GASTROENTEROLOGY NOTES

UPPER GI DISORDERS

Achalasia: Botulinum injections are most effective of all the options for relieving a lower oesophageal sphincter restriction which leads to achalasia. Nifedipine, nitrates or sildenafil can also be used, but are less effective. Surgically, *Heller's oesophageal myotomy* is the best treatment option, it can be done via an abdominal incision or laparascopically.

BCS is a good mnemonic for **Barrett's** dysplasia.
Barrett's Columnar replaces Squamous in Barrett's oesophagus. This is also known as small intestinal (columnar) metaplasia. There is increased risk of oesophageal adenocarcinoma.

Nitrates, caffeine and alcohol can help relieve symptoms by relaxing lower oesophageal tone. Not all patients with **GORD** should undergo an OGD (should be considered if GI bleeding or symptoms of dysphagia occur). Oesophagitis is present in half of GORD patients. Oesophageal manometry or oesophageal motility study measures the strength of the lower oesophageal sphincter. This would rule out achalasia.

A **Mallory-Weiss** tear occurs in the mucous membrane typically in the lower oesophagus. Mallory-Weiss tears are usually caused by forceful or prolonged vomiting or coughing. They may also be caused by epileptic convulsions. The tear may be followed by vomiting bright red blood or by passing blood in the stool. The incidence is 4 in 100,000 people.

Achlorhydria (absence of gastric acid secretion) can be caused by immune destruction to the stomach wall, malnutrition and marijuana use. The *pentagastrin test* is used as a diagnostic aid for evaluation of gastric acid secretory function.

HEPATITIS

Hepatitis A is a picornavirus.
Hepatitis B is a hepadnavirus.
Hepatitis C Virus is a flavivirus. It is a single-stranded RNA virus.

Hepatitis B

A positive **anti-HBc** (IgM) and **HBsAg** suggests acute infection. When the infection resolves, **HBsAg** becomes negative and **anti-HBc** (IgG) is positive. In patients who have been vaccinated, HBsAg is negative and anti-HBs is positive.

HbcAg is the first detectable antigen in acute infection but is also detectable in chronic infection. HbsAg is detectable in chronic infection.

HbsAb is a sign of previous infection or immunisation.

HBeAg (not HBcAg) is the best marker of infectivity, and is used as an important criteria for selection of patients who have chronic hepatitis B **for interferon (α-2B)**

therapy. HBV DNA and HBeAg levels are measured in response to the therapy and undetectable levels would be considered successful treatment.

10% of patients with **hepatitis B** develop chronic infection
(as compared to **hepatitis C** where 80% develop chronic infection).

30% of patients with **hepatitis C** develop hepatocellular carcinoma over 30 years.
20% develop cirrhosis over 20 years.
The treatment options are ribavirin or PEG (polyethylene glycolated) interferon.
IFN α is only effective in clearing the virus in 25% of patients.

Meta-analysis of data strongly suggests a two to three-fold enhanced efficacy of *interferon-ribavirin* combination therapy over interferon monotherapy in all major subgroups of chronic hepatitis C patients. In hepatitis C, response to therapy is determined by normalisation of hepatic transaminases and undetectability of hepatitis C RNA in plasma.

Hepatitis D (delta) is a superimposed infection to Hepatitis B.

Hepatitis E causes acute illnesses, and does not result in a chronic carrier state. It is usually transmitted in a faeco oral route (similar to hepatitis A). It occurs mostly in developing countries and is widespread in India, Asia, Africa and Central America.

Hepatitis G virus or GBV-C does not appear to cause progressive liver disease.

Autoimmune hepatitis occurs in younger to middle aged women. 25% present as acute hepatitis, but the onset is usually insidious. Amenorrhoea is relatively common. It is associated with hyperglobulinaemia rather than hypoglobulinaemia. 60% are associated HLAB8, DR3 and DW3. The sicca syndrome (xerostomia/dry eyes, keratoconjunctivitis sicca) may occur.

LIVER DISEASE

In **hemochromatosis**, the commonest mutation is C282Y. It is found in approximately 90% of cases. The mutation is on chromosome 6, affecting the HFE gene. There is an increased incidence in males.

The serum Fe is elevated (> 300 mg/dL).
The *serum transferrin* saturation is a sensitive parameter of increased Fe and merits evaluation when > 50%.
The *serum ferritin* is increased ferritin of >1000 μmol/l is suggestive (normal <200).
Urinary Fe excretion is markedly increased (> 2 mg/24 h) by the chelating drug deferoxamine (500 to 1000 mg IM based on the size of the patient), and this has been used as a diagnostic test.

In addition, when the Fe content in the liver is significantly increased, an MRI may reflect this change. Liver biopsy had been the gold standard in diagnosis; it now serves only to provide evidence of fibrosis (cirrhosis). Gene assay (Homozygosity C282y mutations) is the also an excellent diagnostic test.

Venesection is preferred therapy . Treatment consists of bi-weekly venesection removing approximately 500 ml per week. Desferrioxamine infusion (another iron chelator) can also be used.

Iron infiltrates the parathyroid glands and can cause hypoparathyroidism.
In **haemochromatosis** , joint deposition of iron occurs, causing arthropathy.
Increased iron deposition in the skin stimulates increased melanin production.
Haemochromatosis is a recognised cause of restrictive cardiomyopathy.
Cardiac damage is commonly seen with ferritin >2,000 ng/l.

Wilson disease : The abnormal gene is the ATP7B gene on chromosome 13. It is autosomal recessive. Kayser-Fleischer rings are often seen on slit lamp, but not always. The best test is hepatic copper concentration (> 250 µg /g of dry weight). .
Typically there is low serum copper levels but high urine excretion of copper. There is low liver production of caeruloplasmin (< 20 mg/dl) in 95% of patients.
Copper deposits can occur in the liver and kidney, hence affecting vitamin D metabolism leading to osteomalacia/osteopenic changes.

Non-alcoholic steatohepatitis (NASH) is a form of liver disease resembling alcoholic liver disease in a patient who does not consume significant amounts of alcohol. The natural course is relatively benign, but liver cirrhosis. together with all its sequelae, may develop; sometimes liver transplantation is indicated. NASH is associated increased prevalence of Insulin resistance/type 2 diabetes. There may also be lipid abnormalities and increased iron stores.

Abdominal tenderness is found in more than 50% of patients with **Spontaneous Bacterial Peritonitis**. Findings on the abdominal examination can range from mild tenderness to overt rebound and guarding. Traditionally, three fourths of SBP infections are caused by aerobic gram-negative organisms (50% of these being *Escherichia coli*), and one fourth of these infections are due to aerobic gram-positive organisms (*streptococcal* species).
An ascitic fluid neutrophil count of > **250 cells/mL** and ascites lactate level of >25 mg/dL are the single best predictors of SBP. A combination of an *aminoglycoside* and *ampicillin* or *cefotaxime* can be used.

Budd-Chiari syndrome is thrombosis of the hepatic vein, the major vein that leaves the liver. Most patients have an underlying thrombotic tendency. About 10% have polycythemia vera, and about 10% have been on the OCP. The most common symptoms in Budd-Chiari syndrome are hepatomegaly, abdominal pain, ascites and jaundice.

Child's Pugh classification includes bilirubin, prothrombin tine, encephalopathy scores, ascites and albumin to measure the severity of liver disease.

Somatostatin its derivative, **octreotide**, and **terlipressin** are often used for emergency treatment of bleeding **oesophageal varices** in patients with cirrhosis of the liver.
Beta blockers (nadolol), nitrates, vasopressin analogues and somatostatin analogues can also be used for reducing rebleeding in oesophageal varices.

Wernicke encephalopathy is a neurologic disorder of acute onset caused by a thiamine deficiency. The condition is characterized by ocular abnormalities, ataxia, and a global confusional state.

Wernicke encephalopathy results from a deficiency in vitamin B-1 (ie, thiamine). The episode may have been precipitated by intravenous dextrose administration which exhausted his vitamin B reserves. B vitamins should be administered to all alcoholic patients requiring dextrose.

The main features of **Korsakoff's psychosis** is short term memory loss and subsequent compensatory confabulation by patient. Other symptoms may include delirium, anxiety, depression, confusion, delusions and insomnia. The treatment is with intravenous thiamine.

Hepatorenal syndrome (HRS) is the development of renal dysfunction in patients with severe liver disease (acute or chronic) in the absence of any other identifiable causes of renal pathology.

BOWEL DISEASE

Crohn's disease is characterised by transmural inflammation, neutrophil infiltrates, lymphoid aggregates, fissures, preservation of crypt architecture and noncaseating granulomata.

Ulcerative colitis is typified by mucosal inflammation, general inflammatory cell infiltration, goblet cell mucus depletion and crypt abscesses.

Ulcerative Colitis Apart from episcleritis, UC is also associated with cholangiocarcinoma, amyloidosis, pyoderma gangrenosum, ankylosing spondylitis, sacroiliitis.

X RAY changes
Loss of haustral pattern, lead pipe, and shortened colon on the X ray, suggests *ulcerative colitis*. In **Crohn's disease**, transmural inflammation with formation of fissures, ulcers and granulomata, and cobblestone appearance are seen.

Inflammatory conditions (e.g Wilson's disease) and drugs such as methyldopa and isoniazid can precipitate **chronic active hepatitis**.

Coeliac Disease: Folate levels are usually normal but not B12 in coeliac disease (in Crohns both are decreased). **Dermatitis herpetiformis** manifests as a pruritic rash. It is associated with HLA DQ2 haplotype. *Anti-endomysial antibodies* may be present. Coeliac disease (gluten sensetive enteropathy) is relatively common in Ireland. Gluten is found in wheat, rye and barley.
Biopsy in **coeliac disease** typically shows:
hypertrophied crypts of Lieberkuhn,
villus atrophy,
degenerate surface epithelial cells,
an increase in intraepithelial lymphocytes.

Jejunal biopsy demonstrating improvement with a gluten free diet is the best form of diagnosis. There is an increase in *gastric and small bowel malignancies*.

Dapsone (diaminodiphenyl sulfone) and sulfapyridine are the primary medications used to treat **Dermatitis Herpetiformis** (DH). Dapsone often is used initially; sulfapyridine is substituted in patients unable to tolerate dapsone.

Whipple's disease, may be confirmed by small bowel biopsy. This will show large, foamy PAS positive macrophages in the lamina propria. Whipple's disease affects mainly men aged 30 to 60. It is caused by an infection with *Trophyrema whippelii*. Symptoms of Whipple's disease include diarrhea, inflamed and painful joints, fever, and skin darkening. Severe malabsorption results in weight loss along with fatigue and weakness caused by anemia. Antibiotics such as *tetracycline, co-trimoxazole and penicillin* can be used for treatment (6-12 months).

BILIARY DISORDERS

Chlorpromazine, tricyclic antidepressants, azathioprine, augmentin and erythromycin cause **cholestatic jaundice** and also associated hepatitis.

Primary sclerosing cholangitis is usually seen in males. It is typically associated with ulcerative colitis. A positive pANCA can occur. The best investigation to confirm this is ERCP, which will reveal multiple strictures in the biliary system. 10% of patients with PSC will progress towards developing cholangiocarcinoma.
There is a cholestatic picture (high alkaline phosphatase) on the liver function tests, but not necessarily high bilirubin. pANCA is positive in about 90% of patients with PSC.
Ursodexoycholic acid improves clinical symptoms and reduces biochemical evidence of cholestasis but no effect on morbidity and mortality has been demonstrated

Primary biliary cirrhosis is more common in females and is usually associated with raised IgM levels. The diagnostic hallmarks for PBC include a cholestatic serum biochemistry: increased serum cholesterol, a moderate increase in triglyceride, serum lipaemia and reduced HDL levels. Clinical features include: palmar xanthomas; tuberous xanthomas (particularly on extensor surfaces); tendinous xanthomas are rare. Connective tissue disorders such as Sjogren's syndrome and scleroderma are associated.
Histology shows white cell damage to the biliary epithelium with non necrotising granuloma formation in the portal triad.

Treatment should be ursodeoxycholic acid, and replacement of vitamins A,D, E and K, as well as calcium [risk of osteoporosis]. *Ursodeoxycholic acid* lowers serum bilirubin and symptoms of itching, and prolongs the progression towards requirement for liver transplantation. Liver transplantation does not cure the condition.

Unconjugated hyperbilirubinemia in **Gilbert syndrome** is due to underactivity of the conjugating enzyme system *bilirubin-uridine diphosphate glucuronyl transferase* (bilirubin-UGT) which converts bilirubin to a conjugated, water soluble form.

Crigler Najjar is a more severe form in which the same enzyme is absent and there is neonatal jaundice due to very high levels of unconjugated hyperbilirubinaemia.
Dubin-Johnson syndrome is asymptomatic mild jaundice due to impaired excretion of bilirubin. In contrast to Gilbert's syndrome, the hyperbilirubinemia is conjugated and bile appears in the urine.

MALT lymphoma is the third most common type of non-Hodgkin lymphoma, although it only accounts for about 7-8% of these tumours. MALT lymphomas have been described at almost all extra-nodal sites, but are most commonly found in the gastrointestinal tract (stomach is the commonest).

Low grade gastric MALT tumours which are associated *Helicobacter Pylori* infection respond in over 80% of cases to helicobacter eradication. A proportion of patients will not respond to eradication therapy alone and will go on to more conventional anti-lymphoma therapies such as such as cyclophosphamide, chlorambucil, nucleoside analogues, or radiotherapy.

PANCREATITIS

Coxsackie, mumps, ECHO and hepatitis viruses as well as hypothermia can cause **acute pancreatitis**.

The following are **poor prognostic indicators in acute pancreatitis**:
Calcium < 2.0 (hypocalcaemia rather than hypercalcaemia as a consequence)
WCC > 15
Urea >16
ALT >200
PaO2 <8
Age > 55 years
Glucose > 10

Chronic Pancreatitis
Cullen's sign (periumbilical discolouration) can be present
Grey Turner's sign (flank discoloration) can be present
Purtscher's retinopathy (ischaemic areas in the retina) can be present
lack of digestive enzymes leads to steatorrhoea

In **chronic pancreatitis**, trypsin secretion is reduced. *Trypsin* is required in the processing of dietary B12 which enables absorption and hence B12 deficiency is the most likely.

Causes of a raised **amylase** are:

acute/chronic pancreatitis
pancreatic cysts and carcinoma
perforated duodenal ulcer
ovarian carcinoma
ectopic pregnancy
gallstones
salivary tumour
adenitis
mumps
diabetic ketoacidosis
anorexia

MISCELLANEOUS DISEASES

Peutz-Jeghers syndrome is an autosomal dominant inherited disorder. The cause of Peutz-Jeghers syndrome appears to be a germline mutation of the *STK11* (serine threonine kinase 11) gene in most cases. It is characterized by intestinal hamartomatous polyps in association with mucocutaneous melanocytic macules. A 15-fold elevated relative risk of developing cancer exists in this syndrome over that of the general population.

Carcinoid syndrome is diagnosed by raised urinary 5-HT levels. A precursor of 5HT, tryptophan is highly metabolised and consequently niacin deficiency (**pellagra**) occurs. The three D's dementia, dermatitis (a photosensitive rash) and diarrhoea occur.

Gut Hormones

Secretin is produced by the jejunum. It relaxes the oesophageal sphincter and also stimulates pancreatic enzyme secretion.

Gastrin is secreted by the G cells of gastric antrum. It stimulates parietal cells produce hydrochloric acid. Its production is stimulated by neural reflex pathways and also by direct effect of digested peptides on the G cells. It also stimulates the production of bicarbonate.

Vasoactive intestinal peptide (VIP) promotes intestinal water and electrolyte secretion.

VIPomas [vasoactive intestinal peptide (VIP)] originate in amine precursor uptake and decarboxylation (APUD) cells of the gastroenteropancreatic endocrine system and in adrenal or extra-adrenal neurogenic sites.

Features of VIP syndrome include watery diarrhea, hypochlorhydria, hyperglycemia , hypercalcemia, flushing and hypokalaemia due to diarrhoea.

Initial treatment is directed toward correcting volume and electrolyte abnormalities by using potassium chloride and sodium bicarbonate. *Octreotide* controls diarrhea in 80% of cases. *Glucocorticoids* reduce symptoms in 50% of patients with VIPoma.

Macroglossia can be caused by many rare infiltrative conditions including mucopolysaccharoidosis. TB, thyphoid and rheumatic fever are infections which can lead to macroglossia.

Causes of **parotid swellings**. Viruses include mumps, coxsackie A virus, parainfluenzae virus, CMV and varicella zoster virus, Hypothyroidism.

H pylori antigen can be measured from stool and H pylori antibody (serology) from blood. The antibodies can be present for more than six months and hence is not a good indicator of acute infection.

COX 2 inhibitors such as celecoxib are used as analgesics instead of NSAIDS in patients who are at high risk of upper GI dyspepsia or ulceration. However, there remains an increased risk of ulceration, though less so compared to NSAIDS.

Misoprostol (prostaglandin analogue) and cimetidine are used in treatment of gastro-oesophageal ulceration.

COX 2 inhibitors have also recently been shown to increase the mortality rate of patients with coronary artery disease by blocking the antithrombotic effects of certain prostaglandins.

The symptoms of fevers, weight loss and lower back pain are classical for **retroperitoneal fibrosis**. There is an association with inflammatory conditions such as SLE, rheumatoid arthritis, ankylosing spondylitis, Hashimoto's thyroiditis and glomerulonephrosis. CT or MRI shows can fibrotic para-aortic masses causing ureteric obstruction.

Drugs associated with **retroperitoneal fibrosis** include: methysergide
beta-adrenergic blockers
lysergic acid diethylamide (LSD)
methyldopa
methysergide
amphetamines
phenacetin
pergolide
cocaine

Azathioprine is used to treat retroperitoneal fibrosis.

Retroperitoneal organs are
kidneys,
aorta,
pancreas
ascending colon
most of duodenum