aldosterone, Cortisol
- 21-hydroxylase deficiency —> increased production of androgenic steroids
- Excessive androgen production —> virilisation, sodium retention and hypertension.
- Virilisation - female infants presents with ambiguous genitalia and male babies have normal genitalia which can delay diagnosis
- **Salt wasting crisis** : dehydration, hypotension, electrolyte imbalance, life threatening
- Excess androgen —> precocious puberty - early development of secondary sexual characteristics in both females and males
- Infertility due to hormonal imbalances

| 21 - hydroxylase                                           | 11 - hydroxylase | 17-hydroxylase / side chain enzyme                                                              |
|------------------------------------------------------------|------------------|-------------------------------------------------------------------------------------------------|
| Virilising                                                 | Virilising       | Non virilising in females                                                                       |
| Intersex                                                   | Hypertension     | Intersex in boys                                                                                |
| 70% salt losing form - Addisonian crisis right after birth | Hypokalaemia     | <b>Mineralocorticoid excess</b> can lead to <b>low androgen</b> and <b>low oestrogen</b> levels |

|                             |                               |              |
|-----------------------------|-------------------------------|--------------|
| Ambiguous genitalia         | Can cause ambiguous genitalia | Hypertension |
| Precocious puberty in males | Precocious puberty in males   |              |

### Lab work-up

- high Serum **17-hydroxyprogesterone** —> diagnostic of 21-hydroxylase deficiency
- Corticotrophin stimulation test : assess borderline forms, **gold standard** for **non-salt losing form** —> **DONE IN UK**
- Imaging : Pelvic USG
- Karyotyping and genetic analysis

### Complications :

- sub-optimal growth and development
- Increased risk of obesity
- Insulin resistance
- Hypertension
- Increased risk of cardiovascular disease
- Women - reduced fertility
- Men - increased risk of testicular adrenal rest tumors (TARTs)
- Side effects due to long term steroid use

## 10. Glucocorticoids - Side effects

### Endocrine :

- impaired glucose regulation
- Increased appetite
- Increased weight gain
- Hirsutism
- Hyperlipidemia

### Cushing's syndrome

- moon face
- Buffalo hump
- Abdominal striae

### Musculoskeletal

- osteoporosis
- Proximal myopathy
- Avascular necrosis of femoral head

#### Immunosuppression

- increased susceptibility to severe infection
- Reactivation of TB

#### Psychiatric

- insomnia
- Mania
- Depression
- Psychosis

#### GIT

- peptic ulceration
- Acute pancreatitis

#### Eye

- glaucoma
- Cataracts

- suppression of growth in children
- Intracranial hypertension
- Neutrophilic

Mineralocorticoid - fluid retention, hypertension

#### 11. Cushing Syndrome

- Due to sustained glucocorticoid excess
- Exogenous administration —> oral steroids - most common
- Endogenous source —> Cushing's disease - adrenal adenoma
- Paraneoplastic effects causing high ACTH production —> small cell lung cancer, carcinoid syndrome

ACTH dependent causes :

- Cushing disease - pituitary tumor secreting ACTH producing adrenal hyperplasia
- Ectopic ACTH production - small cell lung cancer

ACTH independent causes :

- Steroids
- Adrenal adenoma
- Adrenal carcinoma
- Carney complex - syndrome including cardiac myxoma
- Micro nodular adrenal hyperplasia

Pseudo-Cushing's :

- mimics Cushing's
- Due to alcohol excess
- False positive dexamethasone suppression test
- Insulin stress test can be used to differentiate

Clinical Features :

- Increased weight
- Psychiatric disturbances - depression, irritability, lethargy
- Proximal muscle weakness
- Gonadal dysfunction - oligomenorrhoea, hirsutism, impotence
- Acne

Clinical signs :

- Centripetal obesity with moon face
- Buffalo hump
- Easy bruising
- Abdominal striae
- Recurrent infections
- Hypertension
- Hyperglycaemia
- Osteoporosis

General lab findings consistent with Cushing's syndrome -  
hypokalemic metabolic alkalosis

Ectopic ACTH production => low potassium levels

Labs / Investigation :

- overnight Dexamethasone suppression test : 1st line



- Dexamethasone 1mg orally at midnight and check cortisol levels at 0900
- Normal response = cortisol levels  $< 50 \text{ mol / L}$
- False positives = pseudo-Cushing : depression, obesity, alcohol excess and liver enzymes inducers
- 24 hours urinary cortisol - raised levels ; normal urinary cortisol  $< 280 \text{ mol / 24 hours}$

#### Diagnostic tests :

- 48 hour lodging dose dexamethasone suppression test
- 0.5 mg Dexamethasone four time daily for 48 hours
- Measure serum cortisol at 0 and 48 hours
- Normal response - cortisol  $< 50 \text{ nmol / L}$
- ACTH  $\rightarrow$  raised Cortisol levels in pituitary / ectopic ACTH
- ACTH will be suppressed in adrenal disease - Cushing syndrome or non ACTH dependent

#### Management

- Metyrapone : normalises cortisol levels where surgery is not possible
- Mitotane - adjunct to chemotherapy
- Primary treatment - surgical resection of tumor
- B/L Adrenalectomy  $\rightarrow$  Nelson's syndrome : high ACTH from removal of negative feedback of Hypothalamic - pituitary - adrenal axis ; causes skin pigmentation

Insulin stress test - to differentiate between true Cushing's syndrome and Pseudo-Cushing's

#### Complications :

- hypertension
- T2DM
- Obesity
- Metabolic syndrome
- Osteoporosis

| Cortisol       | ACTH       | Interpretation                                                         |
|----------------|------------|------------------------------------------------------------------------|
| Not suppressed | Suppressed | Adrenal Adenoma                                                        |
| Suppressed     | Suppressed | Cushing's disease due to pituitary tumour $\rightarrow$ ACTH secretion |

|                |                |                       |
|----------------|----------------|-----------------------|
| Not suppressed | Not suppressed | Ectopic ACTH syndrome |
|----------------|----------------|-----------------------|

## 12. Diabetes Mellitus

- T1DM - weight loss, polydipsia, polyuria
- T1DM - often presents with DKA => abdominal pain, vomiting, reduced consciousness levels
- Fasting glucose  $\geq 7$  mmol/L
- Random glucose of after 75g oral glucose  $\geq 11.1$  mmol/L
- HbA1c  $\geq 6.5\%$  48 mmol/L diagnostic
- Prediabetes => 6.0 - 6.4 / 4 to 47 mmol / L

### Anti diabetic drugs :

#### 1) Insulin - direct replacement of endogenous insulin - Sub-Q

- Main side effects : hypoglycaemia, weight gain, lipodystrophy

#### 2) **Metformin**

- increases insulin sensitivity, decreases hepatic gluconeogenesis
- GI upset, lactic acidosis type B
- First line
- CI in renal failure with eGFR  $< 30$  mL/min

#### 3) **Sulfonylureas**

- Stimulate pancreatic beta cells to secrete more insulin
- Glimeperide, Gliclazide
- Adverse effects : weight gain, fluid retention
- CI - heart failure

#### 4) **Thiazolidinediones**

- Activates PPAR-gamma receptor in adipocytes to promote adipogenesis and fatty acid uptake
- Adv - weight gain, fluid retention
- Pioglitazone
- CI - heart failure

#### 5) **DPP-4 inhibitors - Vidagliptin, Sitagliptin**

- Gliptins
- Increases **incretin levels** which inhibits glucagon secretions

- Increases incretin levels by decreasing their breakdown
- Well tolerated
- Risk of acute pancreatitis

## 6) **SGLT-2 inhibitors - Canagliflozin, Dapagliflozin, Empagliflozin**

- Inhibits reabsorption of glucose in kidney
- Reversible inhibition of SGLT-2 in renal PCT to decrease glucose reabsorption and increase glucose urinary secretion
- UTI, Fournier gangrene
- Normoglycaemic ketoacidosis
- Increased risk of lower limb amputation
- Typically results in weight loss

## 7) **GLP-1 agonists**

- **-tides**
- Incretin mimetic which inhibits glucagon secretion
- Subcutaneous
- Adv - **nausea, vomiting, pancreatitis**
- Weight loss

GLP-1 agonists / mimetics = Exenatide, Liraglutide

- increases insulin secretion
- Decreases glucagon secretion
- Weight loss
- Sub-Q injection within 60 minutes before morning and evening meals

Consider adding Exenatide to Metformin + Sulfonylurea if :

- BMI > 35
- BMI < 35 and insulin is not advised or weight loss is beneficial

## 13. T1DM

- Autoimmune destruction of pancreatic islets of Langerhans → absolute insulin deficiency and hyperglycaemia
- HLA DR4 >> HLA DR3
- Antibodies - Islet-associated antigen (IAA) antibody ; Glutamic acid decarboxylase (GAD) antibody
- C/ F : Polydipsia, polyuria, weight loss, DKA

- Family history of autoimmune conditions
- Annual monitoring of :
  - A. Retinopathy screening
  - B. Nephropathy - kidney profile
  - C. Dyslipidemia - lipid profile
  - D. Hypertension
  - E. PAD and diabetic foot problems
- Insulin regimens :
  1. BD biphasic regimen - twice daily with premixed insulin pen - Novomix
  2. QDS regimen - three the pre meal **ultra-fast acting** and bedtime **long acting**
  3. Continuous sub-q insulin infusions : T1DM where multiple dose regimens of insulin have not provided good control
- Twice daily Insulin Deter is the regime of choice

#### 14. Diabetic Ketoacidosis

- Acidosis + hyperglycaemia + ketonaemia
- Triggered by infection, inadequate treatment, trauma, surgery
- Accumulation of ketones overflow into urine causing Ketonuria and metabolic acidosis with resultant lowering of pH and bicarbonate levels
- **Glucosuria** - diuresis, dehydration, hyperosmolarity, electrolyte imbalances
- C/F : vomititng, abdominal pain, polyuria, dehydration, polydipsia, shock, lethargy, coma, Kussmaul breathing
- Glucose > 13.8, pH < 7.3, HCO<sub>3</sub> < 18, ANion gap > 10, ketonaemia

#### Mx :

- fluid replacement : IV bolus of saline - 5 to 8 litres isotonic saline
- Human soluble insulin - act rapid infusion
- Insulin infusion 0.1 U / kg / hour
- Potassium repellent
- Monitor urine output
- LMWH if increased risk of thromboembolism
- ITU / HDU admission if severe DKA = low GCS, potassium < 3.5, ketone < 6 mmol/L serum, signs of shock, pH < 7.1

#### Complications :

- cerebral edema
- Arrhythmia
- ARDS
- AKI
- Hypokalaemia
- Hypomagnesemia
- Hypophosphatemia
- Thromboembolism
- Aspiration pneumonia

Gastroparesis Rx : Metoclopramide, Domperidone, Erythromycin  
Diabetic neuropathy - rescue therapy with Tramadol

DVLA - Diabetes - HGV license

- No severe hypoglycaemic event in last 12 months
- Full hypoglycaemic awareness
- Adequate control of condition by regular glucose monitoring - twice daily and times relevant to driving
- Possesses understanding of risks of hypoglycaemia
- Group 2 license HGV - complete **VDIAB1I form**

### Group 1 drivers :

- patient can drive as long as they have hypoglycaemic awareness
- Not more than one episode of hypoglycaemic awareness requiring assistance of another person in the last 12 months
- Sulfonylureas —> notify DVLA
- Diet control -> no need to inform DVLA
- Adequate control of sugars - memory blood glucose monitors

## 15. Classification of MODY disorders

| Gene        | Classification                                                               |
|-------------|------------------------------------------------------------------------------|
| Glucokinase | MODY 2 - mild, rarely any complications                                      |
| HNF 1AE     | MODY 3 - progressive beta cell failure but <b>sensitive to sulfonylureas</b> |

|              |                                                               |
|--------------|---------------------------------------------------------------|
| HNF 4AE      | MODY 1 - neonatal hyperinsulinism                             |
| HNF 1B       | MODY 5 - associated with renal anomalies or cysts             |
| IPF-1        | MODY 4, MODY 6-11, MODY X                                     |
| SUR1, Kir6.2 | Hyperinsulinism in infancy and beta cell failure in adulthood |

## 16. Dynamic pituitary functions -

Insulin, TRH, LHRH are given to the patient.

Serum glucose, cortisol, GH, TSH, LH, FSH levels are recorded.

- GH level rises  $> 20 \mu\text{g} / \text{L}$
- Cortisol level rises  $> 550 \text{ nmol} / \text{L}$
- TSH level rises by  $> 2 \mu\text{g}/\text{L}$  from baseline level
- FSH & LH should double

Dopamine antagonist test - using metoclopramide - can also be used in the investigation of Hyperprolactinemia.

Normal response - two fold rise in prolactin.

Blunted prolactin response = prolactinoma

17. Ezetimibe - inhibits cholesterol receptor on enterocytes  $\rightarrow$  decreases absorption of cholesterol on small intestine.

- Ezetimibe : used in primary heterozygous familial and non familial hypercholesterolaemia
- Used in patients where statins are contra-indicated.
- In combination with statin, Ezetimibe is given if serum total or LDL cholesterol is not well controlled

## 18. Familial Hypercholesterolaemia

- Autosomal dominant condition
- High LDL cholesterol  $\rightarrow$  early cardiovascular disease and death
- Mutation in gene which encodes LDL receptor protein.

Clinical Diagnosis :

- Total cholesterol  $> 7.5 \text{ mmol} / \text{L}$

- LDL > 4.9 mmol / L
- Children TC > 6.7 mmol / L and LDL > 4 mmol / L
- Definite FH : tendon xanthomas in patients or 1st or 2nd degree relatives or DNA based evidence of FH
- Possible FH : family history of. MI < 50 years in 2nd degree relatives, below 60 years in 1st degree relative or family history of raised cholesterol

#### Management :

- high dose statins are first line
- 1st degree relatives should be offered screening
- Statins —> stop in women 3 months before conception due to risk of congenital defects

#### 19. Fibrates - particularly raised triglycerides

Activating PPAR alpha receptors causing increase in LPL activity reducing triglyceride levels

Adv - GI side effects, increased risk of thromboembolism

#### 20. Galactosemia

- Autosomal recessive
- Absence of Galactose-1-phosphate Uridyl transferase enzyme
- Causes increased accumulation of galactose-1-phosphate

C/F :

- jaundice
- FTT
- Hepatomegaly
- Cataracts
- Hypoglycaemia after exposure to Galactose
- Fanconi's syndrome

Dx : Urine reducing substances

Mx : Galactose free diet

#### 21. Gynecomastia

Causes :

- Physiological - normal in puberty
- syndromes with androgen deficiency : Kallman's, Klinefelter's
- Testicular failure - Mumps

- Liver disease
- Testicular cancer - seminoma secreting hCG
- Ectopic tumor secretion
- Hyperthyroidism
- Hemodialysis
- Drugs :
  - Spironolactone
  - Cimetidine
  - Digoxin
  - Cannabis
  - Finasteride
  - GnRH agonists - Goserelin, Buserelin
  - Estrogens, anabolic steroids

Rare drug causes :

- TCA
- Isoniazid
- CCBs
- Heroin
- Busulfan
- Methldopa

## 22. Hormone Replacement Therapy

- increased risk of breathing cancer - RR of 1.26 at 5 years of developing cancer - due to addition of progesterone
- Increased risk of endometrial cancer —> oestrogen by itself should not be given to women with a womb
- Increased risk of VTE
- Increased risk of stroke
- Increased risk of IHD

## 23. Hypercalcemia

1. Primary hyperparathyroidism - commonest cause
2. Malignancy - PTHrP release - squamous cell lung cancer, bone metastases, myeloma - increased osteoclastic bone resorption activity
3. Sarcoidosis
4. Vitamin D intoxication
5. Acromegaly



6. Thyrotoxicosis
7. Milk - alkali syndrome
8. Drugs - thiazides, calcium containing antacids
9. Dehydration
10. Addison's disease
11. Paget's disease of bone with prolonged immobilisation

## 24. **Hyperkalemia**

ECG changes - tall peaked T waves, small P wave, widened QRS  
=> sinusoidal pattern and systole

Causes :

- 1) AKI
- 2) Drugs - K sparing diuretics, ACEi, ARBs, Spironolactone, Ciclosporin, Heparin (heparin cause hyperKalemia due to inhibition of Aldosterone)
- 3) Metabolic acidosis
- 4) Addison's disease
- 5) Rhabdomyolysis
- 6) Massive blood transfusion
- 7) Beta blockers can cause high K levels in renal failure patients

25. Predominant hypertriglyceridemia causes :

- T1DM and T2DM
- Obesity
- Alcohol
- Chronic Renal failure
- Drugs - Thiazides, Non selective beta blockers, unopposed oestrogen
- Liver disease

Predominant hypercholesterolaemia causes :

- Nephrotic syndrome
- Cholestasis
- Hypothyroidism

## 26. **Hyperuricemia**

Increased synthesis -

- Lesch Nyan syndrome
- Myeloproliferative disorders
- Diet rich in purines
- Exercise
- Psoriasis
- Cytotoxics

#### Decreased excretion

- Drugs - low dose aspirin, diuretics, Pyrazinamide
- Pre-eclampsia
- Alcohol
- Renal failure
- Lead

### 27. Hypokalaemia with alkalosis

1. Vomiting
2. Thiazide and loop diuretics
3. Cushing's syndrome ( increased cortisol -> activation of mineralocorticoid receptors in distal tubules —> increased reabsorption of sodium and excretion of hydrogen & K ions —> alkalosis)
4. Conn's syndrome - Primary hyperaldosteronism

#### Hypokalaemia with acidosis

- Diarrhoea - non anion gap metabolic acidosis
- Renal tubular acidosis
- Acetazolamide ( inhibits CA enzyme —> inhibits reabsorption of  $\text{HCO}_3$  in proximal tubule —> increased bicarbonate excretion in urine —> acidosis and hypokalaemia)
- Partial treatment DKA

Magnesium deficiency can also be seen with hypokalaemia

#### Hypokalemia with hypertension

- Cushing's syndrome
- Conn's syndrome - adrenal adenoma
- Liddle's syndrome - defective Epithelial Sodium channel

- 11-beta hydroxylase deficiency

### Hypokalemia without Hypertension

- diuretics
- GI loss - diarrhoea, vomiting
- Renal tubular acidosis type 1 and type 2
- Bartter's syndrome - defective NKCC2 channel in ascending loop of Henle due to defective Chloride reabsorption
- Gitelman syndrome - defective thiazide sensitive Na-CL cotransporter; hypomagnesemia

### 28. **Urinary sodium > 20**

#### Hypovolaemic causes :

- diuretics : thiazide, loop diuretics
- Addison's disease
- Diuretic stage of renal failure

#### Euvolaemic causes :

- SIADH
- Hypothyroidism

#### Urinary sodium < 20

#### Sodium depletion, extra-renal loss

- Diarrhoea
- Vomiting
- Sweating
- Burns
- Adenoma of rectum

#### Water excess - hypervolaemic and oedematous patients

- secondary hyperaldosteronism : heart failure, liver cirrhosis
- Nephrotic syndrome
- IV dextrose
- Psychogenic polydipsia

#### Mx - Chronic hyponatremia

- 1) 0.9% Normal saline → can correct hypovolaemic causes
- 2) Euvolaemic → fluid restriction to 500-1000 mL / day; Rx : Demeclocycline, Vaptan
- 3) Hypervolaemic cause - fluid restriction, loop diuretics, +/- captans

Acute hyponatraemia with symptoms :  $< 120 \text{ mmol / L} \Rightarrow$  hypertonic saline 3% NaCl

ADH Receptor antagonists / Vasopressin antagonist : V2 receptor antagonism - selective water diuresis sparing the electrolytes.  
AVOID in hypovolaemic patients.  
CI in liver disease as they are hepatotoxic nature

## 29. Hypoparathyroidism

Primary hypoparathyroidism

- decreased PTH secretion
- After thyroid surgery
- Low calcium, high phosphate
- Treated with **Alfacalcidol**

C/F of hypoparathyroidism are secondary to hypocalcemia -

- 1) tetany
- 2) Perioral paraesthesia
- 3) Trousseau's sign
- 4) Chvostek's sign
- 5) Chronic - depression, cataracts
- 6) Prolonged QT

Pseudohypoparathyroidism :

- target cells insensitive to PTH
- Due to abnormality in G protein
- Associated with : low IQ, short stature, short 4th and 5th metacarpals
- Dx INV : urinary cAMP and phosphate levels following infusion of PTH
- Type 1 - no increase in cAMP / Phosphate
- Type 2 - increase only in cAMP

- Hypoparathyroidism true - increase in both cAMP and Phosphate

### 30. Kallmann's Syndrome

- Cause of delayed puberty secondary to hypogonadotropic hypogonadism
- X-linked recessive
- Failure of GnRH secreting neurons migrating to hypothalamus

C/F :

- lack of smell, anosmia
- Delayed puberty
- Hypogonadism
- Cryptorchidism
- FSH, LH levels are abnormally low / normal
- cleft lip / cleft palate
- Visual / hearing defects

Mx : testosterone supplementation, gonadotrophin supplementation can result in sperm production

31. 11 beta hydroxylase deficiency : CYP11B1 gene defect; autosomal recessive; precocious puberty in both males and females.

32. Glucagonoma - necrolytic migratory erythema - erythematous rash in the groin, extending to lower limbs, buttocks and perineum

Other features of glucagonoma - NC NC Anaemia, weight loss, angular stomatitis.

### 33. Multiple Endocrine Neoplasia

MEN 1 : 3 P's

- Parathyroid - hyperparathyroidism due to parathyroid hyperplasia
- Pituitary
- Pancreas : Insulinoma, Gastrinoma
- Adrenal & Thyroid
- MEN1 gene

MEN IIa

- Medullary thyroid cancer
- Parathyroid
- Pheochromocytoma
- RET Oncogene

#### MEN IIb

- medullary thyroid cancer
- Pheochromocytoma
- RET oncogene

**34. Orlistat - pancreatic lipase inhibitor** —> fecal urgency / incontinence and flatulence.

Liraglutide - GLP-1 mimetic ; management of T2DM and also causes significant weight loss.

BMI > 35, pre diabetic hyperglycaemia

#### 35. Pendred's syndrome

- Autosomal recessive
- Pendred syndrome gene - chromosome 7
- B/L sensorineural deafness, mild hypothyroidism and goitre.
- Progressive hearing loss and delay in academic progression.
- Defect in organification of iodine —> leading to dyshormonogenesis
- MRI brain : 1.5 turns of cochlea ( normal - 2.5 turns )
- Mx : thyroid hormone replacement and cochlear implants

#### 36. Neuroendocrine tumors

- Most common location - gastrointestinal system
- MEN1 - autosomal dominant, MEN1 gene mutation, pituitary, parathyroid, pancreas, adrenal, thyroid medullary
- MEN2 : RET oncogene, autosomal dominant, parathyroid, pheochromocytoma, medullary thyroid
- NF1 - NF1 gene mutation, autosomal dominant
- Gastrinoma - pain, nausea, loss of appetite, bleeding, anaemia, fatigue, shortness of breath
- Glucagonoma - polyuria, polydipsia, necrolytic migratory erythema

- Insulinoma - weakness, confusion, sweating, tachycardia, severe hypoglycaemia, loss of consciousness, seizures
- Carcinoid - flushing, diarrhoea, wheezing, abdominal cramping, oedema
- Non functioning neuroendocrine tumours - obstructive jaundice, abdominal pain, weight loss.
- Most tumours spread to liver - causing pain, loss of appetite, jaundice, and deranged blood tests

### 37. Primary hyperaldosteronism

- Adrenal adenoma = Conn's syndrome
- Most common cause - b/l idiopathic adrenal hyperplasia
- C/F : hypertension, hypokalaemia, muscle weakness
- 1st line investigation - plasma aldosterone/renin ratio - high aldosterone levels and low renin levels
- CT abdomen and adrenal vein sampling is used to differentiate between unilateral and bilateral causes
- Mx : adrenal adenoma => surgery
- B/L adrenocortical hyperplasia => aldosterone antagonist  
Spironolactone

### 38. Primary Hyperparathyroidism -

- Excess secretion of PTH causing hypercalcaemia
- 85% solitary adenoma

C/F :

- polydipsia, polyuria
- depression
- Anorexia, nausea, constipation
- Peptic ulceration
- Pancreatitis
- Bone pain/fracture
- Renal stones
- HTN

A/W : HTN, MEN I and II.

X-ray : pepper pot skull, osteitis fibrosis cystica

Mx : total parathyroidectomy

### 39. Drugs causing raised prolactin :

- Metoclopramide
- Domperidone
- Haloperidol
- Phenothiazines
- SSRI
- Opioids

### 40. **Pseudohypoparathyroidism**

- Type 1 : complete receptor defect
- Type 2 : receptor is intact
- Labs : increased PTH, increased Phosphate, Low calcium
- Other C/F : short 4th and 5th metacarpal, short stature, learning difficulties, obesity, round face

### 41. Remnant hyperlipidemia / Fredrickson type III hyperlipidemia / broad-beta disease / dysbetalipoproteinemia

Associated with apo-E2 homozygosity

High incidence of IHD and PAD

C/F : yellow palmar creases, palmar xanthomas, tuberous xanthomas

Mx : fibre

### 42. **SIADH - Causes :**

- 1) **Malignancy** - Small cell lung cancer, pancreas, prostate
- 2) Neurological : stroke, SAH, SDH, Meningitis, Encephalitis, Abscess
- 3) Infections : Tuberculosis, Pneumonia
- 4) Drugs : Sulfonylureas, SSRI, Carbamazepine, Vincristine, Cyclophosphamide
- 5) Others : Porphyrias, PEEP

Labs : High urine osmolality  $> 100$  mOsm / kg

Urine sodium  $> 40$  mol / L due to action of ADH on renal tubules

Mx : Fluid restriction, Demeclocycline, Vasopressin R antagonists



#### 43. Thiazolidinediones

- Agonists of PPAR-gamma receptor and reduced peripheral insulin resistance
- PPAR-gamma : intracellular nuclear receptor
- Adv : weight gain, fluid retention, liver impairment, increased risk of fractures, bladder cancer

#### 44. Papillary carcinoma thyroid :

- mixture of papillary and colloid filled follicles
- Tumors have papillary projections and pale empty nuclei
- Lymph node metastases present

#### Follicular adenoma :

- solitary thyroid nodule

#### Follicular carcinoma :

- grossly - can be encapsulated
- Vascular invasion ++

#### Medullary carcinoma :

- C cells derived from neural crest
- Serum calcitonin raised levels

#### 45. GLP-1 analogues - Exenatide

- Increases insulin secretion, decreased glucagon secretion
- Weight loss
- Used in combination with insulin to minimise weight gain
- Sub-Q injection 60 minutes before morning and evening meals. NOT after meals
- Both Exenatide and Liraglutide can be combined with metformin / sulfonyurea
- SR Exenatide - can be combined with insulin.

#### Indications :

1. BMI  $\geq$  35 in people of European descent and problems associated with high weight OR
2. BMI  $<$  35 and insulin is unacceptable or weight loss would be beneficial

Criteria : > 1% or 11 mmol/L reduction in HbA1c and 3% weight loss in 6 months to prescribe GLP-1 and continue  
Major adverse effect : nausea and vomiting

Rare cases : severe pancreatitis.

#### 46. **Gestational Diabetes**

Women with previous history of gestational diabetes => OGT as soon as possible after booking.

If first OGT is normal ==> repeat test at 24-28 weeks

Women with other risk factors such as previous macrosomia baby, 1st degree relative with diabetes, BMI > 30, family origin with high prevalence of diabetes —> offer OGTT at 24-28 weeks.

Do not wait until 16-18 weeks.

This patient fulfilled the criteria for a diagnosis of gestational diabetes on her original OGTT at 25 weeks, due to a fasting glucose > 5.6mmol/L. Her glycaemic control has been refractory to lifestyle modifications, and, most recently, the addition of metformin, as her fasting glucose has remained above 5.6mmol/L. At this stage, NICE advise that short-acting insulin should be added to her existing treatment.

Pregnant women with gestational diabetes or pre-existing diabetes  
Targets :

Fasting - 5.3 mol / L

1 hour after meals - 7.8 mol / L

2 hours after meals - 6.4 mmol / L

47. **Tamoxifen** - used in gynecomastia in patients who developed prostate cancer and are taking Goserelin as part of their treatment.

#### 48. **Uterine fibroids** :

- Benign smooth muscle tumor of the uterus
- Menorrhagia - can cause IDA
- Bulk related symptoms - lower abdominal cramping pain, bloating, urinary frequency due to pressure symptoms
- Subfertility

- Polycythaemia - rare case due to autonomous production of erythropoietin
- Dx ; TVS
- Mx : LNG-IUS
- NSAID - Mefenamic acid - menorrhagia
- Tranexamic acid - menorrhagia
- COCP
- Oral progesterone
- Injectable progesterone

Medical treatment to shrink fibroid - GnRH agonists - reduces the size. Short term treatment only.

Surgical - myomectomy, hysteroscopic endometrial ablation, hysterectomy

Complications : red degeneration - haemorrhage into tumor, occurs during pregnancy.

49. Addison's Disease - absence of A + C + D

Aldosterone + Cortisol + DHEA

Addison's C/F :

- lethargy
- Weakness
- Anorexia
- Nausea and vomiting
- Weight loss
- Salt craving
- Hyperpigmentation : increased ACTH
- Vitiligo
- Loss of pubic hair in women : due to reduced testosterone and DHEA levels
- Hypotension
- Hypoglycaemia
- Hyponatremia
- Hyperkalemia
- Addisonian crisis : collapse, shock, pyrexia

50. The correct answer is normal pregnancy. This patient has a normal TSH, with normal fT3 and fT4 levels, suggesting normal thyroid function. The elevated levels of total T3 and T4 can be explained by the high concentrations of thyroid-binding globulin

that are often seen during pregnancy. Although the patient has reported some fatigue and minor weight gain, these symptoms are non-specific in the context of pregnancy and do not necessarily point towards thyroid dysfunction.

51. Parathyroid hormone is the single most useful test in determining the cause of hypocalcaemia

52. The high incidence of parathyroid tumours and hypercalcaemia make serum calcium a useful indicator of MEN type 1 in suspected individuals

### 53. **Urinary incontinence**

- Overactive bladder / urge incontinence : due to detrusor overactivity, urge to urinate is quickly followed by uncontrollable leakage ranging from few drops to bladder emptying
- Stress incontinence : small amounts leaking while coughing
- Mixed incontinence
- Overflow incontinence : due to bladder outlet obstruction -> prostate enlargement

Mx - urge incontinence bladder retraining - **6 weeks**

Antimuscarinics are first line : Oxybutynin IR, Tolteridone IR, Darifenacin OD

Avoid Oxybutynin in frail, elderly women.

Elderly frail women - prescribe Mirabegron

Mx Stress incontinence :

- pelvic floor muscle training
- Surgical : retropubic mid urethral tape procedures
- Duloxetine : combined Noradrenaline and Serotonin reuptake inhibitor
- MOA : increases synaptic concentration of NA and serotonin within the pudendal nerve —> increased stimulation of urethral strained muscles within the sphincter —> enhanced contraction.

54. Galactorrhoea, the spontaneous flow of milk from the breast unrelated to childbirth or nursing, can be associated with primary hypothyroidism. Hypothyroidism can lead to an increase in thyrotropin-releasing hormone (TRH) which stimulates prolactin release leading to galactorrhoea. Primary hypothyroidism is also associated with hyperprolactinaemia, which can cause galactorrhoea.

55. The patient has hyperprolactinaemia with associated galactorrhoea. The causes of hyperprolactinaemia are wide. It is important to note that the patient also has secondary hypothyroidism (low T4 and inappropriately normal TSH) and hypogonadotropic hypogonadism.

**Non-functioning pituitary adenoma** is correct. Non-functioning pituitary adenomas can result in panhypopituitarism due to infiltration of the normal pituitary tissue. Compression of the pituitary stalk can result in hyperprolactinaemia due to decreased transport of dopamine from the hypothalamus to the pituitary. Dopamine acts to suppress prolactin release. Thus a non-functioning pituitary adenoma accounts for all the biochemical abnormalities present in this case.

56. The most appropriate advice for this patient is that he may be able to apply for a HGV licence if he meets strict criteria relating to hypoglycaemia. According to the UK Driver and Vehicle Licensing Agency (DVLA), people with insulin-treated diabetes can apply for a group 2 (lorry or bus) driving licence if they have no episodes of severe hypoglycaemia within the last 12 months, have full awareness of hypoglycaemia, and can show adequate blood glucose monitoring. The patient would need to demonstrate good control of their diabetes and meet these requirements in order to be eligible.

57. Thyroid storm - treatment :

- PCM
- beta blockers : Propranolol
- Anti thyroid Drugs : Methimazole / PTU [
- Carbimazole not given ]

- Lugol's iodine - given 1 hour after PTU as it can avoid worsening the thyrotoxicosis
- Dexamethasone - 4mg IV QDS - blocks conversion of T4 to T3

58. Prednisolone can cause neutrophilic through

- Demargination of neutrophils via the endovascular lining.
- Delayed migration of neutrophils into tissue.
- Release of immature neutrophils from bone marrow.

During bacterial infection, there is an increased 'left shift' seen on microscopy. In 'left shift' neutrophils are produced and released from the bone marrow at an equal rate to their consumption in the circulation.

With steroid use, 'left shift' generally does not occur due to increased production and release of neutrophils from the bone marrow but no neutrophil consumption.

59. Dapagliflozin - **normoglycemic ketoacidosis**

**60. Water deprivation test - nephrogenic DI**

**Urine osmolality after fluid deprivation - LOW**

**Urine osmolality after Desmopressin : LOW**

61. Mucosa-associated lymphoid tissue (MALT) lymphoma is correct. Although this is a rare form of thyroid lymphoma it is associated with a previous history of Hashimoto's thyroiditis and histology shows extranodal marginal B-cells.

- Anaplastic thyroid cancer is rare (1-2% of thyroid cancers). It tends to occur in older and the histology shows spindle and giant cells.

- **Hodgkin's lymphoma** tends to present with more generalised lymphadenopathy, fatigue, weight loss, and night sweats.
- Medullary thyroid cancer originates from the parafollicular cells (C cells), which produce the hormone calcitonin. The associated hormone secretion can cause diarrhoea symptoms. This cancer is often associated with multiple endocrine neoplasia syndromes (MEN) rather than Hashimoto thyroiditis.
- Although papillary carcinoma is the most common type of thyroid cancer (80% of thyroid cancer cases), it tends to be slow-growing

and affects younger patients. They are not associated with a history of Hashimoto's thyroiditis.

**62. T1DM - lipid lowering drugs guidelines :**

NICE specifically state that we should not use QRISK2 for type 1 diabetics. Instead, the following criteria are used:

- older than 40 years, or
- have had diabetes for more than 10 years or
- have established nephropathy or
- have other CVD risk factors

63. Bartter's syndrome is a rare inherited disorder due to mutated NKCC2 channels which presents with polydipsia, polyuria and a tendency to dehydration.

64. NICE recommends that adding metformin should be considered in type I diabetics with a BMI > 25, either on patient preference or to avoid the need to increase their insulin therapy. The other oral diabetic medications are not currently recommended. Weight loss is likely to be beneficial but there is greater evidence for benefit with the use of metformin. A mixed insulin regime might be used if a multiple injection basal-bolus regime was not suited to the patient's lifestyle but is not usually chosen for better glycaemic control.

65. The correct answer is **Short 4th and 5th metacarpals.**

Pendred's syndrome, a form of syndromic deafness, is not associated with short 4th and 5th metacarpals. This feature is typically seen in conditions such as Albright's hereditary osteodystrophy (pseudohypoparathyroidism), which presents with a constellation of symptoms including short stature, round face, subcutaneous calcifications, and resistance to parathyroid hormone.

**Goitre** is indeed associated with Pendred syndrome. This condition results from mutations in the SLC26A4 gene that leads to impaired iodide organification during thyroid hormone synthesis, causing enlargement of the thyroid gland or goitre. However, the goitre usually develops in later childhood or early adulthood and may not be present in all individuals with Pendred's syndrome.

**Autosomal recessive inheritance** is also correct for Pendred's syndrome. It follows this pattern of inheritance where two copies of an abnormal gene must be present for the disease to develop. Both parents must be carriers but typically do not show signs and symptoms of the condition.

**Sensorineural deafness** is a key feature of Pendred's syndrome. The mutation in SLC26A4 gene affects the function of inner ear cells responsible for maintaining fluid balance, leading to swelling and damage that result in sensorineural hearing loss. The severity varies among affected individuals but it often starts before language development.

Finally, **Euthyroid status** refers to having normal thyroid function despite the presence of goitre - another characteristic feature common in patients with Pendred's syndrome. Although they have goitres due to impaired iodide organification caused by mutations in SLC26A4 gene, these individuals are typically euthyroid meaning their thyroid hormone levels (T3 & T4) remain normal because they can compensate for this defect by increasing thyroglobulin production.

66. The Medicines and Healthcare products Regulatory Agency (MHRA) in the UK has issued a warning regarding the use of Exenatide, a glucagon-like peptide-1 (GLP-1) agonist, due to an increased risk of severe pancreatitis and renal impairment. Exenatide works by increasing insulin secretion, decreasing glucagon secretion, and slowing gastric emptying. However, studies have shown a correlation between its use and the development of severe pancreatitis and kidney damage.

**Rosiglitazone** is incorrect because it's not linked with an increased risk of severe pancreatitis or renal impairment according to MHRA. It's a thiazolidinedione which acts primarily by reducing insulin resistance. However, it has been associated with an increased risk of heart failure and bone fractures.

67. In primary polydipsia, the patient drinks excessive amounts of water, causing dilution of the serum and urine, leading to **low**



**serum osmolality and low urine osmolality.** Following water deprivation, the urine becomes more concentrated, and osmolality rises to  $>750\text{mOsmol/kg}$ . Realistically, it would not be necessary to continue to desmopressin in this instance. If the urine osmolality rises to  $>600\text{mOsmol/kg}$  following fluid deprivation, the test can be stopped as diabetes insipidus has been excluded, because the kidneys are obviously able to concentrate the urine appropriately in response to endogenous antidiuretic hormone.

68. Trousseau's sign more specific than Chvotsek's sign in hypocalcemia.

69. This question is asking about a woman presenting with confusion, bradycardia, hypotension who has been diagnosed with a **myxoedemic coma**. It is asking for the first **initial** treatment, thus the correct answer is **hydrocortisone** and **levothyroxine**.

Levothyroxine is used to replace the low levels of thyroid hormone causing the patient's symptoms.

Hydrocortisone is given to treat **adrenal insufficiency**. Patients suffering from a myxoedemic coma due to **secondary hypothyroidism** are at risk of **hypopituitarism** due to the location of the lesion. Thus patients are treated as presumed adrenal insufficiency until it has been ruled out.

70. For patients with established thyroid eye disease the following symptoms/signs should indicate the need for urgent review by an ophthalmologist (see EUGOGO guidelines):

- unexplained deterioration in vision
- awareness of change in intensity or quality of colour vision in one or both eyes
- history of eye suddenly 'popping out' (globe subluxation)
- obvious corneal opacity
- cornea still visible when the eyelids are closed
- disc swelling

71. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men  $> 102\text{ cm}$ , women  $> 88\text{ cm}$
- elevated triglycerides:  $> 1.7\text{ mmol/L}$

- reduced HDL:  $< 1.03$  mmol/L in males and  $< 1.29$  mmol/L in females
- raised blood pressure:  $> 130/85$  mmHg, or active treatment of hypertension
- raised fasting plasma glucose  $> 5.6$  mmol/L, or previously diagnosed type 2 diabetes

## 72. **Insulinoma**

- Unusual symptoms such as visual disturbances, irritability, abnormal behaviour, confusion, amnesia, paraesthesiae, drowsiness
- Symptoms arise after an overnight fast or before meals as a result of hypoglycaemia
- Hypoglycaemic symptoms predominate - weakness, confusion, sweating, tachycardia
- INV : gold standard - 72 hour supervised fasting
- Blood glucose, insulin levels, C-peptide test.
- Mx : surgical excision due to malignant potential of tumors

Glucagon stimulation test : to assess pituitary function - GH production

Sulphonyllurea assay test : helpful in conjunction with 72 hour fast in Insulinoma

Calcium stimulation test : used when USG, CT and MRI often fails to localise the tumor in Insulinoma

Exercise provocation test : rarely used

## 73. Polyglandular syndrome type 1

- Autosomal recessive
- Associated with :
  - A. Hypoparathyroidism
  - B. Mucocutaneous candidiasis
  - C. Adrenal insufficiency
  - D. Primary gonadal failure
  - E. Primary hypothyroidism
  - F. Hypopituitarism / Diabetes insipidus ( RARE )

- Can also have associated malabsorption, pernicious anaemia, vitiligo, chronic active hepatitis, ITP, myasthenia gravis

74. Premature Ovarian insufficiency : Elevated FSH, Low Estradiol; Age < 40 years; Autoimmune causes responsible for ~20% of cases

Occurs in 10% of women with Addison's disease

\*\* All patients with POI are to be tested for FMR1 permutation (Fragile X) regardless of family history.

75. Whipple's triad : clinical symptoms of hypoglycaemia, blood glucose < 3.3 mmol/L and resolution of symptoms after blood glucose is increased to normal range

Most common cause of non-diabetic hypoglycaemia is factitious use of insulins / sulfonylurea

Causes :

**- Iatrogenic / Factitious**

- Endocrine : GH deficiency or adrenal insufficiency due to hypopituitarism / Addison's disease
- Malnutrition and alcohol abuse
- Mesenchymal tumors - insulinoma, fibromas, Sarcomas, and RCC. These tumors secrete IGF-II in large quantities
- Large liver tumors - high metabolic rate created by large cells of tumors can disturb gluconeogenesis in liver
- Genetic : nesidioblastosis, Islet cell hypertrophy —> mutations of ADP dependent K channels of beta cells —> premature calcium release
- Drugs : beta blockers, Fluoroquinolones, Heparin, PPI, Sulfonylureas, Tramadol, Haloperidol, Disopyramide

C/F : hypoglycaemic symptoms

Labs :

- glucose < 2.8
- Insulin > 3 micro units / mL
- Serum C-peptide > 200 pmol / L
- TSH - normal

## 76. SIADH

- hyponatremia
- Low serum osmolality
- Concentrated urine, urinary Na > 40
- Inappropriate urine osmolality, Urine osmolality > 100

Drugs causing SIADH - Sulfonylureas, SSRIs, TCA, Carbamazepine, Vincristine, Cyclophosphamide

\*\* if serum osmolality is low < 275, urine osmolality should be < 100

Alcohol binge drinking - ADH suppression in posterior pituitary gland; picture is similar to cranial diabetes insipidus - hypernatremia, raised serum osmolality, decreased urine osmolality

77. Pneumonia - can cause euthyroid sick syndrome -

TSH - normal / low

Thyroxine - **low**

T3 - **Low**

78. **Elevated oestrogen** levels produced in pregnancy **stimulate** the expression of thyroid binding globulin (**TBG**) from the liver.

- As TBG binds to free thyroxine (fT4) and free triiodothyronine (fT3), an increase in TBG results in an **initial lowering of fT4 and fT3**.
- This in turn causes a secondary increase in thyroid-stimulating hormone (TSH).
- The net result is a new equilibrium between free and bound thyroid hormones with an **increase** in **bound-T3 and T4** but an overall **unaffected fT3 and fT4 level**.
- As it's the fT4 and fT3 that are responsible for clinic features of thyrotoxicosis these cases rarely produce clinical signs or symptoms, nor do they require treatment.

## 79. **Porphyrria cutanea tarda**

- Acquired deficiency in Uroporphyrinogen decarboxylase UROD

- Leads to accumulation of highly carboxylate porphyrinogens in liver which are oxidised to porphyrins and enters the plasma and excreted in urine
- Photosensitive porphyrins are transported to skin and causes photo damage on exposure to light
- This causes derma-epidermal separation and blister formation
- Excess porphyrins in urine causes urine to become reddish or dark

C/F :

- Blistering skin lesions on sun exposed areas of body
- blisters contain serous or serosanguinous fluid
- Increased susceptibility to infections
- Rupturing leads to scarring with hypo- or hyperpigmentation
- Hypertrichosis - cheeks and forearms
- Scarring alopecia
- Red urine due to porphyrins
- Fragile skin

Labs :

A. Elevated plasma and total porphyrins levels

B. LFT - mildly elevated AST and ALT, iron overload

Mx :

- Avoid exacerbating factors - sunlight, excess alcohol, smoking, oestrogen use
- Repeated phlebotomy
- Low dose Hydroxy chloroquine if ferritin > 600 ng/mL
- Reflectant sunscreens containing titanium dioxide or zinc oxide
- Low dose HCQ
- HIV anti retro viral
- Antiviral therapy for Hepatitis C

80. RTA type 1 : associated with -

- SLE
- Vasculitits
- Autoimmune hypothyroidism
- Drugs - Amphotericin B, Lithium
- Marfan syndrome
- Chronic pyelonephritis

- Obstructive uropathy

Mx : Oral supplementation with potassium and  $\text{HCO}_3$

81. Rapid implementation of tight glycemic control in setting of retinopathy is associated with worsening of retinopathy.

82. Breast bud development - first sign of puberty in females  
Delay puberty girls - lack of pubertal signs in girls by the age of 13 years and boys by the age of 14 years

83. This patient has micro adenoma and normal pituitary screen. The tiredness is probably functional and completely unrelated to the microadenoma.

- All of the proposed interventions in the list of options are associated with significant morbidity.
- Some autopsy series have suggested that the incidence of pituitary tumours in people with an unrelated cause of death could be as high as 27%.
- The Endocrine Society guideline for incidental pituitary adenoma recommends that patients who have an incidental finding of a pituitary adenoma should undergo baseline pituitary function tests as in this case to evaluate for hypopituitarism or hypersecretion.
- If baseline biochemistry is normal, the recommendation for follow-up is a six monthly MRI in a patient with a macroadenoma (adenoma > 1cm) and a 12-month repeat MRI for patients with a microadenoma (< 1 cm).
- If the first follow-up MRI is normal, the recommendation is for three yearly MRI scans thereafter for the patient with a microadenoma.
- The recommendation for biochemical surveillance is annual testing of baseline pituitary function in patients with a macroadenoma, but no further biochemical testing is necessary for patients with incidental microadenomas if the clinical evaluation and history remain stable.

84. Acromegaly - increased risk of colon cancer - rise in IGF-1 and changes in enterohepatic circulation and bile salt loss into the GI tract.

85. Hypothalamic amenorrhoea - low gonadotrophin, low estradiol  
Elevated ghrelin causes inhibition of Hypothalamic-pituitary-ovarian axis; alters the GnRH pulses and causing decreased release of FSH and LH.

Secondary amenorrhoea is due to low levels of leptin in women with low body weight.

Anorexia nervosa labs :

- low FSH, low LH
- Low oestrogens and 17-hydroxysteroids
- Free T4 and TSH are normal
- Anaemia with decreased WBC and platelets
- Metabolic alkalosis
- Hypocalcemia
- Hypokalaemia
- Hypomagnesaemia

86. As the survival of HIV-positive people improves, more complications of antiretroviral therapy are becoming apparent. These include a lipodystrophy-type syndrome that is characterised by the loss of peripheral and facial subcutaneous fat, but with increased abdominal and visceral fat deposition. There is also an increase in the size of the dorsocervical fat pad (buffalo hump). This fat redistribution is associated with a group of abnormalities that is usually **associated with insulin resistance, such as impaired glucose tolerance, low high-density lipoprotein (HDL) cholesterol levels and high triglycerides.**

**Glitazones** can be used to treat the condition, although some small trials have proved equivocal.

87. Retrosternal thyroid extension - CT scan

88. In a normal pregnancy, thyroid-binding globulin levels are elevated above non-pregnant levels because of oestrogen-stimulated synthesis.

As a result, total T3 and T4 levels are elevated but biochemically active free T3 and free T4 levels are within normal limits. In contrast, pathological hyperthyroidism (eg, secondary to Graves' disease) is marked by elevated levels of free T3 and free T4 and

suppressed TSH levels. The same pattern of thyroid function abnormalities occurs in transient hyperthyroidism of hyperemesis gravidarum (THHG).

Diagnosis is based on four criteria:

- abnormal thyroid function tests developing in the context of hyperemesis gravidarum
- no evidence of pre-pregnancy hyperthyroidism
- absence of physical examination findings consistent with hyperthyroidism
- negative thyroid autoantibody titre.

**89. Dulaglutide - GLP-1 agonist** : safe in T2DM and CKD

**90. Hypothyroidism - silent pericarditis : pericardial effusion**

has high cholesterol content, unusual secondary pericarditis with cholesterol deposits of gold paint appearance. Pericardial effusion very rarely needs to be treated in its own right and subsides with thyroid replacement therapy.

**91. Hereditary hemochromatosis with loss of libido - give testosterone**

**92. Carney complex** : autosomal dominant condition - inactivating mutation of protein kinase A on chromosome 17

Dx if 2 out of the following OR one feature + affected 1st degree relative

- 1) spotty skin pigmentation
- 2) Myxoma
- 3) Endocrine tumors - primary pigmented nodular adrenocortical disease (commonest), Sertoli cell tumors, GH / PRL producing tumors, pituitary adenomas, thyroid adenomas and ovarian cysts
- 4) Psammomatous melanotic Schwannoma

**93. Charcot's arthropathy** - immobilisation boot for 3-6 months can significantly reduce long-term joint damage and progression of disease. Also can start patient on bisphosphonates in reducing bone turnover

**94. VIPoma** - metabolic acidosis with normal anion gap.



Also called as pancreatic cholera syndrome / Verner - Morrison syndrome / WDHA syndrome

Watery diarrhoea + normal anion gap metabolic acidosis = VIPoma

94. Patients who are overweight without T2DM, bone mineral density is increased. This may be due to increased levels of Oestrone, produced in adipose tissue via conversion of theca androgens.

95. Post partum thyroiditis - transient effect; Rx with Propranolol

96. Hyperthyroidism - significantly lower resting PaCO<sub>2</sub> tension, tidal volume and significantly higher inspiratory flow and PaO<sub>2</sub> .

97. **Levonorgestrel - delays ovulation.**

98. Papillary cancer of thyroid - Near total or total thyroidectomy + RA Iodine + Thyroid hormone supplementation

IF age > 45 years, tumor size > 2 cm

Age < 45 years and tumor size < 2 cm => partial thyroidectomy ONLY

Total thyroidectomy indications :

- medullary cancer > 5mm
- All other cancers > 4 cm
- Metastasis +
- Extra - thyroid spread +
- Lymph node involvement
- B/L spread
- Familial disease

Chemotherapy - Tyrosine kinase inhibitors : Lenvatinib and Sorafenib - for locally advanced / metastatic papillary, follicular or Hurth cell cancer ONLY if RA iodine did not work

Cabozantinib - recommended for medullary thyroid cancer that has metastasised and is not operable.

Thyroid lymphoma - chemotherapy and external beam radiotherapy

99. Complete androgen insensitivity => female external genitalia and cryptorchidism

100. Risk of developing background retinopathy is increased with duration of diabetes mellitus.

97% of T1DM develops background retinopathy 15 years after diagnosis.

101. PCOS - Sex hormone binding globulin - binds to both testosterone and estradiol. It is reduced in insulin resistance and PCOS.

102. GLUT-4 : glycoprotein coded on short arm of chromosome 19.

Insulin binding to GLUT-4 => tyrosine kinase activation and initiation of cascade of secondary intracellular process.

GLUT-4 => channel through which glucose is taken up into muscle and adipose tissue.

GLUT - 1 : non insulin stimulated glucose into cells

GLUT - 2 : transports glucose into beta cells

GLUT - 3 : non-insulin mediated glucose uptake into brain neurone

GLUT - 5 : fructose transporter expressed on apical border of enterocytes into small intestine

103. SIADH findings :

- concentrated urine - Urine NA > 20
- Hyperosmolality > 100
- Hyponatremia Na < 125

- Absence of hypovolemia, oedema, diuretics

Confirmation :

- Serum osmolality  $< 275$
- Urine osmolality  $> 200$
- Urine Na  $\geq 30$

104. Excess thyroid - cessation of menses - decreased oestrogenisation and increased risk of osteoporosis.

105. **Sturge Weber syndrome** - port wine naevus on one side of face; associated with pheochromocytoma.

106. Causes of secondary amenorrhoea in those with no features of androgen excess include:

- **Physiological causes:**

- pregnancy
- lactation
- menopause.

- **Premature ovarian insufficiency**, for example, due to:

- chemotherapy
- radiotherapy
- autoimmune disease.

- **Hypothalamic** dysfunction due to stress, excessive exercise, and/or weight loss (functional hypothalamic amenorrhea). The female athlete triad is a medical condition observed in physically active females (such as distance runners, gymnasts, and dancers) involving low energy availability (with or without eating disorders), menstrual dysfunction, and low bone density.

- Other **hypothalamic** causes, including:

- 1) chronic systemic illness (such as severe cardiac, renal, or liver disease)

- cranial irradiation, infection or head injury.

- Pituitary causes, including:

- 1) prolactinoma and other hormone-secreting pituitary tumours

- 2) head injury and cranial irradiation

- 3) hypopituitarism (for example, after traumatic brain injury)

- Sheehan's syndrome (pituitary infarction after major obstetric haemorrhage).

**Uterine** causes, including:

1. cervical stenosis
2. Asherman's syndrome (intrauterine adhesions).

• **Thyroid** disease (hypothyroidism or hyperthyroidism).

• **Iatrogenic** causes, including:

- contraceptives - extended-cycle combined oral contraceptives, injectable progesterone, implantable etonogestrel (Nexplanon®), and levonorgestrel intrauterine system (Mirena®) may cause amenorrhea

- drugs (such as antipsychotics, which can cause increased prolactin levels) and illicit drug use (in particular cocaine and opiates, which can cause hypogonadism)

- surgery (hysterectomy, endometrial ablation, and ovarian surgery).

• Causes of **secondary amenorrhoea** in those with features of **androgen excess** (such as hirsutism, acne, and virilization) include:

- 1) polycystic ovary syndrome
- 2) Cushing's syndrome
- 3) late-onset congenital adrenal hyperplasia
- 4) androgen-secreting tumours of the ovary or adrenal gland

(rare).

107. Water deprivation test - to identify the cause of polydipsia and/or polyuria.

- 1st step —> confirm polyuria urine output > 3000 mL / 24 hours
- Exclude major metabolic causes - hypercalcemia, hyperglycaemia, hypokalaemia, chronic renal failure
- Primary polydipsia - patient is not dehydrated but water overloaded in the resting state  $Na < 140$
- Cranial DI - failure to concentrate urine due to lack of ADH. High plasma osmolality and low urine osmolality. Administration of DDAVP restores the kidneys to concentrate urine and raises its osmolality.
- Partial cranial DI - initial plasma osmolality is high, weak ADH action, similar effect is seen in primary polydipsia - to differentiate partial cranial DI and primary polydipsia - measure post hydration serum ADH levels

|                           | <b>Initial Plasma Osmolality</b> | <b>Final Urine Osmolality</b> | <b>Urine Osmolality post - DDACP</b> | <b>Final plasma ADH</b> |
|---------------------------|----------------------------------|-------------------------------|--------------------------------------|-------------------------|
| <b>Normal</b>             | Normal                           | > 600                         | > 600                                | High                    |
| <b>Cranial DI</b>         | High                             | < 300                         | > 600                                | Low                     |
| <b>Nephrogenic DI</b>     | High                             | < 300                         | < 300                                | High                    |
| <b>Primary polydipsia</b> | Low                              | 300-400                       | 400                                  | Moderate                |
| <b>Partial Cranial DI</b> | High                             | 300-400                       | 400-600                              | Relatively low          |

108. 50% risk of T1DM in monozygotic twins as concordance rates are higher in monozygotic twins than dizygotic twins.

50% chance of T1DM in unaffected twin.

109. Hypokalemic periodic paralysis : related to muscle voltage gated calcium channel mutation CACLN1A3

CACNA1 - calcium channel

SCN4A - alpha sub unit of sodium channel

110. Development of diabetes in a patient with normal weight + skin tag formation + excessive acne + carpal tunnel syndrome ==> ? Acromegaly

111. Mnemonic for hypercalcemia - VITAMINS TRAP

V - Vitamins A & D

I - Immobilisation

T - thyrotoxicosis

A - Addison's disease

M - Milk alkali syndrome

I - Inflammatory disorders

N - Neoplasia

S - Sarcoidosis

T - Thiazides

R - Rhabdomyolysis

A - AIDS

P - Paget's disease, Parenteral nutrition, Parathyroidism

112. Thyroid replacement therapy —> guided by dose adjusted serum TSH values 4-8 weeks following initiation of therapy.

Within 4 weeks of therapy —> TSH levels may decline

113. Saline suppression test : secondary confirmation of hyperaldosteronism.

114. Primary hypertriglyceridemia (w/o hypercholesterolaemia)

- elevated VLDL : which is associated with even higher risk than elevated LDL
- Lipoprotein lipase and Apoprotein CII deficiency - elevated triglycerides
- Apoprotein CII deficiency : hyperlipoproteinemia type IB / familial apolipoprotein CII deficiency
- C/F : eruptive xanthomas, lipaemia retinalis, retinal vein thrombosis, pancreatitis and hepatosplenomegaly.
- Chylomicrons can be detected in fasting blood sample/

Primary mixed hyperlipidemia

- elevated cholesterol and Triglycerides.
- Premature atherosclerosis
- Remnant hyperlipidemia (= type 3 hyperlipidemia) - rare cause of mixed hyperlipidemia
- Associated with Apoprotein E2

Apolipoprotein E - familial dysbetalipoproteinaemia

Apoprotein AII : found in HDL cholesterol

Lipoprotein B - functions in LDL catabolism; its deficiency resulting in higher levels of LDL

Familial hypertriglyceridaemia - type IV hyperlipoproteinaemia : elevated triglyceride levels, NORMAL cholesterol levels. Due to excess hepatic production of VLDL

Heterozygous for lipoprotein lipase gene inactivating mutations

Autosomal dominant disorder.

Accompanied by insulin resistance, obesity, hyperglycaemia, hypertension and hyperuricaemia

115. Stop lithium and replace with Lamotrigine / Carbamazepine for mood disorders in women who are trying to get pregnant.

116. Osteoporosis - predominantly affects the trabecular bone as the amount of bone is decreased and structural integrity of trabecular bone is impaired.

117. **BP control >> tight glycemic control** - in patients with both T2DM and Hypertension .

118. Thyroid size - USG

119. PCOS - hirsutism and acne

- Co - cyprindiol ( Cyproterone acetate + ethinylestradiol)
- Brand name - **Dianette**
- This blocks the androgen receptors via negative feedback because of presence of ethinylestradiol
- Effective in reducing androgenic acne

120. Incomplete suppression of cortisol following high-dose Dexamethasone is typical of Cushing's disease.

Pituitary tumors respond to exogenous CRH

\*\* Ectopic sources and Adrenal tumors do not respond to CRH

121. Doxazosin - alpha blocker - smallest effect on renin and aldosterone levels.

Drugs having effect on renin and aldosterone : K sparing diuretics, ARBs, ACEi, CCBs, Angiotensin antagonists - hence patients are asked to stop for 4-6 weeks before the test.

122. End stage renal disease due to diabetes is the number one cause in US and UK .

123. MEN1 - affected gene menin gene - located on chromosome 11

124. Pituitary apoplexy - low BP, low sodium, high potassium, vision loss - Addisonian crisis can also occur. Rx : IV Hydrocortisone

125. **Somatostatin receptor** - 7 transmembrane G-protein receptor

Lanreotide - Somatostatin analogue long-acting. Stimulation of somatostatin receptor leads to inhibitor of production of a number of hormones, insulin and secretin.

Somatostatin analogues are used for treatment of acromegaly, pre surgery or after Surgery.

Side effects : GI upset, diarrhoea, abdominal cramps, can precipitate gall stone formation.

126. Dihydrotestosterone - higher affinity than testosterone for androgen receptors and drives the development of secondary sexual characteristics.

DHT also important in development and maintenance of prostate gland and seminal vesicles.

127. Rapidly growing thyroid mass - anaplastic thyroid carcinoma Associated with regional lymphadenopathy and tracheal compression.

128. Karyotypically 46XY - with normal breast development and no pubic or axillary hair.



Due to lack of DHT receptors.

This patient is genotypical male and has testicular feminisation.

Majority of cases occur due to lack of androgen receptors to DHT.

DHT is formed from testosterone by 5-alpha reductase and is responsible for development of male secondary sexual characters.

129. Dysmenorrhea, menorrhagia and pre-menstrual syndrome (>1 in 10 people) - common in women who are prescribed COCP.

DVT and PE 15 per 100,000 pill users

Migraine 1 in 100 and 1 in 1000 users.

130. Gestational diabetes complication - neonatal hypoglycaemia

Infants of DM mother are used to hyperinsulinism. Poorly controlled diabetes means fetal glucose levels are high.

This stimulates fetal islets of Langerhans which can lead to hyperinsulinaemia after delivery and can cause neonatal hypoglycaemia.

131. Sarcoidosis - increased hydroxylation of vitamin D - as in sarcoidosis patients hydroxylation can occur outside the kidney

Mainly in macrophages in the granulomas that are present in Sarcoidosis.

132. Modest hyperprolactinemia is reported in cases of Addison's disease and is glucocorticoid sensitive,

Absence of steroid enhanced hypothalamic dopaminergic tone is thought to lead to hyper-responsiveness of lactotroph to TRH which results in excess prolactin levels.

Hyperprolactinemia can cause cessation of menses.

133. Segmental pattern of flame haemorrhages - branch retinal vein occlusion

134. Isolated FSH deficiency in a male patient with normal LH levels rules out a hypothalamic disorder.

FSH stimulates Sertoli cells in the testes to produce Androgen binding proteins and inhibin.

ABP - responsible for binding testosterone and making it available for spermatogenesis in the seminiferous tubules.

Decreased FSH - decreased ABP - oligospermia.

135. Insulin inhibits Pyruvate decarboxylase.

Insulin upregulates : G-6-PD, Glucokinase, Pyruvate dehydrogenase, glycogen synthetase

136. Fibroblasts are stimulated by both anti-TSH receptor antibodies and activated T cells and are responsible for Glycosaminoglycans GAG deposition.

GAG is hydrophilic and draws water from the surrounding tissues leading to oedema.

And this edema causes pressure on the optic nerve.

Mx : immune modulation with corticosteroid and MMF may be effective.

Teprotumumab - IGF-1 inhibitor - also can be used in treating thyroid eye disease

137. Carbimazole and PTU = THIONAMIDES

138. Ovulation - rise in LH and Progesterone

139. Simple syndrome = MEN2

140. Primary ovarian failure v/s secondary ovarian failure

In primary ovarian failure - FSH and LH will be elevated

Secondary ovarian failure - low or normal FSH and LH

141. Bartter syndrome = increased urinary Calcium excretion, hypokalaemia, metabolic alkalosis and raised Renin & Aldosterone levels.

Increased production of renal prostaglandin E2.

Renal Bx : hyperplasia of juxta glomerular apparatus.

142. Necrobiosis lipoidica - one or more yellowish brown patches which develop slowly over the lower legs for several months.

Round , oval or irregular shape - centre of lesion becomes shiny, pale, thinned with prominent blood vessels telangiectasia.  
At very high risk of secondary bacterial infection.

143. MODY 2 - fasting blood glucose is higher than normal.  
Rise in glucose post OGTT is much lesser than with conventional diabetes.

MODY 2 - mutations of glucokinase gene ; family relatives will have well controlled diabetes with no complications.

144. Lipohypertrophy - injection of insulin at same time multiple times

Lipoatrophy - formation of anti-insulin antibodies which is an immunological side effect of insulin therapy. Frequently seen with use of recombinant and analogue insulins.

145. HLA DR3 - associated with :

- diabetes mellitus
- Autoimmune hepatitis
- Dermatitis herpetiformis
- Graves' disease
- Membranous glomerulonephritis
- Myasthenia gravis
- Addison's disease
- Sjogren's syndrome
- SLE

HLA B47 : congenital adrenal hyperplasia

HLA B27 - Seronegative arthropathies

HLA A28 : Schizophrenia

HLA DR27 : minimal change disease nephrotic syndrome

146. Lid retraction and lid lag - signs of sympathetic overactivity and can occur in any thyrotoxic state not specific to Graves' disease.

147. Testosterone derived from cholesterol and converted by aromatase into estradiol.

Chronic alcohol and obesity are known to increase aromatase activity which leads to feminisation in obese patients or those with alcoholism.

148. Glucagon acts by bypassing the blocked Beta blocker in beta blocker overdose and activates adenylyl cycles and promotes formation of cAMP from ATP. cAMP in turn exerts a direct Beta stimulant action on heart.

149. Hypothyroidism - most common after thyroidectomy - 10% of patients.

Will require levothyroxine indefinitely.

150. Decline in progesterone = shedding of endometrium

151. **Melatonin -**

- synthesised and secreted by pineal gland from Serotonin
- N-acetyl transferase + acetyl CoA converts serotonin to N-acetyl serotonin.
- N-acetyl serotonin is converted to melatonin by **hydroxyindole-O-methyltransferase**
- Exposure to darkness causes activation of hypothalamus by retinohypothalamic nerves
- Results in increased Noradrenaline secretion by post-ganglionic sympathetic nerves (Nervi conarii) that innervate the pineal gland
- Noradrenaline acts by alpha receptors in the pineal gland to increase intracellular cAMP levels which then causes an **increase in serotonin N-acetyltransferase activity**

152. Non classical CAH : deficiency of enzyme 11-beta-hydroxylase

- results in accumulation of adrenal sex steroids mainly DHEA
- Patients with CAH present with symptoms of reduced production of cortisol and over or under production of mineralocorticoids and androgens.

153. **Insulin - HGV license criteria :**

- no severe hypoglycaemic episodes in last 12 months
- Recently started insulin - show three months of blood glucose monitoring on insulin
- Have full hypoglycaemic awareness
- Can show adequate control of their diabetes by regular blood glucose monitoring at least twice daily and at times relevant to their driving
- Can demonstrate understanding of their risks of hypoglycaemia
- No complications of diabetes

154. MODY characterised by :

- raised HDL cholesterol
- Preserved insulin sensitivity
- Low renal threshold for glucose - glycosuria

155. Riedel's thyroiditis - rare chronic inflammatory disease of thyroid gland characterised by dense fibrosis that replaces normal thyroid parenchyma.

- fibrotic process involves adjacent structures of neck and extends beyond thyroid capsule.
- Thyroid function depends on the extent to which the normal thyroid gland has been replaced by the fibrotic tissue.
- It can cause local symptoms such as hoarseness, stridor and dysphagia.
- Medical treatment includes the use of corticosteroids and tamoxifen.
- If patient develops hypothyroidism, levothyroxine can be used.
- In cases of tracheal decompression surgery can be done.

156. **Post partum thyroiditis**

- it is a common thyroid disorder that presents during the first postpartum year.
- It is the occurrence of either transient hyperthyroidism, transient hypothyroidism, or transient hyperthyroidism, followed by hypothyroidism.
- Most women become euthyroid, one year postpartum.
- It is an exacerbation of an underlying auto immune thyroid aggravated by immunological rebound that follows the partial immuno suppression of pregnancy.
- HLA DR3, DR4, DR5 are at an higher risk.
- In women who develop postpartum thyroiditis - CD4+ / CD8+ and CD4+ 2H4+ ratios are elevated during pregnancy and post part.
- Most likely in those who have TPO antibodies are positive 27 times more likely.
- M/C : lymphocytic infiltrate or diffuse destruction - changes similar to Hashimoto's thyroiditis.

156. In pubertal girls, diagnosis between androgen insensitivity and Mullerian agencies can be made by assessing serum testosterone levels, followed by karyotype analysis. Orchidectomy is advised due to risk of testicular cancer.

157. >90% of patient with overt hypothyroidism will have **dyslipidaemia.**

- **Accumulation of LDL cholesterol due to a defective number of cell surfaces for LDL causing decreased catabolism of LDL.**

**158. Paget's disease - multinucleate osteoclasts on bone biopsy**  
**mixed lytic / sclerotic appearance - Paget's disease and metastasis both**

**159.** Screening is recommended for people with MEN2 -

- pentagastrin test is used to screen for medullary thyroid cancer with measurement of calcitonin
- Monitor calcium
- Pheochromocytome - sreening - 24 hour urinary catecholamine estimation or plasma catecholamines.

160. DKA = lipolysis

161. Gitelman syndrome - hypokalemic metabolic alkalosis - NORMOTENSION. With low calcium excretion due to abnormal functioning thiazide sensitive sodium chloride co-transporter

162. Diabetic ulcers : non removable casting to offload pressure on the uninfected fore foot and mid foot diabetic ulcers which allows time for tissue to heal.

163. GLP-1 analogue are **contra indicated** in patients with gastroparesis as they can exacerbate symptoms of gastroparesis.

Exenatide - cannot be used in patients with creatinine clearance < 30 mL/min

164. DPP IV inhibitors can be used in patients with renal impairment.

165. Patients with myxoedema and hypothyroidism - **cardiomegaly, pericardial effusions and heart failure as a complication.**

166. Diabetic gastroparesis : Domperidone.

167. **Familial hypocalciuric hypercalcemia** - autosomal dominant

Associated with loss of function mutation in CaSR gene - encodes for calcium sensing receptor in parathyroid and kidney tissue.

168. **LIRAGLUTIDE - CONTRA INDICATED IN IBD**

**EXENATIDE - CONTRA INDICATED IN GFR < 30**

**SEMAGLUTIDE - SAFE TO USE IN IBD AND RENAL IMPAIRMENT**

169. **HYPERTENSION + OBESITY + T2DM** - AVOID THIAZIDE DIURETICS AND NON SELECTIVE BETA BLOCKERS

170. **Gordon's syndrome** -

- aka **pseudo-hypoaldosteronism** - that mimics **hypoaldosteronism**
- Due to failure of response to aldosterone and levels of aldosterone are elevated due to a lack of feedback inhibition.
- C/F : short stature, severe hypertension, low FeNa, normal renal function, hyperchloraemic metabolic acidosis, **low renin and elevated aldosterone levels.**
- Hyperkalemia \*\*

171. Benign angiofibromas - MEN1

172. Pituitary tumor causing hyperthyroidism will have raised TSH, raised T3 and raised T4.

INV - MRI Pituitary gland

173. Primary hyperparathyroidism surgery indications :

- hypercalcemia
- Impaired renal function
- Renal stones
- Nephrocalcinosis
- Reduced bone mineral density
- Elevated urinary calcium excretion

174. Cushing's - glucocorticoid excess - potassium depletion and sodium and water retention due to increased chloride secretion

ABG = **hypokalaemia hypochloraemic metabolic alkalosis**

175. Studies show increased risk of diabetic embryopathy - anencephaly, microcephaly and congenital heart disease —> directly related to elevated HbA1c levels.  
Increased risk of spontaneous abortions.

176. Deficiency of **cystathione synthase** - **type 1 homocystinuria**



**Branched chain ketoacid dehydrogenase deficiency = maple syrup urine disease**

**Methylenetetrahydrofolate reductase deficiency = high homocysteine levels - seizures, gait dysfunction, developmental delay**

177. Psychogenic polydipsia - low plasma and urine osmolality due to large amounts of water

178. 1st trimester - TSH upper limit 2.5  
2nd trimester TSH upper limit - 3

179. Pheochromocytoma - raised noradrenaline shows extra adrenal tumor - Scanning with MIBG demonstrates sites of sympathetic activity in 90% of cases

Useful when CT / MRI are inconclusive  
MIBG = 131 metaiodobenzylguanidine

180. Exogenous GH -  
- increase in lean body mass  
- Decrease in body fat  
- Improvement in exercise capacity (no change in muscle strength )  
- Increase in Bone mineral density in ONLY men

181. Beta hydroxy butyrate- persist for longer can cause mild acidosis in treatment of DKA

182. Hypopituitarism causes anaemia due to loss of melanocyte-stimulating properties of adrenocorticotrophic hormones.

Postural hypotension, tiredness, slow reacting reflexes due to hypothyroidism and amenorrhoea due to loss of gonadotrophin.

Gold standard test : insulin stress test in patients with ACTH and GH deficiency

Main risk - hypoglycaemia

CI - seizures / IHD / adrenal insufficiency

183. **Oestrogen** - hormone responsible for fusion of epiphyseal plates and cessation of growth, and skeletal maturation.

Growth spurt at puberty due to androgens in males and estrogen in females.

184. Common side effect of Oestrogen therapy - treat tenderness, bloating, nausea, leg cramps, headache.

185. Adrenal insufficiency → TSH levels low

186. Increased prolactin inhibits GnRH through negative feedback mechanism. Decreased GnRH causes decreased FSH and LH

187. Non classical CAH - Hispanic, Yugoslavian, Eastern European Jewish descent

Mx - glucocorticoid supplementation in juveniles.

Adults - flutamide (used as anti androgen) treatment for mild symptoms

188. **Saxagliptin - increased incidence of heart failure**

189. Metoclopramide - binds to D2 receptor on pituitary lactotrophes

190. Glucagon activates adenyl cyclase

191. ADH - cortical and medullary collecting ducts.

192. HNF-1 alpha - MODY 3 - gene on chromosome 12

193. Prednisolone : hydrocortisone = 1 : 4  
Fludracortisone - 50-300 mcg / day

Effectiveness assessed by serum electrolytes, postural BP, suppression of plasma renin activity to normal levels.

194. Maternal thyroid antibodies → higher risk of spontaneous abortions and miscarriage and pre term delivery.

195. Sulphonylureas work via mimicking the role of ATP on potassium-ATP channels from the outside. They act to **block** these channels causing membrane depolarisation and thus **opening of voltage-gated calcium channels**. This process results in the stimulation of insulin release.

196. The correct answer is **Concomitant** use with **insulin**. Pioglitazone, a thiazolidinedione class of drug used in the management of type 2 diabetes mellitus, is known to cause fluid retention and peripheral oedema. This side effect may be **exacerbated** when pioglitazone is used **concurrently** with **insulin**, as **insulin** also has the **potential** to cause **fluid retention**. Therefore, concomitant use of these two drugs increases the risk of developing peripheral oedema.

197. HLA associations:

HLA-DR1: bronchiectasis

HLA-DR2: systemic lupus erythematosus (SLE)

HLA-DR3: autoimmune hepatitis, primary Sjogren syndrome, type 1 diabetes Mellitus, SLE

HLA-DR4: rheumatoid arthritis, type 1 diabetes Mellitus

HLA-B27: ankylosing spondylitis, postgonococcal arthritis, acute anterior uveitis

198. Alcohol binge drinking is the correct answer. Alcohol bingeing can lead to ADH suppression in the posterior pituitary gland subsequently leading to polyuria. This is similar to cranial diabetes insipidus or partial cranial diabetes insipidus and typically causes hypernatremia with a raised serum osmolality and decreased urine osmolality.

199. Calciphylaxis is a rare, but serious, kidney complication. Calciphylaxis is a vasculopathy of small blood vessels characterised by the deposition of calcium deposits in intimal arterioles with the consequent proliferation of intima, fibrosis and thrombosis. It's most often seen in patients with end-stage renal disease, or patients with kidney failure who are on dialysis or have had a kidney transplant, diabetic patients and patients with rheumatoid arthritis. The classical clinical picture is that of a

necrotic and progressive skin ulcer of reticular pattern, mostly in the lower legs and susceptible to local infection

**200. Primary hyperaldosteronism, bilateral renal artery stenosis and Bartter syndrome** are associated with **hypokalaemia** due **raised** serum **aldosterone**.

Aldosterone is elevated in bilateral renal artery stenosis and Bartter syndrome due to reduced renal perfusion. Aldosterone is high in primary hyperaldosteronism due to (most commonly) an aldosterone producing adenoma.

However, serum renin is usually low in primary hyperaldosteronism due to the resulting hypertension causing excessive renal perfusion, which results in decreased renin production (negative feedback mechanism). High renin levels are seen in renal artery stenosis and Bartter syndrome as a mechanism to improve renal perfusion.

Renal artery stenosis is associated with hypertension and may be associated with abdominal bruits caused by turbulent flow within the stenosed arteries.

**Bartter** syndrome is associated with **normotension**.

The commonest cause of bilateral renal artery stenosis is atherosclerosis. However, in this scenario the patient is young and no cardiovascular risk factors are mentioned. Another cause of bilateral renal artery stenosis, which should be considered in this patient, is fibromuscular dysplasia, which can result in a non-atherosclerotic renal artery stenosis.

Renal artery stenosis is associated with hypertension and may be associated with abdominal bruits caused by turbulent flow within the stenosed arteries.

**201. Sipuleucel-T** is used in a form of autologous cellular immunotherapy, mainly in certain types of **prostate cancer** mainly symptomatic or minimally symptomatic metastatic cancer. As an autologous therapy patients undergo leukapheresis where their

own immune cells are collected, undergo treatment and are then are infuse back into the patient's body. As an immunotherapy sipuleucel-T mechanism of action does not affect the androgen receptors.

202. Fibrate drugs - increased risk of DVT

MOA : activating PPAR-alpha receptors resulting in an increase in LPL activity and reducing triglyceride levels.

203. This patient has presented with symptoms in keeping with hypoglycaemia, precipitated by alcohol use. Alcohol results in exaggerated insulin secretion causing hypoglycaemia. The mechanism is thought to be due to the effect of alcohol on the pancreatic microcirculation leading to a redistribution of pancreatic blood flow from the exocrine into the endocrine parts and thus increased insulin secretion. In a young type 1 diabetic it is thought that the pancreas still retains some of its ability to produce insulin, resulting in higher insulin requirements as the disease progresses.

204. Pseudohyponatraemia refers to a laboratory artefact where the measured serum sodium concentration is lower than the actual physiologic concentration. This can occur in conditions with high plasma protein or lipid content, such as hyperlipidaemia, because these substances displace water and hence sodium in the plasma, leading to a falsely low sodium reading.

205. The patient has polyuria, polydipsia and a hypokalaemic alkalosis. Gitelman, Bartter and Liddle syndrome, and liquorice ingestion all cause hypokalaemic alkalosis. These hypokalaemic metabolic alkaloses can be differentiated by blood pressure, age of onset, and serum and urinary biochemistry.

This is a classic case of Bartter's syndrome which presents with polyuria, polydipsia, hypokalemia and a metabolic alkalosis. Whilst Gitelman syndrome remains within the differential diagnosis, the presence of polyuria and polydipsia favour the diagnosis of Bartter's, as these features are not commonly seen in Gitelman. The absence of hypertension makes Liddle syndrome an unlikely diagnosis.

**NKCC2 channel in the ascending loop of Henle** is correct. This is a classic case of Bartter's syndrome which presents with polyuria, polydipsia, hypokalemia and a metabolic alkalosis. The blood pressure is usually normal in this condition. Bartter's syndrome occurs due to defective chloride absorption at the  $\text{Na}^+ \text{K}^+ 2\text{Cl}^-$  cotransporter (NKCC2) in the ascending loop of Henle.

206. Water deprivation test - cranial DI

Urine osmolality after fluid deprivation - low

Urine osmolality after decompression : high

207. Schizophrenia = psychogenic primary polydipsia

208. Evolocumab prevents PCSK9-mediated LDL receptor degradation. Evolocumab binds selectively to PCSK9 and prevents circulating PCSK9 from binding to the low-density lipoprotein receptor (LDLR) on the liver cell surface, thus preventing PCSK9-mediated LDLR degradation. Increasing liver LDLR levels results in associated reductions in serum LDL-cholesterol. Use of evolocumab is associated with a reduction in levels of free PCSK9 and this is taken as a measure of target engagement. it lowers LDL cholesterol by more than 50% in 85% of patients who are treated. Use of evolocumab is endorsed by NICE under certain conditions only, namely that the dosage is 140mg every 2 weeks and LDL cholesterol is persistently above 3.5 mmol/l

209. The correct answer is normotension. The diagnosis here is that of Bartter's syndrome, given the presenting symptoms and the confirmed defect in the  $\text{Na-K-2Cl}$  transporter. It is usually inherited in an autosomal recessive fashion. As loop diuretics work by inhibiting  $\text{Na-K-2Cl}$  Bartter's has a similar effect to furosemide, causing hypokalemia but without hypertension, unlike other endocrine causes of hypokalemia (Conn's, Liddle's and Cushing's syndromes) which cause hypertension.

Bradycardia is not known to be associated with Bartter's syndrome.

Hyperaldosteronism, rather than hypoaldosteronism, is associated with Bartter's syndrome. As well as elevated aldosterone levels, elevated renin levels are seen.

Hypercalciuria, rather than hypocalciuria, is seen. This predisposes infants to develop kidney stones.

Bartter's syndrome is associated with increased production of prostaglandin E<sub>2</sub>, rather than decreased.

210. The history here points towards a diagnosis of **drug-induced acne**, which can be caused by systemic glucocorticoids. Drug-induced acne generally presents with this rash without comedones or cysts, whereas normal acne vulgaris has both comedones and cysts. Drug-induced acne will not respond to normal acne treatment, but will improve once the offending drug is discontinued. Given the dose and length of time that the patient has been taking it there is a risk of adrenal suppression so prednisolone should be gradually withdrawn.

211. SGLT-2 inhibitors have very good evidence for improving cardiovascular and renal outcomes, but canagliflozin should be used with caution here as some evidence suggests an increased risk of foot amputations. Having two ulcers on this right foot should indicate either an alternative SGLT-2 inhibitor or, an alternative medication with a better side effect profile should be used. A better option would be empagliflozin if an SGLT-2 inhibitor were to be used here.

212. **Untreated thyrotoxicosis increases the risk of premature labour'** - this statement holds true too. If left untreated or poorly controlled, hyperthyroidism can lead to several adverse maternal and fetal outcomes including preterm labour, preeclampsia and intrauterine growth restriction among others.

213. The short Synacthen test is a method of excluding adrenal insufficiency. A baseline cortisol level is taken, IV synthetic ACTH is then administered and a second cortisol level is taken 30 minutes later. If the cortisol post ACTH rises to > 420 nmol/L at 30 minutes,

the adrenal response to ACTH is adequate and Addison's disease (adrenal failure) can be excluded.

However, this excludes only primary adrenal failure and does not exclude cortisol deficiency secondary to failure of the pituitary to produce ACTH. The correct answer is therefore pituitary failure due to damage by an enlarging malignancy. The other answers all cause damage to the adrenal gland.

214. The most significant risk of prescribing an oestrogen-only preparation rather than a combined oestrogen-progestogen preparation is the **increased risk of endometrial cancer**.

Oestrogen stimulates the growth of the endometrium, and without the balancing effect of progestogen, there is an increased risk of unopposed endometrial proliferation, which can lead to hyperplasia and eventually endometrial cancer. Combined preparations containing both oestrogen and progestogen help to counteract this risk by providing a more balanced hormonal environment.

215. Hypothyroidism can cause predominantly hypercholesterolaemia, as opposed to hypertriglyceridaemia. This is due to the fact that thyroid hormones play a crucial role in lipid metabolism. In hypothyroidism, there is a reduction in the liver's ability to take up and degrade low-density lipoprotein (LDL) cholesterol, leading to an increase in plasma LDL levels. Additionally, hypothyroidism reduces the activity of lipoprotein lipase, an enzyme that helps break down triglycerides, but this effect isn't as pronounced as the impact on LDL cholesterol.

216. A hard and fixed, non-tender thyroid goitre is suggestive of Reidel's thyroiditis, also known as invasive fibrous thyroiditis. This is a rare condition characterised by a fibrotic process associated with mononuclear cell inflammation. It is associated with fibrosing conditions affecting other areas, including **retroperitoneal fibrosis** and fibrosing mediastinitis. Retroperitoneal fibrosis may not cause symptoms initially and often presents non-specifically with symptoms such as back pain and malaise. A decreased estimated glomerular filtration rate is often present.



217. **Mullerian duct agenesis**, also known as Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome, is an incorrect answer. This condition is characterised by congenital absence or underdevelopment of the uterus and upper two-thirds of the vagina in females with normal 46,XX karyotype and ovarian function. Although primary amenorrhoea would be expected in these individuals, they would typically have normal secondary sexual characteristics including pubic hair growth, which is inconsistent with the clinical presentation described in the question.

218. Carbenoxolone is a synthetic derivative of glycyrrhizinic acid, which is used for the treatment of peptic ulcer. It has mineralocorticoid activity and can cause hypokalaemia (low potassium levels), not hyperkalaemia (high potassium levels).

219. Tomatoes are high in potassium, a mineral that can build up in the blood of patients with chronic kidney disease stage 4 as their kidneys' ability to filter it out is compromised. Consuming too much potassium can lead to hyperkalemia, a potentially life-threatening condition characterised by muscle weakness, irregular heart rhythms and, in severe cases, cardiac arrest. Therefore, patients with advanced kidney disease should limit their intake of high-potassium foods like tomatoes.

220. As a tricyclic antidepressant, lofepramine is the only medication listed that can cause SIADH.

221. Medications that can cause false negative renin:aldosterone ratio results are the following:

- Angiotensin-converting enzyme inhibitors (e.g. ramipril or lisinopril).
- Angiotensin receptor blockers (e.g. losartan).
- Direct renin inhibitors (e.g. aliskiren).
- Aldosterone antagonists (e.g. spironolactone or eplerenone).

222. Patients with alcoholic liver disease have depleted glycogen stores, therefore, treatment with glucagon does not improve blood glucose.

223. Prolactin secretion from the anterior pituitary gland is primarily regulated by inhibition: the hypothalamus produces prolactin inhibitory factors (most notably dopamine), which are released into the hypophyseal portal bloodstream and bind to receptors on lactotrophs in the anterior pituitary, suppressing the release of prolactin. This inhibitory control is unusual among anterior pituitary hormones, which are primarily under stimulatory hypothalamic control.

224. Type 1 diabetes mellitus is caused by autoimmune destruction of the Beta-cells of the pancreas. Identical twins show a genetic concordance of 40%. It is associated with HLA-DR3 and DR4. It is inherited in a polygenic fashion

Type 2 diabetes mellitus is thought to be caused by a relative deficiency of insulin and the phenomenon of insulin resistance. Age, obesity and ethnicity are important aetiological factors. There is almost 100% concordance in identical twins and no HLA associations.

225. NICE guidelines clearly stipulate the circumstances under which parathyroidectomy should be considered in primary hyperparathyroidism. These are listed below:

- Age under 50 years.
- Adjusted serum calcium concentration that is 0.25 mmol/L or more above the upper end of the reference range.
- Estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m<sup>2</sup> although this threshold depends on other factors, such as age.
- Renal stones or presence of nephrocalcinosis on ultrasound or CT.
- Presence of osteoporosis or osteoporotic fracture.
- Symptomatic disease

226.

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## CLINICAL SCIENCES PASSMEDICINE & PASTEST

### 1. Achondroplasia

- Autosomal dominant - ass. With short stature
- Defect in fibroblast growth factor receptor 3 gene - FGFR-3
- Abnormal cartilage giving rise to :
  - A. Short limbs (rhizomelia) and shortened fingers (brachydactyly)
  - B. Large head with frontal bossing and narrow foramen magnum
  - C. Midface hypoplasia with flattened nasal bridge
  - D. Trident hands
  - E. Lumbar lordosis
- Main R/F : advancing parental age at time of conception

### 2. Alkaptonuria / Ochronosis

- Autosomal recessive
- Disorder of Phenylalanine and tyrosine metabolism due to lack of enzyme homogentisic dioxygenase
- Accumulation of toxic homogentisic acid
- Urine - black color - due to filtration of this substance
- Eventually - accumulation in cartilage and other tissues

C/F :

- pigmented sclera
- Urine turns black when exposed to air
- Intervertebral disc calcification —> back pain
- Renal stones

Mx : high dose vitamin C, dietary restriction of phenylalanine and tyrosine

### 3. Antidiuretic hormone

- Secreted by posterior pituitary gland
- Water reabsorption in collecting ducts of kidneys by insertion of aquaporin-2 channels.
- Source : supra optic nuclei of hypothalamus, released by posterior pituitary
- Function : conserves water, promotes water reabsorption in collecting ducts by inserting aquaporin-2 channels
- Increased secretion in : ECF osmolality increase, volume decrease, pressure decrease, angiotensin II

- Decreased secretion in : ECF osmolality decrease, volume increase, temperature decrease.

#### 4. Arachidonic acid metabolism :

- **PGI<sub>2</sub>** : vasodilation, decreased platelet aggregation, decreases uterine tone
- PGE<sub>2</sub> : increased pain, increases temperature, increase uterine tone, increases gastric mucus
- PGE<sub>2</sub> : decreased gastric acid
- Thromboxane TXA<sub>2</sub> : vasoconstriction, increases platelet aggregative
- LTB<sub>4</sub> : neutrophil chemotaxis
- LTA<sub>4</sub>, LTC<sub>4</sub>, LTD<sub>4</sub>, LTE<sub>4</sub> : increases bronchoconstriction

#### 5. Atrial Natriuretic Peptide

- Myocytes of right atrium and right ventricle in response to increased blood volume
- Secreted both by RIGHT AND LEFT ATRIA ( Right >> Left)
- ANP : 28 amino acid peptide —> acts by cGMP
- Degrades by endopeptidases
- Natriuretic - promotes Na excretion
- Lowers BP
- Antagonist against Aldosterone, Angiotensin II

#### 6. Autosomal Dominant disease with complicating factors -

- **non - penetrance** : lack of clinical signs and symptoms despite abnormal gene - **seen in 40% of Otosclerosis**
- **Spontaneous mutation** : new mutation in one of gametes - **80% of individuals with achondroplasia have unaffected parents**

### 7. AUTOSOMAL DOMINANT = STRUCTURAL

### AUTOSOMAL RECESSIVE = METABOLIC

Metabolic + Autosomal Dominant => **Hyperlipidemia type II, Hypokalemic Periodic Paralysis**

Metabolic + X-Linked recessive => Hunter's, G6PD

Structure + Autosomal recessive => **Ataxia telangiectasia, Friedrich's ataxia**

## 8. Brachial Plexus

- Origin - anterior rami C5 to T1 spinal nerves
- Sections : Root, Trunks, Divisions, Cords, Branches (RTDCB)
- Roots : located in posterior triangle; passes between scalene's anterior and medius
- Trunks : located posterior to middle 1/3 of clavicle;
- upper & middle trunk - related superiorly to subclavian artery
- Lower trunk - passes over 1st rib posterior to subclavian artery
- Divisions : apex of axilla
- Cords : lies in the axilla, related to axillary artery
- C5 and C6 = upper trunk
- C7 = middle trunk
- C8 and T1 = lower trunk
- Each trunk divides into anterior and posterior division
- Lateral cord = anterior division of upper and middle trunk
- Medial cord = anterior division of lower trunk
- Posterior cord = posterior division of all three trunks
- Dorsal scapular nerve C5 : rhomboid major, rhomboid minor, levator scapulae muscles
- Long thoracic nerve - C5, C6, C7 roots - Serratus anterior

### Upper trunk

- Nerve to subclavius C5, C6
- Can give a branch to phrenic nerve - called - accessory phrenic nerve
- Suprascapular nerve - supraspinatus and infraspinatus

### Medial cord :

- Medial pectoral nerve - supplies pectoralis minor and major

- Medial cutaneous nerve of arm - skin on medial side of arm
- Medial cutaneous nerve of forearm
- Medial root of median nerve

Lateral cord :

- lateral pectoral nerve - pectoralis major muscle
- Musculocutaneous nerve - motor root to coracobrachialis, biceps brachii, brachialis
- Musculocutaneous nerve : sensory supply lateral border of forearm through its branch lateral cutaneous nerve of forearm
- Lateral root of median nerve

## 8. Brain tumors

- Metastases : most common form of brain tumors. Commonly spread by - lung, breast, bowel, melanoma, kidney
  - Glioblastoma multiforme
- A. Most common primary brain tumor in adults
- B. Poor prognosis
- C. Imaging : solid tumors with central necrosis and a rim enhances with contrast
- D. Causes disruption of BBB and associated with vasogenic oedema
- E. M/C : **pleomorphic tumor cells border necrotic area**
- F. Mx : Surgical, post op Chemo/Radio; Edema = Dexamethasone

## Meningioma

- Second most common primary tumor in adults
- Benign, extrinsic tumors of CNS
- Arises from : Arachnoid cap cells of meninges and typically located next to dura
- Causes symptoms by compression
- M/C : spindle cells in concentric whorls, calcification of Psammoma bodies

## Vestibular Schwannoma

- Benign tumors from 8th CN vestibulocochlear nerve
- Seen in CP angle
- C/F : hearing loss, facial nerve palsy
- NF type 2 associated with B/L Vestibular schwannoma

- M/C : **Antoni A or B Patterns, Verocay bodies - acellular areas surrounded by nuclear palisades**

### **Pilocytic astrocytoma**

- M/C - **Rosenthal fibers - corkscrew eosinophilic bundle**
- Most common primary brain tumor in children

### **Medulloblastoma**

- Aggressive paediatric brain tumor
- Spreads through CSF system
- M/C : **Small, blue cells, Rosenthal pattern of cells with many mitotic figures**

### **Ependymoma**

- seen in 4th ventricle
- Can cause hydrocephalus
- M/C : **Perivascular pseudo-rosettes**

### **Oligodendroma**

- benign slow growing tumor found in frontal lobes
- M/C : Calcifications with fried egg appearance

### **Hemangioblastoma**

- vascular tumor of cerebellum
- Associated with VHL
- M/C : **foam cells and high vascularity**

## **9. Drugs CI in breast feeding**

- I. **Antibiotics** - Ciprofloxacin, Tetracyclines, Chloramphenicol, Sulphonamides
- II. Psychiatric : Lithium, Benzodiazepines
- III. Aspirin
- IV. Carbimazole
- V. Methotrexate
- VI. Sulfonylureas
- VII. Cytotoxic drugs
- VIII. Amiodarone
- IX. Antipsychotics - Clozapine

## 10. Cardiac Action Potential

| PHASE   | DESCRIPTION                   | MECHANISM                                                                                |
|---------|-------------------------------|------------------------------------------------------------------------------------------|
| Phase 0 | Rapid Depolarisation          | Rapid sodium influx; these channels automatically deactivate after few milliseconds      |
| Phase 1 | Early repolarisation          | Efflux of potassium, Chloride                                                            |
| Phase 2 | Plateau                       | Slow influx of calcium                                                                   |
| Phase 3 | Final repolarisation          | Potassium Efflux                                                                         |
| Phase 4 | Restoration of ionic currents | Restored by Na/K ATPase; slow entry of Na into cells decreasing the potential difference |

11.

$$\text{LVEF} = (\text{SV} / \text{ED LV volume}) * 100 \%$$

SV - End Diastolic - End systolic

$$\text{Cardiac Output} = \text{stroke volume} \times \text{HR}$$

$$\text{Pulse pressure} = \text{SBP} - \text{DBP}$$

$$\text{Systemic Vascular resistance} = \text{Mean arterial pressure} / \text{Cardiac output}$$

## 12. Cell Cycle

G1 phase

- Gap 1, cell increase in size
- Determines length of cell cycle



- Under the influence of p53
- Cyclin D / CDK 4, Cyclin D / CDK 6, Cyclin E / CDK2 - regulates transition from G1 to S phase

### S phase

- Synthesis of DNA, RNA and histone
- Centrosome duplication
- Cyclin A / CDK2 - active in S phase

### G2 phase

- Gap 2, cells continue to increase in size
- Cyclin B / CDK1 1 - regulates transition from G2 to M phase

### M phase

- Mitosis - cell division
- Shortest phase of cell cycle

### Phases of Mitosis :

|              |                                                                                                      |
|--------------|------------------------------------------------------------------------------------------------------|
| Prometaphase | Nuclear membrane breaks down allowing the microtubules to attach to chromosome                       |
| Metaphase    | Chromosomes aligned in middle of cell                                                                |
| Anaphase     | Paired chromosome separate at the kinetochores and move to opposite sides of cell                    |
| Telophase    | Chromatids arrive at opposite poles of cell                                                          |
| Cytokinesis  | Actin-myosin complex in centre of cell contracts resulting in it being picked into two daughter cell |

## 13. Cell Organelles

### Rough Endoplasmic reticulum

- Translation and folding of new proteins
- Manufacture of lysosomal enzymes
- Site of N-linked acetylation
- Eg : pancreatic cells, goblet cells, plasma cells

### Smooth ER

- steroid and lipid synthesis
- Eg : adrenal cortex, hepatocytes, testes, ovary

### Golgi apparatus

- modifies, sorts and packages these molecules that are destined for cell secretion
- Addition of Mannose-6-phosphate to protein designates transport to lysosome

### Mitochondria

- aerobic respiration
- Mitochondrial genome as circular DNA

### Nucleus

- DNA maintenance
- RNA transcription
- RNA splicing - removes intervening, non coding sequences of genes from pre-mRNA and joins the protein coding sequences

Lysosome : breakdown of large molecules such as proteins and polysaccharides

Nucleolus : ribosome production

Ribosome : translation of RNA into proteins

Peroxisome : catabolism of very long chain fatty acids and amino acids; results in the formation of hydrogen peroxide

Proteasome : along with the lysosome pathway, it is involved in degradation of protein molecule that have been tagged with ubiquitin

## 14. Childhood Syndromes

### Patau syndrome - trisomy 13

- microcephaly
- Small eyes
- Cleft lip, cleft palate
- Polydactyly
- Scalp lesion

### Edward's syndrome - trisomy 18

- micrognathia
- Low set ears
- Rocker bottom foot
- Overlapping of fingers

### Fragile X

- learning difficulties
- Macrocephaly
- Long face
- Large ears
- Macro-orchidism

### Noonan syndrome

- webbed neck
- Pectus excavatum
- Short stature
- Pulmonary stenosis

### Pierre Robin syndrome

- micrognathia
- Posterior displacement of tongue - can cause upper airway obstruction
- Cleft palate

### Prader-Willi syndrome

- Hypogonadism
- Hypotonia
- Obesity

### William's syndrome

- short stature

- Learning difficulties
- Friendly, extrovert personality
- Transient neonatal hypercalcemia
- Supra valvular aortic stenosis

Cri du chat syndrome - chromosome 5p deletion syndrome

- characteristic cry due to larynx and neurological problems
- Feeding difficulties
- Poor weight gain
- Learning difficulties
- Microcephaly
- Micrognathism
- Hypertelorism

## 15. Collagen types

| <b>COLLAGEN TYPE</b> | <b>NOTES</b>                               | <b>ASSOCIATED CONDITIONS</b>                   |
|----------------------|--------------------------------------------|------------------------------------------------|
| I                    | Bone, skin, tendon                         | <b>Osteogenesis imperfecta</b>                 |
| II                   | Hyaline cartilage, vitreous humor          |                                                |
| III                  | Reticular fiber, granulation tissue,       | <b>Vascular variant of Ehler Danlow</b>        |
| IV                   | Basal lamina lens, basement membrane       | <b>Alport's syndrome, Goodpasture syndrome</b> |
| V                    | Placental tissue, most interstitial spaces | <b>Classical variant of Ehler Danlos</b>       |

## 16. Complement Deficiencies

- C1 - INH deficiency : C1 inhibitor deficiency - hereditary angioedema
- C1q, C1rs, C2, C4 deficiency : classical pathway components, predisposes to immune complex disease - SLE, Henoch Schonlein purpura

- C3 deficiency : recurrent bacterial infection
- C5 deficiency : Leiner disease - recurrent diarrhoea, wasting and seborrhoeic dermatitis
- C5 - C9 deficiency : encodes the membrane attack complex (MAC) ; prone to *Neisseria meningitidis* infection

## 16. Congenital Infections :

### Rubella

- Sensorineural deafness
- Congenital cataracts
- Congenital heart disease - PDA
- Glaucoma
  
- Growth retardation
- Hepatosplenomegaly
- Purpuric skin lesions
- Salt and pepper chorioretinitis
- Microphthalmia
- Cerebral palsy

### Toxoplasmosis

- cerebral calcification
- Chorioretinitis
- Hydrocephalus
  
- anaemia
- Hepatosplenomegaly
- Cerebral palsy

### Cytomegalovirus CMV

- low birth weight
- Purpuric skin lesions
- Sensori neural deafness
- Microcephaly
  
- visual impairment
- Learning disabilities
- Encephalitis, seizures
- Pneumonitis

- Hepatosplenomegaly
- Anaemia
- Jaundice
- Cerebral palsy

## 17. Cytokines

| <b>CYTOKINES</b> | <b>SOURCES</b>         | <b>FUNCTIONS</b>                                                         |
|------------------|------------------------|--------------------------------------------------------------------------|
| IL-1             | Macrophages            | Acute inflammation, induces fever                                        |
| IL-2             | Th1 cells              | Stimulates growth and differentiation of T cell response                 |
| IL-3             | Activated Th1 cells    | Stimulates differentiation and proliferation of myeloid progenitor cells |
| IL-4             | Th2 cells              | Stimulates proliferation and differentiation of B cells                  |
| IL-5             | Th2 cells              | Stimulates production of eosinophils                                     |
| IL-6             | Macrophages, Th2 cells | Stimulates differentiation of B cells, induces fever                     |
| IL-8             | Macrophages            | Neutrophil chemotaxis                                                    |

|                  |                                       |                                                                                                                           |
|------------------|---------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| IL-10            | Th2 cells                             | Inhibits APCs and Th1 cytokine production<br>AKA human cytokine synthesis inhibitory factor<br>Anti inflammatory cytokine |
| IL-12            | Dendritic cells, macrophages, B cells | Activated NK cells and stimulates differentiation of naive T cells into Th1 cells                                         |
| TNF-alpha        | Macrophages                           | Induces fever, neutrophil chemotaxis                                                                                      |
| Interferon-gamma | Th1 cells                             | Activates macrophages                                                                                                     |

### 18. DiGeorge Syndrome

- Primary immunodeficiency disorder
- T-cell deficiency and dysfunction
- Example of micro deletion syndrome - deletion of a section of chromosome 22
- AKA **velocardiofacial syndrome / 22q11.2 deletion syndrome**
- **Autosomal dominant**

### **CATCH 22**

**C** - Cardiac abnormalities

**A** - Abnormal facies

**T** - thymic aplasia

**C** - Cleft palate

**H** - hypocalcemia, hypoparathyroidism

**22** - Chromosome 22 deletion

### 19. Down's syndrome

## C/F

- face : up slanting palpebral fissures, epicanthic folds, Brushfield spots in iris, protruding tongue, small low-set ears, round/flat face
- Flat occiput
- Single palmar crease, pronounced sandal gap between big and first toe
- Hypotonia
- Congenital heart defects
- Duodenal atresia
- Hirschsprung's disease

## Cardiac features :

- endocardial cushion defect - **most common 40%** - AKA AV septal canal defects
- VSD ~ 30%
- Secundum atrial septal defect ~10%
- Tetralogy of Fallot ~5%
- Isolated PDA ~5%

## Later complications :

- sub fertility : males are always almost infertile due to impaired spermatogenesis.
- Females : subfertile and increased incidence of problems with pregnancy and labor
- Short stature
- Repeated respiratory infections
- Hearing impairment from glue ear
- Acute lymphoblastic leukaemia
- Hypothyroidism
- Alzheimer's disease
- Atlanto-axial instability

## 20. Endothelin

- potent, long acting vasoconstrictor and broncho-constrictor
- Prohormone converted to **endothelin-1** by enzyme **Endothelin converting enzyme**
- Acts via G-protein linked to phospholipase C leading to calcium release

## Promotes release of :

- Angiotensin II



- ADH
- Hypoxia
- Mechanical shearing forces

Inhibits release of :

- nitric oxide
- Prostacycline

Raised levels seen in :

- primary pulmonary hypertension
- MI
- Heart failure
- AKI
- Asthma

## 21. Erythropoiesis

- Red bone marrow found in flat bones - vertebrae, sternum, ribs, proximal ends of long bones
- Fetus - erythrocytes produced in liver
- RBC lifespan - 120 days
- Levels of erythrocytes = hematocrit

## 22. **Fabry disease**

- X-linked recessive
- Deficiency of alpha-galactosidase A
- Burning pain / paraesthesia in childhood
- Angiokeratomas
- Lens opacities
- Proteinuria
- Early CVD

## 23. **Fragile X syndrome**

- Trinucleotide repeat disorder

C/F in males :

- learning difficulties
- Large low set ears
- Long face
- Macroorchidism
- Hypotonia

- Autism common
- Mitral valve prolapse

C/F in females : one fragile and one normal X chromosome- normal to mild features

Dx : antenatally by CVS or amniocentesis; analysis of number of CGG repeats using restriction endonuclease digestion and Southern blot analysis

#### 24. HIV immunological reactions :

- Reduction in CD4 count
- Increase in beta - 2 micro globulin
- Decreased IL-2 production
- Polyclonal B cell activation
- Decrease in NK cell function
- Reduced delayed hypersensitivity responses

#### 25. Hypersensitivity

| TYPE                      | MECHANISM                                    | EXAMPLES                                                                                                                                                                                    |
|---------------------------|----------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Type I - Anaphylaxis      | Antigen reacts with IgE bound to mast cells  | Anaphylaxis<br>Atopy - asthma, eczema, hay fever                                                                                                                                            |
| Type II - Cell bound      | IgG or IgM binds to antigen on cell surface  | Autoimmune haemolytic anaemia<br>Goodpasture's syndrome<br>ITP<br>Pernicious anaemia<br>Acute haemolytic transfusion reaction<br>Rheumatic fever<br>Pemphigus vulgaris<br>Bullus pemphigoid |
| Type III - Immune complex | Free antigen and antibody (IgG, IgA) combine | Serum sickness<br>SLE<br>Post - strept GN<br>Extrinsic allergic alveolitis                                                                                                                  |

|                                    |                                                                                                                |                                                                                                                                                                |
|------------------------------------|----------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Type IV - Delayed hypersensitivity | T - cell mediated                                                                                              | Tuberculosis/ Tuberculin skin reaction<br>Graft v/s host disease<br>Scabies<br>Allergic contact dermatitis<br>Multiple sclerosis<br>EAA - chronic phase<br>GBS |
| Type V                             | Antibodies that recognise and bind to cell surface receptors - either stimulates them or blocks ligand binding | Myasthenia gravis<br>Graves' disease                                                                                                                           |

## 26. Interleukin - 1

- Secreted mainly by macrophages and monocytes
- Acts as a co-stimulator of T cell and B cell proliferation.
- Increases expression of adhesion molecules on the endothelium.
- Stimulates the release of endothelium of vasoactive factors such as PAF, NO and prostacyclin.
- Causes **vasodilation** and **increases vascular permeability**.
- One of the mediators of shock in sepsis
- IL-1, IL-6, TNF -> acts on hypothalamus and causes pyrexia.
- Anakinra - IL-1 receptor antagonist; management of rheumatoid arthritis
- Canakinumab : monoclonal antibody targeted at IL-1 beta; used in systemic JIA and adult onset Still's disease

## 27. Innate Immunity

### Neutrophils

- Primary phagocytic cell in acute inflammation
- Granules contain Myeloperoxidase and lysozyme
- Multi-lobed nucleus

### Basophil

- Releases histamine during allergic response
- Granules contain histamine and heparin
- Expresses IgE on cell surface receptors
- Bi-lobed nuclei

### Eosinophil

- Defends against protozoan and helminthic infections

- Bi-lobed nucleus

### Monocytes

- Differentiates into macrophages
- Kidney shaped nucleus

### Mast cells

- Present in tissue and similar in function to basophil
- Releases histamine during allergic response
- Contains histamine and heparin
- Expressed IgE receptors on cell surface

### Macrophages

- Involved in phagocytosis of cellular debris and pathogens
- Acts as antigen presenting cells
- Major source of IL-1

NK cells : induces apoptosis in virus infected cells and tumor cells

Dendritic cells : acts as antigen presenting cell

## 28. Adaptive immunity

### Helper T cells

- Involved in cell mediated immune response
- Recognises antigen presented by class II MHC molecule
- Expressed CD4, CD3, TCR, CD28
- Major source of IL-2
- Mediates acute and chronic graft rejection

### Cytotoxic T cells

- Recognises antigens presented by MHC Class I molecules
- Expressed CD8, TCR, CD3
- Mediates acute and chronic organ rejection

### B cells

- Major cell of humeral immune response
- Acts as APC
- Mediates hyper acute rejection

### Plasma cells

- Differentiated from plasma cells
- Produces large amount of antibody specific to particular antigen

Most abundant antibody - IgG - fixes complements and passes to fetal circulation.

Most commonly produced - IgA

Least abundant antibody - IgE

Breast milk - IgA ; protection on mucosal membranes, transported via transcytosis

Activation of B cells - IgD

Synthesised by plasma cells - IgE

## 29. Inherited metabolic Disorders

### Glycogen storage disorders

|                               |                                              |                                                                                          |
|-------------------------------|----------------------------------------------|------------------------------------------------------------------------------------------|
| Von Gierke's disease - Type 1 | Glucose 6 phosphatase                        | Hepatic glycogen accumulation<br>C/F : hypoglycaemia, lactic acidosis, hepatomegaly      |
| Pompe's disease - type 2      | Lysosomal alpha 1,4 glucosidase              | Cardiac, hepatic and muscle glycogen accumulation, <b>cardiomegaly</b>                   |
| Cori disease - type 3         | Alpha - 1,6 - glucosidase debranching enzyme | Hepatic, cardiac glycogen accumulation. <b>Muscle hypotonia</b>                          |
| McArdle's disease             | Glycogen phosphorylase (myophosphorylase)    | Skeletal muscle glycogen accumulation. <b>C/F : myalgia, myoglobinuria</b> with exercise |

### Lysosomal Storage Disorders

|                              |                         |                                                                                                                                                                         |
|------------------------------|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Gaucher's disease            | Beta glucocerebrosidase | Most common; accumulation of glucocerebrosidase in brain, liver, spleen;<br>C/F : hepatosplenomegaly, aseptic necrosis of femur<br>Increased levels of Acid phosphatase |
| Tay-Sachs disease            | Hexosaminidase A        | Accumulation of GM2 ganglioside within lysosomes.<br>C/F : developmental delay, cherry red spot on macula, <b>normal size liver and spleen</b>                          |
| Niemann - Pick disease       | Sphingomyelinase        | <b>Hepatosplenomegaly</b><br><b>Cherry red spot on macula</b>                                                                                                           |
| Fabry disease                | Alpha-galactosidase A   | Accumulation of <b>ceramide trihexoside</b><br>C/F : <b>angiokeratomas, peripheral neuropathy, renal failure</b>                                                        |
| Krabbe's disease             | Galactocerebrosidase    | Peripheral neuropathy, optic neuropathy, globoid cells                                                                                                                  |
| Metachromatic leukodystrophy | Arylsulfatase A         | Demyelination of CNS & PNS                                                                                                                                              |

\*\* Gaucher's disease - 3 types : 1) non - neuropathic 2) acute neuropathic 3) chronic neuropathic

Rx : Recombinant glucosidase and **glucosylceramide inhibitors - Miglustat are the main treatment strategy**

### Mucopolysaccharidoses

|                          |                         |                                                                                                                                                                              |
|--------------------------|-------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Hurler syndrome - type 1 | Alpha - 1 - Iduronidase | Accumulation of GAG (heparin and dermatan sulphate)<br>C/F : <b>Gargoylism</b> (large head and grotesque facial appearance), <b>Hepatosplenomegaly, YES corneal clouding</b> |
|--------------------------|-------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                             |                     |                                                                                                                                               |
|-----------------------------|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| Hurler Syndrome<br>- type 2 | Iduronate sulfatase | Accumulation of GAGs;<br>C/F : <b>coarse facial features, behavioural problems, learning difficulties, short stature, NO corneal clouding</b> |
|-----------------------------|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|

### 30. Lower limb Anatomy

- Femoral nerve damaged : loss of knee extension and sensory loss to anterior and medial aspect of thigh following stab injury
- Obturator nerve : damaged nerve anterior hip dislocation - unable to adduct thighs
- Lateral cutaneous nerve of thigh : compression at ASIS —> meralgia paraesthetica = pain, tingling, numbness in distribution of lateral cutaneous nerve —> lateral and posterior surfaces of thigh
- Tibial nerve : foot plantar flexion and inversion - loss of sensation over sole of foot. Injured in popliteal laceration, posterior knee dislocation.
- Common perineal nerve : loss of foot dorsiflexion and eversion, cannot use **extensor hallucis longus**; injury at neck of fibula, tightly applied plaster cast - **foot drop** \*\*
- Superior gluteal nerve - **positive Trendelenburg sign** : misplaced IM injection, Pelvic #, posterior hip dislocation - cannot abduct hips
- Inferior gluteal nerve - hip extension and lateral rotation - injury causes difficulty in getting up from sitting position, cant jump / climb stairs.

### 31. McCune - Albright syndrome : random somatic mutation in GNAS gene

Precocious puberty, cafe au lait spots, polyostotic fibrotic dysplasia, short stature

Polyostotic fibrous dysplasia = bone replaced by fibrous tissue - weak bones, deformity, uneven growth

### 32. Membrane receptors

### Ligand gated ion channels

- Mediates fast response
- Nicotinic acetylcholine
- GABA-A, GABA-C
- Glutamate

### Tyrosine kinase receptors

#### Receptor tyrosine kinase

- Insulin
- Insulin-like growth factor -1 IGF-1
- Epidermal growth factor EGF

#### Non receptor tyrosine kinase PIGGET

- Prolactin
- Immunomodulators - IL-2, IL-6, IFN
- Growth Hormone
- G-CSF
- Erythropoietin
- Thrombopoietin

### Granulate cyclase receptors

- Contains intrinsic enzyme activity
- ANP, BNP

### G protein coupled receptors

- Slow transmission, affects metabolic processes
- Activated by wide variety of signals
- 3 main sub-units - alpha, beta, gamma
- G proteins are named according to the alpha subunit

#### Gs :

- Stimulates adenylyl cyclase → increases cAMP → activates protein kinase A
- Beta 1 receptors - NA, Adrenaline, Dobutamine
- Beta 2 receptors : Epinephrine, Salbutamol
- H2 receptors - histamine
- D1 receptors - Dopamine
- V2 receptors - Vasopressin



- Receptors for ACTH, LH, FSH, PTH, Glucagon, Calcitonin, Prostaglandins

Gi :

- Inhibits adenyl cyclase → decreased cAMP → inhibits protein kinase A
- M2 receptors - Acetylcholine
- Alpha 2 receptors - epinephrine, norepinephrine
- D2 receptors - Dopamine
- GABA-B receptors

Gq:

- Activates phospholipase C → splits PIP2 to IP3 + DAG → activates protein kinase C
- Alpha 1 receptors : Epinephrine, norepinephrine
- H1 receptor - histamine
- V1 receptors - vasopressin
- M1, M3 receptors - acetylcholine

### 33. Microtubules

- Helps guide movement during intracellular transport and also binds internal organelles.
- Found in all cells except blood cells.
- Cylindrical structure - composed of alternating alpha and beta subunits which polymerises to form protofilaments
- Microtubules are polymerised - have a negative or positive charge
- Attachment protein = dyenin and kinesin : helps moves the microtubules facilitating the movement of various cell organelles.
- Dyenin - retrograde fashion - down the microtubule - towards the centre +ve → -ve
- Kinesin : anterograde fashion - up the microtubule way from the centre : -ve → +ve

### 34. Molecular Biology techniques

Southern blot - detects DNA

Northern blot - detects RNA

Western blot - detect proteins; uses gel electrophoresis to separate native proteins by 3D structure; EG - Confirmatory HIV test

## ELISA

- Type of biochemical assay used to detect antigens and antibodies
- e.g. - initial HIV test

35. Hypertrophic pyloric stenosis - under production of NO

Lack of NO : promotes atherosclerosis

Sepsis : Increased NO causes septic shock

## 36. Noonan's Syndrome

- Autosomal dominant
- Normal karyotype
- Defect in gene on chromosome 12

C/F :

- Webbed neck
- Widely spaced nipples
- Short stature
- Pectus carinatum
- Pectus excavatum
- Cardiac - **pulmonary valve stenosis**
- Ptosis
- Triangular shaped face
- Low set ears
- Coagulation problems - **factor XI deficiency**

## 37. Oncogenes

Proto-oncogenes may become oncogene via the following processes :

- mutation - point mutation
- Chromosomal translocation
- Increased protein expression

| GENE  | CATEGORY                    | ASSOCIATED CANCER  |
|-------|-----------------------------|--------------------|
| ABL   | Cytoplasmic tyrosine kinase | CML                |
| c-MYC | Transcription factor        | Burkitt's lymphoma |

|                   |                             |                                             |
|-------------------|-----------------------------|---------------------------------------------|
| n-MYC             | Transcription factor        | Neuroblastoma                               |
| BCL-2             | Apoptosis regulator protein | Follicular Lymphoma                         |
| RET               | Tyrosine kinase receptor    | MEN 2A and 2B                               |
| RAS               | G-protein                   | Many cancers - especially <b>pancreatic</b> |
| ERB-B2 (HER2/NEU) | Tyrosine Kinase Receptor    | Breast and Ovarian cancer                   |

Tumor suppressor genes - **loss of function results in cancer**

Oncogenes - **gain of function causes cancer**

### 38. Oncoviruses

| ONCOVIRUS                    | CANCER                                                                                           |
|------------------------------|--------------------------------------------------------------------------------------------------|
| EBV                          | Burkitt's Lymphoma<br>Hodgkin's Lymphoma<br>Post transplant Lymphoma<br>Nasopharyngeal Carcinoma |
| HPV 16/18                    | Cervical cancer<br>Anal cancer<br>Penile cancer<br>Vulval cancer<br>Oropharyngeal cancer         |
| HHV 8                        | Kaposi's sarcoma                                                                                 |
| Hepatitis B                  | HCC                                                                                              |
| Hepatitis C                  | HCC                                                                                              |
| Human T-lymphotropic virus 1 | Adult T cell leukaemia<br>Tropical spastic paraparesis                                           |

**p53 - tumor suppressor gene - chromosome 17p**

Breast, colon and lung cancer.

p53 - prevents entry into S phase until DNA has been checked and repaired

Key regulator of apoptosis

Li-Fraumeni syndrome - autosomal dominant disorder - characterised by early onset of variety of cancers such as sarcomas, breast cancer and leukaemia. Due to mutation in p53 gene.

### 39. Parathyroid disorders

#### Primary Parathyroidism

- PTH - elevated
- Calcium - elevated
- Phosphate - Low
- Urine calcium : creatinine clearance ration  $> 0.01$
- Recurrent abdominal pain - pancreatitis, renal colic
- Changes to emotional or cognitive state

Causes : 80% due to solitary adenoma

#### Primary hyperparathyroidism

##### Indications for surgery

- Elevated serum Calcium  $> 1\text{mg/dL}$  above normal
- Hypercalciuria  $> 400\text{mg/day}$
- Creatinine clearance  $< 30\%$  compared with normal
- Episode of life threatening hypercalcaemia
- Nephrolithiasis
- Age  $< 50$  years
- Neuromuscular symptoms
- Reduction in bone mineral density of the femoral neck, lumbar spine, or distal radius of more than 2.5 standard deviations below peak bone mass (T score lower than -2.5)

#### Secondary hyperparathyroidism

- PTH - elevated
- Calcium - low or normal
- Phosphate - elevated
- Vitamind D levels - **low**

- May have few symptoms
- Complications : bone disease, osteitis fibrosa cystica, soft tissue calcifications
- Parathyroid gland hyperplasia due to low calcium levels
- Chronic renal failure

### Secondary hyperparathyroidism

Usually managed with medical therapy.

Indications for surgery in secondary (renal) hyperparathyroidism:

- Bone pain
- Persistent pruritus
- Soft tissue calcifications

### Tertiary hyperparathyroidism

- Calcium - normal or high
- PTH - elevated
- Phosphate - decreased
- Vitamin D - normal or decreased
- ALP - **elevated**
- Due to - metastatic calcification
- Nephrolithiasis
- Pancreatitis
- Hyperplasia of all 4 glands causes this

### Tertiary hyperparathyroidism

Allow 12 months to elapse following transplant as many cases will resolve

The presence of an autonomously functioning parathyroid gland may require surgery. If the culprit gland can be identified then it should be excised. Otherwise total parathyroidectomy and re-implantation of part of the gland may be required.

## 40. **Phenylketonuria**

- Autosomal recessive
- Disorder of phenylalanine metabolism
- defect in **phenylalanine hydroxylase**, an enzyme which **converts phenylalanine to tyrosine**

- small number of cases the underlying defect is a deficiency of the tetrahydrobiopterin-deficient cofactor, e.g. **secondary to defective dihydrobiopterin reductase.**
- High levels of phenylalanine —> **learning difficulties and seizures**
- Gene for phenylalanine hydroxylase —> **chromosome 12**

### **C/F :**

- Developmental delay
- Fair hair and blue eyes
- Learning difficulties
- Seizures - infantile spasms
- Eczema
- Musty odour due to urine and sweat (sweat = secondary to phenyl acetate, which is a phenylketone)

### **Labs :**

- hyper-phenylalaninaemia
- Phenylpyruvic acid in urine

### **41. Prader Willi syndorme**

- Example of genetic imprinting
- Gene deletion **father - Prader Willi**
- Gene deletion **Mother - Angelman syndrome**
- Absence of active Prader Willi gene on long arm of chromosome 15
- This may be due to:
  - microdeletion of paternal 15q11-13 (70% of cases)
  - maternal uniparental disomy of chromosome 15

### **Features**

- hypotonia during infancy
- dysmorphic features
- short stature
- hypogonadism and infertility
- learning difficulties
- childhood obesity
- behavioural problems in adolescence

42. Reverse transcriptase - DNA polymerase enzyme : involved in transcribing ss RNA into lengths of ds DNA.

Important role in pathogenesis of HIV which allows their genetic code to be integrated into the host genome as DNA.

It allows for segments of DNA to be produced from messenger RNA

43. **Xanthine oxidase** : catalyses the oxidation of hypoxanthine to xanthine and also further catalyse the oxidation of xanthine to uric acid.

Xanthine oxidase inhibitors - treatment option in gout.

Cause of gouty tophi - firm nodules over the extensor surfaces of fingers, hands, forearms, ears.

44. ADPKD in a patient - his brother would like to donate his kidney - screening method **Genetic screening**

NOT Abdominal USG as sometimes patient with ADPKD type 2 can have a normal USG

45. **Klumpke's paralysis** - C8, T1 nerve roots - weakness of intrinsic muscles of hand, long extensors of fingers  
Supplies motor supply to all intrinsic hand muscles (except LOAF)

LOAF - Lateral 2 lumbricals, Opponens pollicis, Abductor pollicis brevis, Flexor pollicis brevis

LOAF muscles supplied by median nerve C6, C8, T1

46. **Gastric adenocarcinoma** - signet ring cells >> mucinous >> papillary >> tubular in descending order of prognosis.

47. **G-proteins : located in cytoplasm**

They are coupled with GPCR which are on the cell membrane

Ligand binding site of G protein are expressed outside the surface through the plasma membrane.

TSH, ACTH, GABA-B

48. Troponin I mutation associated with HOCM —> **Lys183 deletion mutation form - high risk of SCD**

**Troponin T related HOCM - milder disease form of HOCM**

49. G1 phase - cells grow in size and **synthesise mRNA and proteins.**

50. Facial nerve damage during parotidectomy - tendency of food and fluids to collect in buccal sulcus after meals due to paralysis of buccinator muscle

Action of buccinator muscle : empty the buccal sulcus during mastication.

Peripheral injuries of facial nerve - no loss of taste sensation as the chord tympanii fibers pass from the lingual nerve to facial nerve just below the skull and remains intact during peripheral injuries of facial nerve

51. **Intra glomerular thrombi of immunoglobulins** - described in malignant lymphoma.

Nephrotic syndrome and systemic lymphadenopathy

Renal Bx : massive deposition of amorphous material in the glomerular capillary lumens.

## 52. **Lungs Anatomy**

- Left lung 50-100 grams lighter and smaller than right lung
- Each lung has - apex, three surfaces, three borders
- Apex of lung : blunt superior end of lung with the heart placed between them.
- Triangular fascia - **Sibson's fascia supra pleural membrane** - extension of end-thoracic fascia present between pleura and rib cage
- Surfaces of lung - **1) costal surface** - thoracic cage overlying it; **2) mediastinal / medial surface** - includes hilum of lung, **3) diaphragmatic surface** - in contact with diaphragm
- Borders of lung - **1) anterior border** - between the costal and mediastinal surfaces anteriorly; **2) inferior border** - separates the diaphragmatic surface from the costal and mediastinal surfaces



**3) posterior borer** - between the costal and mediastinal surfaces  
C7 to T1

- One alveolar duct culminates into six alveolar sacs
  - Root of lung contents :
    - A. Main bronchus
    - B. Pulmonary artery and veins
    - C. Bronchial vessels
    - D. Nerves
    - E. Fat tissue
    - F. Lymph nodes and lymphatics
  - Anteriorly - lungs extend from second to sixth costal cartilage
  - Anterior border of left lung - moves laterally to level of **fourth costal cartilage to form the cardiac notch** , before moving down to 6th costal cartilage.
  - Inferiorly - lung reaches upto the 8th rib at mid clavicular levels - 10th rib at mid axillary level and 12th rib posteriorly at level of scapula line
  - Oblique fissure - level of T12 vertebra on posterior side to 6th costal cartilage on the front
  - Visceral pleura - mesothelial lining consists of connective tissue and elastic fibers
  - Epithelium of bronchioles - columnar ciliated
  - Pores of Kohn in alveoli allow intra-alveolar communication
- 
- Right bronchial artery - branch of right posterior intercostal artery
  - Left side - two bronchial arteries - branches of descending thoracic aorta
  - Bronchial veins - drain into Azygos vein on **right** , **hemiazygos vein on left.**
  - Lymphatic drainage - **Bronchopulmonary lymph nodes at hilum**
- 
- Nerve supply - from pulmonary plexuses
  - Sympathetic fibers - 2nd to 5th sympathetic ganglion- bronchoconstriction and increases the secretory activity of mucous glands in lung pathways
  - Parasympathetic fibers - vagus nerve - inhibitory to bronchial muscles and glands

53. S1 nerve injury - loss of sensation in lateral aspect of calcaneus, loss of plantar flexion and ankle eversion.

54. Phase 0 of cardiac potential - related to L type calcium channels - reversal of membrane potential from negative to positive.  
Class I anti arrhythmic - Na channel blockers — exert their effect through phase 0 of action potential.

Class I - Quinidine, Procainamide, Disopyramide

Class III anti arrhythmic - Amiodarone, Sotalol - phase 3 of action potential - rapid efflux of potassium

Phase 3 - closure of L type calcium channels.

Class IV - Cardioselective CCBs Verapamil - phase 2 on cardiac potential - rapid influx of calcium happens in this phase via L type calcium channels

\*\*\*Class II anti arrhythmic decrease the slope of phase 4

\*\*\*Class III anti arrhythmics prolong phase 3 - K channel blockers

55. GORD - Los Angeles System

- 1) Grade A : one or more mucosal breaks < 5mm, none of which extends between the tops of mucosal folds
- 2) Grade B : one or more mucosal breaks > 5mm, none of which extends between the tops of mucosal folds
- 3) Grade C : mucosal breaks extending between the tops of mucosal folds, involving <75 % of mucosal circumference
- 4) Grade D : mucosal breaks involving >75 % of mucosal circumference.

\*\*\* Grade C esophagitis - reduced mean lower oesophageal sphincter pressure

56. 7.5 mg Prednisolone = glucocorticoid needs of 75 kg man

57. Oculomotor nerve palsy - CN III

Aetiology :

- ischaemic microangiopathy
- Diabetic cranial mononeuropathy
- Hypertension

- Compression / Transection : PCOM aneurysm, base of skull #, ischaemic stroke involving posterior cerebral artery branches, basal meningitis
- Tentorial herniation, orbital cellulitis, Internal carotid artery aneurysms
- Uncle herniation - CN III travels anteriorly on edge of cerebellar tentorium and can be compressed during increased ICP due to a supratentorial cause.
- CN III nuclei - midbrain - at level of superior colliculus.
- 2 branches - **1) superior branch** : supplies superior rectus and levator palpebrae ; **2) inferior branch** : supplies medial rectus, inferior rectus, inferior oblique, sphincter papillae.

C/F :

- Paralytic squint : adduction weakness
- Eye looks down (hypotonia) and outwards (exotropia)
- Ptosis
- Horizontal diplopia
- Non reactive fixed, dilated pupil
- Ischaemic microangiopathy - pupillary sparing

\*\*\* Light shone on eye causing constriction of pupil on the opposite eye = CN II

\*\*\* laterally deviation - lateral rectus - Abducens nerve CN IV

58. Surfactant - phospholipids (80%) such as DPPC Dipalmitoylphosphatidylcholine (40%), cholesterol (8%) , apolipoproteins (5%). Other proteins besides lipoproteins (5%). Water least amount present in surfactant. Surfactant -increased pulmonary compliance and leads to reduction in atelectasis.

59. Ventilation - controlled by respiratory centre in medulla.

- receives afferents and efferents from peripheral and central chemoreceptors.
- DKA patients increased respiratory driven response to metabolic acidosis.
- Plasma pH sensed by chemoreceptors located in carotid bodies.
- Control of normal ventilation - central carotid chemoreceptors.

- Central chemoreceptors - controls 2/3rd of ventilatory response.
- Carbon dioxide - freely diffuses across the blood brain barrier into the CSF where it hydrates and then dissociates into H<sup>+</sup> ions.

60. Post EPO injection on ESRD patients - check ferritin levels to see if there are adequate iron stores.

Options are : **serum ferritin, percentage hypochromia, transferrin saturations.**

### 61. Cytokines production :

#### MACROPHAGES

1. IL-1
2. IL-6
3. IL-8
4. IL-12
5. TNF alpha - **major levels of production**

#### EOSINOPHILS

1. IL-1
2. IL-2
3. IL-4
4. IL-5
5. IL-6
6. IL-8
7. IL-13
8. TNF alpha - **minor levels of production**

#### MAST CELLS

1. Histamine
2. IL-4
3. IL-5
4. TGF beta

#### Th1 cells :

1. IL-2
2. IFN gamma

#### Th2 cells :

1. IL-4
2. IL-6
3. IL-10

IL-12 : produced by **dendritic cells, macrophages, B cells**

IL-6 : **macrophages and Th2 cells**

## **62. DNA structure & function**

- DNA double stranded structure - nucleotide contains three elements which combine to form the repeating unit that makes up strand of DNA
- Three elements - phosphate group, sugar group, nitrogenous base
- Nitrogenous base - 4 types - adenine, guanine, cytosine, thymine
- Base + phosphate - **backbone of DNA**
- DNA functions - replication and transcription for proteins
- Double strand initially separated at **replication fork - by DNA helices enzyme**
- **mRNA - ss molecule complementary to strand of DNA it is formed from**
- Each chromosome is made up of DNA double helices being tightly wound round proteins known as histones.
- 22 pairs - autosomes; 1 pair - sex chromosome
- RNA splicing takes place within the nucleus itself.
- Splicing - by enzymes **spliceosomes** - composed of **5 small nuclear RNAs and associated proteins - leads to removal of introns and joining together of exons**

\*\* cytoplasm - contains ribosomes which translate mRNA into proteins by use of tRNA

\*\* Golgi body apparatus - responsible for protein transport

\*\* mitochondria - function to produce ATP in eukaryotic cells

## **63. Hypoxia - vasoconstriction in pulmonary vessels**

\*\* this improves the V/Q ration.

Acute response to hypoxia is due to NO.

Systemic response to hypoxia —> increase in sympathetic tone which leads to vasoconstriction except in vital body organs causes vasodilation.

Pulmonary vasculature - hypoxia causes vasoconstriction which redirects blood flow to areas of lungs that are relatively oxygen rich.

64. Biceps femoris muscle - nerve supply by : **Common fibular branch of sciatic nerve**

Peroneus muscle - **superficial peroneal nerve** - branch of common peroneal nerve

Absent knee reflex, loss of sensation over anterior and medial thigh => femoral nerve damage

\*\* Hip adductors - obturator nerve

\*\* **Small part of adductor Magnus —> tibial nerve**

\*\* **Pectineus muscle of adductor -> innervated by femoral nerve**

64. Hypothyroidism - first biochemical change - **increase in serum TSH**

65. Troponin binds to thin filaments - present in area adjacent to thin filaments

66. ANP - 28 amino acid peptide - released in response to atrial stretch.

ANP dilates the **afferent** glomerular arteriole, constricts the efferent glomerular arteriole and increases GFR

67. **Decreased sweating - increased risk of heat stroke**

68. **Acute attacks of acute intermittent porphyria - IV haematin / Haem alginate**

This suppresses the hepatic haemorrhage synthesis that is responsible for acute episodes of AIP. Typical regimen involves giving 3-4 mg/kg/day over the course of 4 days

69. Bleomycin - degrades preformed DNA - single DNA strand scission

Leading to inhibitor of cell division of growth and inhibition of DNA synthesis in tumor cells

70. Leptin increase release of melanocyte stimulating hormone, CRH, GnRH.

Leptin - stimulates production of cortical bone, decreases cancellous bone formation as a response to increased body weight seen in obesity.

Amylin - slowing of gastric emptying

Onset of puberty - leptin & kisspeptin

Obese women —> early menarche

71. Pituitary gland - sella turcica - depression in basophenoid bone.

Optic chiasma - most likely to be compressed by a pituitary tumor

## 72. **Stellate cells of liver - role in liver fibrosis**

- stellate cells have fat droplets
- Located within Disse space where cytoplasmic processes circle sinuses under the endothelial cells
- MAIN role in process of hepatic fibrogenesis responding to mediators released by parenchymal and Kupffer cells
- These mediators causes transformation of Stellate cells into myofibroblasts.
- Transforming growth factor beta initiates this process.
- transformed stellate cells AKA **Ito cells**, stimulates production of ECM collagen types I, III, IV, fibronectin, laminin, chondroitin sulphate, and hyaluronic acid
- Along with products such as collagenase, MMP and MMP inhibitor TIMP-1

- Activation of Ito cells - important mechanism for control of sinusoidal perfusion

Bile duct epithelial cells - pathology of PBC and PSC

Hepatocytes - undergo enlargement due to prolonged cholestasis

Kupffer cells - produces mediators which stimulates Stellate cells to drive the process of fibrosis.

### 73. Kennedy disease

- X linked pseudo bulbar neuropathy
- Trinucleotide disorder
- 40-60 years
- Repeat expansion of gene - 20 years

Trinucleotide disorders :

- 1) Huntington's chorea
- 2) Spinocerebellar ataxia
- 3) Fragile X syndrome
- 4) Myotonic dystrophy
- 5) Friedrich's ataxia

### 74. Normal lung volume

**Peak expiratory flow - 520-700 L / min**

**Total lung capacity - 5-6.5 L**

**Functional residual capacity - 2-3 L**

**Tidal Volume - 500-700 mL**

**Inspiratory Reserve Volume - 3.3 L**

### 75. Genetics Pointers :

- Human genome project- 20,000 genes
- Exons = coding sequences of DNA which code for peptides produced from mRNA
- Introns = exons have spaces of DNA between them called introns; these code for switches that control gene expression in splicing
- Human genome have a higher number of segmental duplications vs other mammals



76. Chromosome 1 = gene for variegate porphyria PPOX gene - autosomal dominant

Chromosome 6 = hereditary haemochromatosis - HFE gene mutation - autosomal recessive with variable penetrance

Chromosome 7 = cystic fibrosis - CFTR gene

Chromosome 11 = Beckwith-Wiedeman syndrome, Jacobsen syndrome, Ewing's sarcoma

### 77. **ATLS -Shock Classification**

- **Grade I** : loss of up to 15% - 750 mL blood volume; BP normal, Tachycardia +/-
- **Grade II** : 15-30% - 750 -1500 mL - SBP normal, tachycardia ++
- **Grade III** : 30-40% - 1500 - 2000 mL - hypotension, tachycardia, fall in urine output [ complete anuria is unlikely]
- **Grade IV** : > 40% - > 2000mL blood loss - anuria and severe shock

78. Thumb abduction - abductor pollicis brevis - median nerve paralysis

Wrist drop - radial nerve due to radial extensors

Inability to abduct and adduct fingers - ulnar nerve

Inability to flex little finger - ulnar nerve

79. Recurrent laryngeal nerve - hoarse voice, paralysis of posterior cricoarytenoid muscle

Interarytenoid muscle - nerve supply both left and right recurrent laryngeal nerve

80. Renin secreted by Juxta glomerular cells and hydrolyses angiotensinogen to produce angiotensin I.

Factors that increase renin secretion :

- Hypotension causing reduced renal perfusion

- Hyponatremia
- Sympathetic nerve stimulation
- Catecholamines
- Erect posture

Renin secretion reduced by : beta blockers, NSAIDs.

Angiotensin II :

- vasoconstriction of vascular smooth muscle leading to raised BP
- Vasoconstriction of **efferent** glomerular arteriole —> increased filtration fraction to preserve GFR;  $FF = GFR / \text{Renal plasma flow}$
- **Stimulates thirst** via hypothalamus
- Stimulate Aldosterone and ADH release
- Increases proximal tubule Na / H activity

Aldosterone - released in response to raised angiotensin II, hyperkalemia, raised ACTH levels.

Aldosterone = retention of sodium in exchange for  $K^+ / H^+$  in distal tubule

81. Neurons in resting state : positively charged externally, negatively charged internally.

Neurons in resting state can conduct action potentials if required.

At rest - neuron cell membranes are less permeable to  $Na^+$  than to  $K^+$ .

Inside of neuron is rich in chloride ions and contains lesser amount of potassium ions.

Outside of neurone = rich in sodium ions and positive on outside.

82. **Parkinson's disease** - increased protein aggregation and Lewy body formation - due to **proteasome dysfunction**.

**Proteasome** - intracellular apparatus responsible for protein degradation.

\*\* Bortezomib - proteasome inhibitor - used for treatment of MS.

83. **Renal Physiology**

- Most accurate laboratory methods for testing GFR : **1) inulin clearance, 2) chromium labelled EDTA 3) Iohexol** : iodine based, non ionic, water soluble contrast agent which is similar to Inulin
- Proximal tubule - 50% of filtered sodium is reabsorbed within the proximal tubule  $\text{Na}^+ / \text{K}^+$  ATPase pump
- The  $\text{Na}^+ / \text{H}^+$  antiporter secretes  $\text{H}^+$  into the lumen and is responsible for 90% of bicarbonate and some chloride reabsorption.
- All the filtered glucose and amino acids are re-absorbed in PCT
- Drugs secreted into tubular filtrate in PCT = Trimethoprim, Cimetidine, Most diuretic (NOT thiazide, Amiloride, Loop diuretics as they are highly protein bound and not filtered at glomerulus)
- Loop of Henle - thick ascending limb - **impermeable to water - allowing for concentration of urine here.**
- 40% of sodium is reabsorbed via  $\text{Na}^+ / \text{K}^+ / 2 \text{Cl}^-$  pump.
- Loop diuretics compete for chloride binding sites on this transporter.
- Distal tubule : 5% of sodium is reabsorbed via  $\text{Na}^+ / \text{Cl}^-$  transporter.
- $\text{H}^+$  ions secreted accounts for urine acidification.
- Thiazide diuretics compete at this transporter in Distal tubule.
- Collecting duct : Aldosterone sensitive Na channels are present.
- Spironolactone binds to cytoplasmic aldosterone receptor.
- ANP : anti aldosterone in action - counteracts against secondary hyperaldosteronism.
- $\text{H}^+$  secreted in the urine in collecting duct - acidifying urine
- ADH increases water reabsorption by opening water channels which are receptors on the basolateral membrane of the collecting duct - these are stimulated by ADH - leading to insertion of aquaporin channels into the luminal membrane.
- Lithium - enters the collecting duct via sodium channels and inhibits the response to ADH.

\*\*\* Bicarbonates are normally completely reabsorbed from the filtrate in PCT.

Decreased  $\text{HCO}_3^-$  - reabsorption causes metabolic acidosis - Type 2 RTA.

PCT damage :

- Albuminuria and proteinuria present as most amino acids and proteins are absorbed by PCT
- PCT damage causes reduced potassium reabsorption - hypokalemia

#### 84. **BRCA1 - DNA repair**

- Repair of double stranded breaks in DNA
- Process is known as **homologous recombination**
- BRCA1 mutation - breaks in DNA accumulate - increasing the chance of malignancy.
- Defective apoptosis - p53
- DNA polymerase mutation - DNA replication - colorectal cancers
- Growth repair gene mutations - increased risk of colorectal cancer
- RB gene - freezing of cell cycle - associated with impaired checkpoint regulation between G1 and S phase of cell cycle.

85. **Bradykinin - potent vasoactive peptide** - involved in inflammatory processes.

- increased vascular permeability
- Promotes vasodilation, pain and contraction of smooth muscle
- Stimulates arachidonic acid metabolism

86. Golgi body - sits adjacent to endoplasmic reticulum.

- responsible for modification of proteins and lipids produced by other cellular organelles.
- Hermansky - Pudlak syndrome - mutation of AP3 gene - responsible for trafficking of specific glycoproteins from the Golgi body.
- Autosomal recessive inheritance

87. Normal breathing - diaphragm drops down by 1 cm, creating an intrathoracic pressure drop of 1-3 mmHg, and air intake of 500 mL

Accessory muscles of respiration relax during passive expiration.

Diaphragm drops by 10 cm - **during exercise**

Rib cage recoils during passive expiration.

88. Cervical rib - history of pain affecting neck and shoulder and selective weakness of **abductor pollicis brevis - C8, T1 nerve roots.**

89. Portal vein supplies 75% of liver, hepatic artery supplies 25% of liver

90. **Intrinsic factor - produced by parietal cells found in fungus of stomach.**

**Stomach cardia - produces mucous**

91. Paget's disease - low ALP

\*\* low serum magnesium => highly active Paget's disease

92. Scala media = cochlear duct —> contains Organ of Corti

\*\*\* Scala media - contains potassium rich endolymph

Organ of Corti —> produces nerve impulses in response to sound vibrations

\*\*\* high frequency waves - are detected in Scala vestibule which is at the base of the cochlea

Low frequency waves are detected in Scala tympani —> which is present at the apex of cochlea

Scala tympani and vestibuli contains perilymph

20-2000 Hz —> normal hearing frequency range

93. Diffusion - fat soluble molecules - e.g. Glycerol - diffused through semi permeable cell membrane.

- they dissolve in the phospholipid bilayer and pass through in direct of concentration gradient.

- Endocytosis : active process where particles are captured within the cell membrane and this can be receptor or non receptor mediated.

- Exocytosis : export of particles out of the cell via secretory vesicles.
- Osmosis : diffusion of water across a membrane in which water diffuses into a solution having a greater solute concentration
- Phagocytosis : active process by which bacteria or other antigenic material is engulfed by macrophages.

94. Regional variations in lung

- Apex is situated above the level of heart - greater volume of blood will preferentially flow to base than apex
- Alveoli at base are compressed by weight of the lungs and therefore smaller in size compared to apex.
- Basal alveoli have **greater compliance** than apical alveoli
- Apex - less blood flow and less ventilation.
- V/Q ratio apex of lung is the greatest
- Increased V/Q ratio = increased PaO<sub>2</sub>, decreased PaCO<sub>2</sub>

95. **Congenital long QT syndrome** - autosomal dominant - genetic mutations affecting potassium channels are the most common.

Beta blockers - initial step in Rx.

2nd line Rx - ICD insertion, stellate gangliotomy.

ICD insertion is first line in those who suffered a cardiac arrest.

96. Carney complex = atrial myxoma + freckles

- high cortisol levels independent of ACTH
- Testicular, thyroid, pancreatic carcinomas are common
- Mutation in **PRKAR1A gene on chromosome 17q23-q24**

97. **Ethylene glycol - hypocalcemia - as end product of ethylene glycol is oxalic acid.**

**Oxalic acid combines with calcium to form insoluble calcium oxalate ; acidosis + kidney disease**

98. Dextrose 50% - 1700 kcal / one litre 1.7 kcal/mL

Dextrose 40% - 1360 kcal / one litre 1.3 kcal / mL

Dextrose 60% - 2040 kcal / one litre 2 kcal/mL

Lipid emulsion 10% - 1.1 kcal /mL

Lipid emulsion 20% - 2 kcal / mL

Lipid emulsion 30% - 3 kcal/mL

Dextrose 50% - 1 litre & lipid emulsion 20% one litre - 2000 kilo calories

99. Ulnar nerve injury at the elbow - inability to grip a sheet of paper between his fingers when the hand is placed flat on the table - test for paralysis of the Palmar interossei muscles - inability to adduct the fingers.

Loss of sweating over the ulnar border of left hand due to damage to sympathetic interruption

4th and 5th digits are held in clawed position if ulnar nerve lesion is at the wrist.

Elbow lesions of ulnar nerve leads to paralysis of long flexors only - NO CLAWING IN ULNAR ELBOW LESION.

**100. 11-deoxycortisol —> precursor to cortisol**

**Deoxycorticosterone —> precursor to corticosterone**

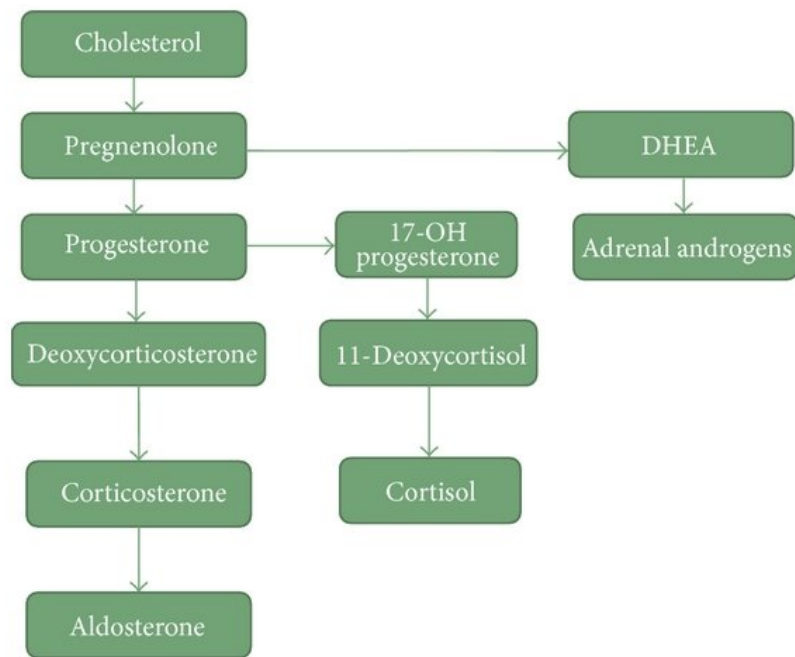
**Corticosterone —> precursor to aldosterone**

**101. Dubin Johnson confirmation - coproporphyrin excretion pattern**

102. Inhalation of fluids - disordered gas exchange - respiratory acidosis.

Metabolic acidosis is due to intravascular volume depletion, hypotension and tissue hypoxia.

Therefore - inhalation of fluids = mixed metabolic and respiratory acidosis.



Caption

Normal / elevated sodium, high urea count, normal / elevated potassium

103. Squamous cells cancers releasing PTHrP -

- lung cancer
- Head and neck cancer
- Cervical cancer
- Vulva cancer

**Other tumors secreting PTHrP :**

- cancers of ovary
- Breast
- Kidney
- Pheochromocytomas
- Pancreatic islet cell tumors

104. **Proofreading occurs** when DNA polymerase travels along a double stranded piece of DNA - when a mismatched pair is recognised, incorrect base is excised.



- Recombination - DNA recombination brings together DNA from multiple source
- Replication : DNA replications is the process of producing two identical copies of DNA from one template molecule
- Retro-transposition : transposition via a RNA intermediate
- Transposition : movement of genetic element from one site to another in a DNA molecule
- Splicing : removal of introns from the primary transcript of a discontinuous gene

105. Respiratory epithelium - cilie - mucociliary escalator has an essential role in clearing debris, including pathogens from the respiratory tract.

- Ciliary dyenin converts chemical energy from ATP into movement, producing rhythmic ciliary beating.
- 100mL mucus is produced by the respiratory tract
- Bronchioles have no cartilage in their walls.
- Bronchioles diameters - 1mm
- Mucociliary escalator moves at 2 cm/min

106. EEG waves

- alpha waves : 8-13 Hz
- Delta waves : < 4 Hz
- Theta waves : 4-7 Hz
- Beta waves : >14 Hz

107. Drugs causing gingival hyperplasia :

- CCB - Amlodipine, Nifedipine, Oxodipine, Verapamil, Diltiazem
- Phenytoin
- Ciclosporin
- Erythromycin
- Hormones
- Acute Myeloid Leukaemia

108. **Hyperphagia - ventromedial nucleus**

Control of BP and HR - dorsomedial nucleus

Memory function - Mamillary bodies

BP regulation, shivering and release of vasopressin : Posterior nucleus

Release of Vasopressin & Oxytocin : Supraoptic nucleus

109. Factors maintaining **pressures** within the **arterial system** :

- 1) peripheral arterial elasticity
- 2) Ventricular systole
- 3) Recoil of elastic aorta

\*\*

- Suction during cardiac diastole - **venous return**
- Residual pressure from blood flow through capillaries - promotes venous blood flow
- Negative pressure during inspiration - **venous blood flow**
- Contraction of external muscles - venous blood flow

110. Monoclonal antibodies target - **plasma cells**

**Two targets for monoclonal therapy in asthma -**

- 1) IgE - in allergic phenotype
  - 2) To target eosinophil maturation via IL-4/IL-5/IL-13 - in the eosinophilic phenotype
- NICE recommends adding monoclonal IgE antibody therapy after 4 or more trials of oral corticosteroids have been completed in the previous year with optimised standard therapy
  - Example - **Omalizumab**
  - severe eosinophilic asthma - Il-5 antibody therapy - **Mepolizumab / Reslizumab / Benralizumab**
  - Il-4/13 antibody therapy - **Dupilumab**

**111. Cytokines involved in fever / sepsis :**

IL-1, IL-6, TNF-alpha

IL-1 - causing vasodilation —> hypotension —> complex cytokine cascade

\*\*\*

IL - 4 promotes class switching to IgE - important in defence against some parasitic disease and in mast cell and basophil degranulation and antigen presentation.

IL - 5 : stimulates eosinophils production in response to parasitic infections and class switching to IgA

IL-8 : along with other mediators - C5a, LTB<sub>4</sub>, - acts as chemotactic factors that lead neutrophils to infection site.

112. Fluorescence in situ hybridisation : fluorescent DNA or RNA probe to bind to specific gene interest for direct visualisation of chromosomal abnormalities

- Eastern blotting - post translational modifications of proteins such as addition of lipids and phosphates.
- Northern blotting : study expression of RNA
- Western blotting : study proteins in a sample
- ELISA : detect antigen and antibodies - color changing enzymes are used in this process.

113. Diabetic nephropathy - Kimmelsteil Wilson nodules - nodular glomerulosclerosis, basement membrane thickening, capillary obliteration, mesangial widening

- Apple green birefringence - Amyloidosis
- Enlarged and hypercellular glomeruli - **Post streptococcal GN**
- Crescent moon shaped glomeruli - **RPGN**
- Wire looping of capillaries - **Diffuse proliferative GN - SLE**

114. Vitamin C - scurvy

- Impaired collagen synthesis and disordered connective tissue as ascorbic acid is a co-factor for many enzymes used in production of proline and lysine.
- Associated with severe malnutrition.
- Also seen in drug and alcohol abuse.

### Clinical Features :

- Follicular hyperkeratosis
- Perifollicular haemorrhage
- Ecchymosis
- Easy bruising
- Poor wound healing
- Gingivitis with bleeding and receding gums
- Arthralgia
- Edema
- Weakness, malaise, anorexia, depression

### 115. Lesch Nyhan Syndrome

- X-linked recessive
- AKA **juvenile gout**
- Defect in purine salvage pathway due to absence of HGPRT enzyme
- HGPRT enzyme catalyses conversion of **hypoxanthine to IMP**
- HGPRT catalyses conversion of Guanine to GMP
- Deficiency of enzyme → hyperuricaemia
- C/F : aggressive behaviour, self-mutilation, intellectual impairment

X-linked dominant - Fragile X syndrome, hypophosphataemic rickets

116. **Early response asthma** - **mast cell degranulation is seen in response to IgE already produced by B cells**; 10-20 minutes peak attained after exposure to allergen and spontaneously resolves in 102 hours

**Late response asthma** - **Eosinophils** which are recruited in response to IL-13 produced by lymphocytes; occurs 3-5 hours after exposure to allergen, resolves in 6-8 hours.

**Attraction of phagocytes** an important feature of Late asthma response.

### 117. Pemphigus vulgaris

- Autoimmune disease caused by antibodies directed against **Desmoglein 3 - cadherin type epithelial cell adhesion molecule**

- **Desmoglein 3 - pemphigus vulgaris**
- **Desmoglein 1 - pemphigus foliaceus**
- More common in **Ashkenazi Jewish population**
- Mucosal ulceration
- Oral involvement 50-70%
- Skin blistering : flaccid, easily ruptured vesicles and bullae
- Bx : **Acantholysis**
- Mx : Steroids, Immunosuppressant

118. **Claudin disorder** -tight junctions disorder Claudine \_ proteins involved in tight junctions between epithelial cells of intestinal and renal cells.

They form a barrier to movement of solutes and ions

Claudin disorders : Neonatal Sclerosing cholangitis

\*\*

Connexins : protein channels between two adjacent cells to allow passage of solutes upto molecular weight of 1000 kDa.

Connexin disorders : connective tissue disorders - oculodendrodigital dysplasia

119. Respiratory alkalosis - salicylate and theophylline

TCA - causes respiratory depression, coma and fits.

120. Hypomagnesemia - exacerbates digoxin toxicity

Hypophosphatemia - worsens cardiac failure by decreasing LV contractility

121. **Neuralgic amyotrophy = Brachial neuritis = Brachial plezitis**

- Autoimmune inflammatory aetiology
- Often occurs after infection, vaccination, traumatic injury, surgery, childbirth
- Intense pain around shoulder and rapid patchy weakness of the affected limb
- \*\* winging of scapula (long thoracic nerve C5-C7)
- Loss of elbow flexion - Musculocutaneous nerve C5-C7
- CSF : mild raised protein, mild lymphocytosis.

**122. Methods to predict 3D structure of protein :**

- 1) **X-ray crystallography** - cannot give information about how the conformation of protein may change over time.
- 2) **Nuclear magnetic resonance spectroscopy**
- 3) **Cryogenic electron microscopy**

**Information about conformational changes of protein : 1) Dual position interferometry; 2) nuclear magnetic resonance**

123. Encapsulation in stem cell derived islet cell transplants - **prevent autoimmune attack** - by introducing barrier (usually alginate) that prevents access by cells of immune system mainly T lymphocytes.

124. Insulin resistance - increased levels of Plasminogen activator inhibitor -1 —> risk factor for Myocardial infarction

**125. Riboflavin :**

- Light sensitive
- Dietary sources - milk, cheese, eggs, liver, yeast extracts, meat extracts
- Involved in **redox process involving the hydrogen transfer chain in mitochondria**
- **Production of ATP**

**126. Inadequate fluid replacement - constipation in enteral feeding**

**Diarrhoea** is common in enteral feeding due to :

- hyperosmolar feeds
- Bacterial contamination
- Low feed temperature
- Reduced intestinal absorptive capacity
- Too rapid or irregular administration
- Lactose intolerance

**127. Anterior mediastinum - thymus**

- Anteriorly by sternum
- Posteriorly by great vessels
- Contents : thymus, lymph nodes, fat and vessels.

- Disorder of anterior mediastinum = thymus, teratoma, terrible Lymphoma, thyroid

128. Radial nerve - via - posterior interosseous branch and superficial branch - supplies skin over first web space and extensor pollicis brevis and longus

### 129. Endothelin

- Constricts **afferent arteriole vasoconstriction**
- Stimulates RAAS
- Leads to release of ANP
- Inhibits action of vasopressin
- Two types of receptors - ET-A and ET-B
- ET-A = vasoconstriction
- ET-B = vasodilation due to NO production.

\*\* Efferent arteriolar dilation = Angiotensinogen II

### 130. ULNAR NERVE - C8, T1

- All intrinsic muscles of hand - **except LOAF muscles**
- LOAF muscles are supplied by median nerve
- Motor - wrist flexion
- Motor supply to - Flexor carpi ulnaris & flexor digitorum profundus ulnar head
- Sensory - medial 1.5 fingers - **hypothenar eminence**
- Damaged in : Medial epicondyle #, claw hand
- Jeanne sign : positive test in ulnar nerve damage due to hyperextension of 1st Metacarpophalangeal joint - Front's thumb sign : adductor pollicis brevis weakness
- Inability to hold card or paper between fingers due to loss of adduction by palmar interossei - CARD TEST
- EGAWA TEST : palm faced flat - patient is asked to move the middle finger sideways- to test dorsal interossei

Complaints : difficulty opening jars or holding a pencil

Weakness of adductor pollicis muscle, dorsal interossei, palmar interossei, 3rd and 4th lumbricals.

Lesions above elbow - Ulnar nerve :

- A. Sleeping with arm hanging over a sharp edge compressing the nerve against humerus - crutches
- B. Supracondylar # of humerus

### MEDIAN NERVE C6, C8, T1

- Motor supply to LOAF muscles , flexor muscles, thenar muscles
- L - lateral two lumbricals
- O - opponens pollicis - thumb apposition
- A - **abductor** pollicis brevis - thumb abduction
- F - flexor pollicis brevis - thumb flexion
- Sensory - palmar aspect of lateral 3.5 fingers
- Damage at wrist : paralysis of thenar muscles, opponent pollicis - **carpal tunnel syndrome**
- Damage at elbow - loss of power in flexor muscles of forearm
- Flexor muscles of forearm - all flexor muscles in forearm are supplied by median nerve **except Flexor carpi ulnaris, and ulnar head of digitorum profundus**
- **Elbow lesion —> loss of pronation of forearm and weak wrist flexion**
- **Ape hand - hand of benediction**

131. T2DM = Normal LDL + Low HDL + Elevated Triglycerides

132. Insulin receptor - tyrosine kinase receptor - **present on cell membrane**

Insulin receptor : involved in intracellular signalling by phosphorylation of intra cellular proteins.

These proteins include - IRS-1 (upregulation of GLUT-4) - responsible for glucose transport

\*\*\* Leprechaunism = Donohue Syndrome = autosomal recessive - mutation causing non functioning of insulin receptor.

133. **Thiazide diuretics :**

- increased delivery of sodium to distal part of DCT



- Increased activation of aldosterone sensitive sodium pump
- Increased sodium reabsorption in exchange for potassium and hydrogen ions
- Causes **hypokalemic alkalosis**

134. Gaucher disease two enzymes elevated : **Acid phosphatase, ACE**

135. Loss of unbuffered gastric acid and can cause metabolic alkalosis in prolonged NG aspiration in post-op lieus if there is inadequate fluid replacement with IV Normal Saline.

Alkalosis is maintained y increased renal  $\text{HCO}_3^-$  reabsorption and  $\text{K}^+$  depletion due to secondary increase in aldosterone.

136. Restrictive lung disease - Idiopathic Pulmonary Fibrosis :

- diffusion capacity is **reduced**
- FEV 1 / FVC - **normal** or **increased**
- TLC - **reduced**

Obstructive airway :

- FEV 1 / FVC : **reduced**
- TLC - normal or increased

137. **Measurement of urine protein immediately on getting out of bed**

Proteinuria can occur because of glomerular damage , tubular damage, increased excretion of LMW protein, secretion of proteins into urine due to UTI.

Young patient - rule out orthostatic proteinuria first.

138. Ileostomies : patients can lose large amounts of Magnesium through their stomas - hypomagnesaemia impairs PTH secretion and causes hypocalcemia that is resistant to an increased provision of calcium.

139. **Azygous lobe of lung** - seen in 0.5% of CXR - normal variant - **reverse comma sign** being the medial end of right clavicle.

Azygous love is formed when the posterior cardinal vein migrates through the upper lobe of right lung.

140. The occurrence of breast and ovarian cancer in multiple members of a family under the age of 45-years-old should strongly raise the suspicion of BRCA1 mutation as the cause for the cancers. The patient meets the screening criteria for BRCA mutations as there are >2 family members with breast cancer <45 years and one family member with both ovarian and breast cancer.

**Polymerase chain reaction** remains the mainstay of **locating mutated oncogenes at present**. The method allows amplification of the mutated gene sequence and the mutated gene sequence can be easily detected on electrophoresis.

141. Bile salts - production is catalysed by **cholesterol 7 - alpha - hydroxylase**

Total bile salt pool - 2.5-5 grams

Total fecal loss of bile salts = 20%

Bile acids concentration in gall bladder = 100-300 mmol / L

Bile salt reabsorption - 80% over **6-8 cycles** \*\*

142. Cardiac abnormalities of DiGeorge syndrome = trunks arterioles, Tetralogy of Fallot.

143. Adrenaline, also known as epinephrine, is a hormone that is only secreted by the adrenal medulla. It plays an essential role in the body's response to stress, increasing heart rate, blood pressure and metabolic rate. In addition, it enhances muscle strength and mental alertness.

**Noradrenaline**, also known as norepinephrine, is not exclusively secreted by the adrenal medulla. While it is indeed produced in the adrenal medulla, it is also synthesized in nerve terminals of the sympathetic nervous system. Noradrenaline acts as both a hormone and a neurotransmitter playing a crucial role in maintaining blood pressure and supporting the fight-or-flight response.

144. Ubiquitination is a post-translational modification process that tags proteins for degradation. The ubiquitin-proteasome system (UPS) is the main machinery for protein catabolism in the cytosol

and nucleus. Proteins tagged with ubiquitin are recognised and degraded by the proteasome, an organelle that disassembles unneeded or damaged proteins into smaller peptides.

Endoplasmic Reticulum :

- Rough ER : translation and folding of new proteins
- Manufacture of lysosomal enzymes
- Site of N-linked glycosylation
- E.G of cells with extensive rough ER = pancreatic cells, goblet cells, plasma cells.

Smooth ER :

- Steroids and lipid synthesis
- E.g. : extensive smooth ER = adrenal cortex, hepatocytes, testes, ovaries.

Golgi apparatus :

- Modifies, sorts and packages these molecules that are destined for cell secretion.
- Addition of Mannose-6-phosphate to proteins designates transport to lysosome

Mitochondrion : Aerobic respiration, contains mitochondrial genome as circular DNA

Nucleus :

- DNA maintenance
- RNA transcription
- RNA splicing - involves removing introns (non coding sequences) from pre-mRNA and joins the exons

Lysosome : breakdown of large molecules such as proteins and polysaccharides

Nucleolus : Ribosome production

Ribosome : translation of RNA into proteins

Peroxisome : catabolism of very long chain fatty acids and amino acids - results in formation of hydrogen peroxide

Proteasome : along with lysosomal pathway, involved in protein degradation that have been tagged with Ubiquitin.

145. Classical hereditary haemochromatosis (HH) is characterised by incomplete penetrance and variable expressivity. Women are less affected than men by iron overload and iron overload-related diseases since menstruation acts as a protective measure due to blood and therefore iron loss.

146. This patient has Fanconi syndrome, of which amphotericin B is a recognised cause.

- This is due to a defect in the cells of the proximal convoluted tubule.
- The proximal tubular cells fail to reabsorb bicarbonate, leading to type 2 (proximal) renal tubular acidosis. T
- The proximal tubular cells also fail to reabsorb glucose and amino acids, explaining the findings of protein ++ and glucose +++ on the patient's urinalysis, in spite of normoglycaemia.
- The patient's blood tests, showing depletion of potassium, calcium and phosphate due to failed proximal tubular reabsorption of electrolytes, further support the diagnosis of Fanconi syndrome.

147. HIV Immunological changes :

- A. Reduction in CD4 count
- B. **Decreased** IL-2 production
- C. **Decreased** NK cell function
- D. **Reduced** delayed hypersensitivity response
- E. **Increased** Beta-2-microglobulin
- F. Polyclonal B-cell activation

148. **Ghrelin** - secreted when stomach is empty and drives increased hunger, levels fall once stomach is full and remains low approximately 3 hours after meal.

Glucose dependent Insulinotropic Polypeptide GIP : incretin hormone that increases gut transit time and has a central effect in reducing obesity

GLP-2 : no effect on appetite; does induce mucosal growth - potential target for short bowel syndrome and radiation induced enteritis.

Leptin - rise in leptin causes decreased appetite.

Peptide YY (PYY) - incretin - appetite suppressant - central effect - delays gastric emptying time.

149. **Liver cirrhosis** : low albumin associated with severe disease drives **relative intravascular volume depletion**.

Aldosterone release is increased as a result and decreased steroid hormone synthesis due to liver impairment.

Both these factors contribute to metabolic alkalosis.

Albumin —> acts as a weak acid and decreased albumin levels causes **metabolic alkalosis**.

150. **Tereparatide** - PTH Analogue - increases osteoblast activity - Procollagen type 1 pro peptides : C-terminal C1CP, N-terminal PINO , Osteocalcin OC

Bone turnover - CTX C terminal cross linked polypeptide

151. P53 - DNA binding protein that induces the expression of a number of genes involved in programmed cell death. P53 gene mutations are implicated in carcinogenesis.

P51 - colon cancer associated peptide : correlate to recurrence of disease

P52 : AKA nF kappa B2 - over expressed in patients with prostate cancer

P54 - helices protein unregulated in certain forms of cancer

P55 - membrane scaffold protein : not related to cancer \*\*\*

152. Right and left renal artery : four in trans-pyloric place at level of L1 - hilum of kidney

- during a trans femoral arteriogram for suspected renal artery stenosis - catheter is passed from the femoral artery through external iliac artery up into the common iliac and into aorta at its bifurcation. From here - catheter is passed up to level of L1 at which right and left renal arteries are located.
- Aorta passes through the diaphragm at T12 vertebra
- Femoral artery lies halfway between ASIS and pubic symphysis
- Aorta → supra renal and gonadal arteries separately above and below the origins of renal arteries on each side.
- Inferior supra renal artery is NOT a branch of aorta

153. **Senescence** - arrest of mitosis : occurs due to DNA damage at telomeres and DNA damage due to non-telomeric sites.

- this DNA damage leads to a DNA damage response
- **Apoptosis** : intrinsic pathway - mitochondrial dysfunction; extrinsic pathway - cell receptor mediated cell death. **DNA fragmentation occurs.**
- **Cellular necrosis** : occurs due to autolysis and is a marker for premature cell death
- **Shortening of Telomeres** : progressive shortening of telomeres is one of the mechanisms of senescence.

154. **UV Radiation - formation of pyrimidine dimers** - energy absorbed by DNA resulting in formation of pyrimidine dimers leading to initiation of apoptosis and inflammatory responses.

155. Triple repeat primed PCR - TP PCR : useful in evaluation of Friedrich ataxia.

- 99% of gene containing part of human DNA sequence have been examined

156. **Alkaptonuria - HLA DR7**

157. PCR

- denaturing dsDNA - 95 degree C
- Annealing of primer 50-70 degree celsius
- Extension of dsDNA molecules - 70 degree C
- RT-PCR Is able to identify transcripts of a given gene by detecting the mRNA coding for the gene
- Cycling of reaction - mixture temperature enable sequential denaturation of the new DNA strand
- Taq polymerase is bacterial origin - *Thermus aquaticus*

158. **Pyramidal tract lesion - extensors in arms and flexors of lower limbs are affected.**

**Weakness of arm extensors and hip flexors**

- as a result of this, because of reduced opposition of other muscle group - arms tend to be held across the body with elbow and wrist flexed
- Leg held in extension with foot drop.

159. **Genetic cloning-** enucleated oocyte fused with the nucleus to form a donor cell.

Process is known as somatic nuclear transfer.

160. Long distance running = fatty acid oxidation

161. **Endothelin 1 = 21 amino acid polypeptide ; potent vasoconstrictor -**

- non elective endothelia antagonist : Bosnian
- Selective Endothelin A receptor antagonist - Ambrisentan

162. **Internal capsule**

- blood supply : lenticulostriate vessels
- End of internal capsule - area between anterior and posterior limbs
- Fibers of optic radiation : lies in posterior limb
- Lentiform nuclei : outer putamen and inner globus pallidus
- Anterior limb lies between the head of caudate nuclei and lentiform nucleus

163. Sarcoid granuloma - asteroid bodies, Langhans Giant cells, Schaumann bodies

Lymph nodes sarcoidosis - Hamazaki - Wesenberg bodies - inclusion bodies of lysosomes with protein, glycoprotein and iron.

164. CSF production by ependymal cells.

- Modified ependymal cells : choroid plexuses
- Astrocytes : maintains biochemical stasis and provides micro-architecture to brain
- Microglia - tissue macrophages
- Oligodendrocytes : forms the myelin sheath that coats axons within the CNS
- Schwann cells - form the myelin sheath that covers axons in PNS
- CSF largely similar to plasma, lesser protein content.

165. TPN requirements :

- Reduced food - Nitrogen 0.15-0.2 g N/kg/day; Calories - 25-30 kcal /kg / day
- Moderate injury / sepsis : Nitrogen 0.2-0.3; Calories - 30-35 kcal/kg/day
- Severe injury : 0.3-0.35 g N/kg/day; Calories 35-40 kcal/kg/day

166. Salt intake - 6 g / day in UK

High salt >1.5 g/100 g salt

Low salt <0.3 g / 100 g salt

Saturated fat intake 30 g/day for men, 20 g/day women

High sugar food > 22.5 g/100 g sugar

Low sugar food < 5 g/100 g sugar

167. Anaemia occurs only in lead poisoning due to inhibition of ferrochelatase enzyme.

Acute intermittent porphyria v/s lead poisoning **please read**

168. Arterial underselling - causes sodium and water retention.

169. **Telomeres**

- Structures at end of chromosomes which in normal cells progressively shorten with each cell division.



- When telomerase is inactivated : shortened telomeres causes cell growth arrest.
- Physiological suppression of telomerase is a tumor suppression and is part of normal ageing process.

170. Cartilage is avascular - receives its nutrition by diffusion from synovial fluid.

Chondrocytes - secrete collagen, proteoglycans

Hyaline cartilage type II collagen.

170. Foam cells - CD68 - monocyte derivative.

171. Botulinum toxin prevents release of acetylcholine

Effect wears off after 12 weeks

Botulinum toxin is immunogenic - can give rise to hypersensitivity reactions

Toxin is produced from **type A neurotoxin**.

172. **Mitosis - Stages :**

1. Interphase
2. Prophase - chromosomes pair up
3. Metaphase - chromosomes line up at equator
4. Anaphase - sister chromatids pulled apart
5. Telophase & Cytokinesis - cell pinched in middle - nuclear envelope develops around the nucleus of each daughter cell, nucleoli reappear and chromosomes unwind

173. Adductor pollicis - **Ulnar nerve** - weakness of adductor pollicis —> **Froment's sign** : patient is asked to hold a piece of paper between their thumb and flat palm as the paper is pulled away - ulnar nerve damage - difficulty maintaining the hold on object leading to compensation by flexing thumb.

174. **Gelatinase : MMP 9 - functions in neutrophil action, angiogenesis, and wound repair.**

**Stromelysin : MMP 3, 10, 11 - degrading a number of tissue constituents including serum collagen subtypes, proteoglycans, fibronectin, laminin and elastin.**

**Enamelysin - MMP 2- - cleave enamel matrix proteins**

**Epilysin : MMP 28 - degrade casein and plays a role in tissue homeostasis and wound repair**

**Interstitial collagenase - MMP 1 - its expression plays a role in progression of rheumatoid arthritis.**

175. Cardiac index and oxygen delivery correlate well with outcome from high-risk surgery.

Survivors after major surgery increase their cardiac index and oxygen delivery in preoperative period above baseline values.

Measurement of mixed venous oxygen saturations requires **pulmonary artery catheter** to sample pulmonary capillary blood.

Simple indicators such as urine output, blood pressure, CVP - correlate poorly with outcome in high risk patients compared with previous cardiovascular disease.

176. **Fovea centralis** : central portion of macula
- disease in macula containing fovea centrals will impact acuity.
  - Macula is rich in **cones**
  - No direct relationship between proliferative retinopathy and frequency of cataracts
  - **Optic papilla** : opening of optic nerve

177. Femoral hernia : lateral and inferior to pubic tubercle.

Inguinal hernia - inguinal triangle

**178. Idiopathic scrotal edema** : allergic condition in children - swollen, erythematous scrotum, can extend to groin and perianal regions. No treatment needed.

- Fournier's gangrene : variant of necrotising fasciitis of scrotum and causes gross oedema, S/C emphysema and patchy necrosis - painful
- Leukaemia : acute painful enlargement of testis and scrotum
- Strangulated hernia : painful irreducible hernia with decreased blood supply

**179. Re-feeding syndrome** : hypophosphataemia - cardiac, respiratory, and neuromuscular failure; others C/F : metabolic encephalopathy due to ATP depletion, AMS, paraesthesia, seizures, coma.

**180. Gas exchange** happens in alveoli - last 7 generations of bronchi.

Bronchi divide upto 23 generations in the lung.

- Equilibration of gases takes about 0.25 seconds in the resting lung, decreasing in high cardiac output states as red cell transit time decreases.
- Initial 16 branches of bronchial tree = conduction zone.

**181. Intense activity with reduced lactic acid** - decreased muscle glycogenolysis- McArdle's disease

**182. Decreased aortic compliance** - with increasing age - aorta is less able to absorb the pulse wave that comes from left ventricular contraction —> increasing the pulse pressure.

**183. Blood buffers** :

- cell and plasma protein
- Hemoglobin - protein and has imidazole side chains and can buffer H<sup>+</sup> ions. Deoxy-Hb better buffer than Oxy-Hb
- Phosphates
- Bicarbonate ions
- Carbonic acid

184. Actin - cytoskeleton - globular protein found in microfilaments of cytoskeleton and in thin contractile filaments of muscle cells.

Alpha actins : muscle cells

Beta and gamma actins : cytoskeleton

Small amounts of actin also found in nucleus.

185. Flexor digitorum superficialis : proximal Interphalangeal joint

- Extensor digitorum - extends medial 4 digits of hand
- Flexor digitorum longus - flexor of 2-5 phalanges of leg - tibial nerve
- Flexion at MCP joints - lumbricals - also extension at interphalangeal joints

186. Cell cycle checkpoint - G1/S and G2/M - p53

Congenital mutation of p53 = Li Fraumeni syndrome

187. Obese patient - CVC Subclavian landmark - 2 cm below mid point of clavicle, and 1 cm laterally.

188. Porphyria cutanea tarda

- Autosomal dominant
- Associated with excessive alcohol intake with or without liver disease
- Deficiency in activity of **Uroporphyrinogen Decarboxylase UROD**
- Blistering skin lesions on sun exposed parts of body
- Hypertrichosis on cheeks and forearms
- Scarring alopecia
- Red urine due to large quantities of porphyrins
- Labs : mild elevates AST, ALT; Elevated plasma and urine total porphyrins, fa porphyrins
- Mx : avoid exacerbating factors,
- Repeated Phlebotomy - preferred over low dose hydroxychloroquine if **ferritin > 600 ng/mL or homozygosity or compound heterozygosity for HFE mutations**
- Low dose hydroxychloroquine

189. Steatorrhoea and malabsorption —> **Lactose intolerance test**

- Involves comparison in blood glucose rise following dose of lactose compared with dose of glucose
- Specific for lactase deficiency
- Definite Dx : lactase of biopsy sample

190. **Irinotecan** - Topoisomerase inhibitor - blocks the breaking and rejoining of phosphodiester backbone of DNA strands

Inhibits microtubule assembly : **Vinca alkaloids**

BCR-ABL Tyrosine kinase inhibitor : **Imatinib**

Competitive inhibition of nucleoside synthesis : **Fludarabine - interfere with DNA sythensis and blocks replication**

Inhibits normal microtubule disassembly : **Taxmen inhibits disassembly of microtubule apparatus during mitosis**

191. **Tetanus toxin**

- Cleaves the specific sites of **Synaptobrevin (VAMP)** - belongs to family vesicle-associated membrane protein.
- Synaptic fusion complex = Synaptobrevin + Syntax + Synaptosome-associated protein **SNAP-25**
- This fusion complex serves to join the membranes of ACh vesicle and nerve cell.
- Botulinum toxin types BoNT/B, D, F, G and Tetanus toxin (TeNT) cleaves specific sites of Synaptobrevin.
- Botulinum toxin types A and E - cleaves SNAP-25 \*\*\*\*
- Synaptobrevin forms SNAP complex together with N-ethylmaleimide sensitive factor (NSF), Calcium and other proteins.

192. **VLDL**

- VLDL formed from triglycerides, cholesterol and apolipoproteins.

- VLDL - transports endogenous products - TGs, Phospholipids, Cholesterol and cholesterol esters.
- Chylomicrons : transport of exogenous products
- VLDL particles are continuously excreted in the liver and contains most of the TGs in the body.
- Main source of energy during prolonged fasting.
- **Apolipoprotein C-II** on its surface
- Binds to capillary endothelium
- Allows for TGs to be progressively removed by LPL
- LPL leaves a particle without TGs and Apolipoprotein C-II → this particle is known as IDL.

Chylomicrons are synthesised post prandially in small intestinal enterocytes.

HDL - takes up cholesterol from cells.

### 193. Riboflavin

- Co-factor of **Flavin adenine dinucleotide (FAD) and Flavin mono nucleotide (FMN)**
- Adverse effect : **Angular cheilitis**
- Formed from **Ribitol - alcohol derived from pentose sugar ribose**
- Dietary sources : liver, milk, cheese, eggs, beer
- Involved in redox process involving hydrogen-transfer chain in mitochondria and production of ATP

### 194. Glucose transporters

#### 1) **GLUT-1 : Widely distributed in fetal cells, Adults -**

**Erythrocytes & endothelial barrier cells like BBB;** responsible for low basal levels of glucose transport to facilitate respiration in mammals. Transporter expression is glucose responsive. GLUT-1 expression unregulated in many tumors. **Bidirectional transporter\***

#### 2) GLUT-2 : transport of monosaccharides including glucose, galactose & fructose from intestinal cells to portal circulation; expressed in hepatocytes, renal tubular cells and pancreatic beta cells, basolateral membrane of small intestinal epithelial cells. . Like GLUT-1, it is bidirectional and allows glucose flow

into and out of liver for glycogenesis and glycolysis, & release of glucose during gluconeogenesis.

- 3) GLUT-3 : high affinity transporter in neurones and placenta; important to preserve energy supply to brain and growing foetus.
- 4) GLUT-4 : insulin-mediated glucose uptake in muscles and adipose tissue; responsiveness to insulin is decreased in patients with insulin resistance; Glitazones are known to increase cell surface expression of GLUT-4
- 5) GLUT-14 : glucose transporter in testes; no role in glucose absorption from gut. GLUT-14 expression is poor prognosis in gastric adenocarcinoma.

195. Hereditary hemochromatosis with liver disease : Dx by LIVER BIOPSY - as iron overload can be found in Kupffer cells of liver which also allows assessment of liver damage and prognosis.

196. Patient of liver transport will have metabolic alkalosis : due to relative volume depletion which is a feature of cirrhosis due to low albumin levels.

Low albumin levels —> low oncotic pressure —> high aldosterone levels —> aldosterone not adequately metabolised due to impaired liver function

Furosemide use in posst-op liver transplant can increase risk of metabolic alkalosis driven by hyperaldosteronism

197. Imatinib - GIST & CML

198. Caspase - abnormalities of cascades causes abnormalities in range of lymphomas and carcinomas.

- in extrinsic pathway of apoptosis - death domains attract intracellular adapter proteins - CD95/FADD = MORT-1, which in turn attracts Procaspase 8
- Procaspase 8 is then modified to form a complex of two small and two large heterodimers - constituting active caspase 8.
- Caspase 8 activates downstream caspases like caspase 3 (executioner caspase) and causes host cell undergoing apoptotic changes - chromatin condensation and cell fragmentation
- Caspase 3 = executioner caspase
- Death domain - attracts intracellular adapter protein CD95/FADD
- MORT1

199. Codons code for amino acids. 61 codons specify the amino acids which form proteins and there are **three stop codons which signify the end of peptide.**

200. **Human mitochondria - circular ds DNA**  
**Nucleus - liner ds DNA**

**Nucleolus - RNA and responsible for assembly of ribosomal RNA**

201. Basophils, eosinophils and mast cells - contain lysosomes can release contents of these granules by degranulation.

- process of degranulation involves lysosomes which are intracellular, fusing with the plasma membrane and discharging their contents.
- IL-5 activity —> key role in up regulating eosinophil activity. Anti-IL 5 agents therefore a therapeutic target in asthma.
- This allows them to act against larger infecting organisms such as Protozoa and Helminths which cannot be engulfed by phagocytosis.
- Phagocytosis : involves chemotaxis, ingestion within a phagosome, intracellular enzymatic degradation and exocytosis.
- Endocytosis of antigenic material - step in antigen presentation

202. Wilson's disease - confirmation - Liver biopsy

Screening - serum ceruloplasmin

Wilson's disease diagnosis is a doubt or sibling or family member screening - ATP7B gene

203. Prostaglandin - inhibited by Aspirin and Glucocorticoids.  
Cyclooxygenase form Prostaglandins.

Synthesised from - straight chain C20 fatty acids, arachidonic acid is the precursor.

Bind to G protein coupled receptors.



204. **Inferior alveolar nerve** : - branch of mandibular division of trigeminal nerve

- all the teeth are anaesthetised in inferior alveolar block
- Mental branch of inferior alveolar nerve also supplies the chin and lower lip which becomes numb in nerve block.
- Inferior alveolar nerve supplies all the teeth of semi-mandible on the affected side including lower incisor teeth.

205. **Heparin inhibits aldosterone secretion → causes hyperkalemia**

206. **Alcohol common cause of hypertriglyceridemia** - all patients with isolate hypertriglyceridemia - counselled on alcohol cessation + exercise levels.

207. **Central scotoma** - depressed vision corresponds to middle visual field and due to **lesion in optic nerve**.

Common causes : MS, Hypertensive retinal disease, vascular lesions.

208. Cortisol levels in normal patient - 0900 hours highest level

Cortisol levels in Cushing's syndrome - 2400 hours highest level

Cortisol levels in Cushings syndrome - shows a circadian rhythm - levels are highest in early morning and fall to their lowest around midnight - 0900 hours level may be within normal limits but midnight levels are not suppressed.

209. Melanocytes : **basal layer of epidermis** - melanocytes are dendritic cells and have **no desmosomes** (intercellular bridges) and have small dark nuclei and clear cytoplasm.

210. **Cholera - GM1 agonism** : Cholera endotoxin B binds to GM1 receptor located on small intestinal mucosal cells. Enter of A1 subunit into secretory cells leads to continuous cAMP activation and increase in cAMP levels leads to massive secretion of water and electrolytes in small intestine.

- GLP receptor antagonism : second phase of insulin response and is a target for agonism in Mx of T2DM.
- GLP-1 receptor antagonism - **Incretin** - treatment of T2DM
- GLP-2 receptor agonism : future treatment target for short bowel syndrome and radiation induced gastroenteritis.
- SGLT1 antagonism - treatment of T2DM in future by blocking glucose absorption.

### 211. **Tay Sachs disease**

- Harmful quantities of fatty substance called **Ganglioside GM2** accumulate in tissues and nerve cells
- Insufficient activity of enzyme called **Beta-hexosaminidase A** which catalyses biodegradation of acidic fatty acid materials known as gangliosides
- Eastern European, Jewish descent
- Child becomes - deaf, blind, unable to swallow
- Muscles atrophy and paralysis is seen
- Dementia, seizures, increased startle reflex
- Cherry red spots in macula
- Simple blood test that checks levels of Beta-hexosaminidase A activity
- Autosomal recessive - both parents must carry affected gene

### 212. **Metabolic response to trauma - increased secretion of :**

- Catecholamines
- Cortisol - remains elevated upto 3 weeks
- Glucagon
- Growth hormone - remains elevated for 8-10 days
- Catecholamine, cortisol and glucagon —> all increase blood glucose levels
- Adrenaline and Glucagon —> act **most rapidly - 4 hours after trauma - by stimulating glycogenolysis**
- Cortisol acts slowly through stimulation of gluconeogenesis
- GH also increased glucose slowly
- Hyperglycaemia can persist for hours to days in trauma patients

### 213. **Interferons**

- Alpha and beta interferons are produced mainly in response to viral infection

- They bind to same cell receptor
- protect the uninfected cells by inducing up regulation of molecules that inhibits viral production of RNA and DNA
- Induces MHC Class I expression leading to enhanced lysis of cells
- IFN - alpha : activates macrophage and neutrophil killing cells.
- IFN - gamma : induces expression of MHC Class II
- IFN - alpha and beta : induces expression of MHC Class I
- IFN - alpha : also upregulates the host response and improves the chances of clearance of atypical mycobacterial diseases

214. Tacrolimus - Calcineurin inhibitor

- **Basiliximab - IL-2 inhibitor - IL-2 promotes T cell differentiation and proliferation**
- **Daclizumab : IL-2 inhibitor**
- **MMF : inhibits monophosphate dehydrogenase - blocks the de novo pathway of purine synthesis ; adverse ; GI upset and marrow suppression**
- **Sirolimus : inhibits receptor - dependent signal transduction of IL-2 and other cytokines via its action on mTOR (mammalian target of Rapamycin) - Adverse effect - causes hyperlipidemia**

215. Spinal cord terminates at the level of L1 - L2

- dural sac in adults extends to the level of S2
- Spinal Extra dural space - contains loose fat which allow ready diffusion of local anaesthetic in an extradural block and extensive vertebral venous plexus of veins
- Lumbar puncture L3-L4 , L4-L5
- Spinal cord length - 18 inches / 45 cm

216. LDL cholesterol contains **apolipoprotein B-100 - ligand for LDL receptor**

- PCSK9 increases LDL receptor **degradation** and when Liver LDL receptor levels fall —> LDL levels rise
- Inhibition of PCSK9 causes fall in LDL
- Concentration of LDLs determined mainly by **rates of hepatic synthesis and peripheral clearance; dietary saturated fat**

**intakes corresponds more strongly than dietary cholesterol intake**

- **HDL cholesterol - involved in reverse cholesterol transport**
- LDL are formed from VLDL and IDL by removing triglycerides and modification in circulation

217. Acute pancreatitis - NG tube feeding - studies have proven this

Persistent vomiting —> Nasojejunal feeding later parenteral feeds

**218. Clearance of drug =**

Urine concentration mg/mL(U) x urine volume produced in mL/min (V)  
/ plasma concentration in mg/mL (P)

For example :

22 mL of 10 mg/mL of IV drug X is given

Plasma concentration at equilibrium is 15 mg/L = 0.015 mg/mL

Urine concentration 150 mg/L = 0.15 mg/mL

Urine volume 1440 mL in 24 hours = 60 mL per hour = 1 mL per minute

$$0.15 \times 1 / 0.015 = 150/15 = 10$$

219. C-peptide cleavage is an example of post translational modification

C-peptide levels **decreased** in insulin overdose

C-peptide levels **increased** in Sulfonylurea abuse

220. Common femoral artery lies on **lateral side of femoral vein and divides 3 cm distal to inguinal ligament.**

- Superficial femoral artery then becomes popliteal artery by passing through hiatus in adductor Magnus
- Posterior tibial artery is felt behind medial malleolus
- Femoral artery thrombosis - PC intervention with angioplasty, locally delivered thrombolytics.

221. LDL Receptor mutation —> development of familial hypercholesterolaemia

Elevated total cholesterol and LDL

Increased secretion of VLDAL is associated with a rise in TGs.

HDL Receptor mutation - early cardiovascular death but NOT rise in LDL

Familial lipoprotein lipase deficiency —> rare and causes marked delevelatio of TG, eruptive xanthomas and recurrent pancreatitis.

222. Inferior / Recurrent laryngeal nerve —> supplies sensation sensory fibers to larynx inferior to vocal cords

- All laryngeal muscles are supplied by recurrent laryngeal nerve except **cricothyroid muscle which is supplied by superior laryngeal nerve - branch of vagus nerve.**
- **Paralysed vocal cord - paralytic position - adducted or lateral from midline and does not move on phonation**
- **Inferior portion of larynx is anaesthetised.**

### **223. Maturation and remodeling of wound - can last upto a year**

- Acute inflammation can last upto 3 days
- Initiating factor originates from platelets activated by mature collagen exposed in wound
- Platelets first aggregate and release active agents - lysosomal enzymes, ATP, serotonin, wound cytokines
- Fibrin clot develops and which completes haemostats and provide strength and support to the wound
- The surface dries to form a scab
- Platelets and microphage factor causes local vasodilatation which produces warmth and increases capillary permeability, which allows serum and white blood cells to accumulate and causes swelling.
- After the initial acute inflammation, macrophages become active as the main agents of demolition removing unwanted fibrin, dead cells, bacteria, and creating fluid fill spaces for granulation tissue.
- Macrophages also release factors that stimulate the formation of new capillary buds during this phase and later, they initiate and control fibroblast activity during repair

- Within the connective tissue randomly oriented, collagen begins to form after a few days, reaching a peak of activity after 5 to 7 days
- Acute Inflammation is the first phase of wound healing.
- Macrophage proliferation is the hallmark of demolition phase
- Ectodermal cells at the edge of the wound, start to proliferate after 24 hours and this can last for up to 3 weeks.

224. Posterior gastric ulcer = **splenic artery - severe haemorrhage**

- Gastroduodenal branch of common hepatic artery can be eroded by posterior gastric ulcer
- Inferior pancreaticoduodenal artery supplies the lower part of 2nd part of duodenum
- Left gastroepiploic artery - greater curve of stomach ulcer
- **Lesser curve of stomach - left gastric artery**

**225. Rapid correction of hyponatremia => central pontine myelolysis or osmotic demyelination syndrome —> due to apoptosis of astrocytes and oligodendrocytes —> loss of water and brain volume shrinks**

226. Clinical description of xanthoma, fleshy lumps over elbows and fat deposits in palmar creases and elevation of cholesterol and TG concentration to almost the same value ==> **familial dysbetalipoproteinaemia**

**Familial dysbetalipoproteinaemia = remnant dyslipidemia = broad beta disease = type III hyperlipidaemia**

- Caused by inherited abnormality of remnant receptor for removal of IDL from circulation by liver
- Labs will show : elevated Total cholesterol, elevated TGs, elevated VLDL and elevated IDL.
- Significant risk of developing coronary heart disease
- Presence of palmar xanthoma —> pathognomic

227. **DNA Helices** - enzymes responsible for separating DNA double helix base pairs

- Defect in DNA helices —> xeroderma pigmentosum, **Cockayne syndrome, or trichothiodystrophy**

- **Nuclease** : enzymes that degrade nucleic acid molecules by cleaving the phosphodiesterase bonds between nucleic acid subunits
- Phosphodiesterase : inactivation of intracellular 2nd messengers such as cGMP and cAMP.
- Restriction endonuclease : cuts DNA molecules at a limited number of specific nucleotide sequences
- Telomerase : enzymes that maintain the ends of eukaryotic chromosomes by synthesising telomeric repeat sequences

228. Middle cerebral arteries - largest arteries that branch the circle of Willis

- MCA termination of internal carotid artery
- Middle meninges artery is a branch of maxillary artery - which itself is a branch of external carotid artery; EDH - middle meningeal
- Middle cerebral artery passes through the lateral sulcus of cerebrum between the temporal and frontal lobes
- Posterior cerebral artery - best visualised by vertebral angiography
- Basilar artery rises from the two vertebral arteries that meet on the under surface of brain stem

229. Faecal incontinence may be associated with **rectal prolapse**

- INV - anal USG used to assess sphincter structure - NOT FUNCTION.
- Anal manometry - **anal function**
- History points : regular usage of pads or anal plugs; ability to defer defecation by > 15 minutes; use of constipating medicines
- Involuntary faecal incontinence is controlled by internal anal sphincter
- Voluntary faecal incontinence is controlled by external anal sphincter
- Faecal incontinence - associated with sphincter damage and atrophy, constipation, pudendal neuropathy

230. Posterior descending artery - posterior portion of IV septum and posterior left ventricular free wall.

231. Cavernous sinus - lies on either side of body of sphenoid and receive blood through facial veins

- Facial veins = superior and inferior ophthalmic veins
- sphenoid veins, middle cerebral veins also drain into cavernous veins.
- Anterior facial veins - drains the face and upper lip which is a high risk of spread of infection
- Occipital vein drain directly into jugular venous system
- Venous drainage of chin directly into jugular venous system
- Pinna of ear- maxillary vein - and drains into jugular venous system
- Skin over parotid gland - maxillary vein —> jugular venous system

### 232. **Acyclovir**

- Active form of aciclovir —> acyclovir triphosphate which is formed by host cell kinases
- Allows it to incorporate into viral DNA polymerase resulting in chain termination
- Viral DNA polymerase unable to function and replication of virus is halted.
- Peak plasma concentration - after 1-2 hours of oral administration
- Rapidly eliminated - hence multiple daily oral doses required.
- In herpes simplex virus - the viral thymidine kinase is responsible for phosphorylating acyclovir to aciclovir monophosphate
- After monophosphorylation - the host cellular kinases converts the drug monophosphate to triphosphate form

233. BRCA1 - Autosomal dominant inheritance

### 234. **Hypermobile Ehler-Danlos : most common type**

- 13 types of Ehler Danlos are present
- Hypermobile type : associated with hyper mobile joints, but skin features are **less prominent** than other subtypes.
- Systemic features include - increased chances of asthma, mild valve regurgitation, GI symptoms - constipation, hiatus hernia.
- Blue eyes
- Normal chest development



Classical Ehler Danlos :

- More severe dermatological features - including hyper elastic skin that splits easily
- Increased risk of easy bruising
- Cardiac features - aortic root dilation are seen more commonly than in Hypermobility types.

235. **Latex associated food** - Kiwi fruit, Avocado, Banana, Chestnut, Papaya, potato, tomato

236. Female carriers of DMD - develops symptomatic cardiomyopathy.

237. **Eastern blotting** : evaluates post- translational modification of proteins such as by lipidation or phosphorylation.

238. Cystic fibrosis - recurrent sinopulmonary infections with evidence of infections due to immunodeficiency in other organs like Pancreas (hint : raised glucose)

239. Von Willebrand disease - **Chromosome 12**

240. **Genomic imprinting** = depending on the phenotype on the gene deleted from mother or father.

Mother - Angelman syndrome

Prader Willi - **Chromosome 15**

241. **Hurler syndrome type I** - autosomal recessive due to **defective chromosome 4p**.

C/F : intellectual disability, corneal clubbing, cafe au lait spots, cardiac disease - death common in the first decade.

242. **Free light chains in urine** - **pathognomic** of Myeloma  
- proteinuria - nephrotic syndrome is found in >30% of patients with Myeloma

243. Normal tryptase levels and normal IgE levels => it is NOT Anaphylaxis

- Scombrotoxin fish poisoning : spoiled fish that has accumulated high levels of biogenic amines - mainly histamine
- Amines are not. Destroyed by cooking
- MX : Similar to anaphylaxis.

#### 244. **Cryoglobulinaemia**

- Type I : **Monoclonal - IgG or IgM** - Waldenström's Macroglobulinaemia (IgM), Multiple Myeloma (IgM)
- Type II : Mixed monoclonal and polyclonal - Hepatitis C, HIV, Rheumatoid arthritis, Sjögren's syndrome, Lymphoma
- Type III - only polyclonal - Sjögren's, Rheumatoid arthritis
- Type II & III → **Rheumatoid factor +ve**
- Hepatitis B - not associated with Cryoglobulinaemia
- Raynaud's phenomenon - ONLY Type I Cryoglobulinaemia
- Other C/F : vascular purpura, distal ulceration, arthralgia, renal - diffuse GN
- Labs - Low C4, Raised ESR
- Mx : Immunosuppression, Plasmapheresis

#### 245. **Turner Syndrome**

- 45 XO
- Definitive diagnosis : **Karyotyping**
- Classical Turner - 45 XO - one entirely missing X chromosome
- Mosaic Turner - majority of cells have partial or missing X chromosome; other cells may have one or two X chromosomes
- Genetics : random event, non disjunction, mosaic.
- PAR1 genes implicated in Turner syndrome

Clinical features :

- Short stature
- Underdeveloped ovaries
- Minimal pubertal development
- Primary amenorrhoea
- Infertility
- Short webbed neck
- Broad chest
- Widely spaced nipples
- Wide carrying angle
- Downward slanting eyes
- Low set ears, low hairline

- Swollen hands and feet
- Cardiac : Bicuspid aortic valve, coarctation of aorta, partial anomalous venous drainage
- Kidney - risk of UTIs, Hypertension
- Hypothyroidism
- Diabetes
- Obesity
- Lymphoedema
- Skeletal - Osteoporosis, Scoliosis, 4th Metacarpal bone shorter
- Cognitive : difficulties with spatial visualisation, weak non verbal skills, **normal intelligence**

246. Specific test for anaphylaxis for drug - Skin prick test to that drug

247. Severe combined immunodeficiency

- most common : X-linked due to defect in common gamma chain
  - protein used in receptors for IL-2
- Other cause : adenosine deaminase deficiency (ADA)
- ADA enzyme : eliminates deoxyadenosine which is toxic to lymphocytes and is generated when DNA is broken down
- ADA also converts Deoxyadenosine to **Inosine**
- Mutations in ADA gene —> reduces or eliminates activity of ADA and allows for build up of deoxyadenosine
- Immature lymphocytes are vulnerable to deoxyadenosine
- C/F : current bacterial, Viral and fungal infections
- Reduced T cell receptor excision circles
- Stem cell transplantation may be successful

248. **P1 receptor - G protein coupled membrane receptors - preferentially bound by adenosine**

- **Predominantly involved in mast cell function and eosinophil apoptosis - functions as a brake in an activated immune system**

249. Finnish / Scandinavian - Northern Europe - Alpha 1 anti trypsin deficiency - common

250. **Partial lipodystrophy**

- Type 2 MPGN - dense deposit disease

- Renal Bx : intramembranous immune complex deposits with dense deposits
- Low circulating levels of C3
- High levels of C3b nephritic factor
- C3b nephritic factor is antibody to C3 converts (C3bBb)
- C3b nephritic factor - **induces lysis of adipocytes**
- **Recurrent infections are rare**
- **Associated with Type 2 MPGN, SLE, POEMS = polyneuropathy, organomegaly, endocrinopathy, monoclonal immunoglobulin, skin changes syndrome**
- **Also associated with Diabetes**

251. Bacteria opsonised by antibodies and complement are more effectively phagocytosed than those opsonised by antibodies alone.

- Primary goal of complement system is to destroy the invading pathogens - process involving deposition of large quantities of C3b on a target.
- Process of coating target with complement to promote elimination is now as **Opsonisation**
- Opsonisation occurs extremely rapidly in less than five minutes.
- Once a target is coated, it can be recognised by cells bearing complement receptors
- Cellular immunity of T cells comes into play to protect against bacteria
- Humoral immunity can only **identify** the pathogen
- Phagocytosis is an innate function that can happen independently or through opsonisation
- Endotoxin AKA lipopolysaccharide - bacterial product that is capable of producing immune responses by triggering the innate system through linkage with **CD14 found on monocytes and macrophages.**

## 252. Pseudohypoparathyroidism

- Target cell insensitivity to PTH due to **loss of function mutation in G-protein**
- Type I : complete receptor defect; infusion of PTH - no rise in cAMP or phosphate
- Type II - cell receptor intact; infusion of PTH only cAMP rises, not phosphate
- Elevated PTH, Low calcium, Elevated phosphate

- Short 4th, 5th metacarpals
- Short stature
- Learning difficulties
- Obesity
- Round face

253. Mitochondrial disorders - **optic atrophy, neuropathy, diabetes mellitus, diabetes insipidus, epilepsy, sensorineural hearing loss.**

254. Hashimoto's thyroid's - **Antithyroid microsomal and antithyroglobulin antibodies +++ - chronic autoimmune thyroiditis**

255. Highest negative predictive value = highest sensitivity  
SLE - ANA highest sensitivity but less specificity.

256. Protein losing enteropathy - **low total cholesterol**

- In glomerular diseases - nephrotic syndrome - protein loss is determined by molecular weight and charge
- In protein losing enteropathy - leakage of individual serum proteins is **independent of molecular weight**
- For this reason - low cholesterol levels are seen in protein losing enteropathy as cholesterol molecules are having higher molecular weight - they are not lost in nephrotic syndrome
- Low albumin - both Nephrotic and protein enteropathy
- Low IgG - nephrotic and protein enteropathy
- Protein loss in urine - frothy urine - seen in both
- Protein losing enteropathy - vitamin K coagulopathy is **rare** even if there is loss of fat soluble vitamin complexes.

257. **Peutz Jeghers syndrome - lentigines - hyperpigmented areas - seen around nose and mouth, on hands and feet, within oral cavity.**

- Hamartomas associated with PJ syndrome - increased risk of intussusception in children and can cause GI bleeding.

258. **Hyper-IgM syndrome**

- CD40 ligand deficiency also called as this

- Undetectable levels of IgA, IgG and IgE
- Normal or high levels of IgM and IgD
- Role of **CD40 ligand in B-cell maturation and isotope switching**
- Hyper-IgM : **B cell defect which usually presents with recurrent sinopulmonary infections.**
- **Increased risk of P.jirovecii pneumonia**
- **Can develop chronic cryptosporoidal infections —> leads to sclerosing cholangitis and liver failure**
- **Increased risk of malignancy - especially abdominal cancer.**

259. **Vecuronium** - responsible for 60-70% of allergic reactions related to anaesthesia.

Antigen responsible —> quaternary ammonium group present in other drugs, food, cosmetics and hair products.

Patch testing arranged after 4 weeks of event

Serum tryptase elevated at time of attack.

260. **Pemphigoid gestations : bullous disorder - in 2nd or 3rd trimester** - urticarial lesions and blisters on anterior abdominal wall surrounding the umbilicus.

Perilesional skin Bx - linear C3 deposition at derma-epidermal junction.

261. Alkaptonuria - chromosome 3 - autosomal recessive

262. MGUS - asymptomatic premalignant clonal plasma cell proliferative disorder defined by : **presence of serum monoclonal protein (M-protein) at a concentration < 3 g/dL, bone marrow with < 10% of monoclonal plasma cells and absence of end organ damage { lytic bone lesions, anaemia, hypercalcemia, renal insufficiency, hyper viscosity}**

- **MGUS is there in >3% of White population over > 50 years**

- Premalignant condition - progression to multiple myeloma at rate of 1% per year.

263. **Porphyrias :**

**Acute intermittent porphyria**

- Deficiency of **porphobilinogen deaminase (PBGD)**
- Sweden population \*\*\*\*

- Autosomal dominant inheritance
- **Chromosome 11**
- Precipitating factors :
  - A. Alcohol
  - B. Drugs - barbiturates, sulphonamides, carbamazepine, OCP, Phenytoin, Rifampicin
  - C. Infections
  - D. Starvation

Clinical Features :

- Autonomic neuropathy - abdominal pain, constipation, vomiting, tachycardia, hypertension, postural hypotension
- Dark or red urine on standing
- Respiratory failure - **bulbar paresis**
- Cerebellar signs
- SIADH
- Psychiatric features : delirium, confusion, agitation, anxiety.
- Abdominal and psychiatric features **commonly seen**

**LABS**

- Elevated Urinary Uroporphobilinogen.
- Elevated serum delta-ALA, and Porphobilinogen.
- Other labs : hyponatremia (SIADH)
- Increased serum cholesterol, serum iron, and T4
- impaired glucose tolerance,

Mx :

- Mild acute attack - **IV Haemin**
- Alternative - IV Glucose 300 g Dextrose (10 % glucose)
- Recurrent non cyclic attacks - IV Haem alginate 3mg/kg
- Frequent recurrent cyclic attack in **women : Preventative GnRH Analog**

**Complications : Hypertension, Chronic renal failure, HCC**

**264. Variegate porphyria**

- Autosomal dominant
- Defect in **Protoporphyrinogen oxidase**
- Photosensitive blistering rash
- Abdominal and neurological symptoms

- More common in **South Africans**

265. C1 inhibitor deficiency - hereditary angioedema - \*\* refractory to steroids

Mx : **C1 inhibitor administration OR administration of specific bradykinin inhibitor ICATIBANT**

266. X-linked recessive : ONLY males are affected

- Affected males : gives children with unaffected sons and carrier daughter.
- Affected males receive the X linked recessive copy from heterozygous female carrier.
- Heterozygous carrier female —>
  - A. 50% chance of male child being affected
  - B. 50% chance of female being carrier.
  - C. 25% chance of all children being affected
  - D. 25% chance of carrier children
- NO MALE TO MALE TRANSMISSION SEEN

267. Selective IgA deficiency - more likely than general population to have IgG2 deficiency - leading to recurrent bacterial infections. Increased risk of pernicious anaemia and gastric carcinoma.

268. **Birch apple syndrome - apple, celery allergy - throat and mouth become itchy after eating apples with symptoms of allergic rhinitis related to birch tree pollen.**

**Oranges - worsens asthma**

269. **Periodic fever syndrome**

- Few syndromes in adults include -
  1. Familial Mediterranean Fever
  2. Tumor necrosis factor receptor associated periodic syndrome (TRAPS)
  3. Hyper IgD syndrome
- Hereditary periodic fever syndromes - rare heritable disorders characterised by short, recurrent attacks of fever and severe localised inflammation - that occurs periodically or irregularly



- They lack high titre antibodies or antigen specific T cells
- AKA Auto-inflammatory diseases
- Fever - Low levels of IgA increases risk of mucosal infections

#### 270. **Action of Tumor necrosis factor**

- TNF - cytokine produced by **activated cells of monocyte phagocytic system majority**
- Hypothalamus : stimulation of Hypothalamic-pituitary-adrenal axis by stimulating release of corticotropin releasing hormone (CRH)
- **Suppresses appetite** by action on hypothalamus - mediated via leptin
- Induces fever
- Liver - **stimulates acute phase response** - leading to increase in CRP
- Induces insulin resistance
- Prostaglandins release
- Helps in neutrophil migration and chemotaxis
- Macrophages : stimulates phagocytosis and production of IL-1
- Increases insulin resistance on tissues
- High TNF levels —> shock like symptoms
- Low TNF levels —> **cachexia**

#### **HPA Axis activation - TNF and IL-1**

271. Isotype suppression levels more a feature of Myeloma than Waldenstrom's macroglobulinaemia

Myeloma - increased IgA and IgG are present  
Waldenstrom's - normal IgA and IgG, raised IgM

272. Hereditary hemorrhagic Telangiectasia - Osler Weber Rendu syndrome

- Autosomal dominant
- History of telangiectasia and bleeding episodes
- Defect in protein called **Endoglin - receptor for TGF-beta and has a role in tissue repair and angiogenesis**

273. Low levels noticed during inflammation - Albumin, Magnesium, Zinc, Transferrin

274. **Gaucher's disease** - decreased levels of enzyme glucocerebrosidase

Acid phosphates high in serum - diagnostic confirmation

275. **Marfan syndrome** - early diastolic murmur - aortic valve incompetence - secondary to aortic root dilatation - major feature of Marfan syndrome.

2 major OR 1 major + 2 minor

Major skeletal criteria :

1. Pectus carinatum
2. Pectus excavatum
3. Reduced Upper : lower segment ratio  $< 0.85$
4. Increased arm span to height ratio (normal 1:1)
5. Positive thumb sign, and wrist sign - **Steinberg sign and walker-murdoch sign**
6. Thoracolumbar lordosis  $> 20$  degree
7. Progressive collapsing foot deformity
8. Protrusion acetabula

Minor skeletal criteria :

1. Moderate pectus excavatum
2. Hyperflexible joints
3. High arched palate - unusually high and narrow palate
4. Specific facial appearance - hypoplasia, retrognathia, maxillary hyperplasia and enophthalmos

276. Prader Willi - increased Ghrelin, hyperphagia, obesity, hypogonadism

Ghrelin receptor - arcuate nucleus and hypothalamus.

Leptin deficiency - contribute to weight gain and is involved in the pathogenesis of lipodystrophy

277. **Allele** - defined as one of a number of alternative forms of the same gene or same genetic locus.

- genes may exist in number of forms which may lead to a loss or Gain of mutation.

- Genetic polymorphisms so common in obesity and diabetes mellitus.
- Examples : TCF7L2 mutation that leads to loss of incretin effect
- PPAR-gamma mutation that are associated with increases insulin resistance.

278. IgG2 deficiency : increased susceptibility to infections with polysaccharide-coated bacteria including H.influenzae, accounting for multiple presentations with otitis media and respiratory tract infections.

- IgG class deficiency —> overall level of IgG may be normal or slightly reduced.
- COmmon variable deficiency —> IgG1 deficiency present as part of wider picture.

278. Primary Sjogren's : dry eyes, dry mouth, bilateral parotid enlargement, constitutional upset, joint polyarthralgia, Raynauds with ANA +ve and RhF +ve

279. **Linkage analysis** : quite common for a gene mutation not to be found in a family member even if gene for condition is known.

- Linkage analysis can be performed using micro satellite markers.
- Testing both affected and unaffected members —> allele carrying the mutation can be tracked through the family.

- **DNA sequence analysis** : mutation detection technique.
- Chromosome analysis : used to look at gross chromosome structure.
- Microarray analysis : gene expression technique.

280. Kearns Sayre syndrome

- mitochondrial disorder
- Rearrangements of mitochondrial DNA - including deletions and duplications
- Sensorineural hearing loss
- Retinitis pigmentosa
- Muscle weakness
- Ataxia
- Recurrent stroke
- Cardiomyopathy

- IDDM / T1DM

**\*\*Usher syndrome : hearing loss + retinitis pigmentosa.**

**281. Behçet's disease : post capillary vasculitis**

- Skin, eyes, joints, GIT and vascular bed
  - Small or large arteries as well as veins \*\*
- **Takayasu's arteritis** - large vessel vasculitis; pulseless limb + fever + raised inflammatory markers. Confirmatory Dx : PET Scan.
  - **Churg Strauss / Eosinophilic granulomatosis with polyangiitis** : small to medium vessels.
  - **Granulomatosis with polyangiitis** : ANCA associated; small to medium vessels
  - **Polyarteritis Nodosa** : medium sized vessels.

**282. Majority of ANA are IgG type**

**283. Mutations in mitochondrial DNA → abnormalities in energy metabolism which can lead to impaired glucose tolerance, dyslipidaemia, and muscle weakness.**

- **Resveratrol** : plant derived phenol
- PPAR- $\delta$  agonists
- Improved mitochondrial oxidative metabolism leads to increase in HDL cholesterol
- Mitochondrial dysfunction = **elevated triglycerides**

**283. SLE inflammatory marker - active disease - normal CRP  
Active disease - Elevated ESR.**

**\*\* elevation of ESR without CRP elevation is typical of SLE.**

**Raised CRP in SLE - underlying infection.**

Lymphopaenia : typical blood abnormality in SLE patients

**284. B cells can undergo somatic hypermutation.**

- B cells have surface IgG and MHC Class II
- B cell identifies an antigen - it can undergo somatic hypermutation - an enzyme makes random mutations in the antibody variable region genes
- B cells also undergo isotope switching - switching through immunoglobulin class
- B cells have surface bound IgG (NOT Plasma cells)

### 285. **Hyperacute rejection of renal transplant - HLA-C**

- Anti HLA-C IgG antibodies are implicated in hyper acute rejection
- Specifically HLA-CW5 subtype play a role in hyper acute rejection of renal transplant.

286. Vitamin D resistant rickets - X-linked dominant —> symptoms occur in both males and females —> but females carry two X chromosome copies so have less severe disease.

287. Isolated IgD deficiency can be seen in patients of Basque region - Northern Spain  
Isolated IgD deficiency - no treatment required.

### 288. **Cystic Fibrosis - percentage of disease in population**

- Autosomal recessive

Scenario - father is healthy - does not have CF

Therefore —> father is carrier / both genes normal

- Population carrier frequency —> 1/25 chance of father being carrier.
- Chance of father passing the gene -  $1/25 \times 1/2 = 1/50$
- Mother of child had a sister with CF who died.
- Parents of the mother are carriers Xx
- CF gene = X
- Normal gene = x
- If mother is healthy —> she has 2 out 3 chances of being a carrier. 1/3 times she is normal.
- Chances of passing gene is 2/3 multiplied with 1/2 = 1/3.
- Chances of couple having child with CF =  $1/3 \times 1/50 = 1/150$ .

### 289. **X-linked adrenoleukodystrophy**

- Rare cause of Adrenal insufficiency
- Mutations in ABCD1 gene

- ABCD1 gene codes for —> **ALD - peroxisomal membrane transporter protein**
  - \*\*\* sometimes misdiagnosed as multiple sclerosis.
  - Adrenomyeloneuropathy or adrenoleukodystrophy = peripheral neuropathy + myelopathy with or without adrenal failure
  - Assay of long chain fatty acid are markedly elevated - useful to confirm diagnosis
  - Mx : Lorenzo's oil
- Autosomal recessive leukodystrophy - presents in neonates and fatal before age of 20 years - developmental delay, deafness, and visual impairment

290. Sick cell anaemia - due to abnormal beta globin chain subunit of adult Hb. HbS is formed which has a valine substitution for glutamic acid at position 6 of beta globin chain.

#### 291. Contact dermatitis - **Type 4 hypersensitivity**

- Type 4 HS RXN is due to accelerators or chemicals used in the manufacturing process - delayed hypersensitivity - nickel hypersensitivity.
- Type 1 HS RXN : development of hives/urticarial type rash very rapidly after wearing gloves - latex proteins themselves and can have cross reactivity with certain fruits - kiwi, banana, papaya, chestnut, tomato, potato
- Type 2 HS RXN : antibody against cellular insoluble antigen - Goodpasture's disease
- Type 3 HS RXN : immune complex deposition - SLE
- Type 5 HS RXN : Autoimmune disease - receptor mediated - Graves disease, Myasthenia gravis

#### 292. **Anti-LGI 1 antibodies**

- Associated with LGI I encephalitis - leucine rich Glioma inactivated-1 antibody
- NMDA Receptor encephalitis - paraneoplastic feature : psychiatric manifestations more common, associated with Ovarian teratomas in women, common Afro-American population. **C/F** : agitation, hallucination, delusion, disordered thinking, seizures, insomnia, dyskinesia, autonomic instability. Mx - IV steroids, Immunoglobulins, Rituximab

- LGI 1 encephalitis - memory loss, confusion, seizures .

293. **KRAS mutation - codes for GTPase** : pancreatic adenocarcinomas, increased **rp16isk** of colo cancer and leukaemia Syndrome has been identified with lesions consistent with **ichthyosis is also seen** .

-**p16** : 30% of patients with chronic pancreatitis

- **NRAS mutation** : malignant melanoma

- p53 : associated with pancreatic cancer in only 50% of pancreatic adenocarcinoma

- Rb gene : Retinoblastoma, bladder cancer

294. Canavan;s disease : progressive neurological degeneration due to a defect in aspartoacylase

Gaucher's disease : Jewish descent

295. Tendon xanthomata, total cholesterol elevated > 7.5, LDL > 4.9 = heterozygous familial hypercholesterolaemia

- Familial HDL deficiency : premature cardiovascular disease with normal LDL cholesterol levels.
- Familial mixed hyperlipidemia : rise in LDL and triglycerides
- Heterozygous familial hypertriglyceridemia : rise in TGs
- Homozygous familial hypercholesterolaemia : total cholesterol in the range of 12-15 or more and very early myocardial infarction

296. **Homozygous C1q deficiency - SLE**

- increased association with SLE is because complement activity is associated with clearance of circulating immune complexes
- If immune complexes are not cleared —> tissue deposition and inflammation can occur.
- Anti-C1q antibodies : associated with hypocomplementemic urticarial vasculitis - rare autoimmune disease - recurrent urticaria - nettle rash; Dx confirmed by at least 2 of the following features : venulitis on skin biopsy, arthritis, ocular inflammation, abdominal pain, positive Cq1 antibodies to immune complexes.

297. CLL - malignancy of B cells

298. **Wolfram DIDMOAD - Autosomal recessive - WFS1 gene**

**299. Huntington - CAG repeats - chance %**

- 26-35 CAG repeat = 0% chance
- 36-39 : reduced penetrance - higher likelihood of developing disease phenotype 66%
- 40-55 CAG repeats - 100% likelihood of developing disease - Huntington's disease
- $\geq 56$  CAG repeats - early disease onset and severe progressive phenotype - called as Juvenile Huntington's disease

**300. Hereditary Non Polyposis Colorectal Cancer**

- Autosomal dominant
- Two main forms
- Lynch I : no family history of other cancers
- Lynch II : other cancers in family - endometrial, ovarian, urinary tract
- Diagnosed according to Amsterdam criteria :
  1. At least three relatives over two generations with colorectal cancer - one being a first-degree relative of the other two with at least one case diagnosed below 50 years of age.
- Genes of HNPCC are involved in **repairing DNA sequence mismatches**.

301. Achondroplasia - occur as a result of sporadic gremlin mutation - risk of further children being affected is less than 1%.

302. Desmopressin should be given in Hemophilia A - with factor VIII levels less than 5%.

303. Ehler Danlos - Kyphoscoliotic type - **autosomal recessive**.

304. Mycophenolate Mofetil can be given in SLE especially in the context of lupus nephritis

Mycophenolate - anti purine drug - selectively depletes B cell and T cell - due to which neutropenia is **rare**.

305. HLA - DP, DQ, DR  $\rightarrow$  **Class II antigens**

**HLA - A, B, C, g  $\rightarrow$  Class I antigens**



306. Two most common mutations of Hereditary Hemochromatosis  
- **C282Y & H63D**

307. **Moxonidine - central acting anti-hypertensive —> associated with angioedema.**

**Other drugs associated with. Angioedema —> ACEi, ARBs**

308. **Pantothenate kinase-associated neurodegeneration**

- Autosomal recessive
- Pyramidal and extra pyramidal signs
- Dementia
- Optic atrophy
- **Eye of the tiger sign on MRI - deposition of iron in basal ganglia**

309. **Calcineurin inhibitors - IL-2 production reduces**

**Calcineurin - is a phosphatase which induces transcription of IL-2**

**IL-2** - essential for clonal expansion and survival of T lymphocytes

Calcineurin inhibitors \_ Tacrolimus, Ciclosporin —> inhibits calcineurin —> decreased IL-2 production —> less T lymphocyte mediated transplant rejection —> also reduced t-regulatory cell activity.

\*\* Calcineurin inhibitors can have a downstream effect and reduce IL-1, IL-6, IL-10 and TNF-alpha levels.

Main action still IL-2 inhibition.

310. **Myotonic Dystrophy**

- Autosomal dominant disorder
- Expansion of CTG repeats that lies on 3' end of DMPK gene on chromosome 19
- Normal individuals <35 repeats
- Affected individuals > 50 CTG repeats
- CTG repeats 50-80 associated with early onset cataracts, classical MD disease

- Most severe form - **congenital MD** - IUGR, Severe hypotonia, muscle weakness and feeding difficulties.

### 311. **Dubin Johnson Syndrome**

- Autosomal recessive
- High prevalence of 1:1300 in Iranian Jews
- Genetic mutation of **canalicular multi specific organic anion transporter (cMOAT)**
- Aka as multi drug resistance protein
- Impaired transport of non-bile salt organic anions —> conjugated hyperbilirubinaemia

\*\*\*\*\*

Gilbert's missense mutation UGT1A1 gene => **autosomal dominant**

Gilbert's mutation promoter region of UGT1A1 gene => **autosomal recessive**

312. **SKin prick test** : Wheal size has a high positive predictive value for sensitisation to a specific allergen.

### 313. **Mantoux test**

- Intradermal skin tests - where an injection of 0.1 mL of purified protein derivative (PPD) is given intradermally in the solar surface of forearm using **tubercular syringe and small gauge needle**.
- Amount of induration should be measured 2-5 days after the injection
- Transverse diameter of induration should be measured in millimetres using a ruler.

314. IgA deficiency —> commonnin anaphylaxis reactions; recurrent infections of GI tract.

IgG deficiency —> recurrent otitis media and sinopulmonary infections.

315. **Most common genetic disorder => sex-linked disorder**  
E.g. - red-green colour blindness, haemophilia A, B

Autosomal dominant single gene disorder - 1:1000

Autosomal recessive single gene disorder - 1:300 to 1:400

Single polygenic disorder - raised LDL Cholesterol outside of familial hypercholesterolaemia - 1:100

### 316. Neonatal Lupus - anti-Ro antibodies

- Placental passage of maternal anti-Ro antibodies
- Anti-Ro antibodies leads to **abnormalities of calcium transport and heart block —> by interfering with automaticity or action potential genesis at the sinus node**
- Some neonatal babies may require chronotropic support for a few days after birth

**\*\* ONLY ANTI-RO (ANTI - SSA) AND ANTI-LA (ANTI-SSB) ANTIBODIES CAN CROSS PLACENTA**

### 317. Screening for medullary thyroid cancer - Pentagastrin and calcium infusion test and measurement of calcitonin

- Family history of MEN2 —> total thyroidectomy in childhood to prevent development of carcinoma is recommended
- **Follicular carcinomas** - associate with **Gardner's syndrome** and **Cowden's syndrome**
- **Papillary carcinoma** - familial papillary carcinoma of thyroid - mutations on chromosomes 1 and chromosomes 8.
- Papillary cancer of thyroid - also associated with Gardner's syndrome, and Cowden's syndrome.

### 318. Early treatment of bladder carcinoma in situ —> BCG intra-vesical filling

BCG vaccination protection last 10-15 years

BCG is 70-80% effective against severe TB infection.

### 319. Facial abnormalities in DiGeorge Syndrome -

- Abnormal ears
- Shortened Philtrum
- Micrognathia
- Hypertelorism
- IgA and IgG isotypes response to infection **impaired**
- T-cell levels are reduced

- B-cell levels normal

320. Epstein Barr Virus - virus cross the mucosal epithelium to infect B cells present in mucosal lymphoid tissue.

Can also infect - dendritic cells, mononuclear cells, plasma cells, smooth muscle cells.

In B-lymphocytes → virus is quiescent ; allows it to hide from T-lymphocyte surveillance.

Despite B cells being infected by EBV → does not lead to an immunological response → this phenomenon is known as **latency**.

321. Hereditary Spherocytosis → **spectrin and ankyrin deficiency**

**This is the most common station in Northern Europe population.**

**\*\*Protein 4.2 mutations in Hereditary Spherocytosis - Japanese population**

\*\* Isolated Spectrin defects accounts for 15-30% in Northern Europe populations.

**Isolated ankyrin - RARE**

322. **Xeroderma Pigmentosum** - nucleotide excision repair defect

- Characterised by photosensitivity with severe sunburn in infancy
- Development of numerous spots resembling freckles, larger atrophic lesions, associated with telangiectasia and multiple solar keratosis.
- Autosomal recessive pattern
- Defect in **nucleotide excision repair**
- Deficiency in repair of DNA damaged by UV radiation, and chromosome breakage.
- Develops multiple malignant cutaneous neoplasms at an early age - suffer from severe ophthalmic and neurological abnormalities.

**\*\* Base excision repair defect - Colon cancer**

Ligase deficiency - development of ovarian cancer

Mismatch repair - esophageal, gastric, head & neck cancers

Protein kinase - colon

### 323. Humoral immunity - splenectomy

- Splenic macrophages are important in clearing opsonised encapsulated bacteria.
- Pneumococcal antigens fall into T1-2 antigen class and presence of functional spleen is crucial for determining immunological response.

### 324. **SLE - activation of classical complement pathway**

- Due to large number of dsDNA. And other immune complexes that form and fix complement.
- These immune complexes get deposited in kidney
- Gram negative bacteria -> activates **alternative complement pathway**

### 325. **Allergic Reaction**

- **Early phase reaction** : occurs within minutes, or even seconds following allergen exposure.
- Immediate or Type I hypersensitivity reaction.
- Due to release of histamine and mast cell degranulation, production of leukotrienes, Pgs, cytokines due to allergen-specific IgE molecules binding to mast cell receptors.
- Late phase reaction : late phase of type I reaction - develops 8-12 hours after allergen exposure and is mediated by mast cells.
- Products of early phase reaction including chemokine and molecules —> act on endothelial cells and causes endothelial cells to express molecules such as vascular cell adhesion molecule and selectins.
- This results in recruitment and actuation of leukocytes from the blood into the site of allergic reaction.
- Th-2 cells and the cytokines they produce leads to further recruitment of mast cells and eosinophils and class switching happens in plasma cells to IgE isotype.
- Risk factors for late reaction anaphylaxis :
  1. Severe initial presentation of anaphylaxis

2. Requiring more than one dose of adrenaline
  3. Delay in adrenaline administration > 30-60 minutes
- Resuscitation guidelines recommends a minimum of 6 hours observation after resolution of symptoms.
  - Recommends if 2 doses of adrenaline are needed to treat allergic reaction or there is a history of previous biphasic reaction.

### 326. Homocystinuria - Celtic region, republic of Ireland

- reduced activity of homocysteine beta synthase
- G307S mutation is most common cause of homocystinuria in patients of Celtic origin
- Guthrie heel prick test - 1 in 65,000
- Autosomal recessive

\*\* Mexican descent — —> 5,10-methylene tetra hydrofolate reductase deficiency (5,10-MTHFR) => high levels of homocysteine

### 327. Classical Complement pathway

- C1 - complex is composed of :
  - a) 1 molecule of C1q
  - b) 2 molecules of C1r
  - c) 2 molecules of C1s
- Classical complement pathway is initiated - this occurs when **C1q binds to IgM or IgG complexed with antigen.**
- End result of classical complement activation is formation of membrane attack complex which is responsible for disrupting the cell membrane of bacteria, leading to cell lysis and death.

\*\*\*

- C2 complement is responsible for joining with C4 to form C3 convertase.
- C3b component of C3 is responsible for joining with C4b2a to form C5 convertase
- C4 is responsible for joining with C2 to form C3 convertase
- C5 is cleaved to form C5a - potent anaphylatoxin and C5b - which recruits the components of MAC.

\*\*\* Properdin is X-linked component of alternative pathway and patients of this deficiency will likely have history of male relatives who have died from meningitis.

Alternative complement pathway = C5-C9

**328. Kupffer cells : tissue macrophages** - found in lining sinusoids of liver and account for nearly 90% of tissue macrophages of the body

Tissue macrophages - two types : **fixed or wandering**

Fixed type of tissue macrophages :

- kupffer cells
- Microglial cells
- Mesangial cells - kidney
- Osteoclasts
- macrophages of reticuloendothelial system

Wandering macrophages :

- macrophages of serosal cavities - pleura, peritoneum, pericardium
- Alveolar macrophages

**329. Nickle allergy - type IV delayed hypersensitivity**

- Delayed hypersensitivity or cell mediated reactions
- It is a T-cell dependent phenomenon
- Local cytokines release produces the typical response of these contact reactions
- Classical example of Type IV delayed HS RXN → tuberculin skin test
- SKIN PRICK TEST - ONLY Type 1 HS RXN

**330. Bullous pemphigoid** : uncommon in elderly patients > 60 years; lesions develop at sub epithelial layer; Direct IF → gold standard for diagnosis of pemphigoid, detecting immunoglobulin binding and complement deposits within the tissue.

**331. Unilateral dermatitis - focal cause - irritant contact dermatitis**  
Absent minded contact - between nail and eyelids can cause this - allergy to nail varnish and nail polish remover.

Chemical that can lead to this include : toluene, sulphonamide, formaldehyde resin.

Bilateral eyelid dermatitis - can be seen in mascara allergy

**332. Thalidomide : irreversible peripheral neuropathy**

**Other adverse effects :** teratogenesis, drowsiness, constipation, weight gain.

Thalidomide and its derivatives - used in management of leprosy, HIV infection, myeloma and melanoma.

333. Systemic mastocytosis : recurrent flushing, wheeze, urticaria, and itching

334. Remnant hyperlipidaemia / familial dysbetalipoproteinaemia / remnant hyperlipidaemia —> **fibrate + statin**

335. Desmopressin (DDAVP) + Tranexaic acid = vWD before major surgery

**336. Co-repression**

- Glucokinase activity in liver is down-regulated by binding with glucokinase regulatory protein (GKRP)
- Co-repression : by binding to GKRP - action of glucokinase is down regulated or repressed
- Small increases in Glucose leads to release of glucokinase from GKRP
- Insulin acts via SREBP1c to up regulate production of glucokinase and a number of promoter genes are also involved
- Mutations in glucokinase coding gene —> loss of function responsible of MODY-2

337. Missense mutation - lateration in nucleotide sequence that converts a codon for one amino acid into a codon for a different amino acid —> protein that functions abnormally

Repeat mutation : short DNA sequences are repeated a number of times, results in abnormal protein function

Nonsense mutation : alteration in nucleotide sequence that changes a triplet coding for amino acid into a termination codon.



Point mutation : single nucleotide change in DNA molecule

338. Pseudo - dominant inheritance : carriage of certain autosomal recessive conditions is particularly high.

339. Placental syncytiotrophoblasts. Contains specific Fc IgG receptors which binds the IgG and facilitates its transport into fetal circulation.

- IgG is major antibody present in human serum, potent activator of complement system.
- Along with IgA in breast milk, maternal IgG provides immunity to neonate until its own immune system develops.

340. Recurrent skin infections - reflects colonisation that will require clearance procedures

- pemphigus is associated with sloughing blisters caused by intra-epidermal lesions
- Eye involvement - mucous pemphigoid AKA cicatricial pemphigoid that involves the mucous membrane classically conjunctiva.
- Herpes gestations - affects the abdomen - unique in pregnant and patients with trophoblast tumors
- Epidermolysis bullosa acquisita - antibodies against type IV collagen, rarely associated with HLA DR2

341. Antigen binding site of antibodies are variable domains from each heavy and light chain of antibody

342. COL3A1 = vascular Ehler Danlos

COL5A1 = classical Euler Danlos

PLOD1 gene = kyphoscoliosis Ehler Danos

343. Thoracic aortic aneurysm - highest mortality turners

344. C3 deficiency = **autosomal recessive**

345.

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## RHEUMATOLOGY

### PASTEST

#### 1. Denosumab

- Secondary prevention of fractures in osteoporotic patients with any value of GFR
- 60mg Subcutaneous injection every 6 months
- Contraindicated in : hypocalcemia and hypophosphataemia
- Monoclonal antibody - targets RANK ligand
- Common adverse effects : joint pain, muscle pains
- Alendroate - contraindicated in GFR < 35
- Strontium ranelate - can be used but high **risk of MI**

#### 2. Enteropathic arthritis

- Arthritis + recurrent episodes of bloody diarrhoea + erythema nodosum
- Inflammatory oligoarthritis —> associated with IBD
- Aphthous mouth ulcers
- Iritis
- Erythema nodosum
- Mx : steroids
- Do stool microscopy to rule out infective causes

#### 3. Osteoarthritis

- Commonly affects the 1st capo-metacarpal joint
- De Quervian tenosynovitis - first dorsal compartment of the wrist —> tendons of abducot policies longus - pain at dorsolateral aspect of wrist with referral pain toward thumb or lateral forearm
- Finkelstein's test : +ve

#### 4. Pyrophosphate arthropathy

- CPPD crystals in fibrous and crystal cartilage
- Shedding of crystals provokes attacks of pseudo gout
- Clinically - sudden onset of pain , inflammation and swelling of knee
- Xray : calcification of articular cartilage or meniscus - chondrocalcinosis
- Synovial fluid - CPPD crystals

- R/F : pseudogout - osteoarthritis, hypothyroidism, hyperthyroidism, hypomagnesemia, haemochromatosis, hypophosphataemia

### 5. Brodie's abscess

- X-ray features : lytic lesion with sclerotic margins in upper tibial metaphysis
- Localised abscess present deep within the bone near the site of metaphysis
- Deep boring pain

### 6. Arteritis Ischaemic optic neuropathy - altitudinal defects - bottom up or top down - common in vascular disorders of optic nerve head - due to ischaemia

- background disease of giant cell arteritis
- Elevated ESR and CRP

### 7. Osteomyelitis - contiguous spread of infection into bone from soft tissue, direct traumatic infection or from haematogenous spread

- haematogenous spread - mono microbial
- Infection or direct trauma - **polymicrobial**
- Periosteal reaction cannot be seen until 7 days

### 8. Raloxifene

- SERM - both estrogenic agonist effects on bone and lipid metabolism; estrogen-antagonist effects on uterine endometrium and breast tissue
- Most common adverse effects : hot flushes, leg cramps
- Increased risk of blood clots
- Beneficial effects : lowering of total and LDL cholesterol \*\*\*
- Improvement of BMD
- Raloxifene - reduces fracture risk at spine  
NO REDUCING RISK OF FRACTURE AT HIP
- Raloxifene v/s Tamoxifene : Raloxifene —> **does not raise TG or HDL levels; no troublesome effects** - oestrogen such as vaginal spotting or breast tenderness.

### 9. Polymyalgia Rheumatica

- Symmetrical arthritis

- Polyclonal increase in globulins is associated with inflammation of PMR
- Early morning stiffness, hip and shoulder girdle
- Transient synovitis can be present
- \*\* carpal tunnel syndrome is seen in 15% of cases

## 10. **Takayasu's arteritis**

- Chronic autoimmune inflammatory condition - large and medium sized arteries
- Transmural fibrosis and stenosis with occlusion
- Pulseless disease
- CD4+ and CD8+ cells aid in the inflammatory process forming granulomas and prompting chronic gradual process of inflammation

C/F :

- Renal artery stenosis - hypertension
- Carotid artery involvement - stroke, dizziness, headaches
- Jaw claudication, mesenteric ischaemia, heart failure

Labs :

- ESR > 20
- Clinical basis diagnosis

## 11. Scleroderma with pulmonary fibrosis and renal disease —> **Anti-SCL70**

CREST features —> Anti centromere antibody; Mx : Bosentan, Sildenafil

MCTD - anti-U1 RNP antibody

Anti-U3 RNP antibody —> cardiac involvement, myositis, pulmonary hypertension in diffuse systemic sclerosis.

12. Hydroxychloroquine —> retinopathy

D-penicillamine —> pancytopenia

## 13. **Chronic Fatigue Syndrome = Myalgic Encephalomyelitis**

- Short flu like illness at the point of symptom onset
- Mainstay of treatment is multi-disciplinary management with role of rest and sleep management

#### 14. **Arthritis mutilans - Psoriatic arthritis**

- Affects 5% of patients
- Attrition of bones and cartilage resulting in loss of joint and marked instability
- Encasing skin appears invaginated and telescoped
- Traction can pull the finger back to its original length
- Occurrence of nail changes seen normally in psoriatic arthritis also seen - pitting, horizontal ridging.

#### 15. **Psoriatic Arthritis**

- Autoimmune
- Nail changes, Distal interphalangeal joint arthritis, dactylitis and paravertebral calcification
- Associated with HLA-B27
- Nail changes - pitting and onycholysis
- DIP joint arthritis
- Dactylitis
- NSAIDs
- DMARDs - Leflunomide, Sulfasalazine, Ciclosporin, MTX
- Anti TNF alpha inhibitors : Adalimumab, Etanercept, Golimumab, Infliximab

16. Rheumatoid arthritis - cardiac tamponade - chest pain, dyspnoea, low BP and small voltage cardiac complexes on ECG.

#### 17. **Thoracic outlet syndrome**

- Disappearance of pulse on abducting the arm above shoulder levels
- Pain, numbness and tingling of upper limb
- Autonomic features : cold hands, swelling or blanching of fingers
- Doppler - can show impingement of blood flow
- Adson's manoeuvre
- 2 types of TOS - vascular and neurogenic  
Neurogenic most common
- Vascular TOS - arterial or venous
- Associated with congenital anomalies : cervical rib, protracted transverse process, muscular deformities, fibrous tissue abnormalities
- Pancoast tumor, hyperostosis and osteomyelitis

- Dx : Spurling's test - axial compression on patients head as it is stretched and laterally fixed
- Adson manoeuvre - shoulder extended and slightly abducted - radial pulse decreases when patient extends neck and turns towards the side of arm being tested

18. Massive synovitis and knee effusions : earliest sign of RA in x-ray

19. Felty syndrome - HLA DRW4  
HLA B8DR3 - Sjogren's

## 20. **Adult Still's disease**

- Incidence of 1-3 per million
- Fever - evening times, > 39 degrees
- Arthralgia
- DIP involvement \*\*\*
- Still's rash - salmon pink, maculopapular, on trunk, thighs, arms or axillae which appears during fever spikes
- Rash can appear on palms, soles, face.
- Rash at site of skin trauma - Koebner phenomenon
- Hepatosplenomegaly
- Polyserositis
- +/- generalised lymphadenopathy
- Rare features : dry eyes, dry mouth
- Myocarditis
- Restrictive lung disease
- Liver or kidney disease
- Panophthalmitis
- Epilepsy
- Intravascular coagulopathy or haemophagocytic phenomenon
- Amyloidosis

21. HLA B8 - primary biliary cholangitis  
HLA B51 - Behcet's disease  
HLA DQ2 - coeliac disease  
HLA D3 - T1DM

22. Synovial fluid in gout - needle shaped crystals

### 23. **Features of scleritis :**

- Gradual onset
- Severe, boring eye pain, radiating to forehead, brow and jaw
- Pain worse with movement of eye and at night
- Localised or diffuse red eye
- Associated watering
- Photophobia
- Radula decreases in vision +/- diplopia
- 50% of cases are bilateral
- Scleromalacia perforans - presents with minimal symptoms
- Posterior scleritis - quiet eye, severe symptoms

24. MTX - microcytic anaemia - raised MCV

Ciclosporin - microangiopathic hemolytic anaemia

Leflunomide - myelosuppression

HCQ - can provoke G6PD crisis

25. **Anti Jo-1 syndrome** : polymyositis + lung fibrosis; CK ++++;  
myoglobinuria ++++/

CK > 5000 —> myoglobin crystallisation in kidneys —> acute tubular necrosis

### 26. **Polyarteritis nodosa PAN**

- Medium sized arteries
- Middle aged men
- Associated with Hep B and HIB and Hep C
- Transmural inflammation of arteries —> aneurysm formation —> infarction and ischaemia of tissues

C/F :

- General - fever, weight loss, myalgia
- Skin - lived reticularis, cutaneous and sub cutaneous nodules, purpura, necrotic ulcer
- GIT : Post radial abdominal pain, bowel necrosis, perforation
- Renal - most commonly involved, AKI or CKD, hematuria, proteinuria
- Neurological - mono neuritis multiplex, stroke

- Bx : lesions of varying stages of inflammation, necrotising inflammation with fibrinoid necrosis and fibrosis
- Angiography - multiple micro aneurysms, **rosary sign**
- Mx : oral corticosteroids
- Complications : MO, heart failure, bowel perforation, stroke

## 27. Rheumatoid Factor

- **Antibody against epitomes of Constant region Fc portion of IgG1**
- Active rheumatoid arthritis —> RF complexes are present in synovial fluids and IgG producing B cells
- B cells in rheumatoid joints also synthesis antibodies to some cartilage components such as collagen type II
- Anti-CCP antibodies associated with more rapid disease progression

## 28. IL-1 triggers episodes of acute gout

## 29. Drug induced lupus :

- Carbamazepine
- Sodium valproate
- Ethosuximide
- Isoniazid
- Penicillamine
- Sulfasalazine

## 30. Calcific tendinitis : deposits of **calcium hydroxyapatite crystals** - **rotator cuff muscles near the humeral attachment region.**

Supraspinatus tendon, infraspinatus and subscapularis

## 31. Reactive arthritis : Joint aspiration : giant macrophages, no organisms seen

## 32. **Adalimumab : anti TNF alpha agent** - addition to MTX and Sulfasalazine in treatment of severe skin and joint disease due to Psoriasis

## 33. Anti TNF - Etanercept - CI are : co-morbid multiple sclerosis, hepatitis B, hepatitis C, Heart failure, pulmonary TB reactivation



Etanercept + Sulfasalazine combination can decrease WBC count.

34. Prolapsed cervical disc = affects the C5 / C6 and C6 / C7 vertebrae; central protrusions can lead to symptoms of spinal cord compression; posterolateral protrusions can cause stiff neck, pain radiating to arm, weakness of muscle affected by nerve root, and depressed reflexes.

35. Leflunomide - teratogenic

Cyclophosphamide - can reduced sperm count, higher doses can lead to irreversible azoospermia —> irreversible infertility

MTX - teratogenic , oligospermia and chromosomal breaks in men reducing fertility

Sulfasalazine - reversible oligospermia and male infertility

36. Rhomboid shaped weakly positive birefringent - pseudogout

Spindle shaped, negatively birefringent - MSU crystal - gout

Rhomboid shaped, negative birefringent - cholesterol crystals

37. Popliteal cysts - Baker's cysts - rheumatoid arthritis

38. Rheumatoid arthritis - women - pregnancy - HCQ, NSAID, TNF alpha inhibitors - **SAFE**

**39.** HLA DR3 - T1DM, Graves, Myasthenia gravis

HLA DR4 - NORTHERN EUROPE

HLA DR1 - SOUTHERN EUROPE

40. Rheumatoid arthritis - **bronchiolitis obliterans**

Non productive cough and dyspnoea.

CXR - may show military or diffuse nodular pattern.

Other causes of Bronchiolitis obliterans :

- toxic fume inhalation
- Bone marrow transplantation
- Post heart / lung transplant
- Infection - viral, Mycoplasma
- Penicillamine
- SLE
- Polymyositis

RA & Lung involvement :

- Bronchiectasis
- Pleural effusions
- Lung nodules
- Interstitial fibrosis
- Bronchiolitis obliterans
- Caplan syndrome ( Pneumoconioses + Rheumatoid nodules)

41. RA —> Elevated TNF alpha, IL-1, IL-6, TGF-beta, Fibroblast growth factor, PDGF

42. **Avascular Necrosis** - flattening and loss of right femoral head on X-ray is consistent with avascular necrosis. This is a known complication of sickle cell disease - single glutamic acid substitution to valine at position 6 of beta globin polypeptide chain. Heterozygote frequency of sickle cell disease —> >20% develop secondary osteoarthritis.

43. Rheumatoid arthritis - synovial fluid - **marked vascular proliferation on synovial membrane —> thickening of synovial membrane and proliferation into folds and fronds may also be seen.**

**Synovial fluid in RA is turbid with neutrophil - NOT** a diagnostic feature.

Viscosity of synovial fluid **decreased in RA - increased in OA.**

44. **Diffuse systemic sclerosis - increased risk of maternal deaths;** reactivation of quiescent scleroderma can occur during

pregnancy and increased frequency of small and pre-term babies as well as renal and cardiac complications for the mother.

- Therapeutic abortion must be considered in these patients.
- Worst possible outcome in pregnancy - **scleroderma renal crisis**
- Serious cardio-pulmonary complications.

45. **Trimethoprim x MTX toxicity** - both are folate antagonists; leads to MTX toxicity

- Rx of MTX toxicity —> colonic acid residue and treating her neutropenic sepsis.
- **Co-trimoxazole (septrin)** another folate antagonist that should not be prescribed in combination with MTX.

46. **Premier's disease : bilateral idiopathic avascular necrosis of scaphoid bone**

- Mx : conservative analgesia, and physiotherapy, surgery

47. Hereditary Haemochromatosis - distinct radiological findings :

- 1) isolated chondrocalcinosis
- 2) hypertrophic osteoarthritis
- 3) hook-like osteophytes on metacarpal heads

48. **Osteomalacia - X-ray : translucent bands, Looser's zones - pseudo fractures**

- osteomalacia : characterised by back pain, muscle weakness and bone tenderness.
- Due to vitamin D deficiency
- Raised ALP and low calcium
- PTH maybe elevated - **secondary hyperparathyroidism** - phosphaturia

Bone expansion and sun-ray appearance :

- chondrosarcoma
- Metastatic tumour in bone
- Osteogenic sarcoma
- Ewing's sarcoma

49. **Genetic factors - single most important influencing factor for attaining peak bone mass density** - birth weight is closely correlated to risk of osteoporosis and body morphology including fat mass have a strong genetic component.

50. Polymyositis / Dermatomyositis - **Muscle biopsy diagnostic test**

51. **Paget's disease** : bowing of legs, deafness ( due to compression of 8th cranial nerve due to neural foramina narrowing ) and +ve family history with raised ALP (due to increased bone turnover)

52. Guidelines for managing lupus nephritis :

- patient with clinic evidence of active previously untreated lupus nephritis should have renal biopsy
- Class I and Class II —> excellent prognosis
- Class III, IV and Class V —> high dose steroids + adjunctive cyclophosphamide / MMF
- Azathioprine >> MMF in women with child bearing potential due to lower teratogenicity.
- Class VI - glomerulosclerosis —> advanced disease - **not treated**
- All patients with background lupus nephritis - HCQ mandatory
- Proteinuria > 0.5 g/24 hours —> administer ACEi / ARBs
- Maintain BP at 130/80 or below

53. Rheumatoid arthritis - pleural effusion - **low glucose, exudate, low pH < 7.2, high LDH.**

**Large amounts of cholesterol may be present in long standing rheumatoid pleural effusions**

54. **SLE criteria - 4 out of 11 :**

- 1) malar rash
- 2) Discoid rash
- 3) Photosensitivity
- 4) Oral ulcers
- 5) Arthritis
- 6) Serositis
- 7) Renal disorder - proteinuria or +++ persistently or cellular casts
- 8) Neurological disorder - seizures or psychosis
- 9) Haematological disorder - haemolytic anaemia / leukopenia <4,000, thrombocytopenia

- 10) Immunological disorders - raised anti-native DNA antibody binding or anti-Sm antibody or +ve for anti-phospholipid )  
11) ANA in raised titre in absence of drugs

55. Rheumatoid arthritis - positive squeeze test eliciting pain over metacarpal joints ; **elevated levels of TNF-alpha**, IL-1, IL-6, FGFR, PDGF.

IL-6 can be targeted by **Tocilizumab**

56. **Sjogren's syndrome - labial gland biopsy** - diagnosis of Sjogren's syndrome depends on finding foci of periductal infiltrate of at least 50 lymphocytes and/or plasma cells at a density of more than one focus per 4 mm<sup>2</sup>.

57. Ankylosing spondylitis - Adalimumab - for patients who do not respond to NSAIDs and conservative treatment.

58. Rheumatoid arthritis - upper GI bleed - **Piroxicam** - anaemia and raised blood urea levels.  
Inhibition of COX-1 causes reduced PG synthesis in stomach which in turn causes unwanted GI bleeding and inflammation.

59. Polymyositis - symmetrical proximal weakness - due to muscle inflammation seen in polymyositis.  
EMG - typical triad of changes with myositis : 1) spontaneous fibrillation potentials at rest. 2) polyphasic or short duration potentials on voluntary contraction, 3) salvos repetitive potentials on mechanical stimulation of nerve

60. Staphylococcal discitis - haematogenous spread of Staph aureus infection at the time of procedure

### 61. **Granulomatosis with Polyangitis**

- Necrotising granulomatous vasculitis that affects small to medium sized arteries, capillaries and veins - AKA Wegener's granulomatosis
- Lungs - cough, hemoptysis
- Kidneys - hematuria, proteinuria

- URT - nasal obstruction, epistaxis, rhinitis, saddle nose deformity, sub-glottic stenosis
- Skin - rashes, ulcers
- Eye - scleritis, episcleritis, conjunctivitis
- Ear - chronic ear infections, hearing loss
- CNS - mononeuritis multiplex, cranial nerve —> proptosis
- GIT - GI bleeding, abdominal pain, diarrhoea
- cANCA +ve in >90% of individuals
- Biopsy - necrotising granulomas with associated vasculitis
- Mx : high dose steroids, cyclophosphamide.

**62. 3 out of 10 criteria to be present in PAN :**

- 1) weight loss of 4 kg or more
- 2) Lived reticularis
- 3) Testicular pain / weakness
- 4) Mononeuropathy / polyneuropathy
- 5) DBP > 90mmHg
- 6) Elevated urea and creatinine
- 7) Hepatitis B infection
- 8) Abnormality on arteriography
- 9) Bx - polymorphonuclear neutrophils

63. Tennis elbow : pain on attempting chair raise test : lateral epicondylitis - wrist extension or supination against resistance with elbow extended provokes pain.

- chari raise text is useful in determining diagnosis
- Patient stands behind chair and attempts to raise it by putting their hands on top of chair back and lifting.

64. Calcium 1000 mg/day, vitamin D 800 IU, 1 g/kg body weight protein intake

65. **Scheuermann's disease** : affects those between 13 and 16 years go age; normal ossification of ring epiphyses of several thoracic vertebrae is affected. Deforming forces are greatest at anterior border of thoracic vertebrae so vertebrae are **narrower anteriorly - resulting in kyphosis.**

**Irregular upper and vertebral end plates with loss of disc space height.**

\*\*\* Congenital absence of neural arch —> kyphoscoliosis.

\*\*\* Anterior displacement of one thoracic vertebra upon another occurs in spondylolisthesis

\*\*\* Osteophyte formation on posterior facet joints is seen in osteoarthritis

66. Etanercept - TNF agents - for Ankylosing spondylitis who have failed two courses of steroids.

Lumbar X - ray - lateral views of thoracolumbar spine —> erosion and sclerosis of anterior corners and periostitis of waist of vertebrae

67. Reactive arthritis- single joint involvement - good response to intra-articular corticosteroid injection.

68. Rheumatoid arthritis poor prognosis :

- female sex
- Positive IgM RF
- Anaemia developing after 3 months of onset
- Anti CCP positivity
- Gradual onset over few months

69. **Prepatellar bursitis**

- tenderness of patella on palpation
- Erythema of knee
- Crepitus of knee
- Fluctuant oedema over lower pole of patella

70. Primary v/s Secondary Raynaud's phenomenon

|               | Primary Raynaud's   | Secondary Raynaud's      |
|---------------|---------------------|--------------------------|
| Age           | 30 years            | > 50 years               |
| Sex           | Female              | Male                     |
| Tissue damage | Absent              | Digital Ulcers, gangrene |
| Symmetry      | Symmetrical attacks | Asymmetrical             |

|                     |          |                                                   |
|---------------------|----------|---------------------------------------------------|
| Capillary scope     | Negative | Positive                                          |
| Auto-antibodies     | Negative | Positive                                          |
| Associated diseases | NONE     | Scleroderma, SLE, other connective tissue disease |

71. Ankylosing spondylitis - earliest X ray feature : **blurring of upper and/or lower vertebral rims at the sacroiliac junction - best seen on a lateral x-ray.**

**This is caused by an enthesitis at the insertion of inter-vertebral ligaments.**

**Persistent enthesitis —> can cause bony spurs - syndesmophytes**

Fusion and sclerosis of sacroiliac joints and calcification of intervertebral ligaments occurs at a later stage.

72. MRI of sacroiliac joint : main lesion in certain patients are spinal ankylosis with sacroiliac joint involvement.

Earliest changes such as bone marrow edema are visible on MRI - which is more sensitive than X-ray.

Uveitis is common and may occur in 25% of patients with AS.

73. RA in feet - swelling of metatarsi-phalangeal joint

Mid and hind foot RA can cause flat medial arch, loss of flexibility in foot

74. C4 complement deficiency - **SLE early onset**

**Early onset most associated with C1q, C4 deficiency**

**C1 and C4 - equal sex distribution**

**C2 - sex distribution reflects non complement associated SLE and occurs slightly alter**

**Complement activation - used for monitoring of SLE disease**



### **C3 deficiency - atypical HUS**

75. Paget's disease - lumbar spine most commonly involved

76. TNF - alpha

- raised levels leads to increased insulin resistance due to phosphorylation of Insulin receptor Substrate - 1 IRS-1
- Neutrophil chemoattracts, stimulates macrophage phagocytosis and helps drive the acute phase response
- TNF alpha acts on wide variety of cells - hypothalamus, liver, neutrophils, macrophages
- Its gene is present on chromosome 6
- Lipopolysaccharide increases TNF-alpha production

77. Osteoporosis - normal / high ALP, normal calcium, normal PTH, normal phosphate

78. Most typical form of RA - chronic and persistent

79. Early sign of Ankylosing spondylitis - retention of lumbar lordosis during spinal flexion

80. Osteomalacia - Looser's zones - linear areas of low density surrounded by sclerotic border

81. Erosive inflammatory osteoarthritis - gull-wing of inverted T pattern of erosions

82. Rheumatoid Arthritis - Pleurisy and pleural effusion are most commonly seen.

83. One of the earliest symptoms of osteoarthritis - **limited range of movement**

84. Paget's disease X ray findings : **increased trabecular pattern and cortical thickening of right hemipelvis.**

85. Cervical spondylolisthesis - forward displacement of one vertebra upon another. Most common cause of this in elderly age

group - osteoarthritis of posterior intervertebral joints which become unstable and permit vertebral displacement.

86. Etanercept - fusion protein - inhibition of TNF alpha and beta (both) - functioning as decoy receptor - preventing binding to cell surface TNF receptor - preventing TNF mediated cellular responses.

Etanercept mimics the inhibitory effects of naturally occurring soluble TNF receptors - as a fusion protein has a longer half life.

Anti CD 20 - Rituximab

Anti CD3 - Muromumab

Anti CD52 - Alemtuzumab

87. **Osteochondritis dissecans** - local necrosis of articular cartilage and its underlying bone —> loose body leaving the surrounding bone.

- Medial femora condyle is most commonly affected and condition is seen in adolescents and young adults.
- Either 3 or 4 loose bodies are present
- Wasting of thigh muscles implies long standing arthritis and loose bodies due to cartilage damage.
- Children and adolescents with open growth plates (juvenile OCD)
- Adults with closed growth plates (Adult OCD).
- Peak incidence 6-15 years, males >>> females
- R/F : trauma, male, genetic
- C/F : knee pain and swelling, typically after exercise; knee catching, locking or giving away; painful clunk when flexing or extending the knee indicating involvement of lateral epicondyle
- Signs : joint effusion, external tibial rotation when walking (medial epicondyle involvement), tenderness on palpation of articular cartilage of medial femoral condyle
- **Wilson's sign for detecting medial epicondyle lesion** with knee at 90 degree flexion and tibia internally rotated , gradual extension o joint leads to pain around 30 degree, external rotation of tibia at this point relieves the pain

- **X- ray : subchondral crescent sign or loose bodies.**
- **MRI** : cartilage damage, visualising loose bodies, stage and assess stability of lesion

88. Pyrazinamide - ATT - strong urate retention agent - causes >80% reduction in renal clearance of uric acid

Metabolite of Pyrazinamide → Pyrazinoic acid - oxidised by xanthine oxidase and is likely responsible for hyperuricaemic effect

89. Tennis elbow - lateral epicondylitis - resistance against wrist extension causes the pain.

90. Reactive arthritis - keratoderma blennorrhagica - aseptic abscesses on soles and palms

**91. Eosinophilin fasciitis**

- Swelling and tenderness of forearms with induration of skin
- Carpal tunnel syndrome
- Flexion contractures of fingers
- Peripheral blood eosinophilia
- Hyper-gammaglobulinaemia

92. SLE joints involvement - most common - > 80% of patients with SLE have joint involvement  
Joint involvement - soft tissue swelling

**93. Anti-Ro antibodies - recognises the cardiac 5-HT<sub>4</sub> serotonin receptor - and inhibits serotonin - activated calcium L channels.**

**There is an associated lupus rash which disappears by 6 months**

94. Paget's disease X-ray : sclerotic phase of bone expansion, thickening of trabecular and de-differentiation (loss of distinction between cortex and medulla)

Osteomalacia X-ray : anticonvulsants like Phenytoin and Phenobarbital → can induce liver enzymes and leads to increased

breakdown of 25-hydroxycholecalciferol —> causes osteomalacia - X-ray shows Looser's zones - pseudo fractures - linear areas of low density surrounded by sclerotic borders

95. Psoriatic arthritis - MTX indicated to control skin lesions and arthritis.

Etanercept - TNF-alpha inhibitor - highly effective in the treatment of severe skin and joint disease but only recommended when disease is still active despite two conventional disease modifying agents

96. G6PD deficiency - acute gout

- Accumulation of Glucose-6-phosphate —> enters the hexosemonophosphate shunt and leads to **increased production of pentose sugars.**
- These pentose sugars acts as substrate for PRPP synthesise and results in increased production of purines
- Purines undergo catabolism to uric acid
- Hypoglycaemia in G6PD also increases catecholamine levels which increases glycogenolysis in muscles
- This causes lactic acidosis
- Lactic acid and uric acid compete for excretion and this causes **decrease in uric acid excretion —> increased uric acid levels —> gout .**

97. Sjogren's syndrome - keratoconjunctivitis sicca, otitis media, hepatosplenomegaly are common.

98. **Ankylosing spondylitis - renal involvement - three types :**

- 1) AA Amyloidosis : more common when disease is present for longer duration. Kidneys are usually enlarged on USG and biopsy shows amyloid - apple green birefringence in polarised light
- 2) NSAID induced nephropathy
- 3) IgA nephropathy - hematuria and hypertension

99. **Trochanteric bursitis :**

- Hip pain on resisted abduction

- Also called as greater trochanteric pain syndrome - due to gluteus medius or minimus tendinopathy with mild involvement of regional bursae
- NSAID - mainstay of management of trochanteric bursitis

**100. Reflex sympathetic dystrophy** - complex regional pain syndrome - Sudden's atrophy - pain is often severe and disproportionate to signs and follows a non-anatomical distribution.

Skin changes are caused by associated autonomic dysfunction

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## PSYCHAITRY

### PASSMEDICINE & PASTEST

#### 1. Acute Stress Disorder

- First 4 weeks after traumatic event
- Intrusive thoughts - flashbacks, nightmares
- Dissociation. - being in a daze, time slowing
- Negative mood
- Avoidance
- Arousla - hyper vigilance, sleep disturbance
- CBT - 1st line
- BZD - Rx -> actue symptoms - agitation, sleep disturbance

#### 2. Alcohol Withdrawal

- Choric alcohol use —> GABA inhibition
- Inhibitor of NMDA glutamate transmission
- Symptoms start at 6-12 hours - tremors, sweating, tachycardia, anxiety
- Peak incidence of seizures at **36 hours**
- Peak incidence of delirium tremens : **48-72 hours** : coarse tremors, confusion, delusion, auditory and visual hallucinations, fever, tachycardia
- 1st step - admit to hospital for monitoring of withdrawals
- 1st line Rx : long acting BZDs -> chlordiazepoxide, diazepam
- Hepatic failure - Lorazepam

### 3. Antipsychotics :

|                            | Typical Antipsychotics                                                           | Atypical Antipsychotics                                  |
|----------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------|
| <b>Mechanism of Action</b> | D2 Receptor antagonist - blocks dopaminergic transmission in mesolimbic pathways | Acts on variety of Dopamine receptors - D2, D3, D4, 5-HT |
| <b>Adverse effects</b>     | Extrapyramidal effects, <b>hyper-prolactinaemia</b>                              | <b>Metabolic effects more common</b>                     |
| <b>Examples</b>            | Haloperidol<br>Chlorpromazine                                                    | Clozapine<br>Risperidone<br>Olanzapine                   |
|                            |                                                                                  |                                                          |

Extra-pyramidal side effects :

- Parkinsonism
- Acute dystonia - sustained muscle contraction - torticollis, oculogyric crisis; Rx - Procyclidine
- Akathisia - severe restlessness
- Tardive dyskinesia : late onset of choreoathetoid movements, abnormal involuntary, chewing and pouting of jaw

\*\* use of anti psychotics in elderly : increased risk of stroke and increased risk of venous thromboembolism

Other side effects :

- antimuscarinic - dry mouth, blurred vision, urinary retention, constipation
- Sedation
- Weight gain

- Raised prolactin - galactorrhea ( due to inhibition. Of tuberoinfundibular pathway)
- Impaired glucose tolerance
- Neuroleptic malignant syndrome - pyrexia, muscle stiffness
- Reduced seizure threshold - increased risk with atypical drugs
- Prolonged QT - Haloperidol \*\*

### **Atypical Antipsychotics :**

- Decreased risk of EPS
- Weight gain ++
- Clozapine - agranulocytosis \*\*\*
- Hyperprolactinaemia
- Examples : clozapine
- Olanzapine - increased risk of dyslipidemia and obesity
- Risperidone
- Quetiapine
- Amisulpride
- Aripiprazole - good side effect profile

### **4. Benzodiazepines**

- Enhances the inhibitory neurotransmitter GABA by **increasing frequency of chloride channels**
- Uses of BZDs -
  1. Sedation
  2. Hypnotic
  3. Anxiolytic
  4. Anticonvulsant
  5. Muscle relaxant
- Withdraw does in steps of about 1/8 of daily dose every fortnight.
- BZD withdrawal :
  - A. Insomnia
  - B. Irritability
  - C. Anxiety
  - D. tremor
  - E. Loss of appetite
  - F. Tinnitus
  - G. Perspiration
  - H. Perceptual disturbances
  - I. Seizures

## 5. **Charles - Bonnet syndrome**

- Persistent or recurrent complex hallucinations - visual or auditory  
- occurring in **clear consciousness**
- Background of **visual impairment**
- Insight - preserved
- Risk factors :
  1. Advanced age
  2. Peripheral visual impairment
  3. Social isolation
  4. Sensory deprivation
  5. Early cognitive impairment
- Associated with : **age related macular degeneration > glaucoma > cataract**

6. **Delusional parasitosis** : rare condition - **fixed, false belief that they are infested by bugs**

## 7. **Medications that trigger anxiety :**

- salbutamol
- Theophylline
- Corticosteroids
- Antidepressants
- Caffeine

## 8. **Stages of grief :**

- denial : includes feeling numbness and also pseudo-hallucinations of the deceased - auditory and visual
- Anger : against family members and medical professionals
- Bargaining
- Depression
- Acceptance

Features of atypical grief reactions :

- delayed grief : occurs when more than 2 weeks passes before grieving begins
- Prolonged grief : maybe present upto 12 months

## 9. Mania and hypomania



## Mania

- lasts for at least 7 days
- Causes severe functional impairment in social and work setting
- May require hospitalisation due to risk of self-harm or others
- May present with psychotic symptoms

## Hypomania :

- a lesser version of mania
- Lasts for < 7 days, typically 3-4 days
- Can be high functioning
- Does not impair functional capacity in social or work setting
- Does not exhibit any psychotic symptoms

Presence of psychotic symptoms - delusions of grandeur, auditory hallucinations helps differentiates mania from hypomania

## Symptoms common to both mania and hypomania :

- mood : predominantly elevated, irritable
- Speech & thought : pressured, flight of ideas, poor attention
- Behaviour : insomnia, loss of inhibitions, increased appetite.

## 10. Lithium

### **Adverse effects :**

- nausea/ vomiting
- Diarrhoea
- Fine tremors
- Nephrotoxicity - nephrogenic DI - polyuria
- Thyroid enlargement - can lead to hypothyroidism
- ECG - t wave flattening / inversion
- Weight gain
- Idiopathic intracranial hypertension
- Leucocytosis
- Hyperparathyroidism —> hypercalcemia

## 11. OCD —> Y-BOCS scale

- mild functional impairment : CBT - including exposure and response prevention (ERP), 2nd line - SSRI or more intensive CBT
- Moderate functional impairment : SSRI or more intensive CBT ; if SSRI contraindicated —> **can use Clomipramine**

- Severe functional impairment : SSRI + CBT or consider Clomipramine

## **12. Personality Disorders :**

### **Cluster A - Odd or Eccentric**

- paranoid
- Schizoid
- Schizotypal

### Cluster B : Dramatic, Emotional or Erratic

- Anti-social
- Borderline
- Histrionic
- Narcissistic

### Cluster C : Anxious & Fearful

- obsessive - compulsive
- Avoidant
- Dependent

### Cluster A - Odd or Eccentric

#### Paranoid

- Hypersensitivity and unforgiving attitude when insulted
- Unwarranted tendency to question loyalty of friends
- Reluctance to confide in others
- Pre-occupation with conspirational beliefs and hidden meaning
- Unwarranted tendency to perceive attacks on their character

#### Schizoid :

- indifference to praise and criticism
- Preference for solitary activities
- Lack of sexual interactions
- Lack of desire for companionship
- Emotional coldness
- Few interests
- Few friends or confidants other than family

#### Schizotypal :

- ideas of reference - some insight is retained
- Odd beliefs and magical thinking

- Unusual perceptual disturbances
- Paranoid ideation and suspiciousness
- Odd eccentric behaviour
- Lack of close friends
- Inappropriate effects
- Odd speech without being incoherent

Cluster B - dramatic, emotional or erratic

Antisocial :

- failure to conform to social norms with respect to law
- More common in men
- Deception - repeatedly lying, use of aliases. Conning others for personal profit or pleasure
- Impulsiveness or failure to plan ahead
- Irritability and aggressiveness. - repeated physical fights and assaults
- Reckless disregard for safety of self or others
- Consistent irresponsibility
- Lack of remorse - indifferent or rationalising having hurt, mistreated or stolen from another

Borderline :

- efforts to avoid real or imagined abandonment
- Unstable personal relationships
- Unstable self image
- Recurrent suicidal behaviours
- Affective instability
- Chronic feelings of emptiness
- Difficulty controlling temper

Histrionic:

- inappropriate sexual seductiveness
- Need to be centre of attention
- Rapidly shifting and shallowing expression of emotions
- Suggestibility
- Self dramatisations

Narcissistic :

- grandiose sense of self importance
- Fantasies of unlimited success, power or beauty

- Sense of entitlement
- Lack of empathy
- Chronic envy
- Excessive need for admiration
- Arrogant and haughty attitude

Cluster C : Anxious & Fearful :

Obsessive - compulsive -

- occupied with details, rules, lists, order, organisation or agenda to the point that the key part of activity is gone
- Extremely dedicated to work and efficiency to elimination of spare time activities
- Meticulous, scrupulous, rigid about etiquettes

Avoidant :

- unwillingness to be involved unless certain of being liked
- Preoccupied with ideas that they are being criticised or rejected in social situations
- Views self as inept and inferior to others
- Social isolation accompanied by craving for social contact

Dependent :

- difficulty making everyday decisions without excessive reassurance
- Need for others to assume responsibility for major areas of their life
- Lack of initiative
- Unrealistic fears of being left to care for themselves
- Extensive efforts to obtain support from others
- Unrealistic feelings that they cannot care for themselves

### **13. Post partum mental health problems**

- Edinburgh post natal depression scale
- Score > 13 = depressive illness of varying severity
- Sensitivity and specificity >90%
- Baby blues : 3-7 days following birth and is more common in primigravida; anxious, tearful and irritable
- Post natal depression : ~10 % of women, starts within a month and peaks at 3 months. Reassurance, support, CBT, SSRI - Sertraline and Paroxetine recommended.

- Fluoxetine - not recommended due to long half life
- Puerperal psychosis : onset within the first 2-3 weeks after birth; severe swings in mood and disordered perception. Admission \*\*\*

#### 14. Schizophrenia

- First rank symptoms - auditory hallucinations, thought disorders, passivity phenomenon and delusional perceptions.
- Auditory hallucinations - two or more voices discussing patients in third person, thought echo, voices commenting on patients behaviour.
- Thought disorders : thought insertion, thought withdrawal, thought broadcasting.
- Passivity phenomenon : bodily sensations being controlled by external influences; actions/influences / feelings
- Delusional perceptions : two stage process - normal object perceived then secondary sudden intense delusional insight into objects

#### Other features :

- Impaired insight
- Negative symptoms - blunting of affect, anhedonia, logia ( poverty of speech) , avolition (poor motivation), social withdrawal
- Neologisms - made up words
- Catatonia

#### Schizophrenia - poor prognosis :

- strong family history
- Gradual onset of low IQ
- Prodromal phase of social withdrawal
- Lack of obvious precipitant

#### GOOD PROGNOSIS :

- Older age onset
- High IQ
- Sudden onset
- Short duration of episode
- Obvious precipitating factor
- Strong support system
- No psychiatric history

- Postitive symptoms predominate

### 15. **Selective Serotonin Reuptake Inhibitors**

- Citalopram and fluoxetine - currently preferred SSRI
- Sertraline - post MI
- Young adolescents - **Fluoxetine**

Adverse effects :

- GI symptoms most common side effect
- Increased risk of GI bleeding - cover with PPI
- Caution : increased anxiety and agitation after starting SSRI
- FLuoxetine and paroxetine —> higher propensity for drug interactions.
- Hyponatremia

Citalopram and QT interval - maximum daily dose is 40mg for adults, 20 mg for patients > 65 years, 20mg —> hepatic impairment.

Warfarin / Heparin —> give Mirtazapine

Triptans -> increased risk of serotonin syndrome

MAO inhibitors —> increased risk of serotonin syndrome

SSRI abrupt withdrawal - discontinuation symptoms :

- increased mood change
- Restlessness
- Difficulty sleeping
- Unsteadiness
- Sweating
- Paraesthesia
- GI - cramps, pain, diarrhoea, vomiting

SSRI - 1st trimester - smal risk of congenital heart defects

\*\*\* SSRI - 3rd trimester —> persistent pulmonary hypertension of newborn

Paroxetine - increased risk of congenital malformations - particularly in the first trimester.

Paroxetine - higher risk of discontinuation syndrome

16. SNRI - inhibits reuptake and increases concentration of serotonin and NA in the synaptic cleft.

Examples : Venlafaxine, Duloxetine

17. Sleep paralysis : transient paralysis of skeletal muscles - occurs during REM;

Paralysis - occurs after waking up or shortly after falling asleep

Hallucinations : images or speaking that appear during paralysis

Mx - Clonazepam may be used

### 18. **Tricyclic Antidepressants**

- Inhibition of reuptake of Serotonin (5-HT) and Noradrenaline
- Inhibition of Serotonin : increased concentrations in synaptic cleft, enhancing serotonergic neurotransmissions.
- Inhibition of noradrenaline : blocking reuptake of NA increases its concentration

Other effects of TCA :

- **antagonism of histamine receptors** : drowsiness
- Antagonism of muscarinic receptors : dry mouth, blurry vision, constipation, urinary retention
- Antagonism of adrenergic receptors : postural hypotension
- Lengthening of QT interval

Neuropathic pain - low dose amitriptyline - also used in prophylaxis of headache both tension and migraine

\*\* Lofepramine - lower incidence of toxicity in overdose

Less sedative TCA - Imipramine, Lofepramine, Nortriptyline

19. The most appropriate strategy for this patient is to switch to the equivalent diazepam dose then slowly withdraw over the next 2 months. This approach is recommended because diazepam has a longer half-life than temazepam, which allows for a smoother and more gradual withdrawal process. Additionally, UK guidelines support using diazepam as the preferred benzodiazepine for withdrawal due to its long half-life and availability in lower doses, which facilitates gradual tapering.

20. Atypical antipsychotics, also known as second-generation antipsychotics, are more associated with weight gain than conventional or first-generation antipsychotics. This side effect is particularly common with medications such as olanzapine and clozapine. The mechanism of weight gain involves the antagonism of serotonin 5-HT<sub>2C</sub> and histamine H<sub>1</sub> receptors, resulting in increased appetite and reduced satiety.

21. Dosulepin, a tricyclic antidepressant, was previously prescribed for managing depression and anxiety. However, due to it posing a significant risk in overdose, it is rarely used and not recommended particularly as a first-line agent or in patients with a high risk of overdose. In excessive amounts, dosulepin can lead to life-threatening complications, including cardiac arrhythmias, seizures, and respiratory depression. Its toxicity arises from the blockade of various receptors, such as histaminic, cholinergic, and adrenergic receptors. The narrow therapeutic index increases the likelihood of severe adverse effects even with a slight overdose.

22. Amoxapine is a tetracyclic antidepressant used to treat depressive disorders. It possesses a unique chemical structure, combining tricyclic and neuroleptic properties. One notable aspect of amoxapine is its relatively safer drug profile in overdose compared to some other tricyclic antidepressants. In instances of overdose, amoxapine tends to produce milder toxicity symptoms. This is attributed to its metabolite, amoxapine-2-OH, which acts as a serotonin reuptake inhibitor, potentially mitigating the severity of adverse effects associated with overdose.

**Desipramine** is a tricyclic antidepressant primarily used to treat depressive disorders. Desipramine has a relatively safer drug profile in overdose compared to some other tricyclic antidepressants attributed to its selective inhibition of norepinephrine reuptake, which leads to a milder side effect profile and reduced toxicity. Desipramine's lower affinity for receptors associated with adverse effects, such as anticholinergic and cardiovascular effects, contributes to its decreased risk of severe complications in overdose situations.



**Lofepramine**, a tricyclic antidepressant, is known for its relatively safer drug profile in overdose compared to some other tricyclic antidepressants. Its active metabolite, desipramine, is produced in smaller amounts, leading to reduced toxicity. Lofepramine's selective inhibition of norepinephrine reuptake, coupled with a lower affinity for receptors associated with adverse effects, contributes to its diminished risk of severe complications in overdose.

**Nortriptyline**, a tricyclic antidepressant, has a relatively safer drug profile in overdose when compared to other tricyclic antidepressants, primarily attributed to its selective inhibition of norepinephrine reuptake, leading to a more favourable side effect profile and reduced toxicity. Nortriptyline's lower affinity for receptors associated with adverse effects, such as anticholinergic and cardiovascular effects, contributes to its diminished risk of severe complications in overdose.

23. PTSD : intrusive memories, avoidance, negative changes in thinking and mood, and changes in physical and emotional responses.

24. Illness anxiety disorder - hypochondriasis - persistent belief in the presence of an underlying serious disease.

25. Duloxetine - inhibitor of serotonin and Noradrenaline reuptake

26. Cyclothymic disorder - chronic course - no symptom free interval longer than two months which does not fit with this patient's history

27. Co-morbidity for other severe mental disorders is greater than 50% in individuals with severe drug dependence.

Mood disorders, anxiety disorders, psychotic disorders are commonly present.

28. Cotard syndrome - nihilistic delusional ideation where a patient believes they are dead or non-existent. It is associated with depression.

Capgras syndrome - delusional disorder where a patient believes someone close to them has been replaced by an impostor.

Couvade syndrome - sympathetic pregnancy where the biological fathers suffer the symptoms of pregnancy in the 1st and 3rd trimesters.

De Clerambault's syndrome - delusional syndrome where the patient think another person who is wealthy or famous is in love with them.

Fregoli delusion - patient believes that different people are in fact the same person in disguise.

29. Lofepramine is a third-generation tricyclic antidepressant (TCA) and is considered the safest in overdose due to its lower cardiotoxicity compared with other TCAs. This reduced cardiotoxicity is because lofepramine has less affinity for cardiac fast sodium channels, which are responsible for the life-threatening arrhythmias associated with TCA overdose.

30. Tyramine containing food - cheese, pickled herring, Bovril, Oxo, Marmite, brood beans

31. Generalised Anxiety Disorder - Citalopram

32. Serotonin Syndrome :

- Complication when combined with other drugs such as :
  - A. Tricyclic antidepressants
  - B. Monoamine oxidase inhibitors
  - C. St John's Wort
  - D. SSRI, SNRI
  - E. Lithium
- Can also be caused by overdose of SSRIs.

Clinical features :

- Tremor
- Akathisia
- Diarrhoea
- Hypomania

- Agitation
- Drowsiness, coma
- Myoclonus
- Hyperthermia
- Seizures
- Pronounced autonomic symptoms - tachycardia, high BP, sweating, mydriasis, hyperactive bowel sounds
- Diagnosis confirmed by Hunter Serotonin Toxicity Criteria
- Mx : IV fluids, BZDs to manage agitation, Cyproheptadine
- Complications : metabolic acidosis, rhabdomyolysis, DIC
- Seizures, pneumonia, respiratory failure

### **33. Frontotemporal dementia - C9orf72 - hexanucleotide repeat expansion of GGGGCC in C9orf72 gene**

Also associated with Motor Neuron Disease

Amyloid Precursor protein - APP - familial onset Alzheimer's disease.

Presenilin 1 - PS1 gene - familial Alzheimer's disease - PS1 gene defect leads to defective activity of gamma secretase which in turn drives accumulation of amyloid pre-cursor protein.

MAPT - Mutations are associated with Fronto-temporal dementia with Parkinsonism, Progressive supra-nuclear palsy and corticobasal degeneration.

34. Electroconvulsive therapy - severe depression for patients who are at risk to their life and urgent treatment is needed.

Indications for ECT in depression include :

- depressive stupor or catatonia
- Psychotic depression
- Refusal of food and drink
- Patient is dangerously suicidal
- Situations where a delay in effects of antidepressant medication will result in a serious health risk

### **35. Attention Deficit Hyperactivity Disorder**

#### Overview :

- Difficulty maintaining attention
- Hyperactivity
- Impulsive actions
- Affects 1 in 20 children; Males >>> females
- R/F : genetic, environmental - neglect, social deprivation, antenatal problems - maternal alcohol and/or drug abuse, obstetric problems - Low birth weight

#### Clinical Features :

- Easily distracted
- Unable to sit still/be quiet
- Associated with impulsivity
- Antisocial behaviour
- Soft neurological signs

#### Diagnosis:

- Symptoms repeat on 2 or more occasions
- Present for at least 6 months and interfere with social, academic or occupational functioning
- 

#### Management:

- Support programmes and parent education
- Group and individual psychological treatment - behavioural modification
- Exercise and balanced diet
- Drug treatment :
  1. **Methyphenidate ( Ritalin)**
  2. Amphetamines ( Adderall)
  3. Dextroamphetamine (Dexedrine)
  4. SNRI ( Atomoxetine)

### 36. **Generalised Anxiety Disorder**

#### Overview :

- Neurosis - anxiety - symptoms of anxiety that are inappropriate and excessive
- Can lead to avoidant behaviour and low mood
- Somatic symptoms - tension, autonomic arousal, hyperventilation

- Commonly associated with other psychiatric problems - schizophrenia, dementia, depression, alcoholism
- R/F - ages 35-54, being divorced or separated, living alone, lone parents
- Protective factors : cohabiting, married

C/F :

- Cognitive symptoms - apprehension, fear of death, losing control, going mad; hyper vigilance
- Somatic symptoms - autonomic arousal ( palpitations, accelerated heart rate, sweating, trembling or shaking, dry mouth)
- Chest / abdomen : difficulty breathing, feeling of choking, chest pain/ discomfort, nausea or abdominal stress
- Mental state - dizziness, depersonalisation, feeling of losing control, fear of dying

Management :

- CBT
- SSRI - Escitalopram, Paroxetine

### 37. Oculogyric crisis - **Mx : Procyclidine - anti-cholinergic**

1) Acute dystonia(Rx with anticholinergics:  
Benztropine,diphenhydramine,trihexiphenidyl)

2) Akathasia aka ants in the pants(Rx with lowering the dose,adding benz or beta blockers)

3) Tardive Dyskinesia (Rx with newer APM)

4) Neuroleptic Malignant Syndrome (Rx with Dantrolene and bromocriptine)

38. Vascular dementia - seizures are more common.  
Because of neuronal irritability in areas where there is vascular compromise.

Vascular dementia has more acute onset.

39. **Dyslexia** : reading and writing difficulties in an otherwise normal intelligence individual is likely **due to dyslexia. Males >> females**

40. **Projection** - defense mechanism whereby an individual attributes an uncomfortable/immoral act onto other people as a means of diverting attention away from themselves - in order to alleviate pressure of feelings of guilt, by wanting to believe that everybody else is similar.

Altruism - acting in a selfless manner in order to benefit other people

Denial : refusal to acknowledge a true fact

Intellectualisation : use of reasoning to support a particular view point or action.

Sublimation : filtering of behaviour to ensure that only socially acceptable forms of behaviour are displayed.

41. Narcolepsy - classical tetrad :

- 1) chronic daytime sleepiness - hypersonia
- 2) Hypnagogic/hypnopompic hallucinations
- 3) Sleep paralysis
- 4) Cataplexy

INV : multiple sleep latency EEG - they fall asleep in less than 8 minutes, was of patients with Narcolepsy often include REM sleep and presence of two or more naps containing REM sleep is virtually diagnostic of narcolepsy

Mx : day time stimulants - Modafinil and Night Time - sodium oxybate

42. Repression - use of conscious efforts to forget unpleasant events.

- prolonged repression can cause behavioural and emotional problems
- Repression can lead to disorganised thought process and social isolation

- Further complications - depression, anxiety, paranoia

Retrogression - process where an individual returns to a state of earlier development - adopting child-like characteristics as a form of defence mechanism in response to difficult or traumatic situation.

Catharsis - process of realising strong or repressed emotions or feelings by bringing them into consciousness and results in relief for the individual.

43. Thiazide diuretics - greatest risk with Lithium

44. Alcohol Dependence Syndrome - key features :

- Strong desire or compulsion to drink, difficult in controlling levels of drinking
- Physiological withdrawal symptoms
- Evidence of tolerance
- Progressive neglect of alternative pleasures or interests
- Persistent drinking despite clear evidence of harmful effects
- Narrowing of the drinking repertoire
- Reinstatement of drinking after periods of abstinence

45. **Passive - aggressive** : covert aggression expressed through passivity, masochism, and self defeating behaviour. Such an individual is often angry and often angers others.

Usual result is deterioration of interaction, with even greater anger and passive-aggressiveness.

46. **External locus of control** - patient is making external factors in the environment accountable for her actions.

- Patients with mental health problems and social maladjustment - usually have an external locus of control.
- Socio-cognitive perspective in personal control suggests that we learn to see ourselves as controlling the environment in which we live, or being controlled by external factors in our environment

Internal locus of control : direct our beliefs to make ourselves accountable for actions.

47. Risk of developing referring syndrome is directly related to the amount of weight loss during episodes of anorexia, and rapidity of weight gain. BMI < 15 predicts higher risk of referring syndrome.

48. Buspirone - partial serotonin receptor agonist - 5-HT 1A - response to treatment is delayed and may take up to 2 weeks.  
Main side effects of Buspirone : dizziness, headache, excitement, nausea

49. OCD - low intensity intervention → SSRI Rx (OR) intensive CBT with exposure-related prevention

Severe functional impairment - SSRI + Intensive CBT with exposure related prevention.

50. St John's Wort

- Hypericum perforatum
- Popular herbal remedy for treating mild depression
- MOA : up-regulation of serotonin and dopamine
- Up-regulated cytochrome P450 enzyme

51. Alzheimer's disease findings :

- neurofibrillary tangles with associated protein tau
- Senile plaques
- Extracellular deposits of amyloid beta peptides
- Cerebral amyloid antipathy
- Hippocampal sclerosis

52. Temazepam : long acting BZD - not recommended for sepsis related delirium

Haloperidol - contraindicated in Parkinson's disease

Trazodone - TCA used over long term as a treatment for depression

53. Delirium tremens :

- occurs around 3-4 day after cessation of consumption
- C/F : coarse tremor, agitation, confusion, delusion, visual hallucinations.
- Fever, sweating, tachycardia may also occur.



- Co-existent hypoglycaemia and Wernicke-Korsakoff syndrome also occurs
- IV Vitamin B
- Sedation with Chlordiazepoxide

54. Oppositional defiant disorder - problems in relating to authority figures. Psychotherapy is the mainstay of therapy to allow individuals to modify their response in certain situations.

55. Compliance therapy - psychological therapy that aims to educate the patient about the nature of their condition, its treatment and need for treatment.

Any negative cognition or problems regarding the treatment can be challenged by the therapist and may help in this patient.

56. Beta blocker - drug induced mood disorder - can cause depression, erectile dysfunction, fatigue, headache, and nightmares.

57. Buspirone - nasal congestion  
Generalised skin rashes are also commonly seen

Movement disorders are rarely seen with Buspirone therapy - both muscular rigidity and Parkinson's disease.

58. Subgroup of patients with **OCD** have now been identified who are characterised by **prepubertal acute onset group A beta-haemolytic streptococcal infection pharyngitis**.

**Basal ganglia** has been involved in this process.

59. Lithium takes **5-7 days for achieving steady state**.

NICE guidelines state that Serum Lithium levels should be checked 1 week after starting and 1 week after every dose change until levels are stable.

Samples should be taken 12 hours after a dose.

- Once stable - monitoring should be at 1-2 month intervals for the first 6 months, and then 3-6 months intervals.
- Weekly monitoring after initiation and after each dose change — every 3 months for the first year — every 6 months thereafter.

- Before starting lithium therapy —> thyroid function, renal function and ECG should be checked.
- Thyroid and renal function to be checked every 6 months on Lithium therapy.

**60. Undoing - performance of an activity - symbolically reverses previous behaviour or thought.**

**This defence mechanism is present in individuals who feel either conscious or unconscious guilt.**

**Compensation :** unconscious defence mechanism by which one attempts to make up real or fancied deficiencies. It is also a conscious process in which one strives to make up for real or imagined defects of physique, performance skills or psychological attributes.

**61. Lewy body v/s Alzheimer's -** Lewy body has 1) fluctuating consciousness levels, 2) varying levels of alertness, 3) significant day time somnolence, visual hallucinations ++

**62. Ganser syndrome -**

- approximate answers
- Somatic conversion
- Pseudo-hallucinations
- Subsequent amnesia
- Apparent clouding of consciousness

**63. Derealisation -** subjective feeling of altered reality of the environment. Person may complain of the world seeming like a dream or as if it's real.

**Depersonalisation :** subjective feeling of altered reality of the self; person may feel as if they are not their normal self, they need to wake up from their present state or that they feel unreal.

**64. Fronto-temporal dementia :** associated with gradual degeneration of frontal and/or temporal lobes and is characterised by alteration in behaviour in social situations and progressive issues with speech and language.

65. Depressive pseudo-dementia :

- In depression, apparent cognitive deficit if present is typically acute and recent, whereas, the apparent cognitive deficit of dementia is insidious.
- Depressed patient will often communicate a sense of distress or agitation and will complain of their cognitive difficulties, unlike truly demented patients who may appear unaware and confabulate.
- Patients may make comments expressing that relatively straight forward tasks are too difficult for them, or that they lack the volition to attempt them.
- Other symptoms of depression such as - diurnal mood variation, early morning waking, biological symptoms etc should be looked for.

Agitated behaviour and increased confusion, and wandering t bed time —> Alzheimer's dementia.

66. Treatment resistant schizophrenia - **Clozapine**

67. **Cyclothymia** - mood swings cycling from mild depression to hypomania (elevated mood and overactivity without psychotic features or significant functional impairment). It resembles a mild form of bipolar affective disorder. It is usually diagnosed in early adulthood and has a life long course.

68. **Fragile X syndrome - most common hereditary cause of mental disability.**

- shorter than average height
- Larger than average head circumference
- Macro-orchidism
- Characteristic facial appearance - large forehead with supra-orbital fullness, long face, long nose, prominent jaws, high arched palate, and large ears.
- Pale irises
- Associated conditions with Fragile X syndrome are :
  - (1)Epilepsy
  - (2)Strabismus
  - (3)Otitis media

- (4) Sinusitis
- (5) Joint dislocation
- (6) Orthopaedic problems
- (7) Apnoea

69. Patients with major depressive disorder - two weeks after commencing treatment with SSRI - patient can commit suicide. Greatest risk is after partial response to antidepressants.

70. Regression - return to less mature levels of functioning. Occurs when there are high levels of stress and anxiety and are not alleviated by more mature defences such as intellectualism and humour.

71. Ganser syndrome

- mimics the symptoms of psychosis
- Pseudo-hallucination
- Patients have poor eye contact with prolonged periods of staring and giving approximate answers - **vorbeireden**
- Somatic conversion
- Amnesia

72. Post partum depression :

- presence of guilty thoughts
- Irritability and inability to sleep
- Thoughts of worthlessness and inability to cope
- Not enjoying the baby
- Suicidal ideation
- High score on Edinburgh post natal depression scale

73. **Thioxanthenes : Chlorprothixene , Flupenthixol**

74. Atypical anti psychotics - Aripiprazole, Amisulpride, Clozapine, Olanzapine, Risperidone, Quetiapine

75. **Counter-transference : therapist's own feelings, emotions and attitudes towards the patient;** therapist needs to be aware of these feelings and to screen out those that are seeming only from him and to take notes of those spoken by the patient.

Transference : unconscious process in which the patient transfers to the therapist feelings and emotions that were experienced in another part of patient's life.

Resistance : plates to words and actions of a patient that act to obstruct them from gaining access to their unconscious - refusing to talk about a certain problem

Transitional object : selected by an infant for self soothing like blanket or toy, its role is to help with the separation-individuation process

76. Prader Willi syndrome - limiting access to food to control weight gain

76. **Isolation** : separation of thought from its attached emotional tone there making it tolerable.

77. **Obsession** - repeated senseless thoughts that pre-occupy a person's mind or intrude a mind. Recognised as patient as irrational and are unsuccessfully resisted.

78. Sodium valproate - 2nd line drug for bipolar disorder if lithium is not tolerated or contra indicated.

79. TCA side effects

- Anti cholinergic : dry mouth, blurry vision, constipation, urinary retention, acute glaucoma
- Anti alpha adrenergic - postural hypotension, tachycardia
- Anti histaminergic - sedation, weight gain
- Quinidine like action - prolonged QT, flattened T waves, negatively inotropic

80. Anorexia nervosa - **zinc deficiency**

81. Haptic hallucination : sensation of being touched, strangled or feeling of insects crawling under the skin, occurs in cocaine abuse. Cocaine can also cause acute toxic psychosis, with marked agitation, paranoia, auditory visual hallucinations.

Haptic hallucinations seen in : cocaine abuse, alcohol withdrawal, schizophrenia.

82. Lesch Nyan syndrome - gene locus : **Chromosome Xq26-27**

83. **Cortical dementia :**

- damage to cerebral cortex
- Critical role in memory and language
- Alzheimer's, FT dementia, CJ disease

Sub cortical dementia :

- damage to areas beneath the cortex and disruption in the fronto-striatal connections
- Early frontal lobe problems such as planning difficulties, poor verbal fluency, personality change, task switching
- Basal ganglia involvement - psychomotor slowing with reduced verbal output, slowed rate of response and reduced alertness
- Parkinson's, Vascular dementia, multiple sclerosis, NPH, Huntington, Wilson's.

84. Short term lithium therapy - less than 4 weeks - can develop **fine tremors**.

85. Risperidone - **significant hyperprolactinaemia**

86. **Premack principle** - patient is exhibiting learned behaviour according to reinforcement hierarchy.

Classical conditioning : learning a new behaviour in response to a stimulus where the behaviour and stimulus are linked together.

Operant conditioning : type of learning in which a behaviour is changed by the behaviour's consequences such as reward or punishment.

Extinction : condition learned behaviour disappears over time if it is not reinforced.

Incidental learning : learning occurs without any intention to learn

87. Splitting : defence mechanism whereby people do not integrate the good and bad qualities of the people. Seen in borderline personality disorder.

88. Cotard syndrome is characterised by a person believing they are dead or non-existent. It tends to be related to depression.

Capgras syndrome is characterised by a person believing their friend or relative had been replaced by an exact double.

Couvade syndrome is also known as 'sympathetic pregnancy'. It affects fathers, particularly during the first and third trimesters of pregnancy, who suffer the somatic features of pregnancy.

De Clerambault's syndrome is characterised by a person believing that another individual (often a celebrity) is deeply in love with them. It typically affects females.

Othello syndrome is when the patient believes their partner is cheating on them. They may be threatening or stalk their partner. This seems to affect males more than females.

89. Tyramine is usually metabolised in the GIT by MAO.

- due to MAO-inhibitors - tyramine enters the circulation and increases release of Noradrenaline
- Vasoconstriction, and increase in BP
- Nausea, palpitations, headache, dilated pupils
- Severe cases - delirium, hyperpyrexia, cerebral haemorrhage and death
- Foods high in tyramine include meat and yeast extracts, matured cheese, red wine, and broad beans.

90. Hypnagogic hallucinations - improved sleep hygiene

91. IQ levels

- 50 to 69 : mild
- 35 - 49 : moderate
- 20 to 34 : severe
- < 20 : profound

92. Tuberous sclerosis :

- TSC1 - chromosome 9q34 - 40% of cases
- TSC1 - encodes for protein **hamartin** - has a tumor suppressant role
- TSC2 - chromosome 16p13 - encodes for **tuberin** - likely to cause mental disability

93. Delusions can be categorised into different types:

- Delusions of Reference - belief that a special meaning lies behind something 'innocent' in the public domain, eg a song, book, newspaper or TV programme is about them; or the way objects are arranged in a room or cars parked in the street has a specific reference to them.
- Delusions of Control - belief that they are being controlled by an external force or having thoughts inserted, removed or broadcasted from their mind. They often cite things such as electricity, radio waves or aliens as the mediator.
- Delusions of Guilt - a false feeling of remorse or guilt that they have committed a horrible crime and 1 should be punished; or are responsible for a disaster such as a flood or earthquake.
- Delusions of Replacement - when a patient believes a person or people in their life, eg their partner or close relative, have been replaced by an impostor who looks and talks exactly like that person.
- Paranoid Delusions - these are the most common type of delusions and often involve the theme of being followed, harassed or conspired against; or the belief that people or organisations (eg MI5, police, employer) are plotting to harm the patient.
- Grandiose Delusions - belief that they have exceptional talent, abilities, worth, or that they may be famous. For example, patients may believe themselves to be God, a billionaire or have superpowers.

94. Alcohol Dependence syndrome - partial opioid antagonist - reduces alcohol cravings

95. Grief - stages :

1. Stage 1 - stage of numbness - initial reaction to loss of loved one. Shock and disbelief.



2. Stage 2 - stage of pining - thoughts, feelings, and behaviours that accompany the bereavement. Grief can be normal. Preoccupation with the deceased in order to counteract feelings of separation anxiety. Anger, irritability, and depressive features are common. Anxiety may escalate to hyperventilation and panic attacks. Pining or yearning or longing or searching
3. Stage 3 - disorganisation and despair - desire to withdraw and disengage from others and activities that they regularly enjoyed. Feelings of pining and yearning become less intense while periods of apathy, meaning an absence of emotion, and despair increase.
4. Stage 4 - reorganisation and recovery - returns to a new state of normal, weight regained, energy levels increase, interest in normal activities resumes.

96. Wernicke's encephalopathy - neuronal loss in mamillary bodies  
Chronic alcohol use - cerebral and cerebellar atrophy and ventricular dilation.

**97. Spiral defect - visual field - positive finding that indicated non organic cause**

**98. Huntington's disease - expansion of unstable triplet sequence - CAG - in the first exon of a gene near the telomere of chromosome 4p**

**The gene has been identified as IT 15 —> codes for protein Huntington**

**CGG repeat - FMR1 gene - fragile X**

**CTG - DMPK gene - myotonic dystrophy**

**GCG - PABPN1 gene - oculopharyngeal muscular dystrophy**

**GAA - FXN gene - Friedrich's ataxia**

**99. Clozapine** : atypical antipsychotic - used in treatment of schizophrenia who are unresponsive or intolerant of at least two other drugs

- adverse : neutropenia, agranulocytosis
- Weekly blood counts are required for the first 18 weeks of treatment and then every 2 weeks up to a year and then monthly maintenance blood tests
- All patients on Clozapine - **registered on Clozaril Patient Monitoring Service**
- Other adverse effects : hyper salivation, sedation, weight gain, reduces seizures threshold

100. An oculogyric crisis is a dystonic reaction, typically associated with the use of antipsychotic medications. It presents as sustained, often painful, upward deviation of the eyes. Procyclidine, an anticholinergic drug, is used in the management of extrapyramidal symptoms caused by antipsychotics. It works by blocking the action of acetylcholine in the central nervous system, which helps to reduce muscle stiffness and spasms.

101. Charles-Bonnet Syndrome. This classically presents as recurrent visual or auditory hallucinations in patients with failing eyesight. It is thought that as the brain receives less visual stimulus than it is used to, it begins to fill in the gaps with previously stored images. Hallucinations can either be simple as in patterns or lines or complex as in people or animals. They are usually pleasant hallucinations and most patients retain insight. In this patient with a history of cataract Charles-Bonnet syndrome is most likely.

102. The most suitable pharmacological treatment for a 24-year-old female with bulimia who has not responded to cognitive behaviour therapy is **high-dose fluoxetine**. Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) and has been shown to be effective in reducing binge eating and purging behaviours associated with bulimia. The National Institute for Health and Care Excellence (NICE) guidelines recommend high-dose fluoxetine (60 mg daily) as the first-line pharmacological treatment for adults with bulimia nervosa.

103. NICE guidelines current suggest index cases of schizophrenia should now be commenced on an atypical antipsychotic as first-line. On starting antipsychotic treatment this patient has developed dyslipidaemia, as displayed by the lipid blood tests, and significant

weight gain. Several atypical antipsychotics can be associated with these adverse effects however **olanzapine** has a relatively higher risk comparatively. Olanzapine is believed to cause higher deregulation of hepatic lipid metabolism resulting in this increased hyperlipidaemia and weight gain.

**Aripiprazole** has, however, been associated with the movement disorder akathisia and therefore this should be monitored.

**Quetiapine** is believed to have a **higher affinity to  $\alpha$ 1-adrenergic and histamine-1 receptors** and therefore patients may be at high risk of **orthostatic hypotension and transient sedation**.

104. The correct answer is **50%**. This is because the concordance rate for schizophrenia in monozygotic twins, who share 100% of their genetic material, is around 50%. This suggests that while genetics play a significant role in the development of schizophrenia, they are not the only factor involved. Environmental factors and other non-genetic influences also contribute to the risk of developing this condition.

105. **Amitryptiline & Dosulepin** (also known as dothiepin) is considered the most toxic tricyclic antidepressant (TCA) in overdose. It has a narrow therapeutic index and can lead to serious complications such as cardiac arrhythmias, seizures, and even death due to its significant anticholinergic and sodium channel blocking effects. The British National Formulary (BNF) advises against its use wherever possible due to the high risk of fatal toxicity.

106. **Delusional parasitosis** is the correct answer, as this patient is presenting with signs and symptoms consistent with 'Morgellons' which is regarded as a form of delusional parasitosis. Reported fibres or inanimate materials are often found to be common household/clothing materials (e.g. cotton). Skin lesions are consistent with chronic excoriations and the scooped-out lesion is consistent with repetitive picking of lesions. The hypopigmented patches are healed lesions. Sparring of the area between the

scapula indicates the area the hands are unable to reach, and no lesions were evident there.

107. This patient has no historical or clinical findings of neurological disease. The likely diagnosis here is **conversion disorder** - a psychiatric condition where psychological stress is unconsciously manifested as physical, neurological symptoms. This was most likely triggered by recent domestic abuse and stress. This patient also has a positive drop-arm test in which the patient unconsciously exhibits a controlled drop to prevent the arm from hitting their face.

108. An obsession is defined as an unwanted intrusive thought, image or urge that repeatedly enters the person's mind. Compulsions are repetitive behaviours or mental acts that the person feels driven to perform. A compulsion can either be overt and observable by others, such as checking that a door is locked, or a covert mental act that cannot be observed, such as repeating a certain phrase in one's mind.

109. Borderline personality disorder is marked out by instability in moods, behaviour and relationships.

Diagnosis is confirmed by the presence of at least 5 of the following symptoms;

- 1) Extreme reactions including panic, depression, rage, or frantic actions to abandonment, whether real or perceived
- 2) A pattern of intense and stormy relationships with family, friends, and loved ones, often veering from extreme closeness and love to extreme dislike or anger
- 3) Distorted and unstable self-image or sense of self, which can result in sudden changes in feelings, opinions, values, or plans and goals for the future (such as school or career choices)
- 4) Impulsive and often dangerous behaviours, such as spending sprees, unsafe sex, substance abuse, reckless driving, and binge eating

5) Recurring suicidal behaviours or threats or self-harming behaviour, such as cutting  
Intense and highly changeable moods, with each episode lasting from a few hours to a few days

6) Chronic feelings of emptiness and/or boredom

7) Inappropriate, intense anger or problems controlling anger

8) Having stress-related paranoid thoughts or severe dissociative symptoms, such as feeling cut off from oneself, observing oneself from outside the body, or losing touch with reality.

110. Venlafaxine is a serotonin-norepinephrine reuptake inhibitor (SNRI) that has been shown to be effective in the treatment of post-traumatic stress disorder (PTSD). It works by increasing the levels of serotonin and norepinephrine in the brain, which can help improve mood, reduce anxiety, and alleviate symptoms associated with PTSD. According to UK guidelines, selective serotonin reuptake inhibitors (SSRIs) such as sertraline and paroxetine are considered first-line treatments for PTSD; however, SNRIs like venlafaxine can also be used if SSRIs are not effective or not tolerated.

111. The clinical (e.g. seizures, mydriasis, urinary retention) and electrocardiographic features are most in keeping with tricyclic overdose. These agents block sodium channels resulting in CNS and cardiovascular toxicity in overdose in the form of seizures and ventricular dysrhythmias. Tricyclics mediate their cardiotoxic effects via blockade of myocardial fast sodium channels (e.g. QRS prolongation, tall R wave in aVR), inhibition of potassium channels (e.g. QTc prolongation), and direct myocardial depression.

112. **Acute paranoid schizophrenia.** This condition is characterised by the presence of delusions, hallucinations, disorganised speech and behaviour. The patient's fear of catching avian flu from seeing migrating birds in her garden, despite no reasonable risk, can be seen as a delusion. Furthermore, the belief that her husband's socks on the washing line alerted her to this

danger suggests a degree of thought disorder - another key feature of schizophrenia.

113. Othello's syndrome is pathological jealousy where a person is convinced their partner is cheating on them without any real proof. This is accompanied by socially unacceptable behaviour linked to these claims.

114. Anorexia features

- most things low
- **G's** and **C's** raised: **g**rowth hormone, **g**lucose, salivary **g**lands, **c**ortisol, **c**holesterol, **c**arotinaemia

115. Olanzapine, like other atypical antipsychotics, is known to block serotonin receptors (especially the 5-HT<sub>2</sub> subtype) as well as D<sub>2</sub> , D<sub>3</sub> , D<sub>4</sub> dopamine receptors

116. This is a classical presentation of pseudodementia - the most common mimic for dementia amongst elderly patients. Although there is evidence of some cognitive impairment, the key feature present is a global memory loss affecting both short and longer-term memory, over a short history of four weeks with reluctance to engage with clinical assessment. These symptoms, coupled with the recent loss of her husband, indicate a severe reactive depressive episode.

117. Antipsychotic medications, such as quetiapine, can increase the risk of cerebrovascular events, including stroke, in elderly patients. This increased risk is particularly relevant for those with dementia-related psychosis. It is important to consider the potential benefits and risks when prescribing antipsychotics in this population.

The Medicines and Healthcare products Regulatory Agency (MHRA) in the UK has issued a warning about an increased risk of venous thromboembolism (VTE) in elderly patients using atypical antipsychotics. These drugs, which include clozapine, risperidone, olanzapine, and quetiapine among others, are often prescribed for the management of schizophrenia and bipolar disorder. They act by

blocking dopamine D2 receptors in the brain which helps to reduce psychotic symptoms. However, they can also cause hyperprolactinaemia and weight gain which may increase the risk of VTE.

118. This most likely represents Charles Bonnet syndrome. Reassurance is usually the best treatment, helping people to understand and come to terms with their hallucinations. It is importance to ensure there is not an alternative cause e.g. infection, psychosis, dementia (particularly Lewy body dementia), intoxication, metabolic abnormalities, focal neurological illness.

119. Haloperidol is a first-generation, 'typical' antipsychotic commonly used for a number of purposes. Apart from its use as an antipsychotic in psychiatric patients, it is often used in the context of delirium as seen here. It also plays a role in the management of nausea, especially in the palliative setting. It binds to numerous receptors, with different affinities for each. Primarily, it antagonises the dopamine **D 2 receptor**.

Blocks dopaminergic transmission in **mesolimbic pathways**.

120. Patients with personality disorder have disturbances in behaviour and personality that result in considerable personal and social distress across all areas of life. Borderline or emotionally unstable personality disorder is characterised by emotional instability, impulsive behaviour and intense but unstable relationships with others. Patients often fear abandonment of those close to them and may idolise these people. As in the patient described, they often have feelings of emptiness, poor self-image and recurrent attempts at self-harm. There is an association between the development of borderline personality disorder and history of trauma or abuse in childhood.

121. depression can mimic dementia. The key defining factor which distinguishes the two diagnoses is the pattern of memory loss: depression typically causes global memory loss, whereas dementia is more commonly a short-term memory loss. As such,

the correct answer is **memory loss of recent events** because it is the only option which suggests a diagnosis of dementia rather than depression. One would expect this patient to describe a global memory loss involving short-term, long-term and working memory loss.

122. Peduncular hallucinosis is a rare neurological disorder that causes vivid visual hallucinations in dark environments which last for several minutes. They typically occur after a midbrain stroke. This diagnosis is less likely given the history of blindness.

123. **Anton's syndrome** is a rare symptom of brain damage occurring in the occipital lobe characterised by cortical blindness, but will not accept they are blind despite being told that they are. They don't have visual hallucinations

124. **Paroxetine**, a selective serotonin reuptake inhibitor (SSRI), has the highest incidence of discontinuation symptoms amongst all SSRIs. This is primarily due to its short half-life which leads to rapid plasma clearance. As a result, abrupt cessation or missed doses can lead to withdrawal symptoms such as dizziness, sleep disturbances, mood swings and irritability.

**Fluoxetine** has the lowest risk of causing discontinuation symptoms among all SSRIs due to its long half-life and active metabolites. It allows for a more gradual decrease in blood levels even when treatment is abruptly stopped.

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MOCK - 1

PATEST

70% - 70 OUT OF 100 Qs

1. NSAID - vWD - NSAID use must be discussed before hand with a haematologist because of their effect on platelet aggregation.

2. Gluten sensitive enteropathy - IgA deficiency

3. HIT type 2 - immune complex mediated - occurs 5-10 days after administration of heparin due to formation of **antibodies against PF4-heparin complex**.



4. Progressive Multifocal Leukoencephalopathy - HIV positive patients - acute presentation - progressive white matter demyelination - subacute with memory impairment, mood changes and progressive focal neurology.

MRI - Multiple bilateral T2 hyperintense lesion.

Infects **oligodendrocytes in immunocompromised patients.**

5. Post exposure prophylaxis HIV - 3 antiretrovirals for 1 month.

6. African continent disease :

- arthropod borne disease - yellow fever, dengue, African trypanosomiasis, Leishmaniasis, Onchocerciasis, Rickettsioses
- Viral hemorrhagic fever - Ebola, Marburg, Crimean-Congo hemorrhagic fever

7. Acute tubular necrosis - 95% of patient go onto make full recovery. 5% patients require long term renal replacement therapy.

8. Theophylline - adverse effects :

- effects on CNS - headache, insomnia, agitation, seizures
- Severe nausea and vomiting
- GI irritation - vomiting, peptic ulceration
- Metabolic disturbances - hypokalaemia, metabolic acidosis.
- Theophylline toxicity - hypotension, ventricular and supra ventricular arrhythmia may occur when drug concentrations are > 25 mcg / mL

9. Amino Acid absorption - Jejunum

- Caecum - major site for absorption of water, bacterial metabolism of free fatty acids
- Proximal stomach - dietary proteins is digested into polypeptides in the stomach by action of pepsin and acid.
- Distal stomach : further digestion of dietary protein by stomach acid and pepsin activity.

10. Anti tubercular drugs side effects:

- **Isoniazid** - peripheral neuropathy - slow acetylators are at higher risk of developing peripheral neuropathy
- **Pyrazinamide** : hepatotoxicity

- **Ethambutol** : retinal injury and permanent loss of visual acuity, restriction of visual fields, and color blindness.
- **Rifampicin** : hepatotoxicity, reddish color to body fluids
- **Streptomycin** : ototoxicity, nephrotoxicity.

### 11. **Doxapram - respiratory stimulant**

- Centrally acting respiratory stimulant with severe respiratory distress where it may improve respiratory function sufficiently for survival.
- Usual dosing regimen is  $\rightarrow$  1-4 mg/min given as IV infusion
- Drug is contraindicated in **hyper metabolism state, hyperthyroidism, pheochromocytoma**
- **Adverse effects** - hypertension, cough, headache, sweating, dizziness, nausea, vomiting, urinary retention.
- Doxapram - Contra indications :
  - A. Heart disease
  - B. Epilepsy
  - C. Cerebral edema
  - D. Stroke
  - E. Status asthmatics
  - F. Hypertension
  - G. Hyperthyroidism
  - H. Pheochromocytoma
- It is incompatible in infusion with aminophylline,  $\text{NaHCO}_3$ , Furosemide as Doxapram has pH of 3.5-5.0 and risk of gasformation and precipitation when mixed with other agents.
- Half life is short, and duration of action is between 5-10 minutes after IV administration.

12. **PCOS** - high LH, normal / low FSH, Normal Oestradiol, High Testosterone, low SHBG, High DHEA, insulin resistance, dyslipidemia

### 13. Beta 2 adrenoreceptors effects :

- decrease in gut motility
- Relaxation of pregnant uterus
- Arteriolar dilatation
- Bronchial smooth muscle relaxation
- Decreased bronchial secretions
- Lipolysis

- Gycogenolysis
- Gluconeogenesis

#### 14. **Pityriasis lichenoides et varioliformis acuta**

- Rare skin condition of unknown ethology
- Burning pain, rash on trunk and limbs
- Scattered papules and small nodules with fine peripheral scale
- Pronounced haemorrhage crust on surfaces
- Dx - skin biopsy
- Mx : topical corticosteroids, anti inflammatory antibiotics, phototherapy, and systemic immunosuppressants.

#### 15. **Lichen planus**

- Itchy, violaceous, polyclonal, flat topped rash most commonly developing over the wrist, and ankles.
- Pale, lacy network develops and often found in mouth
- Presence of Wickham's striae - fine, white, lacy pattern over the papules is characteristic.
- Koebner phenomenon - lichen planus - where the rash colonises sites of trauma after few days
- Associated with liver disease, Hepatitis C, PBC, chronic active hepatitis.
- Lichen planus responds to potent or very potent topical steroid

16. Pleural TB - pleural biopsy microscopy and culture - under thoracoscopic or radiological guidance

#### 17. **Kennedy syndrome - spinal bulbar muscular atrophy**

- Proximal weakness and cramps
- Wasting
- Fasciculations
- Weakness and hyporeflexia are seen
- Perioral fasciculations are diagnostic
- Androgen insensitivity is seen as part of the syndrome - gives rise to gynecomastia and infertility
- CAG trinucleotide repeat

#### 18. QT interval shortening - **Digoxin, Ouabain**

Beta blockers - QT interval neutral

### Causes of **prolonged QT**

1. Hypokalaemia
2. Hypomagnesemia
3. Hypocalcemia
4. Hypothermia
5. Congenital long QT syndrome
6. Myocardial ischaemia
7. Post cardiac arrest
8. Raised ICP

### Drug causes of **prolonged QT** :

- 1) anti arrhythmies : Class Ia - Disopyramide
- 2) Class Ic - Flecainide
- 3) Class III - Amiodarone, Sotalol
- 4) Antipsychotics - Haloperidol, Quetiapine, Olanzapine
- 5) TCA - Amitriptyline
- 6) Anti depressants - Citalopram, Venlafaxine
- 7) Antihistamines - Terfenadine, Loratidine
- 8) Antibiotics - Erythromycin, Clarithromycin

19. Category 1 Pneumoconioses - least severe, fewer opacities and normal lung markings visible

Category 2 - less severe, number of opacities but normal lung markings visible

Category 3 - most severe - increasing density of small opacities, no visible lung markings

20. Number of cell lines have been approved for use in embryonic stem cell studies.

- ensuring that only target cells are transplanted into a suitable device
- If other cells are transplanted —> then it is possible they may continue to divide and leads to formation **of tumor within the device.**

De-differentiation : transformation of adult stem cells

21. L5 nerve root - ankle dorsiflexion, extension / dorsiflexion of great toe

S1, S2 - ankle plantar flexion

S1 - eversion of foot

L4 - inversion of foot

L2, L3, L4 - knee extension

22. Lead poisoning- basophilic stippling, clover leaf morphology, interstitial nephritis, proximal tubular dysfunction, motor neuropathy, anterior uveitis or iritis, gingival blue black or grey line

23. Triose phosphosphate isomerase deficiency

- rare autosomal recessive metabolic disorder
- Neonatal haemolytic anaemia
- Cardiomyopathy
- Splenomegaly
- Increased risk of infection
- Wasting, weakness and spasticity of muscles
- Death in early childhood

24. Causes of autonomic neuropathy :

CNS Causes :

- 1) multiple system atrophy
- 2) Parkinson's disease
- 3) Wernicke's encephalopathy
- 4) Syringomyelia / syringobulbia

Peripheral nervous system

- 1) familial dysautonomia - Riley Day syndrome
- 2) Familial amyloidosis
- 3) GBS
- 4) DM
- 5) Tabes dorsalis
- 6) Alcoholic nutritional neuropathy
- 7) Lambert Eaton

25. Causes of bile acid malabsorption :

- metformin
- Colchicine
- Ileal resection - terminal ileal disease - Crohn's disease - disrupts the enterohepatic circulation causing excessive bile salts to enter the colon
- Cholecystectomy

26. Casts in urine -

- fatty casts / oval bodies : nephrotic syndrome
- Hyaline casts : dehydration, exercise or diuretics
- RBC casts : glomerulonephritides
- Renal tubular epithelial casts : renal tubular necrosis, kidney transplant rejection
- Waxy casts : chronic kidney disease
- White blood cell casts : urinary tract infection

27. Wolff Parkinson White syndrome type B

- first heart sound is due to closure of mitral and tricuspid valves and denotes the end of diastole
- Loud first heart is due to mitral stenosis
- Mitral stenosis - normal splitting of S2
- Second heart sound is due to close of aortic valve followed by pulmonary valve
- Delayed A2 - LBBB, aortic stenosis, HOCM
- Delayed P2 - WPW type B, RBBB
- WPW type B -loud S1, reversal of S2 P2 f/b A2

28. X-linked adrenoleukodystrophy

- ABCD1 gene
- Gene encodes for ALD - peroxisomal membrane transporter protein
- Most common adult phenotype is adrenomyeloneuropathy - combination of peripheral neuropathy + myelopathy
- Assay of long chain fatty acids is useful for diagnosis
- Lorenzo's oil treatment
- Autosomal recessive adrenoleukodystrophy - neonates or young children - deafness, developmental delay, visual impairment

29. Rheumatoid arthritis - pleural effusion :

- low pH

- Low glucose
- High LDH
- High cholesterol
- Exudate

30. D-Penicillamine → pancytopenia, acute tubulointerstitial nephritis

31. RTA type II - urinary pH can be lowered below 5.3 after ammonium chloride administration.

RTA type I - we cannot lower urine pH as it is due to failure of collecting ducts to secrete hydrogen ions.

32. Duke A stage of colon cancer

- colonoscopy - yearly for the first two years
- Afterwards every 3 years
- CEA used to monitor for recurrence

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## DERMATOLOGY PASSMEDICINE & PASTEST

1. Acanthosis Nigricans

- Symmetrical, brown, velvety plaques - neck, axilla, groin.

Causes :

- type 2 diabetes mellitus
- gastrointestinal cancer
- obesity
- polycystic ovarian syndrome
- acromegaly
- Cushing's disease
- hypothyroidism
- familial
- Prader-Willi syndrome
- drugs
  - combined oral contraceptive pill
  - nicotinic acid

Pathophysiology - insulin resistance —> hyperinsulinaemia —> stimulation of keratocytes and dermal fibroblast proliferation Vira interaction with IGFR 1

## 2. Acne Vulgaris

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

Mx :

- mild to moderate - 12 week course of topical combination therapy is first line
  - (a) Fixed combination of **topical adapalene with topical benzoyl peroxide**
  - (b) fixed combination of **topical tretinoin with topical clindamycin**
  - (c) fixed combination of **topical benzoyl peroxide with topical clindamycin**
- moderate to severe acne :
- 12 week course of one of the following options :
  - a fixed combination of topical adapalene with topical benzoyl peroxide
  - a fixed combination of topical tretinoin with topical clindamycin
  - a fixed combination of topical adapalene with topical benzoyl peroxide + **either oral lymecycline or oral doxycycline**
  - a topical azelaic acid + either oral lymecycline or oral doxycycline
- **Minocycline** - not used because of irreversible hyperpigmentation
- a topical retinoid (if not contraindicated) or benzoyl peroxide should always be co-prescribed with oral antibiotics to reduce the risk of antibiotic resistance developing. Topical and oral antibiotics should not be used in combination



- Gram-negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs

Following patients to be referred to a dermatologist :

- patients with acne con globate acne : rare and severe form mostly in men that presents with extensive inflammatory papules, suppurative nodules and cysts on the trunk
- Acne with scarring
- Acne with persistent pigmentary changes
- Mild to moderate acne not responding to two completed courses of treatment
- Moderate to severe acne not responding to previous courses including oral antibiotic.

Pathophysiology is multifactorial

- **follicular epidermal hyperproliferation** resulting in the formation of a **keratin plug**. This in turn causes obstruction of the pilosebaceous follicle. Activity of sebaceous glands may be controlled by androgen, although levels are often normal in patients with acne
- colonisation by the anaerobic bacterium *Propionibacterium acnes*
- inflammation

### 3. Actinic Keratoses

- Common premalignant condition due to chronic sun exposure
- Small, crusty, or scaly lesions
- Pink, red, brown or skin colour
- On sun exposed areas
- Multiple lesions ++

Mx:

- sun avoidance, sunscreen
- Fluorouracil cream - 2 to 3 week course - skin will become red and inflamed
- Topical diclofenac - mild AK
- Topical Imiquimod

4. Alopecia areata : autoimmune condition - localised, well demarcated patches of hair loss. At the edge of hair loss - small, broken, exclamation mark hairs.

- Hair will regrow in 50% of patients by end of 1 year, and 80-90% eventually.
- Other treatment options : topical minoxidil, topical corticosteroids, phototherapy

#### 5. Bullous pemphigoid

- Autoimmune conditions causing sub-epidermal blistering of skin
- Secondary to development of antibodies against hemidesmosomal protein BP180 and BP230
- More common in elderly patients
- Itchy tense blisters typically around flexures
- Blisters heal without scarring
- No mucosal involvement - mouth is spared
- IF - IgG and C3 at dermo-epidermal junction.
- Mx : oral corticosteroids, immunosuppressants.

6. **Eczema herpeticum** - HSV 1 or 2; atopic eczema association; rapidly progressive painful rash.

O/E : monomorphic, punched out erosions - circular, depresses, ulcerated lesions

Mx : IV Aciclovir

#### 7. **Erythema multiforme** :

- Target lesions
- Seen on hands / feet before spreading to torso
- Upper limbs >> lower limbs

Causes :

- viruses - HSV, Orf (Paradox virus)
- Idiopathic
- Bacteria - Mycoplasma, Streptococcus
- Drugs - Penicillin, Sulphonamides, Carbamazepine, Allopurinol, NSAIDs, Nevirapine, OCP
- SLE
- Sarcoidosis
- Malignancy

## 8. **Fungal nail infections : Mx -**

- limited involvement - < 50 % nail affected, ≤2 nails affected, more superficial white onychomycosis - **topical treatment with 5% amorolfine nail lacquer** - 6 months for finger nails, 9-12 months for toenails
- Extensive involvement - due to dermatophyte infection - **Oral terbinafine** - 6 weeks to 12 weeks fingernails, 3-6 months for toe nails
- More extensive involvement due to Candida infection : **oral itraconazole** - pulsed weekly therapy.

9. The Koebner phenomenon describes skin lesions that appear at the site of injury. It is seen in:

- psoriasis
- vitiligo
- warts
- lichen planus
- lichen sclerosus
- molluscum contagiosum

## 10. Lichen planus

### Features

- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, with a 'white-lines' pattern on the surface (Wickham's striae)
- Koebner phenomenon may be seen (new skin lesions appearing at the site of trauma)
- oral involvement in around 50% of patients: typically a white-lace pattern on the buccal mucosa
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:

- gold
- quinine
- thiazides

## 11. Livedo Reticularis

### Causes

- idiopathic (most common)
- polyarteritis nodosa
- systemic lupus erythematosus
- cryoglobulinaemia
- antiphospholipid syndrome
- Ehlers-Danlos Syndrome
- homocystinuria

## 12. Malignant Melanoma

### Types :

- 1) Superficial Spreading : 70% of cases; arms, legs, back, chest; growing moles
- 2) Nodular : most aggressive, second most common; sun exposed skin, red or black lump or lump which bleeds or oozes
- 3) Lentigo maligna : less common, chronic sun exposure, older patients
- 4) Acral lentiginous : rare form, nails, palms and soles; sublingual pigmentation (Hutchinson's sign)

### Major diagnostic criteria :

- change in shape
- Change in size
- Change in colour

### Secondary minor criteria

- diameter  $\geq 7$  mm
- Inflammation
- Oozing or bleeding
- Altered sensation

0 - 1 mm  $\rightarrow$  1 cm margin of excision

1 - 2 mm  $\rightarrow$  1 - 2 cm

2 - 4 mm  $\rightarrow$  2 - 3 cm

$> 4$  mm  $\rightarrow$  3 cm margin

## 13. Onycholysis

Onycholysis describes the separation of the nail plate from the nail bed

### Causes

- idiopathic
- trauma e.g. Excessive manicuring
- infection: especially fungal
- skin disease: psoriasis, dermatitis
- impaired peripheral circulation e.g. Raynaud's
- systemic disease: hyper- and hypothyroidism

14. **Pityriasis versicolor** - yeast *Malassezia furfur* - hypopigmented, well demarcated macules covered in a very fine scale. Most often occur on chest, back, and abdomen. Macules go often unnoticed until the patient tans the surrounding skin. Treatment -> topical clotrimazole or ketoconazole

### 15. **Porphyrria cutanea tarda**

- Most common haptic porphyria
- Defect in **uroporphyrinogen decarboxylase**
- Or due to hepatocyte damage due to alcohol, hepatitis C, Estrogen.
- Photosensitive rash with blistering and skin fragility on face and dorsal aspects
- Hypertrichosis
- Hyperpigmentation
- Labs - elevated uroporphyrinogen, pink fluorescence on Wood's lamp
- Mx : Chloroquine, Venesection if ferritin > 600 ng/mL

### 16. **Psoriasis - exacerbating factors :**

- trauma
- Alcohol
- Beta blockers
- Lithium
- Anti malarial - chloroquine, hydroxychloroquine
- NSAIDs
- ACE inhibitors
- Withdrawal of systemic steroids
- Streptococcal infection —> guttate psoriasis.

## 17. **Pyoderma gangrenosum**

- Neutrophilic dermatosis
- Dense infiltration of neutrophils in the affected tissue.

Causes :

- idiopathic
- IBD - Crohn's=, Ulcerative colitis
- SLE, RA
- Myeloproliferative disorders
- Lymphoma
- Myeloid Leukaemia
- Monoclonal gammopathy IgA
- Granulomatosis with polyangitis
- Primary biliary cirrhosis

Mx : Oral steroids - 1st line treatment.

Ciclosporin, Infliximab may have a supportive role.

## 18. **Topical Brimonidine - alpha adrenergic agonist -**

predominant erythema / flushing in acne rosacea.

Mild to moderate papules / pustules in rosacea —> topical ivermectin is 1st line ; alternatives - topical metronidazole or topical azelaic acid

Moderate to severe rosacea —> topical ivermectin + oral doxycycline

Referral —> rhinopyoma

## 19. **Anti-envoplakin —> number of antibodies are observed in paraneoplastic pemphigus.**

- **Envoplakin**
- **Periplakin**
- **Bullous pemphigoid antigen I**
- **Desmoplakin**
- **Desmoplakin II**
- **Plectin**
- **Alpha 2 macroglobulin like - 1**

- **Antibodies to pemphigus vulgaris ( desomoglein 3)**
- **Antibodies to pemphigus foliaceus (desomoglein 1)**

## **20. Sezary syndrome** - type of T cell cutaneous lymphoma

- pruritic
- Erythroderma typically affecting palms, soles and face
- Atypical T cells
- Lymphadenopathy
- Hepatosplenomegaly

## **21. Skin disorders associated with malignancy**

| <b>Skin disorder</b>               | <b>Associated malignancies</b>                                              |
|------------------------------------|-----------------------------------------------------------------------------|
| Acanthosis nigricans               | Gastric cancer                                                              |
| Acquired ichthyosis                | Lymphoma                                                                    |
| Acquired hypertrichosis lanuginosa | GIT and lung cancer                                                         |
| Dermatomyositis                    | Ovarian and lung cancer                                                     |
| Erythema gyratum repens            | Lung cancer                                                                 |
| Erythroderma                       | Lymphoma                                                                    |
| Migratory thrombophlebitis         | Pancreatic cancer                                                           |
| Necrolytic migratory erythema      | Glucagonoma                                                                 |
| Pyoderma gangrenosum               | Myeloproliferative disorders                                                |
| Sweet's syndrome                   | Haematological malignancy -<br>Myelodysplasia - tender, pruritic<br>papules |
| Tylosis                            | Oesophageal cancer                                                          |

## **22. Tinea incognito** - worsening of fungal rash due to steroid cream application

## **23. Toxic epidermal necrolysis**

- Immune complex mediated hypersensitivity —> type IV HS RXN
- Flu like prodrome —> f/b red/purple rash which then forms blisters / forms bullae affecting skin, mucous membranes, eyes and genitalia
- HLA B1502 , HLA B1508

- HLA B1502 → marker for carbamazepine induced Steven Johnson Syndrome and TEN in Han Chinese; delayed hypersensitivity → T cells are involved.

Drug causes :

- Allopurinol
  - Cephalosporin
  - NSAID
  - Phenytoin
  - Carbamazepine
  - Sulfa group antibiotics
  - Sulfasalazine
  - Sertraline
  - Antiviral - Nevirapine
- 
- Skin lesions most commonly found on palms and soles, trunks, hands
  - Macules → papules → vesicle bullae → widespread erythema
  - Bullae can rupture and give rise to secondary infections
  - Target lesions \*\*\*
  - Areas of central necrosis
  - Nikolsky sign positive
  - SCORTEN system - predicts mortality
  - Age >40, presence of malignancy, HR > 120, Epidermal detachment > 10% of body surface, serum glucose > 14, bicarbonate < 20, serum urea > 10
  - ≥ 5 score → 90% mortality
  - IV Fluids
  - Daily ophthalmology review
  - Emollients and dressings
  - Surgical interventions
  - Lung care - physiotherapy, aspiration, steroids

Long term sequelae -

1. Permanent skin changes including pigmentation
2. Scarring
3. Temperature sensitivity
4. Nail dystrophy
5. Perfect erosions of mucous membranes
6. Vaginal, anal and urethral strictures



## 7. Hair loss

\*\* Fluid loss —> increased viscosity —> plus inflammation = increased risk of VTE

24. This patient has metastatic melanoma.

- One of the treatment choices in this situation is checkpoint inhibitors, of which nivolumab is an example.
- Checkpoint inhibitor induced colitis is an inflammatory condition affecting the colon (colitis), which is caused by cancer immunotherapy (checkpoint inhibitor therapy). Symptoms typically consist of diarrhea, abdominal pain and rectal bleeding.
- It is a monoclonal antibody that binds the programmed cell death protein 1 (PD-1) receptor on T cells preventing it from binding to its ligands on normal cells.
- PD-1 is a checkpoint protein found on the T cells that prevent it from attacking normal cells in the body.
- It binds to programmed cell death protein 1 ligand (PD-L1), expressed in normal cells, and this binding helps the T cells identify the cell as being native & not foreign.
- Some cancer cells also express these receptors and evade the normal immune response.
- Monoclonal antibodies can block the binding of PD-1 or PD-L1 and boost the immune response, thereby have the potential to help fight cancer.
- Some examples of PD-1 inhibitors are **nivolumab**, **pembrolizumab** etc.
- These medications are associated with a myriad of immune-mediated adverse effects.
- Some common ones are diarrhoea, pneumonitis, nephritis, rash and pruritis.
- The preferred management for this condition is moderate to high potency topical steroids. In severe cases, stop the checkpoint inhibitor, and consider systemic steroids.

25. **Porphyrria cutanea tarda (PCT)** is a type of porphyria characterized by photosensitivity, bullae formation on sun-exposed areas, and fragile skin that can easily tear or blister. The patient's

history of hypertrichosis also supports this diagnosis, as it is a common feature in PCT.

26. A history of a non-healing ulcer at the site of a burn injury should be investigated immediately for SCC. Squamous cell carcinomas arising in chronic wounds tend to be more aggressive so early diagnosis and biopsy are important to prevent metastatic disease. They can also be seen in other chronic wounded, scarred or inflamed skin e.g. skin overlying focus of osteomyelitis, scars, radiotherapy scars and venous ulcers.

SCC = keratin pearls

27. According to the British National Formulary (BNF) and National Institute for Health and Care Excellence (NICE) guidelines, oral erythromycin is considered safe for use in pregnancy if topical treatments are ineffective. It's a macrolide antibiotic that has anti-inflammatory properties which can help reduce acne lesions.

**28. Chronic plaque psoriasis Mx :**

- Regular emollients - helps with scale loss and reduces pruritus
- **1st line** : potent topical corticosteroid OD + vitamin D analogue OD
- Apply steroid and vitamin D analogue both separately
- **2nd line** : no improvement after 8 weeks —> vitamin D analogue **twice daily**
- Short acting dithranol may be used.

Secondary care management :

- Phototherapy - UV B light is the choice - 3 times a week
- Photochemotherapy - Psoralen + UV A (PUVA)
- Adverse effects - ageing of skin, increased risk of SCC

Systemic therapy :

- Oral MTX is used first line
- Ciclosporin
- Systemic retinoids
- Biologicals - Infliximab, Etanercept, Adalimumab
- Ustekinumab —> IL-12 and IL-23 blockers

## Guttate psoriasis : Ultraviolet B Phototherapy

29. Eczema herpeticum —> occurs when existing areas of eczema are super-infected with HSV or HZV.

Mx : IV Acyclovir

Additional Abx may be required if there are signs of superimposed bacterial cellulitis, tenderness or pus formation.

30. Necrobiosis lipodica - rare condition affecting the diabetics; painless and can ulcerate following injury,

Rx - topical or intra-lesional steroids.

31. Benign Skin Lesions :

- Angiomas - overgrowth of blood vessels; red pigmentation; blanches under pressure
- Pyogenic granulomas : trauma causes overgrowth of blood vessels; dark red nodules; grows quickly, +/- bleeding
- Lentigines - Liver spots : due to sun exposure, in children; brown macules
- Seborrhoeic keratosis - Basal cell papillomas - greasy and smooth lesion, looks stuck on, pigmented
- Dermatofibroma - pigmented papules / nodules. Symmetrical and regular border, overgrowth of fibrous tissues

32. Porphyria cutanea tarda

- Photosensitivity
- Blistering resulting in scars and milia (tiny inclusion cysts)
- Skin fragility
- Hypertrichosis and sclerodermatous changes
- PCT = deficiency of uroporphyrinogen decarboxylase
- Raised levels of urinary uroporphyrin

33. Basal cell carcinoma - nodular type

- lesions are described as pearly - impressions of being shiny or translucent
- There may be a rolled edge or central depression
- Small central scab or ulcer
- BCC - head and neck
- Mohs' microscopic surgery - where tissue sparing is important - lips, eyelid —> entire cut surface of the excision specimen is

checked histologically for clearance, making wide margins unnecessary

### 34. Pemphigus vulgaris - \*\*\* mucosal involvement

- Ulceration, flaccid blisters on trunk
- **Split is superficial** —> blister roof is fragile and easily disrupted to leave erosions
- Bullous pemphigoid - split is deep and occurs at derma-epidermal junction —> thick blister roof, prominent tense blister (erosions less likely) ; NO mucosal involvement; IF - linear IgG and C3 deposition.
- Blisters can be extended with gentle lateral pressure - Nikolsky's sign
- Typical changes on skin biopsy and direct IF —> intraepidermal split just above the basal layer, with evidence of **acantholysis. IF = IgG deposition**
- Associated with Ashkenazi Jewish origin - antibodies against Desmoglein 3
- Systemic corticosteroids
- Steroid sparing agents like MMF / Azathioprine

### 35. Zinc deficiency clinical features :

- Anorexia
- Lethargy
- Diarrhoea
- Growth retardation
- Delayed sexual maturation
- Hypogonadism & hypospermia
- Alopecia, dermatitis, paronychia
- Intellectual disability, impaired nerve conduction and nerve damage
- Hepatomegaly
- Immune disorders and increased susceptibility to infections

### 36. Lichen planus - itchy, violaceous, polygonal, flat-topped papular rash affecting wrists and ankles

\*\* pale lacy network in mouth known as Wickham's strain  
Koebner phenomenon typically seen

### 37. Toxic Epidermal Necrolysis drugs :

- sulphonamides
- Ampicillin
- Carbamazepine
- Sodium valproate
- Allopurinol
- Phenytoin
- Corticosteroids
- Piroxicam
- Paroxetine

38. Pyoderma gangrenosum - autoimmune hepatitis, primary biliary cholangitis (PBC) - nodules in the area which broke down to form a boggy ulcer with a raised inflammatory border.

39. Acne rosacea : blepharitis, conjunctivitis, keratitis  
Topical antibiotics —> Metronidazole gel

\*\* Ocular symptoms - oral tetracycline

40. The patient presents with a monomorphic rash characterised by punched-out erosions approximately 2mm in diameter, extensively involving her face and neck. Among the provided options, this presentation aligns most closely with eczema herpeticum. This dermatological emergency is predominantly observed in children with an existing history of atopic conditions. The causative agents are either HSV-1 or HSV-2 viruses, and the condition can be life-threatening. Therefore, it necessitates admission for intravenous aciclovir.

41. Antibodies against **desmoplakin I** are seen in **paraneoplastic pemphigus**.

- **Antibodies against desmoplakin II** are also seen in **paraneoplastic pemphigus**.
- **Antibodies against desmocollin 1** are found in **subcorneal pustular dermatosis type of IgA pemphigus**.
- **Antibodies against desmoglein 1** are formed in **pemphigus variants** such as pemphigus foliaceus, pemphigus erythematosus and fogo selvagem

42. This patient has presented with a classic description of livedo reticularis, a discolouration of the skin resulting from reduced blood flow through the arterioles that supply the cutaneous capillaries, commonly affecting the lower limbs. Livedo reticularis may be idiopathic in nature but is usually secondary to another condition, often some form of vasculitis. The autoimmune vasculitis **systemic lupus erythematosus** (SLE) is one of the commonest conditions associated with the diagnosis and therefore should be investigated for if not already established in this patient.

\*\*\* **hypercalcemia** - may be associated with livedo reticularis due to raised serum calcium levels deposition in capillaries, reducing blood flow.

\*\*\* Livedo reticularis - can be seen in **Graves' hyperthyroidism** as a rare manifestation.

43. Keloid scar - more common in young, black adults. **Rarely seen in children.**

44. In fact, some studies have suggested that valproate may even have a beneficial effect on psoriasis due to its anti-inflammatory properties.

45. The patient exhibits features of hyperthyroidism and diffuse goitre. Coupled with ophthalmopathy, her condition is indicative of Graves' disease. The third component of the classic triad of Graves' disease is pretibial myxoedema. This condition is characterized by bilateral, symmetrical, non-pitting, scaly thickening of the skin **with an orange-peel appearance**. Pretibial myxoedema most commonly occurs over the lower legs, particularly on the pretibial areas or dorsum of the foot.

#### 46. **Onycholysis**

- Idiopathic - excessive manicuring or wetting of nails
- Thyrotoxicosis
- Dermatological disease - psoriasis, fungal infection, dermatitis
- Systemic disease - impaired circulation, hypothyroidism, hyperthyroidism
- Raynaud's

47. Lichen planus shows Koebner phenomenon - new disease lesions at site of skin injury

**True Koebner phenomenon** —> Lichen planus, Psoriasis and Vitiligo

48. Photosensitive drugs :

- Doxycycline
- NSAIDs
- Retinoids
- Diuretics - thiazide and loop
- Amiodarone
- Diltiazem
- Enalapril
- Quinidine
- Phenothiazines
- Sulfonylureas

49. **Acute Intermittent Porphyria**

- Defect in enzyme **uroporphobilinogen deaminase**
- Women >> men; **northern Sweden population**
- **UROS gene defect on chromosome 10 \*\*\*\***
- Precipitating factors :
  - A. Alcohol
  - B. Fluctuations in female sex hormones
  - C. Infections
  - D. Starvation
  - E. Drugs - Barbiturates, Sulphonamides, Carbamazepine, Phenytoin, OCP, Rifampicin
- Porphyrins have reddish color and URO breaks down to form uroporphobilin - brownish pigment causes deep red urine
- Increased urinary excretion of both porphyrin precursors and porphyrins.

C/F :

- autonomic neuropathy - abdominal pain, constipation, vomiting, tachycardia, HTN, postural hypotension
- Dark red urine
- Respiratory failure - bulbar paresis
- Cerebellar signs

- Hypothalamic dysfunction
- Hyponatremia - SIADH or GIT losses
- Psychiatric - delirium, confusion, agitations, disorientation, hallucinations

Dx : Urinary porphobilinogen, urinary total porphyrins, serum PBG

Acute attacks - hyponatremia, hypomagnesemia, and hypovolaemia

\*\* increased serum cholesterol, serum iron and T4

LFT - sulfobromophthalein retention

Mx : Mild acute attacks - IV haemin

Alternative - IV glucose - 300 g of dextrose 10% glucose

\*\* Frequent recurrent cyclic attacks in women —> GnRH Analogues.

#### 50. **Sweet's syndrome**

- Triggers are - drugs, infection, underlying cancers
- Skin lesions - plum coloured and may be papules, plaques or nodules
- Mucosa involvement +/- , blisters +/-
- Fever +++ , neutrophilia +++
- Dx : skin biopsy

#### 51. **Dermatitis herpetiformis**

- **HLA B8, DQ2, DQ3**

- Skin Bx : sub-epidermal blisters with neutrophil micro abscess in dermal papillae
- IF - +ve for IgA staining

52. Psoriasis - Th 17 cells —> IL-17 —> Ixekizumab = anti IL-17 antibody - treatment of active psoriasis and reducing risk of occurrence.

#### 53. **Melasma / Chloasma**

- Hormone stimulated increased melanogenesis on face
- More common in darker skin types



- Estrogens - Either endogenous or exogenous plays an important role
- Precipitated in pregnancy or estrogen containing contraceptives
- Worsened by skin exposure
- Usually symmetrical - affecting the cheek area and upper lip - forehead
- Rigorous skin protection

#### 54. **Darier's disease**

- **Autosomal dominant** condition with characteristic cutaneous features
- Warty papules and plaques in seborrhoeic areas - central chest, back, scalp, flexures, palmar pits
- Nail changes - nail atrophy, dystrophy
- Secondary infection of lesions —> crusting and malodour
- Mx : Retinoid acitretin symptomatic cases

55. Non Hodgkin's Lymphoma —> Paraneoplastic pemphigus; appears to worsen in patients with NHL.

Rx - high dose corticosteroids.

56. Erythema gyratum repens - paraneoplastic eruption with **wood-grain** pattern and figurate erythema seen in patients with **lung cancer**.

57. Hair products and hair dyes, henna —> **para-phenylamine diamine**

\*\*\* topical steroids are treatment of choice.

58. NF-1 - chromosome 17 —> peripheral neurofibromatosis. Cafe au lait patches, axillary freckling.

Estrogen responsive —> increase in size during pregnancy and axillary freckling.

**Autosomal dominant**

59. Immunosuppression — > common cause of atypical shingles —> multi dermatomal shingles ; Mx - IV Acyclovir

60. **Cheiroarthropathy** - stiff hand syndrome - prolonged duration of diabetes and presence of microvascular complications

Condition of frozen shoulder + carpal tunnel can be part of cheiroarthropathy.

Improved glucose control + physiotherapy.

### 61. **Secondary syphilis**

- Develops 4-12 weeks after primary infection
- Macular or papular rash → symmetrical on trunk, limbs, palms and soles
- Rash is pale pink and non-pruritic
- Confluent plaques = condyloma lata - moist flexures
- Erosions may be present on mucosa surfaces
- Muscle and joint pains, generalised lymphadenopathy
- Patchy alopecia \*\*\*

### 62. Behcet's disease

- cutaneous : erythema nodosum, acneiform lesion, pathergy (abnormal response to tissue injury)
- GIT - abdominal pain, diarrhoea
- CNS - meningitis, confusion, headache
- Vascular - large vessel disease can lead to venous thrombosis, and arterial vasculitis and aneurysms.

63. Guttate psoriasis is a type of psoriasis that presents as small, erythematous papules and plaques with fine scaling, often triggered by a preceding streptococcal infection such as tonsillitis. In this case, the patient's recent history of exudative tonsillitis, along with the description of the rash involving the torso and limbs with erythematous lesions and fine scale, strongly supports the diagnosis of guttate psoriasis.

64. The patient has an itchy vesicular rash on the buttocks with a background of coeliac disease. This is highly likely to be dermatitis herpetiformis which is associated with coeliac disease. If biopsied, the lesions will demonstrate IgA deposition in the dermis on immunofluorescence.

65. The patient presents with a blistering rash on the face and dorsal hands provoked by sunlight and alcohol. In addition, there is hypertrichosis (excessive hair growth in non-androgen-dependent areas of the body). These findings suggest a diagnosis of porphyria

cutanea tarda. This can be inherited or acquired due to hepatocyte damage (i.e. hepatitis C infection or alcohol excess). In the setting of negative testing for hepatitis C and the absence of alcohol excess, this is likely due to an inherited defect in uroporphyrinogen decarboxylase. Hepatitis C is a common cause of porphyria cutanea tarda and serology should always be checked in suspected cases.

66. Primary herpes simplex infection, caused by the *Herpes Simplex Virus (HSV)*, can lead to a condition known as erythema multiforme. This is a type of hypersensitivity reaction that presents as a rash with target-like lesions or 'bull's-eye' appearances. It often occurs following certain infections, including HSV.

**Erythema ab igne** is incorrect because it is a skin condition caused by long-term exposure to heat or infrared radiation, not related to an infection like HSV. It presents as a mottled, red-brownish discolouration of the skin and does not develop after herpes simplex infections.

**Erythema nodosum** is also incorrect. Erythema nodosum is an inflammatory condition that causes tender, red nodules under the skin, typically on the shins. Although it can occur in response to various triggers such as infections, drugs and diseases like sarcoidosis and inflammatory bowel disease, it isn't usually associated with herpes simplex infections.

Erythema nodosum is a type of panniculitis, an inflammation of the subcutaneous fat. It typically presents as painful, erythematous nodules on the shins and is usually self-limiting. In most cases, the lesions will resolve spontaneously without scarring within 1-2 months.

The option **Erythema chronicum migrans** isn't correct either. This rash is characteristic of Lyme disease, which is caused by the bacterium *Borrelia burgdorferi*, transmitted through tick bites. It typically starts as a small red spot at the site of the tick bite and expands over time to form a large round rash.

Finally, **Erythema marginatum** is incorrect because this rash is most commonly associated with rheumatic fever - an inflammatory disease that can develop after an infection with group A Streptococcus bacteria causing strep throat or scarlet fever - not with primary herpes simplex infection. The rash appears as pink rings on the torso and inner surfaces of the limbs which come and go for as long as several months.

67. **Topical eflornithine** acts on the hair follicle to inhibit hair growth. It is the first-line treatment for facial hirsutism and results are usually seen after 6-8 weeks. Hair growth returns if the use of this treatment is stopped.

68. This child has presented with the classic progression of eczema herpeticum where a disrupted skin barrier, often secondary to another condition such as atopic eczema, is infected by herpes simplex virus 1 or 2. Coxsackievirus A16 or vaccinia virus can also cause the infection. The condition presents with a rapidly increasing rash along with other symptoms including fever, lymphadenopathy and bowel changes. Eczema herpeticum is a severe, disseminating infection that can progress to multiple end-organ-failure rapidly and therefore requires **IV aciclovir** urgently if suspected.

69. Various small bowel diseases that cause destruction or malfunction of the gut mucosa and malabsorption lead to zinc deficiency. This has similarly been noticed in patients on total parenteral nutrition (TPN) who do not receive zinc - resulting in acrodermatitis herpetiformis causing peri-orificial dermatitis and alopecia.

Selenium deficiency can contribute to fatigue, hair loss, weight gain, joint and muscle pain.

Iron deficiency can contribute to fatigue, weakness, pale skin, chest pain, shortness of breath, headache, dizziness and cold peripheries.

Vitamin B12 deficiency can cause a smooth tongue, nerve problems like numbness or tingling, pale skin and weakness.

Folate deficiency can cause a lack of energy, pale skin, palpitations, headaches and loss of appetite.

70. Seborrheic dermatitis, which is believed to be due to several factors including an inflammatory response to the fungus *Malassezia furfur*, commonly affects areas of the body high in oil-producing glands such as the scalp, face and chest. Although the condition affects approximately 2-5% of the general population it is significantly associated with immunocompromise and can affect 85-95% of patients with **HIV**. Although the exact mechanism is not fully understood it is likely that immunocompromised patients are at increased risk due to the overgrowth of the *Malassezia* yeast.

## HIV & Parkinson's disease

71. **Erythema gyratum repens** - associated with internal malignancies - is characterised by a number of concentric, erythematous, from either flat to slightly raised bands with fine white scale in waves located at the leading edge of erythema. Their appearance may represent a wood-grain pattern. It can often precede a diagnosis of typically lung cancer by an average of nine months.

72. **Skin biopsy** is the gold standard test used to diagnose dermatitis herpetiformis which is the condition being described in this case. A punch biopsy is taken from the periphery of the lesion and is observed under direct immunofluorescence microscopy. The results will show granular deposits of immunoglobulin A (IgA) within the dermal papillae.

73. Pompholyx eczema (also known as dyshidrotic eczema) is a type of vesicular hand dermatitis. It is more common in young adult females and is commonly related to sweating, with flares during hot weather and humid conditions. It manifests as recurrent crops of vesicles and/or blisters on the palms which can cause intense itching and burning. The vesicular stage is usually followed by a dry, desquamating phase in which the skin can peel, crack or crust.

Although the aetiology is unknown triggers include 1

- humidity e.g. increased sweating (due to climate, hyperhidrosis)
- irritants e.g. water, detergents, metals (nickel)
- lifestyle e.g. smoking
- drug use e.g. aspirin and COCP
- fungal infections

74. The most likely diagnosis in this case is **Erythrasma**.

Erythrasma is a superficial skin infection caused by the bacterium *Corynebacterium minutissimum*. It typically presents as well-defined, pink or brown patches with fine scaling and superficial fissures in intertriginous areas such as the groin, axillae, and inframammary folds. The condition is often asymptomatic and can be confirmed by observing coral-red fluorescence under Wood's lamp examination due to the presence of porphyrins produced by the bacteria.

75. The correct answer is **allergic contact dermatitis**. The patient's history of having her hair dyed 2 days ago, along with the distribution of the rash around her hairline but sparing the scalp itself, strongly suggests an allergic reaction to a component in the hair dye. Allergic contact dermatitis is a type IV hypersensitivity reaction that occurs when an allergen comes into contact with the skin, causing inflammation and a vesicular rash.

76. Pemphigoid gestationis = BLISTERS

77. This case presents a patient with suspected hereditary haemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu syndrome. HHT is an inherited condition characterized by an **autosomal dominant pattern of inheritance and age-related penetrance**, with the majority of individuals manifesting symptoms such as recurrent epistaxis (nosebleeds) during adolescence.

In cases where HHT is suspected, it is imperative to conduct a family history and consider referral for genetic testing. Most cases are attributable to mutations in the endoglin or ACVRLK1 genes,

though mutations in other genes, including SMAD4, RASA1, and BMPR9, may also be causative.

Autosomal dominant with age related penetrance.

78. Seborrhoeic dermatitis - otitis externa and blepharitis

79. Granuloma annulare - papular lesion with hyperpigmentation on central depression; oral surfaces of hands and feet - extensor aspects of arms and legs

80. **Necrobiosis lipoidica diabetorum**. This condition is a rare skin disorder of unclear aetiology, often associated with diabetes mellitus. It typically presents as shiny, atrophic, yellow-brown plaques on the shins with telangiectasia and occasional ulceration. The patient's age, the location of the lesion and its description fit this diagnosis.

81. **uroporphyrinogen decarboxylase**, leading to the presentation of porphyria cutanea tarda (PCT). Uroporphyrinogen decarboxylase converts uroporphyrinogen III into coproporphyrinogen III, one of the many reactions in synthesizing heme. The patient has a new blistering rash on sun-exposed areas of the body after a holiday to a country with a hot climate, implying photosensitivity. Given the familial history and raised urinary uroporphyrinogen the most likely diagnosis is PCT.

82. Onycholysis - Drugs - **Doxycycline, Tetracyclines, Psoralens**  
Onycholysis - pemphigus vulgaris.

Arsenic poisoning - **Mees' line** —> **transverse lines across nail plate**

83. **Kaposi's sarcoma**

- associated with HHV-8
- Tends to present with red, purple or brown cutaneous nodules or plaques.
- Typically affects legs, head and neck.
- Can be seen in elderly, non immunocompromised
- HIV associated Kaposi, endemic KS (Africa - young individuals)

- KS can affect lymph glands and internal organs

#### 84. **Alopecia areata**

Autoimmune associations -

- vitiligo
- Thyroid disease
- Pernicious anaemia
- Rheumatoid arthritis
- Diabetes
- 1/3 of patients have positive family history

#### 85. **Necrobiosis Lipodica**

- Poorly responsive to treatment
- Unusual complications of diabetes, can occur in non-diabetes patients also
- Small vessel damage leading to partial necrosis of dermal collagen and connective tissue —> histiocytic cellular response
- Skin over shins commonly involved
- Erythematous plaques that develop yellowish - brown plaques discolouration with atrophy and prominent telangiectasia
- Females >>> males

#### 86. Pityriasis rosea - human herpes virus - 7

- Recent viral infection
- Herald patch usually on trunk
- Erythematous, oval, scaly patches with longitudinal diameters of oval lesions along lines of Laugier - fir tree appearance
- Tear drop scaly papules on trunk and limbs
- Mx : self limiting ; UVB Phototherapy

#### 87. Ane rosacea - Management

- Simple measures : sunscreen, camouflage creams
- Predominant erythema / flushing -
  - A. Topical briminodine gel - only if there is limited telangiectasia
  - B. Briminodine - topical alpha adrenergic agonist
- Mild to moderate : topical ivermectin / topical metronidazole / topical azelaic acid
- Moderate to severe : topical ivermectin + oral doxycycline



- Referral if treatment resistant for surgery

88. Mastocytosis is a diverse group of disorders characterised by the expansion and accumulation of mast cells in one or more organ systems. There are several subtypes and the diagnostic criteria will be outlined below.

Indolent:

No B or C findings

**Smouldering = 2 or more B findings** (B = burden of disease):

- Bone marrow >30% mast cells and/or Tryptase >200 ng/ml and/or KITD816V mutation with a variant allele frequency (VAF) of >10%
- Signs of dysplasia or myeloproliferation without frank associated haematological neoplasm, and a normal FBC
- Hepatomegaly without liver dysfunction and/or splenomegaly without hypersplenism

**Aggressive = 1 or more C findings** (C = cytoreduction-requiring i.e. organ dysfunction):

- One or more cytopenias (Hb <100, platelets <100, neutrophils <1.0)
- Hepatomegaly with liver dysfunction
- Osteolytic lesions or fractures
- Splenomegaly with hypersplenism
- Malabsorption with weight loss due to GI infiltration

Aggressive systemic mastocytosis is correct. The patient has clinical and biochemical features to support a diagnosis of mastocytosis. The rash described is urticaria pigmentosa. The raised monocytes and positive urinary histamine add further weight to the diagnosis. A bone marrow aspirate, trephine, cell markers, and cytogenetics would be required to make the diagnosis definitively. The presence of end-organ dysfunction (e.g. Hb < 100 and platelets < 100) favours the diagnosis of aggressive systemic mastocytosis in this case.

89. Any melanoma > 1 mm depth —> **sentinel lymph node biopsy**

90. **Lupus pernio : AKA chronic cutaneous lupus** : persisten red to purple indurated plaques and nodules which mostly affects the nose, cheeks, ear and fingers.  
Associated with Sarcoidosis.

91. **Acral lentiginous melanoma**

- Normally seen on sole of the foot and palm of hand
- Irregularly pigmented macules
- Thicker palpable areas may appear if it progresses
- Breswlo thickness and presence of ulceration

92. Erythema ab igne —> prolonged exposure to moderate heat —> epidermal changes including atypia and dysplasia —> increased risk of SCC.

93. Lichen sclerosus on glans penis —> **balanitis xerotica obliterans**

94. SCC —> capable of spreading via lymphatic channels; may arise from areas of actinic keratosis / Bowen's disease / chronic scars or wounds; excise is curative and Radiotherapy is effective overall.

~10% of SCC metastasise via lymphatics

Higher risk of metastasis —> large tumor size and depth, poor differentiation, site including nose, upper lip and mucosal.

95. Pyoderma gangrenosum associations :

- IBD
- Rheumatoid arhtritis
- Myeloid leukaemia
- Myelofibrosis
- Myeloma
- Monoclonal gammopathies
- Arthritides
- Diabetes
- Multiple myeloma

96. **Pseudoxanthoma elasticum**

- skin appearance is of yellow papules arranged in a linear or reticular configuration
- Skin resembles of a plucked chicken
- Renal vascular hypertension
- PVD and claudication
- Premature coronary artery disease
- MVP
- Bleeding from GIT - **upper GI haemorrhage**
- Angioid streaks ~85% of patients → linear grey or dark-red streaks with irregular edges lying beneath the retinal vessels
- Visual loss may occur due to macular involvement by a streak or scarring
- Visual acuity declines in young patient
- Skin biopsy : elastic fibers of dermis are short and fragmented; abnormal fibers are basophilic and can be seen on H&E stains; can also elicit granuloma formation.
- Special stain → Van Kossa stain → can reveal calcium deposits

97. Psoriasis → independent risk factors for cardiovascular disease

Associated with → obesity, hypertension, hyperlipidaemia, type II diabetes, metabolic syndrome, CVD - myocardial infarction

98. **Psoriasis** → epidermis is invaded by large number of T-lymphocytes → induce keratinocyte proliferation

This also causes local inflammation with unregulated production of TNF-alpha, IFN-gamma and IL-12 cells.

Elevated TNF-alpha correlates well with flares of psoriasis.

99. Acanthosis nigricans → Gastrointestinal tumor, insulin resistance, acromegaly, Cushing's syndrome, endometrial carcinoma

100. Cutaneous T-cell lymphoma

- Sezary syndrome
- Mycosis fungoides
- Classical cutaneous presentation with erythroderma - middle aged male
- SS → severe end of spectrum

- MF —> patches of erythematous skin changes
- SS —> widespread erythematous skin changes +/- keratoderma accompanied by leukaemia infiltration of bone marrow
- Histology of skin and marrow = common canal proliferation of T cells CD +ve T helper cells .

#### 101. **Pityriases lichenoides et valrioliformic acuta PLEVA**

- Initial area of erythema developing rapidly into pus filled papules

Associated with :

- toxoplasmosis
- Epstein Barr virus - atypical lymphocytes on blood
- HIV
- CMV
- Parvovirus 5th disease
- Staph. Aureus septicemia
- Group A beta haemolytic streptococcal infections

102. Sweet's syndrome - acute febrile neutrophilic dermatosis characterised by fever, neutrophilia and erythematous tender skin lesions. Associated with haematological malignancy - myelodysplasia  
Tender purple plaques.

#### 103. **Erysipelas = St Anthony's fire**

- Superficial form of cellulitis caused by group A streptococcus - Streptococcus pyogenes
- Distinctive warn, red, tender skin lesion with induration and sharply defined, raised, rapidly advancing border
- Vesicles or bullae may develop
- Desquamation of area may occur after 7-10 days
- Face is affected
- Raised WBC
- Culture of aspirated fluid —> low organism yield
- Mx : IV / oral penicillin.

104. Leukocytoclastic vasculitis —> **purpuric papules**

105. Pityriasis lichenoides - **optical tacrolimus - applied twice daily**

106. Peristomal pyoderma gangrenosum —> **topical tacrolimus**

**107. Granuloma inguinale**

- Caused by *Klebsiella granulomatis*
- Gram negative bacilli that reproduces within neutrophils, plasma cells and histiocytes.
- Painless, indurated nodule that progresses to a heaped up ulcer
- Presence on infected mononuclear cells - **Donovan bodies** - **diagnostic**
- Mx : doxycycline or TMS

**108. Granuloma annulare / necrobiosis papulosis** - associated with T1DM and T2DM, autoimmune thyroiditis and hyperlipidaemia  
- annular, skin coloured or pinkish plaque  
- Mx : topical / intralesional corticosteroid

109. *Microsporum canis* - dogs or cats ; bright green fluorescence on Wood lamp examination.

**110. Alopecia areata**

- Single or multiple, discrete, round patches of hair loss
- Non scarring alopecia
- Exclamation mark hairs - short tapered hair
- Nail pitting
- Associated with —> vitiligo, thyroid disease, pernicious anaemia, RA, DM
- Topical or intra-lesional steroids .
- Topical minoxidil
- Janus kinase inhibitors — new avenue for treatment

111. Panton valentine leukocidin PVL toxin by *Staph aureus* —> responsible for recurring skin infections.

TSST-1 - toxic shock syndrome toxin - sunburn rash, malaise, high fever, hypotension

Enterotoxin - food poisoning

Serine protease C - ScpC : Streptococcus pyogenes : immune down regulation of host and development of soft tissue infections.

\*\*\*\* Culture of intestinal secretions = Salmonella chronic carrier status - culture of intestinal secretions, faeces or urine.

\*\*\* **Spontaneous intracranial hypertension**

- headache is better when lying flat (idiopathic intracranial hypertension - headache worse when lying flat)
- Mechanism of SIH : insidious CSF leak that leads to low pressure of CSG - orthostatic headache
- Nausea, vomiting, horizontal diplopia, unsteadiness or vertigo
- Altered hearing, neck pain/stiffness, inter scapular pain, visual field abnormalities.
- Headache - gradual , sudden or thunderclap
- Dx : confirmed by measuring CSF opening pressure
- Low CSF opening pressure - **dry tap**
- MRI : pachymeningeal enhancement - sagging of brain, tonsils descent and posterior fossa crowding.
- Mx : bed rest, analgesia, increased fluid intake, epidural blood patch.

\*\*\* **Elevated thrombin time with normal retiplase time —> unfractionated heparin in sample.**

\*\*\* **Occlusion of Middle cerebral artery**

Superior division of MCA occlusion causes :

- dominant hemisphere involved : expressive aphasia
- C/L hemiparesis affects face, hand and arm, **sparing** the leg
- C/L hemisensory deficit same distribution
- **NO** homonymous hemianopia

Inferior division of MCA :

- C/L homonymous hemianopia
- Impairment of cortical sensory functions such as agraphaesthesia and stereognosis on C/L side of body
- Lack of awareness - anosognosia
- Neglect of and failure to recognise opposite side of body
- Neglect of contralateral side of external space

- Dressing apraxia
- Constructional apraxia

\*\*\* **MDR-TB**

- DOTS is recommended
- At least 5 drugs are recommended - one of which is **quinolone**
- Treatment for 9-12 months
- Treatment failure : positive culture after 4 months of therapy

\*\*\* **Liver abscess Rx : Ceftriaxone + Metronidazole**

\*\*\* **Cyclophosphamide** - prodrug that is metabolised by liver into **4-hydroxyl cyclophosphamide** —> decomposes into alkylating species + choloacetaldehyde + acrolein

**Acrolein —> hemorrhagic cystitis**

**Co-administration of mesna decreases risk of bladder toxicity.**

\*\*\* Acute pyelonephritis = Rx : oral co-amoxiclav / ciprofloxacin

\*\*\* **Paradoxical emboli - patent foramen ovale**

- right atrial pressure >>> left atrial pressure —> PFO opens and allows venous debris to enter into arterial circulation
- Typically during valsalva such as straining to pass stool, childbirth or during diving
- PFOs - requires valsalva during an ECHO with **agitated saline** to visualise them
- Bubbles can be seen entering the left atrium

**Partial anomalous pulmonary venous drainage** : between 1 to 3 pulmonary veins opens into right atrium instead of left atrium; can cause cyanosis, clubbing

**Holmes - Adie pupil :**

- anisocoria - difference in pupil size may be physiological usually < 2 mm difference or pathological or pharmacological

- **Pathological causes** : damage to sympathetic pathway and damage to parasympathetic pathway —> causes impaired dilatation and constriction respectively.
- Sluggish accommodation / light near dissociation with absent or poor constriction is indicative of Holmes - Adie pupil.
- **Anisocoria due to Holmes Adie pupil** : more appreciable in light than dark due to damage of parasympathetic nerve supply o ciliary ganglion causing impaired constriction and dilated pupil.
- Dx : confirmed by **low dose Pilocarpine (0.125%)** —> constriction in affected eye ONLY due to hypersensitivity of sphincter pupillae

### **Argyll Robertson pupil :**

- tertiary stage of syphilis
- Accommodation present
- No constriction of pupil to light
- BUT pupils are B/L involved and irregularly smaller than usual
- MORE NOTICEABLE in dark. \*\*\*\*
- Iris atrophy ++
- Dx : Syphilis serology

### **Horner's syndrome :**

- result of damage to sympathetic supply to eye
- Affected pupil - constricted with **normal response to light and normal accommodation**
- Anisocoria - **more pronounced in dark (similar to Argyll Robertson) due to impaired dilatation**
- **Mild ptosis with +/- anhydrous**
- Pharmacological test —> **Apraclonidine and cocaine to confirm diagnosis and level of injury**

\*\*\*

**Yellow discolouration** - digoxin toxicity

**Blurred vision** - direct consequence of dehydration or hyperglycaemia

**Blue discolouration** - Sildenafil - due to crossover inhibition of retinal PDE-6 activity.

**Loss of colour vision** - optic neuritis

**Loss of night vision** - retinitis pigmentosa



\*\*\* LDL particles are the main carriers of cholesterol. these particles can deposit lipid into the walls of peripheral vasculature. There is a strong association between total and LDL-cholesterol concentration and increased risk of CAD.

\*\*\* **Nitrous oxide inhalation** - predominant sensory neuropathy and associated myelopathy (weakness, combination of increased and decreased reflexes and sensory neuropathic signs)

- clinical syndrome that develops is indistinguishable from Vitamin B12 deficiency.
- Nitrous oxide - interacts with via B12 —> **selective inhibition of methionine synthase**
- Symptoms worsen in individuals and appear earlier with a underlying vit B12 deficiency.

\*\*\* **Crigler Najjar syndrome**

- autosomal inheritance
- Type 1 : autosomal recessive
- Type 2 : autosomal recessive with pseudo-dominance
- Severe unconjugated hyperbilirubinaemia results from an absence (type 1) or decreased levels (type 2) of **glucoronyl transferase**.
- Pre hepatic problem hence liver histology is normal.
- Only patients with type 2 can survive till adulthood

\*\*\* **tropical sprue**

- presents several months after people native to tropical areas migrate to temperate climate
- C/F : diarrhoea - malabsorption, steatorrhoea.
- Megaloblastic anaemia with vit B12 and folate deficiencies /
- Mx : 4-6 weeks of Ampicillin or tetracycline

| Dysfunction                  | Effects                                                      |
|------------------------------|--------------------------------------------------------------|
| Vestibular nuclei            | Vomiting, vertigo, nystagmus                                 |
| Inferior cerebellar peduncle | I/L cerebellar signs - ataxia, dysmetria, dysdiadochokinesia |

|                                                     |                                                                                        |
|-----------------------------------------------------|----------------------------------------------------------------------------------------|
| Central tegmental tracts                            | Palatal myoclonus                                                                      |
| Lateral spinothalamic tract                         | C/L deficit in pain and temperature                                                    |
| Spinal trigeminal nucleus & tract                   | I/L loss of pain and temperature                                                       |
| Nucleus ambiguus - vagus and glossopharyngeal nerve | I/L laryngeal, pharyngeal and palatal hemiparalysis; hoarseness, diminished gag reflex |
| Descending sympathetic fibers                       | I/L Horner syndrome                                                                    |

\*\*\* **Type III vWD :**

- **increased APTT and increased BT**
- Total absence of vWF
- Causes prolonged BT as absence of vWF will lead to decreased platelet adhesion to endothelium
- Factor VIII levels are also decreased in vWF type III → hence prolonged APTT.

\*\*\* **Hemophilia A & B = normal Bleeding time.**

**Factor VII deficiency - prolonged Prothrombin time**

\*\*\* **Bone marrow karyotype is most important prognostic marker in AML**

**Patients w with genetic change such as t(8;21) or chromosome 16 inversion -- low risk of relapse**

**High risk of relapse = changes in chromosome 5 or 7**

\*\*\* **Modified Glasgow Criteria - Acute Pancreatitis**

|                   |              |
|-------------------|--------------|
| Age               | > 55 years   |
| pO <sub>2</sub>   | < 8 kPa      |
| WBC               | > 15,000     |
| Corrected calcium | < 2 mmol / L |
| ALT               | > 200        |
| LDH               | > 600        |
| Glucose           | > 10         |

|         |      |
|---------|------|
| Urea    | > 16 |
| Albumin | < 32 |

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## MEDICAL OPHTHALMOLOGY PASSMEDICINE & PASTEST

### 1. Acute angle closure glaucoma

- Raised IOP
- Secondary to impairment of aqueous humour outflow
- R/F : hypermetropia (long sightedness), pupillary dilatation, lens growth associated with age.

#### C/F :

- severe pain - ocular or headache
- Decreased visual acuity
- Symptoms worse in darkness due to mydriasis
- Hard, red eye
- Haloes around light
- Semi dilated non reacting pupil
- Corneal edema - dull or hazy cornea

#### Mx :

- direct parasympathomimetic - **Pilocarpine** - contraction of ciliary muscle —> opening of trabecular meshwork —> increased aqueous humour outflow
- Beta blocker - **Timolol** - decreased aqueous humour production
- Alpha 2 agonist - **Apraclonidine** decreased aqueous humour outflow and increases uveoscleral outflow
- IV **acetazolamide** : decreased aqueous humour production
- Definitive Mx : laser peripheral iridotomy.

### 2. ARMD

- Advancing age, females >> males
- Smoking +++ increase risk
- Family history increases risk
- **Dry ARMD** : atrophic, presence of drusen - yellow round spots in Bruch's membranes

- **Wet ARMD** : exudative or neovascular macular degeneration; **choroidal neovascularisation**; leakage of serous fluid and blood can result in **rapid loss of vision, worst prognosis**

### **C/F :**

- gradual reduction in visual acuity - for near field objects
- Difficulty in dark adaptation and worsening of night vision
- Photopsia (flickering or flashing lights)
- Glare around objects
- Visual hallucination - Charles Bonnet syndrome

INV : slit lamp M/C, fluorescein angiography - for guiding anti VEGH therapy.

Mx : Combination of Zinc + Vit A + Vit C + Vit E

- anti VEGF “ limits the progression of wet ARMD - **Ranibizumab, Bevacizumab, Pegaptanib**

### **3. Angioid rental streaks**

- Irregular dark red streaks radiating fro optic nerve head
- **Degeneration, calcification and breaks in Buch’s membrane**

### **Causes :**

- pseudoxanthomas elasticum
- Ehler Danlos syndrome
- Paget’s disease
- Sickle cell anaemia
- Acromeglay

### **4. Anterior Uveitis**

AKA **Iritis**

- anterior portion of urea - inflammation - iris and ciliary body
- Associated with HLA B27

### **Clinical Features :**

- acute onset
- Ocular pain

- Pupil may be small
- **Intense photophobia**
- **Blurry vision, red eye**
- Ciliary flush - ring of red spreading outwards
- **Hypopyon - pus and inflammatory cells in the anterior chamber**

Associated with : 1) AS 2) Reactive arthritis 3) UC, Crohn's, 4) Behcet's disease 5) Sarcoidosis - **bilateral lesions seen**

## 5. CRAO

- Rare cause of sudden visual loss
- Due to thromboembolism (atherosclerosis) or arteritis (GCA)
- Sudden, **painless**, U/L visual loss
- RAPD +++
- Cherry red spot on pale retina

Mx : IV steroids for GCA

## 6. Central Retinal Vein Occlusion

- Sudden **painless** loss of vision
- R/F : increasing age, HTN, CVD, Polycythemia, Glaucoma
- Fundoscopy - widespread hyperaemia, several retinal haemorrhages - stormy sunset
- Branched retinal vein occlusion : vein in the distal venous system is occluded —> blockade of retinal veins at AV crossings -> limited area of fundus being affected

Mx - macular edema —> anti VEGF injections

Retinal neovascularisation —> laser photocoagulation

## 7. Diabetic Retinopathy

- hyperglycaemia —> increased retinal blood flow —> damage to endothelial cells and pericytes
- Endothelial dysfunction —> increased vascular permeability —> exudates seen on fundoscopy.
- Pericyte dysfunction —> micro aneurysms formations
- Retinal ischaemia —> neovascularisation

## **Non proliferative DR**

1. **Mild NPDR** : 1 or more micro-aneurysm
2. **Moderate NPDR** : micro aneurysm, blot haemorrhages, hard exudates, cotton wool spots = soft exudates, venous beading, venous looping
3. **Severe NPDR** : blot hemorrhages and micro aneurysm in all 4 quadrants, venous beading in 2 quadrants, IRMA in 1 quadrant.

IRMA = intra retinal micro vascular abnormalities

4. Mx : Severe / very severe —> pan retinal laser photocoagulation

## **Proliferative DR**

- retinal neovascularisation - causes vitreous haemorrhage
- Fibrous tissue anterior to retinal disc
- T1DM more common
- Panretinal laser photocoagulation - 50% develop in reduction in vision due to scarring of peripheral retinal tissue; **decrease in night vision due to rods loss as they are located in peripheral retina.**

## **Maculopathy :**

- hard exudates and background changes on macula.
- T2DM more common
- Mx : anti VEGF

## **8. Herpes Zoster Ophthalmicus**

- Hutchinson's sign : rash on tip or side of nose —> indicates nasociliary involvement — risk factor for ocular involvement
- Mx : oral antiviral for 7-10 days - **start within 72 hours**
- Severe infection - IV antiviral
- Secondary inflammation of eye - topical corticosteroids
- Complications : ocular - conjunctivitis, keratitis, episcleritis, anterior uveitis, ptosis, post herpetic neuralgia.

## **9. Horner's syndrome**

Congenital Horner's - **heterochromia** - **difference in iris colour**

## **Anhidrosis : Causes :**

- **Central lesions** : anhidrosis of face, arm and trunk
  1. Stroke
  2. Syringomyelia
  3. Multiple Sclerosis
  4. Tumour
  5. Encephalitis
- **Pre ganglionic lesions** : anhidrosis of face
  - Pancost's tumor
  - Thyroidectomy
  - Trauma
  - Cervical rib
- **Post ganglionic lesions** : NO anhidrosis
  1. Carotid artery dissection
  2. Carotid aneurysm
  3. Cavernous sinus thrombosis
  4. Cluster headache

\*\* Apraclonidine - alpha adrenergic agonist : pupillary dilatation in Horner's syndrome - due to denervation supersensitivity  
Also causes mild pupillary constriction in normal pupil due to down regulation of NE release at synaptic cleft.

10. Trochlear CN 4 diplopia - supplies the superior oblique muscle  
- **depresses the eye and rotates it inwardly - lesions of this nerve - outward rotation and torsional element to diplopia.**

**Horizontal diplopia** : recti muscles for horizontal movements fails to move in a conjugate manner —> medial or lateral rectus  
Lateral rectus - CN 6 - abducens

**Episodic diplopia** - Myasthenia gravis, thyroid eye disease, multiple sclerosis and squint decompensation

**Diplopia worse at night** - myasthenia gravis

Diplopia worse for far distance than near distance - rule out CN V pathology.

### 11. **Mydriasis - Causes :**

- third nerve palsy
- Pheochromocytoma
- Traumatic iridoplegia
- Congenital
- Holmes Adie pupil

Drug causes :

- topical mydriatics - atropine, tropic amide
- Sympathomimetic - amphetamines, cocaine
- Anti cholinergic : TCA

### 12. **Multiple Sclerosis - Optic neuritis**

- poor discrimination of colours
- Red desaturation
- Central scotoma
- U/L decrease in visual acuity
- Pain worse on eye movement, RAPD +++
- MRI : lesions disseminated in space and time
- Presence of lesion in the other eye as evidenced by abnormal visual evoked potentials
- CSF : lymphocytes, oligoclonal bands
- MRI - shows plaques

### 13. **Papilloedema**

- swelling of optic disc bilaterally
- Venous engorgement is the first sign
- Loss of venous pulsate
- Blurring of optic disc margin
- Elevation of optic disc
- Loss of optic cup
- **Paton's lines - concentric radial retinal lines cascading from optic disc**

**Causes :**

- SOL - neoplastic, vascular
- Malignant hypertension
- Idiopathic intra cranial hypertension



- Hydrocephalus
- Hypercapnia
- Vitamin A toxicity
- Hypothyroidism and hypocalcemia

Giant cell arteritis : affects the large and medium sized arteries

- occlusive vasculitis causes optic nerve ischaemia —> optic disc swelling and leading to sudden, unilateral vision loss
- Arteritic anterior ischaemic optic neuropathy AION

14. 3rd cranial nerve palsy with pupil involvement —> **suggestive of compression —> urgent intracranial scan**

**Ischaemia of CN III —> diabetes —> pupil sparing \*\*\***

#### **15. Posterior communicating artery aneurysm**

- CN III emerges in the **inter-peduncular fossa** - passes between the posterior cerebral and superior cerebellar arteries
- It pierces the dura at the **lateral clinoid process to enter the lateral wall of cavernous sinus**
- PCOM artery aneurysm - headache, I/L dilated pupil
- New onset, pupil involving isolated CN III palsy - **rule out SAH**

#### **16. Same day referral -**

- acute glaucoma
- Corneal laceration
- Contact lens related ulcer
- Corneal ulcer
- Endophthalmitis
- Intra ocular FB insertion
- Trauma
- Chemical injury

**\*\*Adenovirus - most common cause of infective conjunctivitis**

#### **17. Posterior vitreous detachment**

- **Painless**
- **NO loss of vision**

- R/F - increasing age, highly myopia (short sighted)
- Appearance of floaters
- Flashes of light in vision
- Blurry vision
- Cobweb across Visio
- Dark curtain descending down
- Signs : **Weiss ring on ophthalmoscopy**

18. **Parinaud syndrome** : lesion in dorsal midbrain - id-dilated pupils, upper lid retraction, paralysis of upward gaze.

19. **Asymmetric diabetic retinopathy**

- suspicion of ocular ischaemic syndrome on the side affected worse
- OIS - due to atherosclerosis
- Visual loss with or without pain
- Raised IOP, rubeosis iridis
- Anterior chamber cells
- Cataract
- Retinal haemorrhages
- Neovascularisation of disc and retina
- Cotton wool spots and micro-aneurysms
- **INV of choice : Fluorescein angiography and carotid doppler USG**

20. **Ehler Danlos - normal anterior chamber = no lens dislocation**

**Sudden loss of vision with normal anterior chamber = retinal detachment**

21. **Cornea verticillata** - vortex keratopathy - side effect of Amiodarone - rarely due to HCQ, Tamoxifen, Fabry disease

**Band keratopathy** - calcium deposition in chronic eye disease or due to hypercalcemia

**Corneal arcus** - hyperlipidemia in elderly

**Hudson Stahli lines** : iron deposition and normal ageing

**22. Duane syndrome** : congenital condition and commonly presents in childhood;

Failure of abduction of affected eye, with retraction of globe on adduction and narrowing of palpebral tissue. Adduction may be affected in type 2 or 3 Duane's syndrome.

**23. Refsum disease - cerebellar ataxia, peripheral neuropathy, deafness, ichthyosis.**

**Cause of Retinitis Pigmentosa :**

- Refsum disease
- Usher syndrome
- Abetalipoproteinaemia
- Lawrence Mood Biedl syndrome
- Kearns Sayre syndrome (mitochondrial inheritance)
- Alport syndrome ( X linked dominant )

**Central retinal vein occlusion**

- sudden loss of vision in one eye
- Affects retinal changes in all 4 quadrants
- Dilated tortuous retinal veins
- Cotton wool spots
- Macular edema
- Optic disc swelling

Branch retinal artery occlusion —> painless visual field loss.  
Affected retinal area would be pale with a branch distribution.  
No other signs seen

**Branch retinal vein occlusion** - branch distribution with same signs as central retinal vein occlusion

**Central retinal artery occlusion** - sudden, painless loss of vision, pale retina, cherry red spot on macula

**24. CN III Palsy** - pupil on opposite side reacts normally to light shone into the affected eye

- pupil on affected side - dilated, fixed pupil - as the CN III brings parasympathetic pupillomotor nerve fibers to iris sphincter
- Pupil of affected side of CN III palsy will be impaired - to both direct light and consensual (light shone into opposite normal eye)
- Pupil of affected side will be unreactive to light or accommodations
- CN III palsy - pupil size different will be greater in bright light because of failure of constriction.

\*\*\* **Anisocoria** - pupil size is different in bright and dim light.

## 25. **Heterochromia iridis conditions :**

- congenital Horner's
- Pigment dispersion syndrome
- Sturge-Weber syndrome
- Waardenburg syndrome

## 26. **Retinitis pigmentosa**

- Degeneration of photoreceptors and retinal pigment epithelium
- Progressive loss of vision and peripheral vision
- **Autosomal recessive 60% of cases**
- **Autosomal dominant 20-25%**
- **30% of cases —> spontaneous mutations**
- **Associated diseases :**
  - A. Usher syndrome - neurosensory hearing loss + RP
  - B. Refsum's disease
  - C. Kearns Sayre syndrome
  - D. Bardet Biedl syndrome
- INV : pigmented bony spicules on retina fundal appearance
- Waxy disc pallor
- Attenuation of retinal blood vessels
- **Worst prognosis - X linked RP**

27. Stargadt's disease = autosomal recessive causing macula disease and cone dysfunction

28. Sarcoidosis = granulomatous uveitis - bilateral

29. **CMV Retinitis = sectorial areas of necrotising retinitis with haemorrhages** - brush fire appearance - unilateral or bilateral - can cause visual loss with macula or optic nerve involvement.  
Mx : Oral Valganciclovir

30. The patient's symptoms and signs are suggestive of blepharitis, a common chronic bilateral inflammatory condition of the eyelid margins. Initial management should involve a combination of eyelid hygiene measures such as warm compresses to loosen crusts, mechanical removal of lid debris with cotton-tipped applicators or clean washcloth, and lid massage to express meibomian secretions. This approach can help control symptoms and prevent complications.

31. Drugs which may precipitate acute glaucoma include anticholinergics and tricyclic antidepressants

32. **Panretinal laser photocoagulation** is correct. The findings described are in keeping with proliferative retinopathy, which is more common in type 1 diabetics and 50% are blind within 5 years. Following treatment around 50% of patients develop a noticeable reduction in their visual fields due to the scarring of peripheral retinal tissue.

33. **Intravenous antimicrobial** is required in hospitals for patients with orbital cellulitis due to the risk of cavernous sinus thrombosis and intracranial spread. All patients with a clinical diagnosis of orbital cellulitis MUST be admitted with an ophthalmic opinion sought as soon as possible.

34. Ulcerative colitis, Ankylosing spondylitis —> HLA B27 associated —> anterior uveitis —> conjunctival injection with cells and flare in the anterior chamber and photophobia.  
+/- —> keratin precipitates, fibrin, synechiae, hypopyon

35. Cone opsin —> adaptation in light; different types - red, green and blue portions of visible light spectrum.

Melanopsin —> photopigment in retinal ganglion cells which are involved in circadian rhythms and pupillary responses.

**Panopsin / Opsin 3 : protein encoded by Opsin- 3 gene —> outside the eye [ liver, testes, brain and pancreas ]**

36. ARMD - anti oxidants are contraindicated because of : Beta-carotene has been found to increase the risk of lung cancer and hence antioxidant dietary supplements are not recommended for smokers.

**37. Hyphaema :**

- occurs when bleeding from iris vessels fills the anterior chamber with blood
- Strict rest
- DO NOT DILATE
- Hyphaema if large - and does not disperse quickly - can cause corneal staining
- Acute stage of hyphaema —> RBC clog the trabecular meshwork and decreased drainage of aqueous humour and corneal edema
- IV carbonic anhydrase inhibitors to lower the IOP
- Common side effect : **tingling of fingers**

**38. Vogt - koyanagi - Harada syndrome : oculocutaneous disease** - systemic condition seen in Japanese, Hispanic and Asian populations.

- **anterior uveitis, retinal detachment**
- **Choroiditis**
- **Optic disc edema**
- **Cutaneous changes : vitiligo, alopecia, poliosis.**

**39. Syphilis eye involvement :**

- uveitis
- Arterial and venous vasculitis similar to Behcet's disease
- Madarosis (loss of eyelashes)
- Conjunctivitis
- Argyll Robertson pupil
- Optic neuritis

- Scleritis

40. Radiation optic neuropathy - abnormality of anterior visual pathway

Ischaemic disorder of optic nerve - months to years after RT to brain, orbits and paranasal sinuses.

41. **6th CN Palsy :**

- loss of unilateral **abduction**
- Double vision maximal in direction of gaze of affected eye
- False image is outer image
- False image arises in affected eye
- Adults commonly - microvascular

42. Microaneurysms - fluorescein angiography

43. Vitamin A toxicity is a rare cause of papilloedema. In this case, she is likely to have been taking retinoids for psoriasis.

44. Primary Open Angle Glaucoma Mx :

- Prostaglandin analogues - Latanoprost - **increases uveosacral outflow - Once Daily - Adv :** iris pigmentation brown colour, increased eyelash length
- Beta blockers - Timolol, Betaxolol - **reduced aqueous humour production** - CI in asthma and heart block
- Sympathomimetics - Brimonidine - alpha 2 adrenergic agonist - reduced aqueous humour production and increases outflow - AVOD if taking MAO-inhibitors and TCAs; adv : **hyperaemia**
- CA Inhibitors - Dorzolamide, Acetazolamide - reduced aqueous humour production - systemic absorption can cause sulphonamide like reaction
- Miotics - **Pilocarpine - muscarinic receptor agonist - increased uveosacral outflow (like PG analogues)** - adv : constricted pupil, headache, blurry vision

45. The correct answer is **black bone spicule-shaped pigmentation in the peripheral retina**. Retinitis pigmentosa (RP) is a group of inherited retinal disorders characterized by progressive degeneration of the photoreceptors, leading to vision

loss. The classic fundoscopic finding in RP is black bone spicule-shaped pigmentation in the peripheral retina, which occurs due to the migration and proliferation of retinal pigment epithelial cells into the outer retina. This finding is highly suggestive of RP and supports the diagnosis in this patient with a family history and worsening vision.

46. Hypopyon + Normal pupil rxn is keratitis'  
hypopyon + small pupils fixed is Ant uveitis

47. This is because fluorescein angiography is a key investigation in assessing the extent of neovascularisation, which is a feature of wet or exudative age-related macular degeneration (AMD). In this procedure, a fluorescent dye is injected into the bloodstream and pictures are taken as the dye passes through the blood vessels in the retina. This allows for the visualisation of any abnormal blood vessels, leaks or blockages.

48. **Red eye - glaucoma : severe pain, haloes, semi dilated pupils**

**Red eye - anterior uveitis - small fixed oval pupil, ciliary flush.**

49. **Meibomian cyst**, also known as a chalazion, is a granulomatous inflammation of a Meibomian gland in the tarsal plate of either upper or lower eyelid. It usually presents as a painless swelling on an eyelid without any associated watering or redness unless secondarily infected or inflamed which again does not fit with this clinical scenario.

50. **Pinguecula** is a common degenerative condition characterised by yellowish patch or bump on conjunctiva near cornea (usually on nasal side). It tends to be asymptomatic but may cause discomfort or foreign body sensation particularly in dry conditions. Given that our patient has presented with persistent watery eyes and erythema at inner canthus rather than any discomfort or foreign body sensation makes pinguecula unlikely diagnosis here.



51. Heterochromia, a condition where the two eyes are different colours, can be associated with Horner's syndrome. This is a neurological disorder that results from damage to the sympathetic nerves supplying the eye. Symptoms of Horner's syndrome include ptosis (drooping of the upper eyelid), miosis (constriction of the pupil), anhidrosis (lack of sweating), and heterochromia. The heterochromia in Horner's syndrome is usually partial and more commonly seen in patients who acquire the condition at a young age.

52. Argyll-Robertson pupil is one of the classic pupillary syndromes. It is sometimes seen in neurosyphilis. Typically the pupil accommodates but doesn't react. A mnemonic used for the Argyll-Robertson Pupil (ARP) is Accommodation Reflex Present (ARP) but Pupillary Reflex Absent (PRA)

#### Features

- small, irregular pupils
- no response to light but there is a response to accommodate

#### Causes

- diabetes mellitus
- syphilis

53. **Vitelliform macular dystrophy** is also an incorrect option. This disorder typically affects central vision due to the accumulation of yellow deposits under the macula, causing distortion or loss of central vision. However, it does not cause night blindness or tunnel vision as described by the patient.

54. Apraclonidine eye drops are initially used to confirm a Horner's pupil. Apraclonidine stimulates both alpha-1 and alpha-2 receptors. When added to the affected eye, it causes pupil dilation by >2mm because of the relative supersensitivity of this pupil to alpha-1 receptor activity. In a normal pupil, however, it causes constriction due to the more potent activity at the alpha-2 receptor which triggers reuptake of noradrenaline in the synaptic cleft.

Hydroxyamphetamine is then used to distinguish between first/second or third order neurones. In other words, it will distinguish

either a lesion in the brainstem, cervical cord, chest or neck and one affecting above the superior cervical ganglion at the carotid bifurcation. In a normal pupil or a first/second order Horner's, the pupil will dilate secondary to increased levels of noradrenaline released from the post-synaptic neurones. In a third order neurone, this will not occur.

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## GERIATRICS

### PASSMEDICINE & PATEST

#### 1. Donepezil and bradycardia

- One of the important possible side effects of the acetylcholinesterase inhibitors (donepezil, rivastigmine and galantamine) is bradycardia (or SA block or AV block).
- Hence these medications might be contraindicated or should be started with caution in patients with conduction abnormalities or those already taking negatively chronotropic medications such as beta blockers, rate-limiting calcium channel blockers or digoxin.
- Other possible side effects include gastrointestinal effects (nausea, vomiting, anorexia, diarrhoea), agitation, hallucinations, syncope; and less commonly gastrointestinal ulcers, seizures, conduction disorders, urinary retention and extrapyramidal symptoms.
- Neuroleptic malignant syndrome is also listed in the BNF as a very rare adverse reaction.

2. The key point here is that this man has an acute confusion with impaired consciousness. Impaired consciousness is seen in delirium but not in dementia. The history is also not long enough to be suggestive of a dementing illness (1 and 2). The suggestion of a personality change is a red-herring here. The dehydration and smell of urine suggest a urinary tract infection which may precipitate an episode of delirium.

3. **Donepezil** is an acetylcholinesterase inhibitor, which along with galantamine and rivastigmine, are first line for management of mild to moderate Alzheimer's dementia.

**Memantine** is an NMDA receptor antagonist, used as a 2nd line or 'add on' treatment for mild-moderate Alzheimer's dementia. It may be used 1st line in severe Alzheimer's.

**Oxybutynin** and **tolterodine** are anti-muscarinic medications used in the treatment of urge incontinence. Immediate release oxybutynin should, however, be avoided in 'frail older women' according to NICE.

**Rotigotine** is a dopamine agonist used in the treatment of Parkinson's disease and restless legs syndrome.

4. The Waterlow scale was developed in 1985 to assess the risk of pressure sore development, helping to drive level of nursing intervention and use of special mattresses to reduce risk. Potential scores range from 1-64. A score greater than 10 indicates an increased risk of pressure sore development, with scores >15 indicating high risk and >20 indicating very high risk. A number of factors are taken into account when assessing patients using the scale including body habitus, continence status, malnutrition, mobility, neurological status and presence of major trauma.

5. Lewy body dementia (LBD) is a type of progressive dementia that leads to a decline in thinking, reasoning and independent function due to abnormal microscopic deposits that damage brain cells over time. Parkinsonian symptoms such as bradykinesia, rigidity and tremor are common in LBD. Additionally, patients with LBD can have significant neuropsychiatric symptoms including agitation. Importantly, these patients are extremely sensitive to neuroleptic drugs like haloperidol and can experience severe exacerbation of their parkinsonian symptoms when exposed to these medications.

6. This patient has frontotemporal lobar degeneration (FTLD). There are 3 subtypes of FTLD including frontotemporal dementia (or Pick's disease), progressive non-fluent aphasia, and semantic dementia. Of the 3 subtypes, this patient has Pick's disease which is characterised by an insidious onset, commonly before 65 years,

and a change in personality and social disinhibition. The positive family history also makes frontotemporal dementia more likely.

7. **Catatonia** is incorrect. Catatonia characteristically presents with mutism, posturing, staring, rigidity and echopraxia/echolalia.

**Dementia** is incorrect. The set of symptoms this patient is experiencing would fit with a diagnosis of dementia, however, the fluctuation of symptoms and the onset over a short period makes delirium the more likely diagnosis.

**Depression** is incorrect. Depression in elderly patients may present with confusion and a decline in functioning (pseudodementia), however, the fluctuation in symptoms and acute onset favours a diagnosis of delirium rather than depression.

**Schizophrenia** is incorrect. It would be highly unlikely for a first presentation of a primary mental illness at age 95, and again the daily fluctuation of symptoms makes this diagnosis less likely.

8. Patients with Alzheimer disease have reduced production of choline acetyl transferase, leading to a decrease in acetylcholine synthesis and impaired cortical cholinergic functioning.

The only role for cholinesterase inhibitors is to improve some cognitive function and improvement in activities of daily living. There is no role for cholinesterase inhibitors in advanced Alzheimer's disease.

9. MRI head is correct. The diagnosis is dementia. The lack of fluctuation and the chronic history make a delirium unlikely. The probable subtype is Alzheimer's disease dementia as evidenced by the insidious onset of memory problems in association with other cognitive deficits such as impaired reasoning and handling of complex tasks, impaired visuospatial abilities and change in personality. There are no specific features to suggest vascular dementia, frontotemporal dementia, dementia with Lewy Bodies or Creutzfeldt-Jakob disease. Structural imaging in the form of CT or MRI head is recommended in the investigation of dementia, both to exclude reversible causes of cognitive decline (i.e. subdural

haemorrhage) and assist with subtype diagnosis. **MRI features suggestive of a diagnosis of Alzheimer's disease, for example, include mesial temporal lobe atrophy and temporoparietal cortical atrophy.**

10. Cranial nerves passing through jugular foramen : **CN 9, 10, 11**

- internal jugular vein passes through jugular foramen
- CN 9,10, 11 and IJV can become compressed in **jugular foramen syndrome**
- CN 9 : glossopharyngeal —> sensory fibers from tonsils, pharynx, middle ear and posterior 1/3 of tongue ; motor fibers to stylopharyngeal muscles
- CN 10 : sympathetic and parasympathetic function; motor fibers to muscles of palate and pharynx
- CN 11 - motor control to sternocleidomastoid and trapezius muscle

**\*\*Geniculate ganglion lesion** : facial nerve palsy and hearing loss

11. End stage dementia - bedridden patient with Neisseria gonorrhoea infection —> **call the police sexual abuse maybe**

12. Creatinine - cation in physiologic pH range - secreted by the organic cation secretory pump.

- this pump can be inhibited by other organic cations.
- Number of drugs can inhibit this pump —> **Trimethoprim, Cimetidine**

**13. Biofilm formation - including urinary catheter and prosthetic surfaces** - failure of antibiotic therapy.

14. GVA - temporal biopsy - classical pattern on biopsy - intimal thickening and transmural inflammation, dense inflammatory infiltrate composed of T cells and histiocytes is present.

15. **Venous ulcer** :

- 2/3 ads of them are due to chronic venous insufficiency
- Leads to venous stasis and increased capillary pressures
- Producing secondary skin changes

- R/F : obesity, history of varicose veins, leg trauma, DVT
- Large and superficial ulcers - granulation tissue in the base
- Peripheral edema, venous eczema, hemosiderin deposition, lipodermatosclerosis and atrophy blanche
- ABPI to rule out arterial disease
- Compression main Mx principle

16. **Lewy bodies** - eosinophilic inclusion bodies within neurones - mainly in the limbic areas.

17. Digoxin - **high degree of protein binding** - widely distributed throughout body tissues. Extensive distribution means that circulating drug concentrations are low.

Digoxin half life : 30 - 40 hours

Renal excretion majority of drug

Water soluble

NOT LIPOPHILIC

18. CLL - immunophenotyping - flow cytometry

19. Digoxin adverse effects :

- disorientation
- Vomiting
- Mental confusion
- amnesia
- Depression
- Yellow visual field discolouration - **xanthopsia**

Beta blockers, statin, Nifedipine —> sleep disturbances

20. Left Homonymous hemianopia - Right distal posterior cerebral artery occlusion

21. **Tonsillar herniation : worsening of stroke - increase BP and bradycardia**

22. **Amantadine** - reduces dyskinesia without worsening motor function - inhibits NMDA receptors rather than any dopamine action. Reduces dyskinesia and improves motor function.

23. Therapeutic CSF large volume removal can help in additional symptomatic relief from VP shunt placement

24. Bullous impetigo in immunocompromised Rx : IV Co-amoxiclav

**25. During Intermittent Positive pressure ventilation :**

- lung volumes are increased
- Pulmonary vascular resistance is increased → increase in RV volume
- Increase in RV volume → decreased LV filling
- Hyperinflation → Prostaglandins release → protective mechanism against lung injury
- Over inflated alveoli → compression of alveolar blood vessels
- Increased intra thoracic pressures during all phases of cardiac cycle
- Inspiration during IPPV → increased intrathoracic pressure → increases RA pressure
- Decreased in venous pressure
- Decrease in afterload → decrease in systemic blood pressure

**26. Barthel Index : measure of physical functioning and ability to perform Activities of Daily living**

- 80 - 100 : normal
- 50 - 79 : moderate reduced ADL
- 25 - 49 : low ADL
- <24 : very low ADL
- Score of ≤ 40 indicates poor chronic prognosis

27. Anti tubercular therapy in patients with severe liver impairment : avoid giving oral forms of ATT as there is high risk of toxicity with Pyrazinamide, Isoniazid, Rifampicin → liver friendly regimen : injectable streptomycin, Injectable Moxifloxacin.

28. Waldstrom's macroglobulinemia : anaemic, low platelet count, hepatosplenomegaly, monoclonal IgM proliferation

Mx : urgent plasmapheresis

Increased IgM levels → hyper viscosity → visual symptoms and retinal changes

29. Actinic keratosis : atypical keratinocytes on biopsy : 5-fluorouracil treatment

30. Brainstem strokes :

- contralateral weakens
- Ipsilateral sympathetic pathway causing Horner syndrome
- Ipsilateral hypoglossal nerve —> tongue weakness on affected side —> deviation of tongue to same side
- Medial longitudinal fascicles involvement —> I/L internuclear ophthalmoplegia
- Sensory loss on C/L side
- Facial sensory loss on I/L side

31. Severe dementia MMSE score < 10 / 30 —> DO NOT GIVE ACETYLCHOLINE INHIBITORS

Prescribe Memantine - NMDA Receptor antagonist

32. Thiazide diuretic & Loop diuretic : hypokalaemia and hyponatremia.

33. Deltoid muscle weakness :

- weakness in drawing the arm forward
- Internally rotating the shoulder
- **Supraspinatus** : initiated the first 30 degree of movement
- Deltoid assists in flexion and medial rotation of shoulders

34. Progressive supra nuclear palsy : axial rigidity + postural instability + vertical supra nuclear gaze palsy + dysarthria + cognitive dysfunction.

\*\* presence of marked postural instability in a Parkinsonism patient should suggest the possibility of PSP

\*\* postural instability is often a **late** features of idiopathic Parkinson's disease.

35. Circumflex artery - branch of Left coronary artery and supplies **posterolateral left ventricle and anterolateral papillary muscle - also supplies SA node**



- **left coronary artery** - arises above the left aortic cusp and divides to form circumflex and left anterior descending arteries
- Posterior inter ventricular artery : arises from right coronary artery and supplies the posterior 1/3 of IV septum

36. K channel antagonist - Amiodarone & Sotalol - delays depolarisation, increases AP duration and increase effective refractory period.

- Ca channel antagonist : Verapamil & Diltiazem
- K channel agonist : Nicorandil → activates K-ATP channels in cardiac mitochondria
- Na channel antagonist : Lidocaine

37. **Lentigo maligna** : pigmented, flat nature of lesion on sun damaged skin

38. Frontal lobe dementia : **failure to draw interlocking patterns : constructional apraxia - lesion to right hemisphere or frontal lobe.**

39. **Receptive dysphasia** : hinders recovery in stroke patients due to difficulties in complying with rehabilitation therapy.

40. CLL Mx : **single agent - CHLORAMBUCIL**

41. ASYMPTOMATIC COLONISATION OF MRSA → TOPICAL DECOLONISATION WITH MUPIROCIN AND CHLORHEXIDINE

42. **Cardiac Amyloid** : heart failure with restrictive filling pattern —  
> seen by dilated atria

- speckled appearance is characteristic of amyloid
- Cardiac amyloid : bradycardia with 2:1 or complete heart block is common

43. **Aspergillus species fungus** :

- **septate hyphae and involvement of sinuses**
- Diabetes is a predisposing factor for infection
- Mx : Amphotericin B

Actinomyces : Gram positive, branching, filamentous bacteria

Mucor : rhino cerebral disease ; aseptate hyphae \*\*\*

Rhizopus : can cause mucormycosis - nasal stuffiness, facial pain and oedema, necrotic block nasal turbinates : aseptate hyphae \*\*\*

#### 44. **Nitrate tolerance : reactive oxygen species formation**

- chronic nitrate therapy —> increases vascular oxidative stress
- Enhanced degradation of NO and reduced bioavailability.
- ROS and Reactive nitrate species —> leads to inhibitor of activation of exogenous source of nitrate

#### 45. Lewy body dementia : core symptoms :

- features of Parkinsonism
- Well formed and detailed visual hallucinations
- Fluctuating cognition with variations in attention and alertness

Other supportive features :

- repeated falls
- Syncope or transient LOC
- Severe autonomic dysfunction - urinary incontinence, postural hypotension
- Neuroleptic hypersensitivity

#### 46. Thiazides adverse effects :

- hypercalcemia
- Hypokalaemia
- Hypomagnesemia
- Hyponatremia
- Hypochloraemic alkalosis
- Worsens glucose tolerance when used with beta blockers

#### 47. **Anton syndrome - basilar artery - cortical blindness due to bilateral occipital lobe infarct**

- occipital lobe is supplied by posterior cerebral arteries from the basilar artery

Middle cerebral artery : parietal lobe and temporal lobe.

Anterior communicating artery - bridge between anterior cerebral arteries - interruption can cause frontal Lob deficit.

Anterior inferior cerebellar artery : nystagmus

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**JAN 2016 PATEST PREVIOUS YEAR PAPER**  
**SCORE 71 %**

1. Macrophages - foam cells are fat laden macrophages in atherosclerotic plaques. They engulf oxidised LDL by process of **endocytosis via scavenger receptors** associated with necrotic foci - increase in local inflammatory response and plaque rupture
2. **Basophils** : predominantly involved in **atherosclerosis** - can be recruited into atherosclerotic plaques by CCL2
3. Extensive bone pain due to metastases + nausea + vomiting => **glucocorticoids** - Dexamethasone
4. Pregnancy - low molecular weight heparin - **Enoxaparin**
5. **Pronator syndrome : compression neuropathy of median nerve at the elbow.**  
**C/F :**
  - compression o median nerve in region of elbow or proximal part of forearm —> pain or numbness in distribution of median nerve
  - Weakness of muscles supplied by anterior interosseous nerve : flexor pollicis longus, flexor digitorum profundus of index fingers, and pronator quadratus.
  - Difficulty grasping objects
6. **Transport of fatty acids within the cell : carnithine acyltransferase I**
  - transport of fatty acyl coA into mitochondrion : via an acyl-carnithine intermediate —> generated by action of carnithine acetyltrasnferase O

- Acyl carnitine —> enters mitochondria —> **carnitine acyltransferase II catalyses regeneration of fatty acyl CoA molecule**
- Carnitine deficiency —> inability to transport fatty acids into mitochondria.
- Most common feature is : **dilated cardiomyopathy in children.**

7. Coarctation of aorta —> commonly associated with bicuspid aortic valve.

8. Best way to confirm cerebral toxoplasmosis —> CSF PCR

9. Birch pollen allergy - apples, cherries, plums, peach

10. Just lateral to left sternal lower border - right ventricle

3-4 cm lateral to lower left sternal border - left ventricle

11. **Schizoid personality disorder** : emotional aloofness, indifference to praise and criticism, absence of bizarre idiosyncratic thinking

12. Ischemic colitis : IV Fluids - due to chronic cocaine abuse —> progressive mesenteric artery disease as a result of arterial vasoconstriction and fibrosis.

Conservative management with IV fluids and analgesia

13. **Common peroneal nerve lesion** :

- weakness of foot dorsiflexion
- Weakness of foot eversion
- Weakness of extensor hallucis longus
- **Preserved foot inversion**
- **Preserved plantar flexion**

L3 lesion - loss of hip adduction and abduction

Knee extension **preserved** : in both common peroneal nerve lesions and L5 radiculopathy.

14. CMV retinitis : immunocompromised individuals - HIV / receiving chemotherapy —> minute of exudates + retinal haemorrhages

Dx : CMV PCR

Rx : IV Ganciclovir

15. Drugs causing acute pancreatitis :

- Azathioprine
- Mesalazine
- Didanosine
- Bendroflumethiazide
- Furosemide
- Pentamidine (toxoplasmosis infection in HIV - aerosolised pentamidine - risk of pneumothorax)
- Steroids
- Sodium valproate

16. Carbamazepine : MOA - voltage dependent sodium channel inhibition

**Ethosuximide : MOA** : voltage gated calcium channel

17. **Somatostatinoma**

- arises from pancreas or GIT
- Characterised by excessive secretion of somatostatins
- **Classic pentad** : Diabetes mellitus + cholelithiasis + weight loss + steatorrhoea + diarrhoea & hypochlorhydria
- 10% of patients with NF-1 = von Recklinghausen's disease => develop somatostatinomas.
- Hormones secreted are : somatostatin, gastrin, insulin, VIP, ACTH, calcitonin, pancreatic polypeptide.

18. Infective Endocarditis : Poor prognosis factors :

- prosthetic valve
- Staph aureus infection
- Depletion of complement levels
- Culture negative endocarditis

IE : Indications for. Surgery :

1) cardiac failure or hemodynamic compromise

- 2) Extensive valve incompetence
- 3) Large vegetations
- 4) Septic emboli
- 5) Septal abscess - aortic root abscess - PR prolongation
- 6) Fungal infection
- 7) Antibiotic resistant endocarditis
- 8) Failure to respond to medical therapy

### **Streptococcus viridans → good outcome of IE**

#### **19. Alpha thalassemia**

- deficiency of alpha chains in Hb
- 2 separate alpha chains are located on **chromosome 16**
- 1 or 2 alpha globin chains affected → hypo chromic, microcytic  
- Hb levels are typically normal
- 3 alpha globin chains are affected → hypo chromic microcytic anaemia + **splenomegaly = HbH disease**
- 4 alpha chains absent : homozygotes - death in utero - hydrops fetalis, Bart's syndrome

#### **20. Ciclosporin → IL-2 inhibitors**

##### **Ciclosporin involved in :**

- allograft immunity
- Delayed cutaneous hypersensitivity
- Allergic encephalomyelitis
- Freund's adjuvant arthritis
- GVH disease

IL-2 = T-cell growth factor TCGF

21. Increased rates of vaccine failure → coeliac disease - HLA types predispose to vaccine failure  
HLA B8, SC01, DQB1, DQA1

22. Juvenile Myoclonic epilepsy : classical EEG pattern - 4-6 Hz bilateral polyspike and slow wave discharges with frontal predominance

**23. Opponens pollicis - originates from flexor retinaculum of hand and tubercle of trapezium  
Passes downward and laterally and inserted into metacarpal bone on radial side.**

**Supplied by recurrent branch of median nerve —> liable to damage during forearm injury.**

**24. Long standing rheumatoid arthritis - finger drop - due to :  
swelling and dorsal subluxation of ulnar styloid**

**25. Immunocompromised with red cell aplasia , rash arthritis =  
Parvovirus B19**

**26. Ropinirole - increased risk taking behaviour and changes in  
sleep patterns.**

**27. IL-1 inhibitor : Canakinumab**

**IL-6 inhibitor : Tocilizumab**

**28. Psoriasis with active skin disease + arthritis = MTX for Rx**

**29. Activation of Parasympathetic nerves : S2-S4 origin - bladder  
contraction and bladder emptying**

**30. Tertiary hyperparathyroidism following renal transplant -  
surgery better outcomes**

**As patients following renal transplant - are taking tacrolimus —>  
Cinacalcet has moderate reduction in exposure hence avoided  
And surgery is preferred.**

**31. Hyponatremia in Mesothelioma : poor outcomes**

**32. PCM overdose - poor outlook - INR > 2 less than or equal to 48  
hours,**

**INR > 3.5 at or before 72 hours**

INR > 6.5 —> Liver transplant

33. Chronic pancreatitis associated malabsorption —> Pancreatin

Bile acid malabsorption due to ileal resection or short bowel syndrome —> Cholestyramine

34. **Prophase** : initial phase of cell division when initial chromosome condensation occurs

**Metaphase** : chromosomes align at the equator of cell prior to cell division into two daughter cells

**Anaphase** : replicated chromosomes moves to opposite poles of the cell

**Telophase** : nuclear membrane reforms in each daughter cell, nucleoli reappear and chromosomes unwind into chromatin

**Interphase** : phase between episodes of cell division

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### MAY 2016 PATEST PAPER

1. Bing eAlcohol drinking : increased response to ADH causing **increased of aquaporin-2 channel in collecting duct** - reduction in free water excretion —> protects against dehydration.
2. Initial chemotherapy in haematological malignancies —> **10 days into treatment — increased risk of neutropenic sepsis**
3. Vinblastin and Vincycline —> binds to micro tubular proteins of mitotic spindle —> prevents polymerisation and causing **metaphase arrest** ; high concentrations of vinblastin can exert complex effects on nucleic acid and protein synthesis.
4. **Etoposide : cell lysis on G2 phase** ; high concentrations = lysis can be observed of cells entering mitosis; low concentrations = prevents cell from entering prophase
5. Cisplatin - inhibits DNA cross linking
6. Doxorubicin - prevents DNA intercalation —> inhibitor of DNA, RNA and protein synthesis



7. Bleomycin - ssDNA scission - inhibition of cell diving, cell growth and DNA sythesis.
8. Chronic stable angina —> Rx : Bisoprolol or cardioselective CCB
9. Parkinsons's disease anti emetics : Ondansetron, Cyclizine and Domperidone
10. Latex allergy food - bananas, kiwis, avocado, chestnuts
11. MODY + renal cysts + family history of diabetes => HNF 1-beta mutation
12. PDE-5 inhibitor : Sildenafil; PDE-4 inhibitor : **Roflumilast (COPD use)**
13. Dual Endothelin A & B receptor antagonist : Bosnian
14. Selective Endothelin A receptor antagonist : Ambrisentan, Atrasentan, Sitaxentan
15. Threadworms : Rx = **Medendazole** followed by second dose 2-3 weeks later
16. Pemphigoid : antibodies at derma-epidermal junction - associated wit hC3 deposition and antibodies are against **type 17 collagen**
17. Sickle cell vasoocclusive crisis : pain management : Opiates - Morphine
18. Hypotesion + Bradycardia - not responsive to Atropine —> Transcutaneous pacing
19. Origin of Left coronary artery : arises above the left posterior aortic cusp
20. Poor prognosis in AML - Age > 60 years, Karnovsky score less than 60% , MDR1 gene +ve, Chromosomal changes t(6;9). 11q23;
21. Bronchiectasis CT findings : tree in bud appearance - multi centrilobular nodules with linear branching pattern connecting them; Other CT features : brachial dilatation, lack of bronchial tapering from proximal to distal regions of lung
22. Sarcoid lung disease : linear bands of fibrosis radiating from hill
23. Bronchiectasis - increased bronchial diameter
24. Cluster headache / Paroxysmal hemicrania overlap => Indomethacin trial
25. **Isoniazid - inhibits bacterial fatty acid synthesis - decreased production of mycotic acid of bacterial cell wall**
26. Gitelman's syndrome - familial hypokalaemia and hypomagnesemia - loss of function in NaCL co transporter in

the DCT ; confirm diagnosis by genetic testing ; autosomal recessive - mutation of SLC12A3 gene ; C/F : low - low normal BP, polydipsia, polyuria, arrhythmia, fatigue, nocturia, hypocalcemia symptoms; **Hypokalaemia, hyponatremia, hypomagnesemia, elevated renin and aldosterone levels, hypocalciuria, high urine K / urine Na / urine Cl**

27. Thin filaments = actin + troponin + tropomyosin
28. Thick filament - myosin
29. Fasciscapulohumeral dystrophy - **DUX4 gene** - leads to muscle death - high tone deafness, retinal changes and cardiac arrhythmias.
30. Primary cause of polyuria in binge alcohol drinking - reduced ADH levels
31. Crohn's disease - erythema nodosum + GI symptoms + raised MCV + nail ridging (via B deficiency)
32. Homonymous hemianopia with macular sparing - contralateral occipital cortex
33. Staph aureus infection pneumonia - flucloxacillin / 2nd line - Erythromycin
34. ACE inhibitor associated angioedema- starts several years after starting the drug
- 35. Origin of posterior cerebral artery : near the intersection with the posterior communicating artery**
36. Anterior choroidal artery : originates from internal carotid artery
37. Anterior inferior cerebellar artery - originates from origin of basilar artery
38. Superior cerebellar artery - posterior to posterior communicating artery
39. Pontine artery : branch of before superior cerebellar and posterior cerebral.
- 40. Trimethoprim - increases creatinine levels** : competes with creatinine for organic anion secretory pump
- 41. Hypercalcemia** - thyrotoxicosis - stimulation of osteoclast cells c-fos protein which is present in osteoclast precursors
- 42. Anaesthetic related hepatitis** : resolution is likely over few days without any interventions
- 43. Severe UC** - long term remission - Azathioprine
- 44. Liver specialist referral in PCM overdose** : INR > 2 within 48 hours of PCM overdose, creatinine > 200, SBP < 90 mmHg, Hypoglycaemia, pH < 7.3

**45. Cystic fibrosis - Pseudomonas infection - Inhaled Tobramycin**

**46. Human genome project :**

- A.** 3.7 Million human Single nucleotide polymorphisms (SNPs) have been identified
  - B.** 99% of human DNA sequence identified
  - C.** Alu repeats - role in human genetic diversity
  - D.** 15,000 full length human cDNA have been identified
  - E.** 30,000 human genes have been identified in 2003
- 

### **MRCP SEPT 2016**

1. Spironolactone - competitive inhibitor of aldosterone receptors - distal portion of distal convoluted tubule - collecting duct.
2. CA inhibitors : proximal portion of PCT
3. Loop diuretics : thick ascending limb of Loop of Henle
4. Non Hodgkin's lymphoma : painless, slow progressive peripheral lymphadenopathy - cold agglutinins present.
5. Viral pericarditis : ST elevation with concave upwards
6. ST Elevation with convex upwards : Myocardial infarction
7. **Anterior hypothalamic nuclei : thermoregulation and circadian rhythms, - located at inferior border of paraventricular nuclei**
8. **Supra schismatic nucleus** : primary regulator of circadian rhythms - receives neural projections directly from retina and projections from lateral geniculate nuclei and superior colliculus.
9. **Lateral pre-optic nucleus** : onset of NREM sleep
10. **Paraventricular nucleus of hypothalamus** : maintains systemic osmotic balance through vasopressin and oxytocin release from posterior pituitary gland
11. **Supraoptic nucleus** : produces vasopressin and oxytocin.
12. Long term hemodialysis - beta 2 micro globulin aggregates in brain
13. Juvenile myoclonic epilepsy Rx : Levetiracetam, Lamotrigine, Topiramate
14. **Dravet syndrome** - severe myoclonic epilepsy associated with significant developmental delay
15. Waldstrom's macroglobulinaemia : Rituximab + Cyclophosphamide + Dexamethasone

16. Poorly controlled T1DM on insulin regime —> **refer to : 72 hour continuous glucose monitoring system assessment**
17. **Evidence of atherosclerosis affecting more than one vascular bed - carotid artery disease and other vessel - increased risk of future cardiovascular death.**
18. **Low BMI => increased risk of cardiovascular death**
19. Haemochromatosis - serum transferrin saturation levels ; haemochromatosis associated with C282Y and H63D mutations
20. Subclavian vein location : 1 cm inferior to junction of middle and medial third of clavicle
21. Anti VEGF injection complication : bacterial endophthalmitis.
22. Rivaroxaban monitoring : **PT levels**
23. **Heparin levels - APTT monitoring**
24. **Platelet function - Bleeding time**
25. **Direct thrombin inhibitors - Dabigatran - fibrinogen levels**
26. Chronic lithium use - reduces both cAMP and non-cAMP related u-regulation of aquaporin 2 channels —> decreased aquaporin 2 gene expression
27. Type 4 RTA —> Aldosterone resistance
28. B cell non Hodgkin's lymphoma - CD20 receptor on B cells - anti CD 20 antibody - Rituximab is used in treatment
29. Damage to **right** parietal lobe —> visual spatial awareness deficit
30. Damage to **left** parietal lobe - deficit in understanding spoken and written languages
31. **Ezetimibe** - inhibits Niemann Pick C1 like protein 1 (NPC1L1) which is responsible for intestinal absorption of cholesterol
32. Fibrates - PPAR alpha agonists - reduces triglycerides
33. **Eltrombopag = stimulates platelet growth and treatment of thrombocytopenia when present in CLD - thrombopoietin receptor antagonist**
34. High risk neutropenic patients with sepsis of unknown origin Rx : Ciprofloxacin + Vancomycin + single dose Gentamicin
35. Christie's guidelines - confirmed neutropenic sepsis - Piperacillin + Tazobactam with gentamicin
36. **Internal carotid artery aneurysm** - exert pressure on Oculomotor nerve which can lead to third nerve palsy

- 37. Supra schismatic pressure - altitudinal visual field defect rather than homonymous hemianopia - akinetic mutism, hypothalamic syndromes can also be seen
- 38. Diabetic neuropathy - **pregabalin** - decreases episodes of urinary incontinence - Pregabalin preferred in patients with urinary retention
- 39. De Quervain's tenosynovitis - entrapment tendonitis - pain during thumb motion
- 40. Calcium salts decreases absorption - levothyroxine, iron, zinc, strontium ran elate and quinolone antibiotics
- 41. Pregnant women with APLA - Aspirin 75mg + Prophylactic dose of LMWH
- 42. Vincristine adverse effects : neuritic pain, sensory loss, paraesthesia, difficulty in walking, slap gait, loss of DTR, ataxia, paresis, foot drop and cranial nerve palsies
- 43. Pneumococcal meningitis - Vancomycin + Ceftriaxone
- 44. Specificity - true negative rate - proportion of negatives that are correctly identified.
- 45. **Elbasvir - inhibitor of HCV NS5A**
- 46. **Dasabuvir - inhibitor of HCV NS5B**
- 47. **Grazopravir - inhibitor of HCV NS 3/4 A**
- 48. SLE - Membranous GN due to lupus nephritis - Rx : Mycophenolate
- 49. **Vertebral artery - direct branch of left subclavian artery**
- 50. **Other branches of left subclavian - internal mammary artery**
- 51. Left Common carotid artery directly arises from aorta
- 52. Basilar artery is branch of vertebral artery
- 53. **Benzbromane & Lesinurad - URAT-1 inhibitor - increases uric acid exertion**
- 54. **IL-1 inhibitor - Canakinumab - used in gout treatment**
- 55. **Allopurinol** - improved renal outcomes in patients with diabetic nephropathy and positively impacts on progression of cardiac failure.
- 56. SVC obstruction due to bronchial mass - **stenting Mx**
- 57. Interleukin - 1 - gout triggers - hence IL-1 inhibitors are used in gout treatment
- 58. Diabetic neuropathy - **with gastroparesis - Domperidone**

- 59. Carbamazepine - HLA B1502 testing before starting  
Carbamazepine - high risk of Steven Johnsons syndrome
- 60. Juvenile dermatomyositis - anti p140 antibodies
- 61. IV Magnesium in asthma - **decreased histamine release - inhibits smooth muscle constriction, decreases histamine release from mast cells and inhibits ACh release**
- 62. Severe refractory colitis - **Ciclosporin**
- 63. Metformin - indirect AMP Kinase activator
- 64. Nintedanib - tyrosine kinase inhibitor** - treatment of IPF
- 65. Mepolizumab** - monoclonal antibody anti eosinophil - binds to IL-5 on surface of eosinophils and reduceing their production and survival
- 66. Long QT type 1 —> potassium channels - codes for slow component outward rectifying potassium current
- 67. Long QT type 4 —> Calcium, sodium and potassium channels
- 68. Long QT type 3 —> sodium channels

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### MRCP JAN 2017

- 1. **Senescence phase of cells - end of mitosis** : progressive shortening of telomeres length due to repeated cell division with cell division stopping once telomeres falls below a critical length
- 2. G0 phase : resting phase - quiescent cells such as hepatocytes and neurones
- 3. G1 - gap 1 phase - cells increase in size - determines length of cell cycle - under influence of p53 - Cyclin D / CDK 4, Cyclin D / CDK6 , Cycline E / CDK2
- 4. S phase - synthesis of DNA, RNA and histones - centrosome duplication - Cyclin A /CDK2
- 5. G2 - gap 2 phase - cells increase in size - cyclin B / CDK1
- 6. M phase - mitosis - shortest phase of cell cycle
- 7. Hereditary spherocytosis - EMA binding test - autosomal dominant pattern of inheritance
- 8. Long QT syndrome Mmx : Atenolol, Propranolol, Metoprolol

9. Heart failure not controlled on ACE I / Beta blocker → with reduced EF < 35% and pulse sinus rhythm < 75 → **Sacubitril - Valsartan ( remove ACEi as ARB (valsartan) and ACEi cannot be given together )**
10. **Sacubitril** - not given in patients with history of angioedema and cough seen in ACEi - as Sacubitril also increases bradykinin levels
11. **Sacubitril** - prodrug → converted into sacubitrilat and **inhibits enzyme neprilysin** - which is responsible for degradation of atrial and brain natriuretic peptide
12. **HF with EF < 35% and PR > 75 bpm sinus rhythm -> Ivabradine - used when increased ventricular rate despite Beta blocker use or when beta blocker is contra indicated**
13. **SSRI** - can cause acute manic episode within 3-4 weeks of starting the drug
14. Guillain Barre- FVC monitoring - FVC < 20 mL/kg → shift to ITU ; FVC < 15 mL/kg → intubate
15. Right homonymous hemianopia - occipital cortex - posterior cerebral artery supply
16. IgE deficiency - parasitic infections
17. IgA deficient - GI tract infection - present on mucosal surfaces
18. Checking HbA1c after blood transfusion - 12 weeks
19. Paroxysmal AF with normal ECG → perform ECG event recorder → transmits the ECG by mobile and can be used when palpitations can occur
20. Haemochromatosis - diagnostic testing - genetic testing for C282Y and H63D mutations followed by liver biopsy for staging.
21. Hypoglycaemia due to alcohol drinking - **reduced gluconeogenesis** - alcohol is associated with reduced availability of pyruvate - as pyruvate is the initial substrate of gluconeogenesis pathway;  
Alcohol also causes redistribution of pancreatic blood flow more flow towards endocrine of pancreas resulting in increased insulin secretion
22. Physiological response to hypoglycaemia : **FIRST** decreased insulin production followed by increased glucagon secretion. GH and cortisol are also released later along with increased Adrenaline and cholinergic transmission.

**23.** Myelodysplasia & myelofibrosis - normal or low WBC count.

**24.** Increased WBC with predominant **lymphocytes** - **CLL**

**25.** Increased WBC with predominant granulocyte origin - neutrophils, basophils and eosinophils - **CML**

**26.** Heyde Syndrome - AS + Angiodysplasia due to vWF multimer deficiency as AS causes increased cleavage of vWF multimer

**27.** Adult male - 2500 kcal/day; adult woman - 2000 kcal/day

**28.** Non small cell Cancer Surgery CI :

1. **Pneumectomy** FEV1 < 2 L, **Lobectomy** FEV1 < 1.5

2. Hilar lymph node > 1 cm size

3. Stage IIIb or IV (metastases present - no surgery)

4. Malignant pleural effusion

5. SVC compression

6. Vocal cord paralysis

7. Tumor near hilum

**29. AML - good prognosis**

- Karnofsky score > 60%
- t(8;21)
- inv(16)
- t(16;16)
- t(15;17)
- NPM1 and CEBPA mutations
- MDR-1 phenotype negative

**AML Poor prognosis -**

- Karnofsky score <60%
- Chromosome -5, -7, 3q26 aberrations
- t(6;9)
- Karyotype 11q23
- FLT3/ITD mutation
- MLL partial tandem duplication
- BAALC over expression
- Mutations in IDH1 and IDH2
- Prior therapy related AML
- Prior myelodysplastic and myeloproliferative

**30.** Streptococcus bovis - gallolyticus associated with Infective Endocarditis - Colon cancer, Chronic liver disease

**31. Oroya fever - Bartonella bacilliformis - endemic to South America**

**Baronella quintana - trench fever - alcoholism and homeless patients - culture negative endocarditis**



32. Pregnancy - early features of Korsakoff syndrome - conjugate gaze palsy, nystagmus, lateral rectus

**33. Fabry's disease :**

- X linked recessive inheritance of lysosomal storage
- Mutation of GLA gene —> defect in enzyme alpha - galactosidase A
- Insufficient breakdown of substances produced from cell turnover - causing defective storage of sphingolipid and endothelial accumulation.
- C/F :
  - i) Pain - neuropathic pain - due to damage of peripheral nerve fibers
  - ii) Kidney : common cause of death is CKD
  - iii) Cardiac : accumulation of sphingolipids causes hypertrophy of cardiac muscle and restrictive cardiomyopathy; arrhythmia - complete heart block, VT, AR, MR
  - iv) Skin - angiokeratomas, anhidrosis or hyperhidrosis
  - v) Raynaud's phenomenon
  - vi) Ocular - cornea verticillata (vortex keratopathy)
  - vii) Clouding of cornea due to lens deposits
  - viii) Fatigue
  - ix) Peripheral neuropathy
  - x) Diarrhoea
  - xi) Osteoporosis
- genetic testing of GLA gene most accurate way
- Most commonest cause of death - cardiovascular or renal failure

34. Pioglitazone - PPAR gamma agonist - increases peripheral insulin sensitivity in muscle and fat - can cause increased fat storage - weight gain ; CI in heart failure and bladder cancer history, decreased eGFR

35. Arcuate scotomas - glaucoma

36. Omeprazole - mixture of R and S isomers

Esmomeprazole - ONLY S isomer of Omeprazole

37. Penicillins resistance - penicillin binding proteins mutations

Quinolones resistance - decreased outer membrane protein F & DNA gyrase mutations

Aminoglycosides resistance - N-acetyltransferase mutation

Macrolides resistance - Ribosomal mutation

38. Glucagon - increased HR via cAMP mechanism and positive inotrope - improves pulse and blood pressure.

Glucagon fails —> external transcutaneous pacing —> Isoprenaline infusion

39. Disseminated Gonococcal infection - Ceftriaxone + Azithromycin

40. HBsAg only marker detected during the first 3-5 weeks after being infected with Hepatitis B

41. HSP - Mx : Analgesia & Observations

42. Acute anterior uveitis - topical corticosteroids

43. Mycobacterium avian infection in HIV negative => daily triple therapy with Ethambutol + Rifampicin + Azithromycin for 15-18 months.

Rifampicin not tolerated - use Rifabutin

44. Severe cavitating MAC infection : Daily Quadruple therapy with Ethambutol + Rifampicin + Azithromycin + Streptomycin

45.  $NRR = 100 \text{ divided by difference in absolute risk}$

46. APC gene - FAP condition - chromosome 5q21-22

47. Atrial fibrillation - anticoagulation for 4 weeks after DC cardioversion.

48. IBD - non invasive - fecal calprotectin

49. Distal weakness + increased tone + hyper reflexia = Conus medullaris

50. **Dasatinib - used when Imatinib resistance is there** - inhibits activity of BCR-ABL kinase and SCR family kinase

**Lapatinib - dual HER2 and EGFR inhibitor**

**Pazopanib = multi targeted Tyrosine kinase inhibitor - renal carcinoma**

**Sunitinib - treatment of renal cancer - similar to Pazopanib**

51. Lesser curve of stomach - left and right gastric arteries

Coeliac trunk - 3 branches - 1) left gastric artery 2) common hepatic artery 3) splenic artery

Common hepatic artery branch —> gastroduodenal artery - supplies blood to proximal duodenum, pylorus and pancreatic head

Greater curve of stomach - left and right gastro-omental arteries

Short gastric arteries - supplies the fundus of stomach - **branches of splenic artery**

52. Assessing prognosis in COPD - BODE index - Airway obstruction by measuring FEV1, BMI, MRC Dyspnoea scale, distance walked in 6 minutes

53. Atrial fibrillation in COPD - Bisoprolol can be used - proven benefit of better control of ventricular rate and overall mortality

54. At risk of neutropenic sepsis - Oral Ciprofloxacin + Vancomycin IV

55. Steven Johnson syndrome - anti desmoplakin antibodies

Pemphigus vulgaris - Anti Desmoglein

Bullous pemphigoid - IgG and C3 deposition

56. RTA Type 1 - rare cause - Primary Biliary Cirrhosis

57. Methanol - formic acid crystals - damages optic nerve

58. Granisetron - 5-HT<sub>3</sub> antagonist - three sites of action :

- 1) vagal nerve terminals in GIT
- 2) CTZ in area postrema
- 3) nucleus tractus solitarius

Anterior hypothalamic nuclei - thermal regulation and regulation of thyroid function

Medial pre optic nucleus - release of gonadotrophin and thermoregulation

Supraoptic nuclei - release of vasopressin and oxytocin

Supra schismatic nuclei - control of circadian rhythms

59. Renal impairment - Warfarin affected - as it is highly protein bound -

Renal failure causes changes in acid base balance - increase in unbound warfarin - bleeding

60. Simvastatin dose adjustment needed in renal impairment if dose is > 10 mg

61. IgA nephropathy - poor prognosis - small amount of haematuria, hypertension, smoking, hyperlipidemia, ACE Phenotype DD, worsening creatinine, greater proteinuria

Good prognosis - frank haematuria, normal creatinine

62. Chronic indigestion - duodenal ulcer - due to vomiting of stomach acid - can also have hypokalaemia, anaemia, elevated bicarbonate and evidence of dehydration

63. LQT1 - IKr channel

LQT2 - IKs channel

LQT 3, 4, 9, 10, 12 - sodium channels

64. Persistent A-fib : Amiodarone

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### MRCP MAY 2017

1. 1,25-OH Vitamin D → increases gut absorption of vitamin D
2. **Acute promyelocytic leukaemia - t(15;17)** - evidence of DIC - retinoid acid receptor gene on chromosome 17 is involved in translocation with promyelocytic leukaemia gene on chromosome 15.  
Burkitt lymphoma - t(8;14)  
Acute myeloid leukaemia with white cell maturation - t(8;21)  
Mantle cell lymphoma - cyclin D1 gene on chromosome 11 - t(11;14)
3. **Kaposi's sarcoma - HHV-8**
4. Turner's syndrome patient presenting in heart failure - **coarctation of aorta** - due to LVF related to increased work load due to coarctation of aorta - causes syncope, SOB  
Turner's syndrome with Bicuspid aortic valve presents only after age of 18 years
5. Median nerve injury at elbow : \*\*\* pronator teres syndrome - **overuse injury** - both sensory and motor symptoms of median nerve compression  
**Carpal tunnel** - associated with median nerve injury leading to motor weakness affecting thenar eminence only; NO sensory loss over thenar eminence.
6. Functional residual capacity - volume of air present in lungs at end of passive expiration.
7. Long QT Mmx : Propranolol, Atenolol, Metoprolol, Nidolol  
High stellate ganglionectomy - used if patients do not respond to beta blockers  
ICD only for LQT patients who present with cardiac arrest non fatal and do not respond to beta blockers or high left stellate ganglionectomy
8. Acute Ischaemic stroke - no role of BP control in thromboembolic stroke if they are outside the window period of 4.5 hours for thrombolysis

**Acute intervention for BP in ischaemic stroke - only when BP is  $\geq 220/120$  or history of IHD, aortic dissection, hypertensive encephalopathy**

9. **Metformin** - reduces hepatic glucose output
10. **DPP-4 inhibitors** : increases glucose dependent insulin release
11. **Sulfonylureas** : increases glucose independent insulin release
12. **Liraglutide** - slows gastric emptying leading to positive weight control
13. **Indications to stop Exercise tolerance test** :  
dizziness; ataxia; pre-syncope; sustained VT; triplet of ectopics; SVT; heart block; ST depression of  $> 2\text{mm}$ , ST Elevation of  $> 3\text{mm}$
14. **Steroid induced psychosis** - seen after 3-4 days of treatment
15. **Coeliac disease** - increased risk of **Squamous cell carcinomas of oesophagus** - perform **UGIE** \*\*\*
16. **Right atrium** - receives deoxygenated blood from SVC, IVC, coronary sinus, anterior cardiac vein.  
**Right ventricles** - connects to lungs via pulmonary artery - carries deoxy blood to lungs

**Blood supply to heart - comes from left and right aortic sinuses within the aorta**

**Right coronary artery** - right marginal branch supplies the right atrium and right ventricle ; posterior IV branch (80% of people) supplies right ventricles and apex

**Left coronary artery - LAD** - LV, RV, IVS

Left Marginal artery - LV lateral wall ; Left Circumflex : supplies LA and LV in 20% of people.

All veins drains into coronary sinus which drains into right atrium - small cardiac vein, great cardiac vein, middle cardiac vein, left marginal vein, left posterior ventricular vein

\*\*\***Small cardiac vein** : runs along the coronary sulcus b/w RA and RV and opens into right eternity of coronary sinus ; receives blood rom posterior portion of RA and RV.

**Great cardiac vein** : begins at apex of heart - drains venous

blood from Left atrium and both ventricles.

**Middle cardiac vein** : at apex, and drains into coronary sinus  
right extremity

17. **Anti VEGF agents** - Nevelizumab, Aflibercept - used when there is no neovascularisation
18. **Azathioprine** - can be used as second line medication for RA and IBD - safe in pregnancy - check TPMT activity levels  
\*\*\* Pregnancy - do not use Leflunomide & MTX.
19. Tinea Cruris - jock itch - topical clotrimazole
20. **Hashimoto's thyroid's - complications** : thyroid lymphoma - diffuse large B-cell lymphomas - due to prolonged antigenic stimulation leading to development of lymphoma
21. **Publication bias** : concern in meta-analyses - especially results of a new class of medication
22. 25-30 mL/kg/day water, 1 mmol/kg/day potassium, Sodium, Chloride, 50-100 g/day glucose
23. **Dendritic cells** - antigen presenting cells via **MHC Class II to T lymphocytes** which then later differentiates into memory T cells and effector T cells.
24. IPF - **Nintenedib, Pirfenidone** - **decreased rate of FVC decline by 125 mL/year.**
25. **Amyloidosis - restrictive cardiomyopathy** - nervous disease and heart failure - biventricular heart failure with elevated JVP on inspiration due to reduced right atrial dilatation .
26. **Lupus nephritis - membranous nephropathy** - already on HCQ —> Add MMF 1 g/day for the first week, increase 2g/d in second week and f/b 3g/day. Total dose period is 6 months.  
**DO NOT STOP HCQ IN LUPUS KIDNEY DISEASE**
27. **Microscopic polyangitis with granulomatosis** - who are experiencing exacerbations on Corticosteroids and Cyclophosphamide - **administer Rituximab - MMF used when Cyclophosphamide & Rituximab show no improvement.**
28. **Terlipressin** - reduced portal blood pressure with reduction of blood circulation in portal vessels.

**29. Section 2 of Mental Health Act** - in a patient without any significant psychiatric history - admission under section 2 is most appropriate and it lasts for a period of 28 days - and **not renewable**.

**Section 3 of MHA** - admission for treatment order which lasts upto 6 months

**Section 5(2) of MHA** : applied for by a doctor - allows a patient to be held in hospital for 72 hours - designed for patients who **are already admitted**.

**Section 5(4)** : designed for nurses to use and can result in patients being held in hospital for upto 6 hours until alternative arrangements can be done

**Section 136** - allows police to hold a patient for upto 72 hours - must be repeated once patient has been assessed either because they have been discharged or detained under section 2 or 3.

**30. Gonorrhoea - pregnant woman** - nine Ceftriaxone 1g IM  
If patient refuses injection or has needle phobia - **Cefixime 400mg PO + Azithromycin 1g PO single dose**

**31. Flecainide - marked depression of fast sodium Channel in heart** - acute onset paroxysmal AF and no evidence of ischaemic or structural heart disease

**32. Wound botulism** - **penicillin // Metronidazole ( penicillin allergic)**

**33. Coeliac disease has a 2nd peak of distribution in 60 years age group patients**

**34. Sporadic CJD** - increased signal intensity in MRI in caudate and putamen - EEG shows periodic wave complexes and the 14-3-3 protein is found in CSF

**New onset variant of CJD** - increased signal intensity in thalamus and seen in younger individuals.

**35. MLH1 mutations** - DNA mismatch repair genes - found in colon cancer, stomach cancer, non small cell lung cancer

**36. Ras family mutations** - **GTPase regulatory gene** - associated in pancreatic cancer



**37. MODY - 5** mutation in hepatic nuclear factor - beta - HNF 1-B - associated with renal cysts and pancreatic atrophy

MODY 2 : Glucokinase mutations

MODY 3 : HNF 1-alpha mutation - responsive to sulfonylureas

**38. PDE 4 inhibitor - Aprelimast - Psoriasis**

**39. Statins CYP3A4 - Erythromycin, Clarithromycin, Ciprofloxacin , Ciclosporin**

**40. Scleroderma renal crisis - ACE inhibitors  
Prednisolone can worsen it**

**41. Relapsing remitting MS** - Dimethylfumarate is used.  
Natalizumab - associated with increase in risk of progressive multifocal leukoencephalopathy

**42. Liddle syndrome** - autosomal dominant - mutations in genes on chromosomes 16p12 - encodes beta and gamma subunits of Epithelial Na channels in collecting duct

**43. Opioids are substrates of CYP2D6 - cannot use SSRI with opiates as it leads to opioid toxicity**

**44. OAT1 inhibitor - Lesinurad - gout treatment**

**45. Thiazide diuretics inhibits KCNQ1 and KCNE3 channels - potassium channels**

**46. Bendroflumethiazide - inhibits Na-Cl symporter**

**47. Loop diuretic - inhibits Na/K/2 Cl transporter**

**48. Pharyngeal pouch** - INV - Barium swallow >>> UGIE

**49. Alcohol abuse** - drives PTH levels up - leads to hypocalcemia - alcohol abuse also has low platelet count

**50. Bullous pemphigoid** - trunk, flexures, axillary and inguinal folds - are commonly involved.

Mucosal lesions are also seen in 10-30% of patients - buccal and palatal mucosa commonly involved.

Rarely - larynx, genitals, and anus are involved.

Associated with Drugs like : **NSAIDs, Furosemide, Captopril, Penicillamine**

**51. Liquorice poisoning - hypokalaemia with hypertension due to 11 Beta hydroxysteroid dehydrogenase type 2 inhibition** - this enzyme is responsible for inactivating cortisol - decreased levels of this enzyme causes high cortisol levels and increased mineralocorticoid levels leading to hypokalaemia and hypertension

Hypokalaemia + hypertension = Conn's , Cushings, Liddle's ,  
11 beta hydroxylase deficiency

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### MRCP SEPT 2017

1. **Buprenorphine** : partial mu and kappa opioid receptor agonist
2. **Congenital Pelger Huet anomaly** - laminopathy associated with mutations in lamin B receptor; **bilobed nuclei in neutrophils and in homozygotes - associated with skeletal abnormalities - shortened limbs**
3. All interossei muscles - deep branch of **ulnar nerve - C8, T1**
4. C4 C5 nerve damage - dorsal scapular nerve - weakness of rhomboid muscles and elevator scapulae
5. C5/C6 - **long thoracic nerve damage, phrenic nerve, supra scapular nerve and lateral pectoral nerve**
6. Indapamide and Chlorthalidone >>> Bendroflumethiazide - as Bendroflumethiazide causes dysglycemia, hyponatremia and hypokalaemia
7. **Anti Zic-4 antibodies** - cerebellar degeneration - associated with **small cell lung cancer**
8. **Anti Yo antibodies** - cerebellar paraneoplastic - **ovarian and breast cancers**
9. **Anti ampiphysin antibodies** - associated with **Stiff person syndrome and encephalomyelitis - breast and lung cancer**
10. **Tocilizumab : Anti IL6 monoclonal antibody** - initial therapy for giant cell arteritis and as add on to reduce corticosteroid dose. Used in **Polymyalgia rheumatica**
11. **Golimumab - anti TNF** : used in treatment of Psoriasis & Psoriatic arthritis
12. FEV1 > 50% and features of no response to steroid / no asthma features —> LAMA + LABA = Umeclidinium / Vilanterol
13. **PDE 4 inhibitor - Roflumilast** - used when no good control of COPD on triple therapy of LABA + LAMA + ICS
14. **Greater curvature of stomach - left gastroepiploic artery**
15. **Gastroduodenal artery** - pylorus of stomach and proximal part of duodenum

- 16. Left gastric artery** - arises from coeliac trunk; runs along superior portion of lesser curvature of stomach - **ulcer in lesser curve can cause massive blood loss**
- 17. Right gastric artery** - arises from hepatic artery proper - lesser curvature of stomach and joins with left gastric artery
- 18. HNF -1 beta : MODY 5-** **renal cysts, pancreatic endocrine loss, epididymal cysts in men, bicornuate uterus in women**
- 19. Patients unsuitable for chemotherapy** - Thalidomide  
Thalidomide alternative - **Bortezomib - proteasome inhibitor - leads to cell cycle arrest and apoptosis**  
**Bortezomib + Dexamethasone - induction therapy in Myeloma for patients < 65 years**

**Myeloma Rx : Bendamustine + Prednisolone**

- 20. Ezetimibe - NPC1 L1** - responsible for intestinal uptake of cholesterol and phytosterols - Ezetimibe reduces cholesterol absorption from gut
- 21. Evolocumab - PCSK9 inhibitor** - reduces serum LDL cholesterol
- 22. Lead poisoning-** Fanconi syndrome, Proximal Type 2 RTA
- 23. Primary CNS Lymphoma** - Epstein Barr Virus - in both immunocompetent and immunocompromised individuals
- 24. Mepolizumab - anti IL-5 monoclonal antibody** - treatment for asthma when there are **elevated eosinophils.**  
**Asthma - elevated IgE levels - SC Omalizumab**
- 25. Abatacept - CTLA 4 immunoglobulin** - used in RA arthritis
- 26. PDE 6 inhibitor** - occurs in high doses of PDE 5 inhibition which causes blue discolouration of vision in patients taking Sildenafil
- 27. PML - JC virus** - multiple white matter lesions on MRI
- 28. Myasthenia gravis** - not responding to Pyridostigmine & prednisolone - **Azathioprine is 2nd line**
- 29. MODY 2 - glucokinase mutation** - diet controlled diabetes - no insulin needed
- 30. Belimumab** - monoclonal antibody - inhibits activation of B-lymphocyte stimulator - BLyS receptor  
Inhibition of BLyS down-regulates B lymphocyte activity —>

used in **SLE patients who fail to gain control despite using Hydroxychloroquine & high dose corticosteroids**

31. LADA with anti GAD antibodies - **Rx with Metformin - which indicates insulin resistance**
32. Anti GBM disease - **always normal ESR values**
33. **Systemic sclerosis - bacterial overgrowth - Metronidazole Rx**
34. **Bile acids - Obeticholic acid - Farnesoid X Receptor agonist** - reduces hepatic dysfunction associated with PBC
35. **PPAR Alpha agonist - Elafibranor** - clinical trials of NASH; Other PPAR alpha agonist - Fibrate
36. **Yersinia - Ofloxacin in renal impairment patients** - Yersinia infection can cause diarrhoea in adults and mesenteric lymphadenopathy -  
**Gentamicin used for Yersinia infection with normal renal parameters**
37. **Hyperthyroidism - pregnancy - early - PTU ; Late - carbimazole**
38. **Tramadol** - increases release of serotonin - when used in combination with antidepressants like TCAs, it can cause serotonin syndrome  
Tramadol when prescribed with CYP3a4 inhibitors - can lead to opiate toxicity.
39. Type 1 errors - incorrectly rejecting the null hypothesis - lack of blinding can lead to false positive result
40. Type 2 errors - small sample size
41. Conduction velocity in heart - **highest in Purkinje fibers**
42. **Early NASH - Liraglutide 3mg OD** - can be used in treatment of obesity where R/Fs such as hypertension , T2DM are present.
43. **Anti - ANNA3 antibodies** - Hodgkin's lymphoma - causes sensory neuropathy and encephalomyelitis

**Anti - Tr antibodies - Hodgkin's lymphoma - cerebellar degeneration**

44. **Lesinurad** - inhibits **URAT1 and OAT4** - leads to increased excretion of uric acid - causes a small increase in creatinine - and can lead to formation of new renal stones

45. **Genital herpes - pregnancy - Acyclovir at 36 weeks - 400mg TID**
  46. **Single episode on pulmonary edema - with evidence of bilateral renal artery atheroma - Rx with Amlodipine 5mg daily**  
Renal artery stenting is reserved for patients with progressive increase in serum creatinine despite good control of BP or recurrent episodes of pulmonary edema present.
  47. **Asthma - increased IgE —> Omalizumab ; Increased Eosinophil —> Mepolizumab**
  48. **Vedolizumab : antibody directed against α4-β7 integrin receptor - IBD Rx**
  49. **Pregnancy - increase thyroxine dose by 50% above baseline**
  50. **Pregnancy with Hepatitis A - provide Hepatitis A vaccine**
  51. **Pregnancy with jaundice in late third trimester - acute fatty liver of pregnancy**
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### **JAN 2018 MRCP PAPER**

1. **Alemtuzumab** - anti CD 52 Monoclonal Antibody - used in treatment of CLL and cutaneous T cell lymphoma, Multiple Sclerosis
2. **Atezolizumab** : Programmed cell death Ligand 1 PD-L1 inhibitor - used in treatment of non small cell lung cancer
3. **Sunitinib** : small molecule kinase inhibitor used in treatment of Renal cell carcinoma
4. **Pure seminoma - LDH elevated in 50% of seminoma (not beta hCG as it is elevated only in 20% of patients)**
5. **Pulsus paradoxus** - exaggerated fall in BP during inspiration > 10 mmHg - **cardiac tamponade, asthma, croup, OSA**
6. **Adult onset Still's disease - C/F** : arthralgia, increased serum ferritin, rash Salmon pink rash, maculopapular, increased rash appearance during fever, lymphadenopathy \*\*\* negative RF and ANA  
Mx : NSAID + Corticosteroids + MTX with Folic acid  
Arthritis - MTX , alternatives - Leflunomide, Tocilizumab  
Refractory to IL-1 and IL-6 therapy —> can use anti-TNF (Adalimumab, Infliximab, Etanercept)

Patient with systemic symptoms - suspected Macrophage

activating syndrome - use **Anakinra / Canakinumab - IL-1 inhibitor**

**Macrophage Activation syndrome - very common in Still's disease :**

Fever, organomegaly, increased ferritin, cytopenia, increases TGs, coagulopathy.

7. **Belimumab** - anti B lymphocyte stimulator antibody - **use in SLE**
8. **Golimumab** - anti TNF drug - psoriasis and psoriatic arthritis
9. **ST depression in V1 - V3 with dominant R wave in V2 - posterior circulation MI** - posterior descending artery which is branch of RCA supplies the posterior wall.
10. Small bowel bacterial overgrowth due to systemic sclerosis Rx - Rifaximin, Tetracyclines, Metronidazole
11. **Soleus muscle - plays a role in prevention of falling forwards on prolonged standing**
12. **Non arteritis ischaemic optic neuropathy** - rapid deterioration of vision against a backdrop of multiple vascular risk factors and partial oedema of optic disc.
13. **Cisplatin - causes cross linking of DNA - adverse effects :** peripheral neuropathy, ototoxicity, hypomagnesemia, atrial fibrillation due to hypomagnesemia , \*\* sometimes can cause Haemolytic Uraemic syndrome
14. **HER-2 antagonist** - Trastuzumab - dilated cardiomyopathy
15. **Pemphigus vulgaris Mx :** Corticosteroids —> Immunosuppressants - Azathioprine / MMF / Cyclophosphamide —> Biological - anti CD20 **Rituximab** —> **IV IG last option**
16. **Hypophosphataemic rickets - X linked dominant - PHEX gene - involved in regulation of FGF-23**
17. **Lymphogranuloma venereum - Doxycycline**
18. **Pancreatic exocrine insufficiency - fecal elastase**
19. **Drug induced Parkinsonism** - symmetrical, less likely to have tremors  
Akinesia with loss of arm swing is an early feature  
Bradykinesia, expressionless face, slow initiation of movement and speech difficulties.

Drugs involved - antipsychotics , metoclopramide,  
Prochlorperazine

20. **Mycophenolate Mofetil therapy adverse effects** : can cause tremors commonly , gum hypertrophy , seizures, GI disturbance Hypertonia, somnolence and symptoms of myasthenia syndrome are also seen
21. Sight affecting macular edema - focal laser therapy  
Anti VEGF therapy **avoided in pregnancy**
22. Normal pressure hydrocephalus - **therapeutic lumbar puncture - can assess response for medical therapy and shunt placement**
23. **Transthyretin amyloidosis - most common inherited form of amyloidosis - autosomal dominant**  
Abnormal formation of transthyretin - protein produced in liver to transport vitamin A and thyroxine - it is a negative acute phase reactant  
Patients with TTA can present any time - **C/F** : peripheral neuropathy, biventricular failure, ventricular wall thickening on ECHO, cardiac failure
24. **Bicalmutamide, Enzalutamide** - Non steroidal anti androgen therapy recommended in patients with metastatic prostate cancer which has become resistant to Goserelin  
**Docetaxel** : treatment for hormone relapsed prostatic carcinoma
25. **Evolocumab - PCSK9 inhibitor** - prevents degradation of LDL receptors and enables more LDL cholesterol to be removed from blood
26. Head injury patients with prolonged admission in hospital come with fever - suspect MRSA - **Linezolid which has good CNS penetration**
27. **Diabetic foot infection : co-amoxiclav**
28. **Acyclovir - DNA polymerase inhibitor**
29. **Sofosbuvir** - RNA polymerase inhibitor - inhibiting NS5B dependent RNA polymerase
30. **Marfan's syndrome - beta blockers / ARB** use as cardioprotective
31. **Trastuzumab - dilated cardiomyopathy - perform ECHO before starting Rx - R/W cardiac functioning every 3 months**

32. **Yersinia infection - tetracyclines, Quinolones, Macrolides**
33. Metformin & GFR : <30 - STOP ; 30-45 - decrease dose
34. Infective endocarditis - episodes of complete heart block - shows paravalvular extension of infection - surgical intervention needed.  
Other indications for Surgery :  
- cardiac failure / hemodynamic compromise  
- extensive valve incompetence  
- large vegetations  
- septic emboli  
- septic abscess  
- fungal infection  
- antibiotic resistant endocarditis  
- failure to respond to medical therapy
35. **Klebsiella pneumonia Rx** : Quinolones, Meropenem, Tazocin
- 

### MAY 2018 PAPER

1. **Osmosis** - passage of **solvent** across semi permeable membrane from low to high concentration.
2. **Reverse osmosis** : passage of **solutes** from high to low concentration across semi permeable membrane.
3. **Diffusion** - movement of molecules from high to low concentration in a solvent pool
4. Acute AIHA due to CLL therapy Fludarabine - **Rx with prednisolone**  
**Prednisolone + rituximab followed by blood transfusion if no response to corticosteroid treatment.**
5. Behavioural changes in **Fronto-temporal dementia** : treat with **SSRI Paroxetine** - SSRI for depression, anxiety, behavioural changes

Fronto-temporal + delusions - low dose atypical antipsychotic

**Topiramate** - can help in compulsive alcohol abuse seen in association with Fronto-temporal dementia.

6. **HLA-DR4** : Pemphigus, Drug induced lupus, IgA Nephropathy, Polymyalgia rheumatica, Rheumatoid arthritis, T1DM



7. **HLA B1502** - Steven Johnson syndrome - Carbamazepine use in Chinese population
8. **HLA B5701** - development of hypersensitivity to **Abacavir** - **HAART treatment - genetic screening before starting patient on Abacavir**
9. Beta blockers - erectile dysfunction
10. Spironolactone - erectile dysfunction, gynecomastia
11. Patient with significant bacterial sepsis + neutropenia => G-Colony stimulating factor can be used.
12. **Peripheral neuropathy** - Cisplatin, Oxaliplatin, Carboplatin
13. **Pembrolizumab** - PD-1 Receptor and immune checkpoint inhibitor - increased risk of autoimmune disease —> T1DM, autoimmune thyroid disease
14. **Dermatitis herpetiformis** - Skin Bx : IgA deposits
15. **Bronchial carcinoid skin presentation - pellagra**
16. **Pancreatic adenocarcinoma** - Necrolytic migratory erythema
17. **SCC of Esophagus - tylosis** - hereditary hyperkeratotic skin lesion
18. **PJ syndrome** - mutation in STK11 gene - tumor suppressor gene - autosomal dominant
19. T helper-2 cells : produces IL-4, IL-5  
IL-4 differentiates naive T cells into T helper 2 cells  
IL-4 —> promotes differentiation of macrophages into M2 macrophages - induces B cell class switching IgE production  
IL-4 : decreased classical M1 macrophage production and IFN-gamma
20. **Carcinoma breast** : CA-125 & CA 27.29 —> detects MUC1 in blood which is a well known marker of breast carcinoma.
21. **Cytokeratin fragment - 21 : non small cell lung cancer**
22. Severe pancreatic exocrine deficiency —> **Creon - pancreatic enzyme supplementation**
23. Active flare of lupus - **Reduced C3, C4, increased C3d (complement degradation product)**  
**Elevated ESR**  
**Elevated CRP - underlying infection**
24. **Allopurinol & Febuxostat** - xanthine oxidase inhibitor which promotes toxic accumulation of 6-mercaptopurine which is a product of Azathioprine.  
Avoid Xanthine oxidase inhibitors with Azathioprine.

25. **HLA B52 - Takayasu arteritis**
  26. **HLA B51 - Behcet's disease, increased susceptibility to Rubella infection**
  27. **HLA DR4** - drug induced lupus, Pemphigoid, IgA nephropathy, Polymyalgia rheumatica, Rheumatoid arthritis, T1DM
  28. **HLA DR2** - Narcolepsy, Goodpasture's Multiple sclerosis, SLE
  29. **Lithium induced hypothyroidism** - Start thyroxine to correct hypothyroidism - do not stop Lithium without discussion
  30. **Tourette syndrome - Atypical antipsychotic - Risperidone**
  31. **Listeria meningitis** - cheese dishes poisoning
  32. **Hepatitis B acute infection** - failed to clear after 4 weeks - **Tenofovir is prescribed.**  
**Tenofovir - nucleotide reverse transcriptase inhibitor**
  33. **Telaprevir, Boceprevir - Hepatitis C treatment** - both are **inhibitors of NS3/4A serine protease**
  34. **Giardiasis Rx** : Tinidazole one off dose
  35. **Membranous nephropathy with worsening proteinuria** - Corticosteroids + Cyclophosphamide
  36. **Graves eye disease Rx** : Prednisolone -> Rituximab —> Cyclosporine
  37. **Commonest cause of transfusion associated morbidity** - **Transfusion associated circulatory overload**
  38. **Scrub typhus** - black eschar , regional lymphadenopathy, pulmonary involvement ; Rx - Doxycycline, Azithromycin if Doxycycline is CI
  39. **Infliximab** - **safe in early pregnancy upto 16 weeks after which it is stopped**
  40. **Scombroid toxin** - accumulation of histamine in inappropriately stored fish - commonly involved fish —> tuna, mackerel, sardine, anchovy, bluefish
  41. **Eczema** - **do not smoke while using emollient as it can catch fire** - **NHS fire advice given**
  42. **Liddle syndrome** - congenital form of hypertension with hypokalemic metabolic alkalosis ; autosomal dominant - mutation of gene on chromosome 16 - Rx —> Amiloride, Spironolactone
  43. **Recurrent uterine prolapse** - ring pessary for patients unfit for surgery
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## JAN 2019 MRCP

1. **Palindromic rheumatism** - recovery of joint function between attacks - anti malarial HCQ are considered the best intervention
2. **Ascending limb of loop of Henle** - impermeable to water , active reabsorption of ions  
**Descending limb of loop of Henle** - impermeable to reabsorption of ions - water is freely absorbed
3. **U waves hypokalaemia** - seen in V2 and V3 - during to electrical change seen with depolarisation of Purkinje fibers and are also present in **hypocalcemia, & hypomagnesemia**
4. Chronic inflammation can be a cause of Amyloidosis in kidney
5. **Right middle lobe consolidation - obscuration of right heart border**
6. **LEft heart border - left upper lobe**
7. **Right upper lobe consolidation - increased opacification above the horizontal fissure - obscures border between lung and clavicle.**
8. Features suggestive of VT over SVT :
  - negative or positive concordance of V1-V6
  - Rsr' with tall first R wave - VT
  - extreme axis deviation - northwest axis - QRS positive in lead aVR and negative in leads I and aVF suggestive of VT
  - absence of typical RBBB or LBBB suggestive of VT
  - QRS > 160 ms suggestive of VT
9. DKA - acetoacetate presence after treatment shows mild positive ketones in urine
10. T-test : to differentiate between the means of two data where data is normally distributed
11. Renal SLE - gradual deterioration of kidney function —> MMF; Renal lupus - life threatening renal vasculitis —> Cyclophosphamide
12. **Goodpasture's syndrome** - Methylprednisolone + Cyclophosphamide
13. **Early Ankylosing spondylitis - MRI of LS spine & pelvis**
14. Frontal lobe - distal segment of anterior cerebral artery
15. **Verapamil - CYP3A4 —> Metabolised by inhibitors like Fluconazole which can increase the effect of CCB which can cause constipation**

16. **Hmeangioblastoma** - common in VHL disease - can cause sub-retinal oedema, retinal detachment or glaucoma - laser photocoagulation and anti VEGF are treatment options
  17. **Schistosoma mansion** —> haptic fibrosis, portal hypertension, variceal bleeding
  18. **Osteosarcoma associated with Long standing Paget's disease**
  19. Facial nerve damage - **just before it emerges from stylomastoid foramen** - as it gives off branches chords tympani
  20. **Central lesion facial nerve** - preservation of facial movements of muscles of forehead due to double innervation of facial nerve from the other side
- 

### **MAY 2019 PAPER**

1. Hereditary spherocytosis - associated with chronic hemolysis, increased reticulocytes, and spherocytes on blood film. Chronic hemolysis —> **bile pigment gallstones**
2. **Juvenile myoclonic epilepsy** - Sodium valproate - males; Levetiracetam - females
3. Entamoeba histolytica - **amoebiasis Rx** : metronidazole + diloxanide furoate
4. Primary pulmonary hypertension - patient pregnant on Bosentan - **switch bosentan for sildenafil** - Bosentan associated with malformations of head, mouth, face.
5. Gout with significant cardiovascular profile - **use Benzbromarone** - **inhibitor of uric acid transporter and non competitive inhibitor of xanthine oxidase** - **regular monitoring of liver function is required**
6. **Cortisol release** - **normal individuals** - highest in morning, lowest in midnight
7. **Cocaine** - **myocardial ischemia** - **GTN infusion & CCBs >>> Beta blockers & BZDs**
8. **Mitral stenosis in pregnancy** - consider percutaneous mitral valvotomy; Mmx with long acting nitrates, diuretics for heart failure, and beta blockers for control of ventricular rate. CI to percutaneous mitral valvotomy - significant valve calcification and presence of left atrial thrombus

9. **MHC Class II molecules are present on dendritic cells - Antigen presenting cells, other APCs** - macrophages, B cells
10. Cardiac myocytes - express MHC Class I antigen - associated with peptide fragments by proteasomal degradation, and flag cells for immune surveillance.
11. Chlamydia in pregnant women - Azithromycin 1g single dose OR erythromycin BD for 14 days
12. **Cyclophosphamide - T cell modulation** - rapidly metabolised in vivo to active metabolites 4-hydroxy-cyclophosphamide + aldofosfamide - **exerts its effects by T cell modulation** - cells which have low levels of alcohol dehydrogenase, CD +ve T lymphocytes
13. **Adalimumab - TNF inhibitor - used in RA** - MOA : blocks the interaction of TNF to p55 and p75 cell surface TNF receptors  
No good response to TNF inhibitors - **Tocilizumab IL-6 inhibitor can be used**
14. **Abatacept - CTLA-4 Immunoglobulin** - blocks T cell co-stimulation causing downregulation of inflammatory activity, IL-2 receptor, IL-6, rheumatoid factor, CRP, TNF-alpha
15. **Carcinoid tumor - measurement of urinary 5-HIAA levels** - fruits such as bananas, kiwi fruit, pineapple, plums, tomato can interfere with the measurement of 5-HIAA
16. HLA-B51 : HLA Class I antigen - **Behcet's syndrome**
17. **Chancroid** - one to two large **painful** ulcers - f/b **enlarged fluctuant inguinal lymphadenopathy** - Rx : **single dose Azithromycin or Ceftriaxone**
18. Psoriatic arthritis - failed 2 DMARD drugs - Add **Golimumab TNF alpha inhibitor**  
Failed Golimumab —> Add IL12 and IL23 inhibitor - Ustekinumab
19. Long term use of Nitrofurantoin —> **Pulmonary fibrosis**
20. **Bullous impetigo** - flaccid bullae with straw coloured fluid - heals with erythematous base - **Staph aureus** - Mupirocin & fusidic acid is the Rx
21. **Flecainide - class Ic anti-arrhythmic - blocks fast sodium channel**
22. **Chlamydia Rx** : single dose Azithromycin 1g OR Doxycycline 100mg for 7 days BD

- 23. Diabetic osteomyelitis with mixed bacterial picture -  
Vancomycin + Ceftriaxone**
- 24. Severe diabetic foot disease Rx : meropenem in penicillin  
allergic**
- 25. Cholesterol emboli Rx : supportive therapy only - dialysis if  
needed**
- 26. Early menopause** - less than a year —> Sequential combined  
HRT ; menopause > 1 year —> continuous combined HRT
- 27. Atypical pneumonia** - Macrolides - Erythromycin,  
Clarithromycin,  
Levofloxacin 750mg OD for 7 days  
Azithromycin 1g one dose f/b 500 mg OD for 7-10 days
- 28. Tacrolimus - extensively metabolised by CYP3A4 system -  
inhibitors can increased Tacrolimus levels -  
SICKFACES.COM**
- 29. Thin basement membrane neuropathy - autosomal  
dominant** - defect in collagen formation - no treatment  
required - presents with only microscopic hematuria

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### MRCP JAN 2020

- 1. Potassium levels > 7 —> QRS prolongation - high grade AV  
block with sinus bradycardia, slow Atrial fibrillation is also  
seen**  
**Potassium levels around 5.5 —> peaked T waves**  
**Potassium at 6.5 levels —> PR prolongation followed by  
flattening of P waves**
- 2. CKD related anaemia** - targets for EPO therapy —> 20%  
transferrin saturation, 100 micrograms/L for ferritin
- 3. >90% of lung cancers can be avoided by quitting smoking**
- 4. Lichen planus** - topical corticosteroids
- 5. CLL irradiated blood** - due to a risk of GVHD due to transfusion  
- **depletion of white blood cells**
- 6. S4 - after P wave**
- 7. Necrobiosis lipodica Rx —> topical corticosteroid followed  
by topical tacrolimus if corticosteroids do not help**
- 8. Pacing wire giving rise to ventricular tachycardia —> insertion  
into coronary sinus**

9. **Lymphogranuloma venereum** - Chlamydia trachomatis  
serotypes L1, L2, or L3 -infects mononuclear phagocytes -  
Doxycycline BD for 21 days
10. **Whipple disease** - IV Penicillin / Ceftriaxone followed by co-  
trimoxazole or tetracyclines for 12 weeks
11. Africa - malaria prophylaxis - Atovaquone / Proguanil ,  
Doxycycline, Mefloquine
12. Ankylosing spondylitis on MRI - osteitis or bone marrow edema  
on short inversion T1 images with lesions of high intensity or  
give dark signal on T1 weighted images or T2 images with fat  
suppression
13. Ulcerative colitis confined to rectum —> corticosteroids +  
Mesalazine enema
14. **Recurrent vaginal candidiasis** - FLuconazole 150mg every 3  
days for 3 dose followed by maintenance dose of 150mg  
weekly for 6 months
15. **Docetaxel - disrupts microtubule formation - renal tubular  
toxicity**
16. **Tocilizumab - anti IL 6 MAb** - treatment of RA
17. Nephrogenic DI - Rx : **Low salt, low protein diet, thiazide  
diuretics** —> not improving : **Amiloride + Thiazide**
18. Bartter syndrome polyuria - improves with NSAIDs
19. BCA-1 : **B lymphocyte chemoattractant** - unregulated in  
tissues subjected to chronic inflammation - chronic arthritis,  
MALT due to H.pylori
20. Presence of suicide note- **highest risk for successful future  
suicide**
21. IgE binds to mast cells and basophils —> massive release of  
histamine during anaphylaxis
22. Pseudoxanthoma elasticum complications - haemorrhage,  
Mitral valve prolapse
23. **Dematofibrosis lenticularis** - autosomal dominant - sclerotic  
bone lesions : osteopoikilosis and melorheostosis, connective  
tissue naevi - complications : bone malignancy, aortic stenosis,  
diabetes
24. **Opioids suitable for patients with raised creatinine -  
fentanyl, alfentanil, buprenorphine**
25. **HLA - siblings - 25% chance of identical HLA match  
50% match** - haploidentical match - chances of sharing half of

HLA of sibling

Identical twins - 100% HLA match

**26. Lithium - HTN - CCB**

**27. Salmeterol - long term partial agonist of beta - 2 receptor; more lipophilic than Salbutamol hence long duration of action -**

**28. Fixed flexion deformity of hip - rectum femurs muscle - other hip flexor muscles :** adductor longus, tensor fascia latae  
- Can be injected with Botulinum A toxin to help with muscle relaxation

**29. NSAID -** can cause inflammation in small bowel wall and proximal colon - microscopic colitis - ulcers, erosions and inflammatory cell infiltrate

**30. Membranous nephropathy -** Loop diuretics to decreased oedema followed by ACEi or ARB

**31. Hemoptysis -** minor symptoms - oral tranexamic acid - central tumors where bronchial artery embolisation cannot be done

**32. Stoma associated pyoderma gangrenosum -** IV Infliximab, Topical tacrolimus, benzoyl peroxide, potassium iodide, nicotine and 5-ASA

**33. Primary progressive Multiple sclerosis - Ocrelizumab**

**34. Relapsing Remitting MS : fingolimod**

**35. Aldosterone sensitive Na - K exchange pump : distal part of DCT**

**36. Microscopic colitis - PPI, NSAID, SSRI**

**37. PPI side effects-** hyponatremia, hypomagnesemia, osteoporosis, microscopic colitis , increased risk of C/diff infections

**38. Acute pancreatitis -** no complaints of vomiting or ileum —> trial of oral feeding

**39. Reticulocytes -** contains ribonucleic acid (RNA)

**40.**

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\*\*\*\* Ischaemic - Purtscher retinopathy - rare form of acute pancreatitis - which may cause temporary or permanent blindness

Severe pancreatitis features :

- age > 55 years
- Hypocalcemia



- Hyperglycaemia
- Hypoxia
- Neutrophilia
- Elevated LDH and AST

Drugs causing acute pancreatitis :

- Azathioprine
- Mesalazine
- Didanosine (anti retro viral drugs)
- Bendroflumethiazide
- Furosemide
- Pentamidine (pneumocystis jirovecii aerosol form Rx)
- Steroids
- Sodium valproate

Upper GI bleed :

**Glasgow-Blatchford score at first assessment - to decide if patients can be managed as outpatient or not - score of 0 → outpatient management**

**Rockall score - used AFTER endoscopy - percentage risk of rebleeding and mortality**

Oesophageal varices - band ligation

Gastric varices - N-butyl-2-cyanocrylate

**Sulphasalazine adverse effects :**

- rashes
- Oligospermia
- Headache
- Heinz body anaemia
- **Megaloblastic anaemia**
- **Lung fibrosis**

Mesalazine side effects : - GI upset, headache, agranulocytosis, acute pancreatitis, interstitial nephritis

C.diff infection -

- Clindamycin
- 2nd and 3rd generation cephalosporin
- PPI

C.diff - releases exotoxin A and B - acts on intestinal epithelial cells and inflammatory cells -> pseudomembranous colitis

C.diff toxin in stool

C.diff antigen - positive only shows exposure to bacteria rather than current infection

1st line - Oral vancomycin

2nd line - Fidaxomicin

3rd line - Vancomycin +/- IV Metronidazole

Recurrent episodes - within 12 weeks - Fidaxomicin

> 12 weeks - Vancomycin / Fidaxomicin

### **Bezlotoxumab - monoclonal Ab against C. Diff toxin B**

\*\* Colon cancer - sporadic mutations ~95% of them

APC gene mutation, activation of K-ras oncogene, deletion of p53, DCC tumor suppressor genes

HNPCC - Lynch syndrome - MSH2 and MLH1 gene are involved - Lynch syndrome patients also have a higher risk of endometrial cancer \*\*

### **FAP - APC gene - chromosome 5 - autosomal dominant**

Variant of FAP = Gardner's syndrome - osteomas of skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on skin

Refractory Crohn's disease and fistulating Crohn's to induce remission - **Infliximab**

**Metronidazole** - isolated perianal disease

## **Hemochromatosis - mutation of HFE gene - chromosome 6**

**\*\*** Babies born to Acute Hep B mothers or mothers chronically infected with Hep B → complete course of vaccination + Hep B Immunoglobulin

Anti-HBs : immunity through exposure or immunisation - **negative in chronic disease**

Anti-HBc : previous or current infection ; IgM anti-hoc appears during acute or recent Hep B infection ; IgG anti-HBc persists

HBeAg - marker of infectivity and HBV replication

HBsAg - ongoing infection - acute = < 6 months, chronic = > 6 months

Anti-HBc : caught - negative if immunised

Hepatorenal syndrome - splanchnic vasodilatation - decreased systemic vascular resistance → underling of kidneys

Hirschsprung's disease - failure of parasympathetic ganglion cells development in Auerbach and Meissner plexus

**Associated with Down's syndrome**

Gold standard INV - rectal biopsy

IBS constipation - use conventional laxatives

**Do not use lactulose**

**Resistance or no change after 12 months of using conventional laxatives → can use Linaclotide**

2nd line - low dose Amitryptiline 5-10 mg

**\*\*** Peutz Jeghers syndrome - autosomal dominant - serine threonine kinase LKB1 or STK11

Hamartomatous polyps causing GI bleeding, intussusception, small bowel obstruction, pigmented lesions on lips, oral mucosa, face, palms and soles.

**\*\* PPIs adverse effects :** hyponatraemia, hypomagnesemia, osteoporosis, **microscopic colitis**, increased risk of C.diff infection  
Microscopic colitis - chronic diarrhoea, colonoscopy + Bx should be considered when patients presents with chronic diarrhoea while taking PPI

Increased risk of C.diff - Clindamycin, Cephalosporins, PPIs

Clinical complications of hypophosphatemia seen in referring syndrome -

1. Cardiac dysfunction - decreased phosphate levels can impair myocardial contractility
2. Respiratory failure - phosphate is essential in ATP production - and for optimal functioning of respiratory muscles - muscles weakness of diaphragm and intercostal muscles
3. Neurological complications - confusion, seizures, coma - due to disturbed ATP metabolism in CNS
4. Blood - reduced 2,3-DPH can shift the curve to left - increased affinity of Hb to Oxygen - reduced oxygen supply to tissues causing tissue hypoxia
5. Rhabdomyolysis - impairs ATP reduction in muscles —> muscle breakdown and rhabdomyolysis

Small bowel bacterial overgrowth syndrome - Rx with Rifaximin / Metronidazole / Co-amoxiclav

Threadworms - Enterobius vermicularis - Mx : **Mebendazole**

### **Whipple's disease C/F :**

- malabsorption - diarrhoea, weight loss
- Large joint arthralgia
- Lymphadenopathy
- Skin - hyperpigmentation and photosensitivity
- Pleurisy, pericarditis
- CNS - ophthalmoplegia, dementia, seizures, ataxia, myoclonus

Jejunal biopsy : PAS granules in macrophages

Mx : Oral Co-trimoxazole for 1 year , sometimes **preceded by course of IV Penicillin**

Wilson's disease - express copper absorption from small intestine - defect in ATP7B gene in chromosome 13

Basal ganglia degeneration - particularly - putamen and globus pallidus

KF rings - green brown in iris periphery due to deposition of copper in Descemet's membrane

RTA - Fanconi syndrome

Hemolysis

**Blue nails**

Reduced total ceruloplasmin

Reduced total serum copper

Increased 24 hour urinary copper excretion

Confirmation INV - genetic analysis of ATP7B gene

Mx : Penicillamine, Trientine hydrochloride, Tetra-thiomolybdate

Antibiotic Mechanism of Action Common Resistance Mechanisms

Penicillins Inhibit cell wall synthesis Beta-lactamase production, altered penicillin-binding proteins (PBPs)

Cephalosporins Inhibit cell wall synthesis Beta-lactamase production, altered PBPs

Vancomycin Inhibit cell wall synthesis Altered cell wall structure

Aminoglycosides Inhibit protein synthesis Enzymatic modification, decreased uptake

Tetracyclines Inhibit protein synthesis Efflux pumps, ribosome protection

Macrolides Inhibit protein synthesis Ribosomal modification, efflux pumps

Quinolones Inhibit DNA replication/repair Target mutations, efflux pumps

Sulfonamides Inhibit folic acid synthesis Altered dihydropteroate synthase

Trimethoprim Inhibit folic acid synthesis Altered dihydrofolate reductase

Rifampin Inhibit RNA synthesis Target mutations, efflux pumps

- Anthrax : bacillus anthracis - Woolsorter's disease - contains tripartite protein toxin - 1) protective antigen 2) oedema factor which increases cAMP 3) lethal factor - toxic to macrophages

**Painless black eschar - cutaneous malignant pustule with no pus**

Anthrax can cause GI bleeding

Rx : **Ciprofloxacin**

- **Bacteriostatic Antibiotics** - Chloramphenicol, Macrolides, Tetracyclines, Sulphonamides, Trimethoprim
- **Abx inhibiting protein synthesis** - Chloramphenicol, Macrolides, Tetracycline, Fusidic acid, Aminoglycosides
- **Aminoglycosides - can cause misreading of mRNA**
- **Inhibits DNA synthesis** : Quinolones, Metronidazole, Sulphonamides, Trimethoprim
  
- Azole ; inhibits 14-alpha demethylase - which reduces ergosterol - P450 inhibition, Liver toxicity
- **Amphotericin B** - binds with Ergosterol forming transmembrane channels leads to monovalent ion leak - **Adv** : nephrotoxicity, flu like symptoms, hypomagnesemia, hypokalaemia
- **Nystatin** - binds with Ergosterol forming transmembrane channels leads to monovalent ion leak
- **Terbinafine** - inhibits squalene epoxidase
- **Griseofulvin** - interacts with microtubules to disrupt mitotic spindles - teratogenic
- **Flucytosine** - gets converted to 5-FU by cytosine deaminase - disrupts fungal protein synthesis by inhibiting thymidylate synthesis
- **Caspofungin** - inhibits synthesis of beta-glucan
  
- Aciclovir : Crystalline nephropathy
- Ganciclovir : Myelosuppression, agranulocytosis

Both Acyclovir & Ganciclovir - guanine analogs, inhibits viral DNA polymerase

- **Ribavirin** - guanosine analog - inhibits IMP dehydrogenase interferes with capping of viral mRNA - **Adv** : Haemolytic anaemia
- **Amantadine** : inhibits unceasing M2 protein of virus in cell - releases dopamine from nerve ending ; **Adv** : confusion, ataxia, slurred speech
- **Oseltamivir** - inhibits Neuraminidase
- **Foscarnet** - **inhabits viral DNA polymerase** - **Adv** : Nephrotoxicity, hypocalcemia, hypomagnesemia, seizures

Genital herpes pregnancy < 28 weeks - acyclovir now and at 36 weeks

> 28 weeks pregnancy - Acyclovir at 36 weeks and Caesarean

- **Brucellosis Rx** : Doxycycline + Streptomycin
- **Campylobacter jejune Rx** : Clarithromycin
- **Cholera Rx** : Doxycycline, Ciprofloxacin
- **Chlamydia Rx** : Doxycycline is 1st line, 2nd line - Azithromycin ; Pregnant - Azithromycin / Amoxicillin / Erythromycin
- **Pseudomembranous colitis - C.diff toxin** : Vancomycin, Fidaxomicin
- **Cryptosporidiosis** : Nitazoxanide - Immunocompromised patients; Rifaximin +/- in severe disease in immunocompromised patients  
Immunocompetent - supportive treatment
- **Cutaneous larva migrans Rx** : Ivermectin / Albendazole
- **CMV Retinitis Rx** : IV Ganciclovir ; alternative - IV Foscarnet / Cidofovir
- **Diphtheria Rx** : IM Penicillin, Diphtheria toxin
- **Typhoid / Paratyphoid Rx** : Azithromycin - mild, Ceftriaxone - severe ; Sensitivity of organism known - Ciprofloxacin
- **Giardiasis Rx** : Metronidazole
- **Gonorrhoea Rx** : IM Ceftriaxone 1mg single dose / Cefixime 400mgg + oral Azithromycin 2g single dose
- **Strongyloidosis Rx** : Ivermectin chronic; ALbendazoe, Thiabendazole
- **Enterobius Vermicularis pinworm** - Albendazole

- **Loa loa - Calabar swellings** - DEC
- **River blindness Onchocerca volvulus** - Ivermectin
- **Toxocara canis - dog roundworm** - visceral larva migrans and retinal granuloma - DEC
- Schistosoma, Paragonimus westermani, Clonorchis sinensis - **Praziquantel**
- Fasciola hepatic - liver fluke - **Triclabendazole**
- **MAC prophylaxis in HIV when CD4 < 100** - Clarithromycin/Azithromycin  
MAC Mx : Rifampicin + Ethambutol + Clarithromycin
- **CNS Toxoplasmosis in HIV** - Rx : Sulfadiazine + Pyrimethamine
- **Primary CNS Lymphoma - EBV** : Steroids + Chemotherapy +/- whole brain irradiation
- **HIV P. Jirovecii infection** - Co-trimoxazole, severe case IV Pentamidine  
Can use aerosolised Pentamidine - but high risk of pneumothorax  
If pO<sub>2</sub> < 9.3 KPa —> **steroids which reduces risk of respiratory failure**  
Prophylaxis - Oral TMP-SMX
- **Mucocutaneous** - topical Paramomycin  
**Cutaneous leishmaniasis** : Sodium stibogluconate / Meglumine antimoniate  
Alternatives : Paramomycin, Pentamidine  
**Visceral Leishmaniasis** - Liposomal Amphotericin B
- Lemierre's syndrome - infection of IJV by Fusobacterium necrophorum - septic pulmonary emboli seen
- **Leptospirosis** : high dose benzylpenicillin / Doxycycline
- **Listeria meningitis Rx** : IV Amoxicillin / Ampicillin + Gentamicin
- **Lyme disease - Borrelia Rx** : Doxycycline / Amoxicillin  
**Disseminated Lyme** - Ceftriaxone
- **Lymphogranuloma venereum** - Doxycycline
- **Meliodosis Rx** : IV Ceftazidime / Imipenem / Meropenem for 10-14 days  
F/B Oral TMP-SX + Doxycycline for 3-6 months
- **Mycobacterium marinum - fish tank granuloma** - Tetracyclines, Fluoroquinolones, Sulphonamides, macrolides
- **PID Rx** : Oral Ofloxacin + Oral Metronidazole (OR) IM Ceftriaxone + Oral DOxy + Oral Metro



- **HIV PEP** : Oral Tenofovir + EMtricitabine + Raltegravir / Lopinavir for 4 weeks
- **Pubic live Rx** : Malathion 0.5% / Permethrin 1% / Phenothrin 0.2% / Carbaryl 0.5%
- **Q fever - Coxiella burnetii** - Rx : Doxycycline
- **Scarlet fever :caused by Group A S.pyogenes** - Oral Penicillin V for 10 days / Penicillin allergic - Azithromycin
- **Schistosoma hematobium** - egg clusters pseudo-papillomas which are calcifications on X-ray - can cause obstructive uropathy and kidney damage - **swimmer's itch** - R/F for SCC of bladder - Rx : **single dose of Praziquantel**
- **HSV - 2** - multiple painful ulcers
- **Syphilis - primary, secondary, tertiary - primary syphilis** - Painless ulcer
- **Chancroid** - painful genital ulcers with U/L painful inguinal LN involvement
- **Lymphogranuloma venereum** - Chlamydia trachomatis - small painless pustule —> ulcer —> painless lymphadenopathy —> proctocolitis Rx => Doxycycline
- Splenectomy blood picture - Howell Jolly bodies, target cells, Pappenheimer bodies
- Co-trimoxazole - Sulfamethoxazole + trimethoprim - P.jirovecii pneumonia - adverse effects of Co-trimoxazole : Hyperkalemia, headache, Steven Johnsons syndrome
- **Syphilis : IM Benzylpenicillin** / Alternative - Doxycycline
- Cysticercosis - Taenia solium (pork) , Taenia saginata (beef) - **Niclosamide**
- **Hydatid disease** : dog tapeworm Echinococcus - liver cysts - **Albendazole**
- **African Trypanosomiasis Rx** - early disease - IV Pentamidine / Suramin; Late disease or CNS involvement - IV Melarsoprol
- **American Trypanosomiasis** : Benznidazole / Nifurtimox
- **Lassa viral hemorrhagic fever** : Ribavirin - excreta of infected African rats or person to person spread
- **Wuchereria Bancroft** - Rx with DEC
- **Yellow Fever** - classic description involves sudden onset of high fever, rigors, nausea & vomiting. Bradycardia may develop.
- A brief remission is followed by jaundice, haematemesis, oliguria

**Nevirapine - P450 inducer - NNRTI**

**Ritonavir - P450 inhibitor - Protease inhibitor**

**Vancomycin - MRSA infections** - inhibits cell wall formation by binding to D-Ala-D-Ala moieties - prevents polymerisation of polypeptides

Resistance : Alteration to terminal amino acid residues of NAM.NAG peptide subunits

### **Pathophysiology of IHD -**

1. Initial endothelial dysfunction
2. Fatty infiltration of sub-ends space by LDL particles
3. Monocytes → macrophages → phagocytose oxidised LDL → **foam cells**
4. Last step - smooth muscle proliferation and migration from tunica media into intima causing formation of fibrous capsule over the fatty plaque

Acute Coronary syndrome secondary prevention drugs

1. Aspirin
2. 2nd anti platelet - Clopidogrel
3. Beta blocker
4. ACE inhibitor
5. Statin

STEMI Criteria : C/D consistent with ACS > 20 mins duration with persistent ECG features in ≥ 2 contiguous leads of -

- 1) 2.5 mm ST elevation in V2-V3 in men < 40 years
- 2) ≥2 mm ST Elevation in V2-V3 in men > 40 years
- 3) 1.5 mm ST elevation in women V2-V3
- 4) 1mm ST elevation in other leads
- 5) New onset LBBB\

Two types of coronary reperfusion therapy - 1) PCI 2) Fibrinolysis

- 1) PCI : presentation within 12 hours of onset of symptoms AND PCI can be delivered within 120 minutes.
  - patient has ongoing ischaemia even after presenting >12 hours - PCI can be considered
- 2) Fibrinolysis : within 12 hours of onset of pain and PCI cannot be delivered in 120 minutes

**PCI** : dual antiplatelet = aspirin + 2nd drug

Drug therapy before PCI :

- Not taking an oral anticoagulant —> Prasugrel
- Taking oral anticoagulant —> Clopidogrel

Drug therapy during PCI :

- radial access - UF heparin with bailout GP IIb / IIIa inhibitor -
- Femoral access - **Bivalirudin with bailout GP IIb/IIIa inhibitor.**

**Fibrinolysis** : should be given an antithrombin drug - repeat ECG 90 minutes - still ST elevation persistent —> PCI to be done.

Following procedure —> **give Ticagrelor**

**Adenosine** - effects increased by Dipyridamole; adenosine effects blocked by Theophylline.

\*\* Avoid in asthma patients due to bronchospasm

Adenosine MOA : transient heart block in AV node; agonist of A1 receptor in AV node - causes hyperpolarisation and increased K<sup>+</sup> outward flux.

**ADP Receptor inhibitors - Clopidogrel, Ticagrelor, Prasugrel, Ticlopidine**

ADP - adenosine diphosphate - one of main platelet activating factors mediated by **G-coupled P2Y1 and P2Y12**

ADP R inhibitors - blocks P2Y12 receptor

**Ticagrelor** - can cause **dyspnoea** due to impaired clearance of adenosine

**Ticagrelor CI** : high risk of bleeding, intracranial haemorrhage, severe hepatic dysfunction.

Caution in asthma / COPD patients as it can cause dyspnoea

**Clopidogrel x PPI - Omeprazole & Esomeprazole** - reduces the anti platelet effects

Absolute CI of Prasugrel - Previous stroke / TIA, high risk of Bleeding (GRACE scoring), Prasugrel hypersensitivity

**Amiodarone - potassium channel blocker** inhibits depolarisation and prolongs AP— **class III**

Long half life - loading doses.

QT prolongation

P450 inhibitor

Nitrate tolerance - only with Standard release Isosorbide mononitrate

**Early diastolic murmur** - aortic regurgitation - increased by handgrip

Aortic regurgitation :

- collapsing pulse
- Wide pulse pressure
- Quincke nail bed pulsations
- De musset's sign - head bobbing
- Mid diastolic - Austin flint murmur - severe AR - due to partial closure of anterior mitral valve cusps caused by regurgitation streams

**Aortic stenosis - Ejection systolic murmur**

- narrow pulse pressure
- Slow rising pulse
- Delayed ESM

- Soft / absent S2
- S4
- Thrill
- Duration of murmur
- LVH or LVF

### **SASMR DARMS**

Systolic : AS, MR

Diastolic : AR, MS

Mid diastolic murmur - atrial myxoma - tumor plop

**ASD** : ESM, fixed splitting of S2

Ostium secundum - more commk, **Holt-Oram syndrome - triphalangeal thumbs + OS ASD**

**Ostium Secundum ASD ECG - RBBB + RAD**

Ostium primum ECG - RBBB + LAD, prolonged PR interval

Associated with abnormal AV valves

Bicuspid aortic valve associated with Turner's syndrome & Left dominant coronary circulation - PDA arises from Lcx

5% of patients also have coarctation of aorta

**Catecholaminergic polymorphic ventricular tachycardia -**

**autosomal dominant** - defect in Ryanodine Receptor RYR2 - found in myocardial Sarcoplasmic reticulum.

-Exercise or motion induced polymorphic VT causing syncope or SCD

Rx : beta blockers, ICD

- Arrhythmogenic RV cardiomyopathy - **ECG abnormalities in V1-3, typically T wave inversion. An epsilon wave is found in about 50% of those with ARV - this is best described as a terminal notch in the QRS complex**

- **Mutation of gene which encodes for components of desmosome**
- Rx : Sotalol, catheter ablation, ICD

**\*\*NAXOS DISEASE - ARVC + PALMOPLANTAR KERATOSIS + WOOLLY HAIR**

**\*\* ACE-inhibitors and beta-blockers have no effect on mortality in heart failure with *preserved* ejection fraction**

Direct thrombin inhibitor - Dabigatran

Haemorrhage adverse effect

Rapid reversal of Dabigatran - **Idarucizumab**

Dabigatran CI in prosthetic heart valve patients

**\*\*\* Dipyridamole - Phosphodiesterase inhibitor - elevates cAMP levels which reduces calcium levels.**

**Ebstein's anomaly :**

- Cyanosis
- Prominent a wave in JVP
- Hepatomegaly
- **Tricuspid regurgitation - PSM worse on inspiration**
- RBBB —> widely split S1 and S2

**Heart sounds**

- S1 : closure of mitral and tricuspid valves
- Soft S1 - long PR, MR
- Loud S1 : MS , L to R shunts, short PR, trail premature beats, hyperdynamic state

**S2**

- closure of aortic and pulmonary valves
- Soft : **AS**
- Loud : Systemic HTN (A2), Pulmonary HTN (P2) , hyper dynamic state, ASD without pulmonary HTN
- Fixed split S2 - atrial septal defect

- Widely split S2 - deep inspiration, RBBB, Pulmonary stenosis, severe MR
- Reversed split S2 - LBBB, severe AS, WPW Type B, PDA

**S3** - due to diastolic filling of ventricle

- LVF - dilated cardiomyopathy
- Constrictive pericarditis - pericardial knock
- MR

**S4** - atrial contraction against a stiff ventricle - P wave on ECG

- AS
- HOCM
- HTN
- HOCM - double apical impulse due to palpable S4

**Palmar xanthoma - remnant hyperlipidemia / type III hyperlipidemia / familial dysbetalipoproteinemia**

Due to defective apoE2 synthesis - **elevated IDL**

**Also seen are tuberous xanthomas**

**Type I hyperlipoproteinaemia :**

- **Type Ia - familial hyper-chylomicronemia** - decreased Lipoprotein lipase - increased Chylomicrons - C/F : acute pancreatitis, eruptive skin xanthomas, HS megaly, lipoma retinalis
- **Type Ib - familial apoprotein CII deficiency** - due to altered ApoC2 - elevated chylomicron - C/F same as Type Ia
- **Type Ic - LPL inhibitor in blood - similar to Type Ia**

**Type II hyperlipoproteinemia :**

- **type II a - familial hypercholesterolemia** - increased LDL levels due to defective LDL receptor deficiency - Rx : Bile acid sequestrates, Niacin, Statin  
C/F : Xanthelasma, Arcus seniles, tendon xanthomas
- **Type II b - familial combined hyperlipidemia : decreased LDL Receptor and increased ApoB - elevated LDL and VLDL**  
Rx : Statins, Niacin, Fibre

Type IV - familial hypertriglyceridemia - elevated VLDL

HOCM - large A waves on JVP

Associated with - Friedrich's ataxia, WPW

ECHO Findings - MR SAM ASH - MR, systolic anterior motion of anterior mitral valve leaflet, Asymmetric hypertrophy

### **JVP waves :**

- A wave : atrial contraction
- Large A wave - seen in increased atrial pressures - TS, PS, Pul HTN
- Absent in atrial fibrillation

Cannon a waves caused by right atrium contracting against a closed tricuspid valve —

regular —> VT, AVNRT ; irregular —> Complete heart block

**C wave** : closure of tricuspid valve

**V wave** : passive filling of blood into RA against closed Tricuspid valve - prominent / giant V waves in TR

X descent - fall in atrial pressure during ventricular systole

Y descent - opening of tricuspid valve

\*\* Inferior & Posterior infarction - acute MR —> papillary muscle rupture —> hypotension, pulmonary edema, systolic murmur.

**PDA** - let subclavicular thrill, collapsing pulse, large volume pulse, wide pulse pressure, apex beat ++

Mx - Indomethacin / Ibuprofen - neoante - inhibits PG synthesis  
If associated with another heart defect - PGE1 to keep the PDA open until after surgical repair.



**Pulsus paradoxus** - greater than normal  $> 10$  mmHg fall in SBP during inspiration  $\rightarrow$  severe asthma, cardiac tamponade

**Slow rising plateau pulse** - aortic stenosis

**Collapsing pulse** - PDA, AR, hyperkinetic state

**Pulsus alterans** - severe LVF

**Bisferiens pulse - double pulse** - mixed aortic valve disease, HOCM

**Jerky pulse** - HOCM

**Warm AIHA - IgG causes hemolysis at body temperatures - extravascular sites**

- idiopathic
- Autoimmune - SLE
- Neoplasia - lymphoma, CLL
- Drugs - methyldopa

Mx : steroids +/- Rituximab

**Cold AIHA - IgM - 4 degree - complement mediated - intra vascular**

- symptoms of Raynaud's and acrocyanosis
- Poor response to steroids
- Lymphoma
- Mycoplasma
- EBV

**Beta thalassemia** - autosomal recessive

**Hairy cell leukaemia** - pancytopenia, splenomegaly, vasculitis, dry tap, TRAP stain +ve

Mx - Chemo - Cladribine, Pentostatin

Immunotherapy 2nd line - Rituximab, IFN-alpha

**Multiple myeloma** - poor prognosis - raised beta-2 micro globulin, low albumin

**Sideroblastic anaemia** - delta aminolevulinate synthase 2 deficiency

Acquired causes of sideroblastic : alcohol, myelodysplasia, lead, isoniazid, Linezolid, Chloramphenicol

## HC MC anaemia

High ferritin, high iron, high transferrin

Blood film - basophilic stippling

Prussian blue stain - ringed sideroblasts

Mx - pyridoxine

## Drugs causing TTP :

- Ciclesonide
- OCP
- Penicillin
- Clopidogrel
- Acyclovir

TTP - fever, Microangiopathic haemolytic anaemia, fluctuating neuro signs due to microemboli, thrombocytopenia, renal failure

CKD - elevated hepcidin levels are due to decreased renal clearance - causes decreased iron absorption from gut and impaired release of stored iron from macrophages and hepatocytes

\*\* Metabolic acidosis inhibits of iron from  $Fe^{3+}$  to  $Fe^{2+}$

## Nephritis syndrome -

1. Rapidly progressive GN - crescentic - AKI - rapid onset - Goodpasture's, ANCA vasculitis
2. IgA nephropathy - Berger's disease - mesangiol proliferative GN

## Nephrotic syndrome :

1. Minimal change disease - Hodgkins, NSAID - steroid responsive - common in children
2. Membranous GN - proteinuria, nephrotic syndrome, CKD - infection rheumatoid, drugs, malignancy
3. FSGS - HIV, heroin, Alports, sickle cell

x

Red / orange urine - Rifampicin, Doxorubicin

Doxorubicin also causes cardiomyopathy dilated

### **HIV associated nephropathy - disease itself or Protease inhibitors like Indinavir can precipitate intratubular crystal deposition**

1. Massive proteinuria causing nephrotic syndrome
2. Normal or large kidneys
3. FSGS with focal or global capillary collapse on renal biopsy
4. Elevated urea and creatinine
5. Normotension

IgA nephropathy associated with - alcoholic cirrhosis, coeliac disease, dermatitis herpetiformis, HSP

Mesangial deposition of IgA

Mesangial hypercellularity - +ve IF for IgA & C3

NO PROTEINURIA

If persistent proteinuria present → ACEi

Active disease → not responding to ACEi → immunosuppression with steroids

25% of patients develop ESRF

Good prognosis - frank hematuria

### **Sirolimus - renal transplant immunosuppression - blocks IL-2 receptor**

### **Monoclonal antibodies - Daclizumab, Basiliximab**

**Erythrasma** is a generally asymptomatic, flat, slightly scaly, pink or brown rash usually found in the **groin** or **axillae**. It is caused by an overgrowth of the **diphtheroid Corynebacterium minutissimum**. Examination with Wood's light reveals a coral-red fluorescence. Topical miconazole or antibacterial are usually effective. Oral erythromycin may be used for more extensive infection

Alpha 1 :

Agonist - phenylephrine

Antagonist - doxazosin

Alpha 1a antagonist - tamsulosin

Alpha 2 -

Agonist : clonidine

Antagonist : Yohimbine

Non selective alpha antagonist - Phenoxybenzamine

Beta 1 :

Agonist - dobutamine

Antagonist - Atenolol

Beta 2 :

Agonist - salbutamol

Non selective beta antagonist - Propranolol

**Carvedilol & Labetalol** - mixed alpha and beta antagonist

Pathways of alpha and beta -

- all are G-protein coupled
- **alpha-1**: activate phospholipase C → IP3 → DAG
- **alpha-2**: inhibit adenylate cyclase
- **beta-1**: stimulate adenylate cyclase
- **beta-2**: stimulate adenylate cyclase
- **beta-3**: stimulate adenylate cyclase

**Severe drug reaction to Allopurinol** - HLA B\* 5801 allele screening

**COCP** - reduces risk of ovarian, endometrial and colorectal cancer

Increased risk of breast cancer and cervical cancer

Increased risk of stroke and IHD

Increased risk of VTE

**Digoxin toxicity precipitating factors :**

- Hypokalaemia - increased binding of Digoxin to ATPase pump
- Renal failure

- Hypomagnemsemia
- Hypoalbuminemia
- Hypothyroidism
- Hypercalcemia
- Hybernaternemia
- Acidosis
- Myocardial ischemia

Drugs causing increased digoxin toxicity -

- Amiodarone
- Quinidine
- Verapamil
- Diltiazem
- Spironolactone
- Cyclosporin
- Thiazides
- Loop diuretics

Common causes of DRESS - extensive skin rash + fever + organ involvement

Labs - low or high WBC, thrombocytopenia, Eosinophilia, abnormal LFT

- allopurinol
- Anti epileptics
- Antibiotics
- Immunosuppressants
- HIV treatment
- NSAIDs

Drugs causing agranulocytosis

- thyroid drugs : Carbimazole, PTU
- Atypical antipsychotics - Clozapine
- Antiepileptics - Carbamazepine
- Abx - penicillin, Chloramphenicol, Co-trimoxazole
- Antidepressants - Mirtazapine
- Cytotoxic drugs - MTX

**JAK2 inhibitor - Baricitinib**

**Monoclonal antibody - Tralokinumab**

**Both are used in Eczema after failure of treatment with Cyclosporine / MMF / Azathioprine**

**Brodalumab - Anti IL-17 - psoriasis treatment**

**Dapsone - dermatitis herpetiformis - when not improving with diet**

**Alzheimer - APO e4 allele carriage**

**Type III hyperlipidemia - APO e2 allele carriage**

**Massive PE - 50mg Alteplase over one minute UV**

**Hereditary hemorrhagic telangiectasia - mutation in ENG gene - causes HHT type 1**

**DPP 4 inhibitors - glucose dependent insulin release**

**Sulfonylureas - glucose independent insulin release**

**ADRB1 - resistance to Beta 1 drugs**

**ADRA1A - resistance to alpha 1 drugs**

**ADRA2A - resistance to alpha 2 drugs**

**ADRB2 - beta 2 drugs**

**EDNRB - gene for endothelin B receptor which is responsible for endothelin 1 degradation and gene dysfunction can be associated with accelerated HTN, pulmonary hypertension and hepatic fibrosis**

**Long standing and extensive psoriasis - cyclosporin as this condition is associated with Th2 cells**

**DR3 - autoimmune hepatitis, Primary Sjogrens, T1DM, SLE**

**Adult Hydrocortisone dose - 15-25 mg/day**

**Prednisolone - Hydrocortisone dose /4 = 4-6 mg/day**

**Immunocompetent host - CMV can cause sore throat and pharyngitis similar to IM picture - Rx with Ganciclovir and Acyclovir**

**Factor V Leiden screening test : Dilute Russell viper venom time**

**Blood samples mixed with snake venom in presence and absence of activated protein C**

**Multiple myeloma bony deposits - whole body MRI**

**Lebers hereditary optic neuropathy** - progressive U/L optic neuropathy and other eye is gradually involved

Fundoscopy - telangiectasia and pseudo-edema of optic disc

**Impaired glutamate transport with increase ROS and oxidative damage**

**Mx - Idebenone**

**Entacapone** - increases the duration of action of Levodopa by blocking the action of enzyme catechol-O-methyl transfer - which metabolises levodopa

Used in combination with levodopa to reduce off phenomena seen with levodopa

MAO B inhibitors such as Rasagiline can also be used to reduce motor fluctuations

Ondansetron - 5 HT3 antagonist - centrally acting - **but can cause QT prolongation - avoid in patients with long QT**

Cyclizine and Diphenhydramine has anti cholinergic actions

Severe depression have excessive sleep due to SSRI —> Use

**Moclobemide - MAO inhibitor**

Antibodies (immunoglobulins) may be divided into 2 main pairs:

- Fab region: antigen-binding fragment - the region that binds to antigens
- Fc region: fragment crystallizable region - the tail region of an antibody that interacts with cell surface receptors

### **Absent ankle jerks (LMN) + Extensor Plantar (UMN)**

- SCD of spinal cord
- MND
- Friedrich's ataxia
- Syringomyelia
- Taboparesis - tertiary syphilis
- Conus medullaris lesions

Acute disseminated encephalomyelitis - MRI : areas of supra and infra tensorial demyelination

Mx :IV glucocorticoids & IVIG

Anti NMDA R encephalitis - OVarian teratoma

- FLAIR sequences —> deep subcortical limb structures
- Anti- MUSK antibody specific to muscle kinase in Myasthenia gravis can be found - no evidence of thymoma and ACh receptor antibodies.

### **Wernicke's aphasia :**

- lesion of superior temporal gyrus
- Supplied by inferior division of MCA
- Sentences that make no sense
- Word substitution
- Neologism
- Word salad
- SPEECH FLUENT - IMPAIRED COMPREHENSION

### **Broca's aphasia :**

- inferior frontal gyrus
- Superior division of MCA
- Speech non fluent, laboured, halting



- Repetition impaired
- Comprehension - intact

### **Conduction aphasia :**

- stroke of arcuate fasciculus
- Speech fluent, comprehension normal
- Repetition poor - aware of mistakes they are making

Brain abscess - 3rd generation cephalosporin + metronidazole

### **Cervical spondylitis myelopathy**

- neck pain
- Wide based, ataxic or spastic gait
- UMN weakness in lower limbs - increased reflexes, increased tone, upping plantar
- Bladder dysfunction - urgency, retention

### **Charcot Marie Tooth disease**

- foot drop
- High arched feet
- Hammer toes
- Distal muscle weakness
- Distal muscle atrophy
- Hyporeflexia
- Stork leg deformity

**Carbamazepine** - blocks Na channels and prolongs refractory period

**Ethosuximide** - blocks T type calcium channels in thalamic neurons

L5 radiculopathy - weakness of hip abduction , loss of inversion , loss of eversion, foot drop

Common peroneal nerve lesion - weakness of dorsiflexion (foot drop), weakness of eversion, weakness of extensor hallucis longus

**Preserved ankle inversion**

**Friedrich's ataxia : GAA repeat on chromosome 9 - Frataxin gene**

- absent ankle jerks, extensor planters
- Cerebellar ataxia
- Optic atrophy
- Spinocerebellar degeneration
- Cardiac —> HOCM
- DM
- High arched palate

Huntington disease - CAG repeat - defect of Huntington gene on chromosome 4

Degeneration of cholinergic and GABA neruons in striatum of basal ganglia.