022 - Pages 526-550

- 022

022

Pages 526-550

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

• porphyria cutanea tarda (PCT) Management of chronic infection • chronic hepatitis C is defined as infection that lasts for more than 6 months.
• Combination therapy
 interferon-alfa and ribavirin
 recommended for those with moderate-sever disease
 (histological diagnosis of significant scarring and/or significant necrotic inflammation). In cases where a liver biopsy carries a high risk (e.g. haemophilia), treatment can be initiated without histological confirmation. currently a combination of pegylated interferon-alpha, ribavirin and a protease inhibitor (e.g. boceprevir, simprevir and telaprevir) is used Genotype 1 hepatitis C have low rates of viral clearance with dual interferon and ribavirin therapy alone. the recommended duration of therapy is 48 weeks Ledipasvir/sofosbuvir modern anti-hepatitis C antivirals, which work via inhibition of NS5A and NS5B can be used without ribavirin or interferon and hence lend themselves well to treatment of hepatitis C in the context of mixed cryoglobulinaemia. Because they can be used without interferon, they do not increase renal inflammation and reduce the viral load, impacting positively on progression of renal impairment. • Duration of treatment: The effectiveness of antiviral treatment depends on the viral genotype; the response is generally better in people infected with genotypes 2 or 3 than in those infected with genotypes 1, 4, 5 or 6. The recommended treatment duration is 24 weeks (genotypes 2 or 3) or 48 weeks (all other genotypes) Both treatment-naïve (new) patients and those who have relapsed following initial response to interferon-alfa should be considered for 6 months of combination therapy. • Cure rates:
 cure rates are now approaching 90%, including for some strains which have been previously difficult to treat • The aim of treatment:
 the aim of treatment is sustained virological response (SVR), defined as undetectable serum HCV RNA six months after the end of therapy • Contra-indications: treatment is not generally recommended in those patients who consume large quantities of alcohol, given the increased risk of liver damage. • Treatment follow-up: the best way to assess response to treatment Viral load • Relapses
 relapse occurs in approximately 5% of people after 5 years. Complications of treatment • Ribavirin - side-effects:
 haemolytic anaemia,
 cough,
 teratogenicity
 Women should not become pregnant within 6 months of stopping ribavirin

• interferon alpha - side-effects:
 flu-like symptoms,
 fatigue,

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 3

Gastroenterology

 depression,
 Peginterferon alfa 2a and 2b are contraindicated in severe psychiatric conditions. leukopenia, thrombocytopenia.
 close monitoring of FBC is recommended, with initial review after 4 weeks of therapy.

Factors Associated with Accelerated Fibrosis Progression Host Viral Nonmodifiable • Fibrosis stage • Inflammation grade • Older age at time of infection • Male sex • Organ transplant

Modifiable • Alcohol consumption • Nonalcoholic fatty liver disease • Obesity • Insulin resistance • Genotype 3 infection • Coinfection with hepatitis B virus or HIV

MRCPUK-part-2-march-2018: A patient with H/O IV drug abuse, deteriorating renal function, spider naevi consistent with chronic liver disease, and the purpuric rash. Hepatitis C is positive. is the most appropriate intervention? Ledipasvir/sofosbuvir Δ hepatitis C with mixed cryoglobulinaemia do not increase renal impairment Ribavirin is less effective than NS5A and NS5B inhibition

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Hepatitis D Hepatitis D virus infection can only occur with coexistent hepatitis B infection.

Virology • Hepatitis D is a single stranded RNA delta virus
• It is an incomplete RNA virus that requires hepatitis B surface antigen to complete its replication and transmission cycle.
• It is transmitted in a similar fashion to hepatitis B (exchange of bodily fluids) and patients may be infected with hepatitis B and hepatitis D at the same time. Hepatitis D terminology: • Co-infection:
 Hepatitis B and Hepatitis D infection at the same time. • Superinfection:
 a hepatitis B surface antigen positive patient subsequently develops a hepatitis D infection. Superinfection is associated with high risk of fulminant hepatitis, chronic hepatitis status and cirrhosis. Diagnosis • made via reverse polymerase chain reaction of hepatitis D RNA.
Treatment • Interferon is currently used as treatment, but with a poor evidence base.

Hepatitis E

Virology • RNA hepevirus • spread by the faecal-oral route • incubation period: 3-8 weeks Epidemiology • common in Central and South-East Asia, North and West Africa, and in Mexico Features • causes a similar disease to hepatitis A, • liver biopsy
 Marked cholestasis is a hallmark histological finding in hepatitis E virus infection. Other liver biopsy features of a hepatitis E patient shows patchy necrosis Management • supportive • In general, hepatitis E is a self-limiting viral infection followed by recovery. Prolonged viraemia or faecal shedding are unusual • a vaccine is currently in development, but is not yet in widespread use Prognosis • does not result in a carrier state • carries a significant mortality (about 20%) during pregnancy • does not cause chronic disease or an increased risk of hepatocellular cancer

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Hepatitis histology • hepatitis E Marked cholestasis
• chronic hepatitis Ground-glass hepatocytes (large hepatocytes containing surface antigen).
• Hepatitis A Hepatocyte swelling, monocyte infiltration, and Councilman bodies
• hepatitis B shows a granular eosinophilic “ground glass” appearance; cytotoxic Tcells mediate damage. • hepatitis C Lymphoid aggregates and a marked increase in the activation of sinusoidal lining cells
• hepatitis D Microvesicular steatosis

Colorectal conditions Colorectal cancer (CRC)

Epidemiology
• Colorectal cancer is the third most common type of cancer in the UK and the second most cause of cancer deaths • Adenocarcinomas comprise the vast majority (98%) of colon and rectal cancers
• Location of cancer (averages) rectal: 40% sigmoid: 30% descending colon: 5% transverse colon: 10% ascending colon and caecum: 15% Risk factors • Colorectal adenomas
• Family history
• Hereditary syndromes
 Familial adenomatous polyposis: 100% risk by age 40
 Hereditary nonpolyposis colorectal cancer (HNPCC): 80% progress to CRC.
• Conditions associated with an increased risk of colorectal cancer
 Inflammatory bowel disease (IBD): ulcerative colitis and Crohn's disease
 Endocarditis and bacteremia due to Streptococcus gallolyticus is associated with CRC. Bovis in the Blood = Cancer in the Colon. Acromegaly
• Diet and lifestyle
 Smoking Alcohol consumption Obesity Processed meat; high-fat, low-fiber diets • Older age
Protective factors • Physical activity • Diet rich in fiber and vegetables and lower in meat • Long-term use of aspirin and other NSAIDs

Risks for colorectal carcinoma Population risk 1 in 40 One first-degree relative more than 45 years old 1 in 17 One first-degree plus one second-degree relative 1 in 12 Two first-degree relatives 1 in 6 Familial polyposis 1 in 2

Which drugs may reduce the risk of colon cancer? Vitamin D Aspirin and NSAID

Types
• There are three types of colon cancer:

1. Sporadic (95%)
2. Hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
3. Familial adenomatous polyposis (FAP, <1%) • Sporadic colon cancer may be due to a series of genetic mutations. For example: allelic loss of the APC gene more than half of colon cancers further gene abnormalities e.g.
   activation of the K-ras oncogene, RAS is an intracellular signaling molecular that acts downstream of the epidermal growth factor receptor (EGFR) to stimulate cell division and growth present in 30-50% of colorectal cancers associated with failure to respond to EGFR based therapies such as the monoclonal antibodies Cetuximab and Panitumumab. The presence of a KRAS mutation is a contraindication to treatment with these agents. Which histopathological subtypes is essential for successful treatment with cetuximab? K-Ras wild type
   Cetuximab is licensed by NICE in metastatic colorectal cancer for K-Ras wild type proven patients who require downstaging prior to surgical resection of liver metastatic disease. always given in combination with chemotherapy
   major side effect acne type rash. deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma • Hereditary non-polyposis colorectal carcinoma (HNPCC) also known as (Lynch syndrome)
   autosomal dominant mutation of DNA mismatch repair genes with microsatellite instability. most common form of inherited colon cancer.
   Around 90% of patients develop cancers, often of the proximal colon, which are usually poorly differentiated and highly aggressive.
   The most common genes involved are: MSH2 (60% of cases) the function of this gene DNA mismatch repair MLH1 (30%)

 Patients with HNPCC are also at a higher risk of other cancers, with endometrial cancer being the next most common association, after colon cancer. The Amsterdam criteria are sometimes used to aid diagnosis: at least 3 family members with colon cancer the cases span at least two generations at least one case diagnosed before the age of 50 years Torre-Muir syndrome, a type of hereditary nonpolyposis colorectal cancer (HNPCC), is characterized by sebaceous adenomas. These lesions are usually present on the face, near the eyes and forehead and appear as yellow papules/nodules.

sebaceous adenomas associated with Torre-Muir syndrome a type of HNPCC

 Polyp cancers represent T1 disease and have been sub-classified.
 The Haggitt system is used for pedunculated polyps and describes the deepest invasion of carcinoma cells within the polyp: Level 1 is limited to the head of the polyp Level 2 is extension into the neck Level 3 is invasion of the stalk, and Level 4 is invasion beyond the stalk but above the muscularis propria. The Kicuchi system describes the depth of invasion in sessile polyp cancers.

• Familial adenomatous polyposis (FAP)
 FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years.
 Patients inevitably develop carcinoma.
 It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5.
 Genetic testing can be done by analysing DNA from a patients white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.
 Patients with FAP are also at risk from duodenal tumours. Oesophago-gastroduo-denoscopy (OGD) surveillance is recommended.
 A variant of FAP called Gardner's syndrome can also feature: osteomas of the skull and mandible,
 retinal pigmentation,
 thyroid carcinoma
 and epidermoid cysts on the skin

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Carcinoembryonic antigen may be used to monitor for recurrence in patients post-operatively or to assess response to treatment in patients with metastatic disease Features • Colorectal cancer on the left side of the body typically presents with bright red rectal bleeding. • Colorectal cancer on the right side of the body typically presents with iron deficiency anemia and melena. Colorectal cancer is the most common cause of iron deficiency anemia in postmenopausal women or in men aged 50 or older. • In the descending colon, colorectal cancer presents as colicky pain and hematochezia. • Colorectal cancer on the left side of the body typically presents with obstruction. • In the ascending colon, colorectal cancer presents as an exophytic mass with iron deficiency anemia and weight loss.

Colorectal cancer: screening

Overview • most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16% • the NHS now has a national screening programme offering screening every 2 years to all men and women aged 60 to 74 years. Patients aged over 74 years may request screening • eligible patients are sent faecal occult blood (FOB) tests through the post • patients with a single positive results are offered a colonoscopy • An uncertain or unclear result will result in a request to repeat up to a maximum of two further tests. Persistent unclear

results require further investigation with consideration of colonoscopy. • A negative faecal occult blood does not exclude an underlying diagnosis of colorectal cancer. • Any patient with symptoms, irrespective of a negative faecal occult blood test, should be investigated for the possibility of underlying bowel cancer as appropriate. At colonoscopy, approximately: • 5 out of 10 patients will have a normal exam • 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential • 1 out of 10 patients will be found to have cancer

Streptococcus bovis bacteraemia and endocarditis is associated with colon cancer (in around half of cases). All patients should, therefore, undergo colonoscopy Colorectal cancer: referral guidelines NICE updated their referral guidelines in 2015. The following patients should be referred urgently (i.e. within 2 weeks) to colorectal services for investigation: • patients >= 40 years with unexplained weight loss AND abdominal pain • patients >= 50 years with unexplained rectal bleeding • patients >= 60 years with iron deficiency anaemia OR change in bowel habit • tests show occult blood in their faeces (see below) An urgent referral (within 2 weeks) should be 'considered' if: • there is a rectal or abdominal mass • there is an unexplained anal mass or anal ulceration • patients < 50 years with rectal bleeding AND any of the following unexplained symptoms/findings:

Chapter 3

Gastroenterology

• -→ abdominal pain • -→ change in bowel habit • -→ weight loss • -→ iron deficiency anaemia Faecal Occult Blood Testing (FOBT) This was one of the main changes in 2015. Remember that the NHS now has a national screening programme offering screening every 2 years to all men and women aged 60 to 74 years. Patients aged over 74 years may request screening.

In addition FOBT should be offered to: • patients >= 50 years with unexplained abdominal pain OR weight loss • patients < 60 years with changes in their bowel habit OR iron deficiency anaemia • patients >= 60 years who have anaemia even in the absence of iron deficiency

Follow-up period for adenomatous colonic polyps • The British Society of Gastroenterology (BSG) guidelines on the follow-up period for adenomatous colonic polyps includes: 5-year interval is indicated for low-risk patients
 (one to two adenomas that are both small, ie <1 cm) 3-year follow up is recommended for medium-risk patients
 (three to four adenomas or one or two adenomas where one adenoma bigger than or equal to 1 cm) 1-year follow-up is recommended for high-risk patients
 (five or more small adenomas or more than three with at least one at or above 1 cm in size). guidance for colonoscopic surveillance Risk profile Definition
Surveillance interval low risk 1 to 2 adenomas that are both small, ie <1 cm) intermediate risk (3 to 4 adenomas or 1 or 2 adenomas where one adenoma ≥ 1 cm) high risk ≥ 5 small adenomas or > 3 with at least one at or above 1 cm in size). Post polypectomy follow-up: • Polyps that are ≤10 mm in size can be removed in a single go with biopsy forceps or snares.
• The need for repeat colonoscopy following polypectomy applies to large sessile adenomas removed piecemeal (that is, multiple snares required). Small areas of residual polyp can then be

treated endoscopically, with a further check for complete eradication in two to three months.
- India ink tattooing aids recognition of the polypectomy site at follow up.
- If extensive residual polyp is seen, surgical resection needs to be considered.
- If there is complete healing of the polypectomy site, then there should be a colonoscopy at one year, to check for missed synchronous polyps, before returning to three yearly surveillance.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

5-year 3-year 1-year

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

Stages • The stages of colorectal cancer are based on the TNM staging system by the American Joint Committee for Cancer (AJCC).

TNM Staging Corresponding Duke's Classification stage Description I
A Tumor confined to intestinal wall (confined to the muscularis propria) II
B Infiltration into the visceral peritoneum, adjacent organs, or perirectal tissue III
C Lymph node involvement IV
D Distant metastases

AJCCC (American Joint Committee) Staging of Colorectal Cancer Primary Tumor (T)
TX Primary tumor cannot be assessed T0 No evidence of primary tumor Tis Carcinoma in situ: intraepithelial or invasion of lamina propria T1 Tumor invades submucosa T2 Tumor invades muscularis propria

T3 Tumor invades through the muscularis propria into pericolorectal tissues T4a Tumor penetrates to the surface of the visceral peritoneum T4b Tumor directly invades or is adherent to other organs or structures

Regional Lymph Nodes (N) NX Regional lymph nodes cannot be assessed N0 No regional lymph node metastasis N1 Metastasis in 1-3 regional lymph nodes

N1a Metastasis in one regional lymph node N1b Metastasis in 2-3 regional lymph nodes

N1c Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis N2 Metastasis in 4 or more regional lymph nodes N2a Metastasis in 4-6 regional lymph nodes N2b Metastasis in 7 or more regional lymph nodes

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 3

Gastroenterology

Distant Metastasis (M)
M0 No distant metastasis M1 Distant metastasis M1a Metastasis confined to one organ or site (for example, liver, lung, ovary, nonregional node) M1b Metastases in more than one organ/site or the peritoneum

Residual tumour (R) classification exists in addition to the TNM classification and the histological grade (G): • RX presence of residual tumour cannot be assessed • R0 no residual tumour • R1 microscopic residual tumour • R2 macroscopic residual tumour. Management: depends upon the stage. • Stage I (Duke's A):
 Definition Carcinoma in situ limited to mucosa or submucosa (T1, N0, M0).
 Management surgery to remove the tumour.
 Additional treatments are not usually needed.
 Follow-up
 Colonoscopy - indicated on an annual basis for the first 2 years, then this should be done 3-yearly Faecal occult blood - should be tested 6-monthly for the first 4 years and then once yearly
 Carcinoembryonic antigen (CEA) - can be used to monitor for recurrence if it is elevated initially
 Prognosis the five-year survival rate exceeds 90%. • Stage II (Duke's B):
 Definition Cancer that extends into the muscularis (B1), into or through the serosa (B2).
 Management surgical removal of the tumour followed by radiotherapy.
 Radiotherapy has been shown to reduce the rate of recurrence.
 The role of adjuvant chemotherapy is less clear in Duke's B than in Duke's C (see below).
 chemotherapy is not typically given as standard. Prognosis the five-year survival rate is 70% - 80%
• Stage III (Duke's C):
 Definition Cancer that extends to regional lymph nodes (T1-4, N1, M0).
 Management surgery to remove the tumour,
 chemotherapy with 5-FU and leucovorin in some patients radiotherapy may also be needed (especially if the tumour is large and invading the tissue surrounding the colon).

 There is no role for adjuvant radiation therapy in patients with colon cancer.
 Adjuvant radiotherapy is useful in patients with rectal cancer in whom the risk for local recurrence is greater. Prognosis The five-year survival rate is less than 60% (40 - 50%) • Stage IV (Duke's D):
 Definition Cancer that has metastasised to distant sites (T1-4, N1-3, M1).
 Management Surgery to remove the tumour or to bypass an obstructing tumour,
 Metastatic lesion resection: 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.
 palliative chemotherapy and/or radiotherapy for symptom relief;
 Trans-arterial chemoembolization & Radiofrequency ablation are used as palliative procedures when the lesions are too numerous or large to resect. use of new agents such as cetumixab (a

recombinant human/mouse chimeric epidermal growth factor inhibitor) or bevacizumab (a recombinant human antivascular epidermal growth factor (VEGF) antibody).
 Prognosis Five-year survival is approximately 5%. Radiation therapy is not a standard modality in the treatment of colon cancers

MRCPUK-part-1-January 2015 exam: A man has hereditary non-polyposis colorectal cancer secondary to a mutation in the MSH2 gene. which other cancers his daughter will most be at risk from? Endometrial cancer

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Dysplastic colonic polyps The British Society of Gastroenterology (BSG) published guidelines on the follow-up period for dysplastic colonic polyps in 2002: • 5-year interval is indicated for low-risk patients (one to two adenomas that are both small, ie <1 cm) • 3-year follow up is recommended for medium-risk patients (three to four adenomas or one or two adenomas where one adenoma bigger than or equal to 1 cm) • 1-year follow-up is recommended for high-risk patients (five or more small adenomas or more than three with at least one at or above 1 cm in size). Polyp characteristics: associated with a higher risk of malignant change:
• polyps greater than 1.5 cm, which are sessile or flat
• Histology demonstrating severe dysplasia, predominantly villous architecture or squamous metaplasia

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 3

Gastroenterology

Peutz-Jeghers syndrome • Peutz-Jeghers syndrome is an autosomal dominant condition • Characterised by: numerous hamartomatous polyps in the gastrointestinal tract. pigmented freckles on the lips, face, palms and soles.
• Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.
• incidence of 1:50,000 live births. Genetics • autosomal dominant • responsible gene encodes serine threonine kinase LKB1 or STK11 Features • hamartomatous polyps in GI tract (mainly small bowel) • pigmented lesions on lips, oral mucosa, face, palms and soles • intestinal obstruction e.g. intussusception • gastrointestinal bleeding Management • conservative unless complications develop • colonoscopy every two years after the age of 25 for evaluation of the presence of polyps and polypectomy.

Capsule endoscopy • Capsule endoscopy is currently used in UK to identify the source of occult gastrointestinal bleeding when an OGD and colonoscopy and failed to show a cause.
• It is particularly useful for identifying pathology in the ileum.

Pseudomyxoma peritonei • Pseudomyxoma peritonei is a rare mucinous tumour most commonly arising from the appendix.
• The disease is characterised by the accumulation of large amounts of mucinous material in the

abdominal cavity. • It is rare, with an incidence of 1-2/1,000,000 per year Treatment • usually surgical and consists of cytoreductive surgery (and often peritonectomy) combined with intra-peritoneal chemotherapy with mitomycin C.

Villous adenoma

Overview • Villous adenomas are colonic polyps with the potential for malignant transformation. • They characteristically secrete large amounts of mucous, potentially resulting in electrolyte disturbances. • often in the rectum and rectosigmoid,
Features: The vast majority are asymptomatic. Possible features: • non-specific lower gastrointestinal symptoms • secretory diarrhoea may occur • microcytic anaemia • hypokalaemia

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Carcinoid tumours Carcinoid syndrome Left-sided valvular lesions are not observed in carcinoid syndrome because the lung metabolizes serotonin (5-HT). Remember the symptoms of carcinoid syndrome as "Be FDR" : Bronchospasm, Flushing, Diarrhoea, and Right-sided valvular lesions. • Carcinoid syndrome occurs in only 5% of patients with carcinoid tumour • usually occurs when metastases are present in the liver and release serotonin into the systemic circulation • The most common originating sites of carcinoid is the small bowel, particularly the ileum;
 Around 55% of all carcinoid tumours arise from the GI tract,
 the most common site of origin is the small bowel (45% of those arising within the GI tract). Within the small bowel, the most common site of origin is the distal ileum. • carcinoid tumors are the most common malignancy of the appendix.
• 5-HT, kinins, prostaglandins and other vasoactive substances are secreted. • may also occur with lung carcinoid as mediators are not 'cleared' by the liver • the caecal-appendiceal region is the commonest location for a carcinoid primary.
• These tumours are slow growing

Features
• flushing (often earliest symptom) the most common feature (occurring in 85% of patients) .often provoked by alcohol. • diarrhoea (75%)and abdominal cramps in the majority of patients. • bronchospasm • hypotension • right heart valvular stenosis (left heart can be affected in bronchial carcinoid) Cardiac abnormalities develop in 50% of patients and consist of tricuspid regurgitation or pulmonary stenosis. Fibrosis of the heart valves is a recognised feature • other molecules such as ACTH and GHRH may also be secreted resulting in, for example, Cushing's syndrome • pellagra can rarely develop as dietary tryptophan is diverted to serotonin by the tumour

Investigation • urinary 5-HIAA 24-hour urine collection for 5-hydroxy-indole-acetic acid (5-HIAA) - excretion is greater than 0.3 mmol. • plasma chromogranin A y • Biopsy of the lesion show cells staining for chromogranin A on histology consistent with a neuroendocrine tumour • Octreotide scanning is positive in up to 85% of cases, however a negative scan does not rule out liver metastases.
• The liver should be imaged by high resolution CT with fine cuts or by USS.
 The sensitivity of USS may be increased by the use of microbubble contrast medium (levovist), which is available at some centres.
• Fasting gut hormones should be measured as neuroendocrine tumours may co-secrete other hormones such as VIP, which may contribute to the diarrhoea. Management • somatostatin analogues e.g. octreotide Octreotide is less likely to be effective if octreotide scan negative, but other analogues such as lanreotide have different affinities for different somatostatin receptor subtypes, which may be present on the tumour. • diarrhoea: cyproheptadine may help • Other Symptomatic management may include hepatic embolisation, hepatic chemoembolisation and chemotherapy.
• echocardiography to screen for carcinoid heart disease (right-sided valvular lesions). Prognosis
• generally good.

Gorlin syndrome causes:

1. gastric hamartomas,
2. basal cell carcinomas,
3. mandibular bone cysts,
4. intracranial calcification,
5. pits on the palms and soles.

Diverticular disease
• Diverticulosis presence of diverticula which are asymptomatic. • Diverticular disease diverticula associated with symptoms typically painless bleeding • Diverticulitis diverticular inflammation (fever, tachycardia) with or without localised symptoms and signs painful, No bleeding Overview • Diverticula are bulging sacs that push outward on the colon wall.can occur anywhere in the colon, but most commonly form near the end of the colon on the left side (sigmoid colon). • A diverticulum consists of a herniation of mucosa through the thickened colonic muscle.
• most common in industrialized countries where diets are lower in fiber and higher in processed carbohydrates.
• Diverticular disease is by far the commonest cause of severe fresh bleeding per rectum. Causes: It is believed diverticula form when there is increased pressure in the colon • Diets low in fiber cause hard stool and slower "transit time" through the colon, increasing pressure. • repeated straining during bowel movements also increases pressure.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

• Drugs: diuretics, and narcotic pain relievers, can increase constipation and increase pressure in the colon. Epidemiology • Approximately 50% of all people have diverticula by the time they are 50

years of age, and nearly 70% of all people have diverticula by the time they are 80 years of age • Diverticular disease is rare in people younger than 40 years • Disease is more virulent in young patients, with a high risk of recurrences or complications. • The most common fistula is colovesicular and then colovaginal fistulas. Risk factors • The main risk factors are age over 50 years and low dietary fibre. • Obesity is an important risk factor in young people. • Complicated diverticular disease has an increased frequency in: patients who smoke, use non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol, and those who are obese and have low-fibre diets Features • Approximately 75% of people with diverticula have asymptomatic diverticulosis • Pain is generally exacerbated by eating and diminished with defecation or flatus. • Other symptoms, such as bloating, constipation or rectal bleeding, may also occur. • Diverticulitis Mechanism may occur if some faeces get trapped and stagnate in a diverticulum, bacteria then multiply and cause infection. Site of the pain Generally, presents with left lower quadrant pain. Asian patients have predominantly right-sided diverticula and will usually present with right lower quadrant pain. Pain may be intermittent or constant and may be associated with a change in bowel habits. Fever and tachycardia are present in most patients One third of patients who develop diverticulitis will develop further complications (perforation, abscess, fistula, stricture/obstruction) Diagnosis: colonoscopy • sensitivities and specificities for CT are significantly better than for contrast enemas. • When an abscess is suspected, CT scanning is the best modality for making the diagnosis and following its course. • Because of risk of perforation, endoscopy is generally avoided in initial assessment of the patient with acute diverticulitis. • Haemorrhage: Flexible sigmoidoscopy is an appropriate initial approach to rule out an obvious rectosigmoid lesion. If no cause is identified, further assessment with non-invasive (nuclear scintigraphy) or invasive (angiography, colonoscopy) techniques can be undertaken in an attempt to localise and treat the bleeding source. Management • asymptomatic No treatment or follow-up needs there may be a prophylactic benefit of a high-fibre diet. The risk of perforation may be increased by the use of NSAIDs and long-term use of opioids. Calcium-channel blockers are associated with a reduction in diverticular perforation but

there is insufficient evidence to recommend their use. • Diverticulitis Broad-spectrum antibiotics to cover anaerobes and Gram-negative rods - eg, coamoxiclav or a combination of ciprofloxacin and metronidazole (if allergic to penicillin). Paracetamol should be used for pain. Recommend clear liquids only; gradually reintroduce solid food as symptoms improve over 2-3 days. Review within 48 hours, or sooner if symptoms deteriorate. Hospital admission should be arranged if symptoms persist or deteriorate. Mesalazine has been shown to be more effective in improving the severity of symptoms, bowel habit, and in preventing symptomatic recurrence of diverticulitis, than antibiotics alone Most patients admitted with acute diverticulitis will respond to conservative treatment, but 15-30% will need surgery. The indications for surgery are: Purulent or faecal peritonitis. Uncontrolled sepsis. Fistula. Obstruction. Inability to exclude carcinoma. CT-guided percutaneous drainage of abdominal abscesses is now used in preference to surgery when feasible. Risk of recurrent symptoms after an attack of acute diverticulitis is about one in three. Recurrent attacks are less likely to respond to medical

treatment and they have a high mortality rate. • Haemorrhage Haemorrhage ceases spontaneously in 70-80% of patients.. Subsequent colonoscopy should be performed to establish the source of the bleeding and to exclude neoplasia. Intra-arterial vasopressin at angiography can control haemorrhage in more than 90% of patients. The benefit is usually only temporary but may allow time to prepare the patient adequately for surgery. Angiographic embolisation of very distal bleeding branches is also effective and safe. Surgery in lower gastrointestinal bleeding is usually reserved until endoscopic or angiographic treatments fail. Segmental resection is most usually done if the bleeding site is clearly identified from a therapeutically unsuccessful angiographic or endoscopic procedure. In patients with persistent bleeding and no angiographic or endoscopic identification of a definite bleeding site, subtotal colectomy may be required. The chance of a third bleeding episode can be as high as 50%, so many authorities recommend surgical resection after a second bleeding episode. • Prognosis Approximately three quarters of patients with anatomical diverticulosis remain asymptomatic. Most complications of diverticulitis are associated with the initial attack, after which the disease tends to run a benign course. Mortality and morbidity are related to complications of diverticulosis, which are mainly diverticulitis and lower gastrointestinal bleeding. These occur in 10-20% of patients with diverticulosis during their lifetime. • Prevention Dietary fibre may prevent development of diverticular disease but, once symptoms develop, the benefit from fibre supplementation is unclear.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

 Physical exercise has also been shown to help prevent the development of diverticular disease.

The presence of mixed Gram-negative and/or anaerobic organisms is highly suggestive of secondary peritonitis due to a perforated large bowel or appendicitis.

Meckel's diverticulum
• Meckel's diverticulum is the vestigial remnant of the omphalomesenteric duct.
• It is normally located in the terminal ileum within ~60 cm of the ileocaecal valve and it averages 6 cm in length. • the diverticulum is frequently located near the ileocecal valve in the small bowel.
• In Meckel diverticulum, there is persistence of the vitelline duct, an embryologic structure necessary for receiving nutrients. When this structure persists, the Meckel diverticulum may contain ectopic tissue, such as the acid-secreting gastric mucosa • Although it occurs much more commonly in children it is an important differential consideration for gastrointestinal bleed in adults. • also quite common in Down's syndrome.
Features • About 50% of these contain ectopic gastric mucosa, commonly leading to clinical presentations of peptic ulceration and haemorrhage. • Other complications of Meckel's diverticulum include
 Diverticulitis Intussusception Perforation Obstruction. Diagnosis • Technetium99m pertechnetate scintigraphy
 Tc-99m pertechnetate accumulates in gastric mucosa and is the study of choice for identifying ectopic gastric mucosa in a Meckel's diverticulum.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 3

Gastroenterology

The picture shows an excised Meckel's diverticulum.

Meckel diverticula: rule of 2’s • occurs in 2% of the population,
• commonly located within 2-feet of the ileocecal valve, • 2-inches in length,
• commonly occurs before the age of two.

Intussusception • Hirschsprung disease is aganglionosis of colon, causing obstruction. It usually presents in neonatal period. • common cause of intestinal obstruction in children in general and in Down's syndrome in particular.
• There is a classic triad in intussusception of:

1. acute abdominal pain,
2. currant jelly stool and
3. palpable abdominal mass, usually in right iliac fossa.

Aorto-enteric fistulae (AEF)
• known to occur following endovascular repair of abdominal aortic aneurysms (AAA) and secondary to aortic grafting of any kind, presumably because of mechanical forces of dislodged or migrating devices. • May occur after aorto-bifemoral graft as treatment for peripheral vascular disease. • Strongly positive faecal occult blood (FOB) suggests significant GI haemorrhage in spite of normal upper GI endoscopy.

Angiodysplasia
Angiodysplasia is associated with aortic stenosis Definition

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

• Angiodysplasia is a vascular deformity of the gastrointestinal tract which predisposes to bleeding and iron deficiency anaemia.
Epidemiology • generally seen in elderly patients (≥ 60 years).
• the most common vascular lesion of the gastrointestinal tract
• Second most common cause of lower GI bleeding in patients >60 years of age. Location of lesion
• the most common site: predominantly located in the proximal colon (77%) (located most commonly in the ascending colon and caecum)
Associations • associated with aortic stenosis,
• In Heyde's syndrome, a syndrome of aortic valve stenosis and colonic angiodysplasia, a possible mechanism is the induction of von Willebrand's disease type IIA by the valvular stenosis. Features • may be asymptomatic,

• gastrointestinal bleeding (estimated incidence of active bleeding being about 10% of affected cases). Diagnosis • Colonoscopy If the initial colonoscopy is negative, the most appropriate next investigation is repeat colonoscopy. Pick up of colonic angiodysplasia, (sensitivity), is only 80% by colonoscopy however, this is why it is advisable to move to a repeat colonoscopy.
 Once two colonoscopies have taken place, moving to capsule endoscopy is a usual next step. • 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. • mesenteric angiography if acutely bleeding Management • Bleeding stops spontaneously in >90% of cases. • endoscopic cautery or argon plasma coagulation • antifibrinolytics e.g. Tranexamic acid • oestrogens may also be used

Heyde's syndrome gastrointestinal bleeding from angiodysplasia in the presence of aortic stenosis.

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 3

Gastroenterology

Anal fissure

Anal fissures are longitudinal or elliptical tears of the squamous lining of the distal anal canal. If present for less than 6 weeks they are defined as acute, and chronic if present for more than 6 weeks. Around 90% of anal fissures occur on the posterior midline

Management of an acute anal fissure (< 6 weeks) • dietary advice: high-fibre diet with high fluid intake • bulk-forming laxatives are first line - if not tolerated then lactulose should be tried • lubricants such as petroleum jelly may be tried before defecation • topical anaesthetics • analgesia topical steroids do not provide significant relief Management of a chronic anal fissure (> 6 weeks) • the above techniques should be continued • topical glyceryl trinitrate (GTN) is first line treatment for a chronic anal fissure • if topical GTN is not effective after 8 weeks then secondary referral should be considered for surgery or botulinum toxin

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Anal fistula
• Goodsall's rule describes the likely location of the internal opening of a fistula-in-ano based on its external opening.
 If the external opening is anterior to the 9-3 o'clock plane, then the fistula forms a direct radial tract and opens internally at the same clock face point.
 If the external opening is posterior to this line then it will generally follow a more circuitous route opening at 6 o'clock.

Inflammatory bowel disease (IBD) Crohn's disease Definition • Crohn's disease is a form of inflammatory bowel disease.
• Commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus. Epidemiology • IBD is more common in white people than in African-Caribbean people or those of Asian origin. • has a lower incidence in non-white races; people of Jewish origin are more prone to inflammatory bowel disease than non-Jews; and Ashkenazi Jews are at higher risk than Sephardic Jews. • slightly more common in females (male to female ratio is 1:1.2) • typically presents in late adolescence or early adulthood. The highest incidence of Crohn's disease in the 15–30 year age • The ratio of Crohn's disease to ulcerative colitis varies between adults and children. In adults, the ratio of Crohn's disease to ulcerative colitis is 2:3, while the ratio in children is much higher (2.3:1). Pathology • cause is unknown but there is a strong genetic susceptibility • inflammation occurs in all layers, down to the serosa. This is why patients with Crohn's are prone to strictures, fistulas and adhesions Features
• non-specific symptoms such as weight loss and lethargy • diarrhoea:
 the most prominent symptom in adults.
 Crohn's colitis may cause bloody diarrhea.
 Nocturnal diarrhoea is indicative of organic disease and is typical of a Crohn's disease flare.
• abdominal pain:
 the most prominent symptom in children.
 often in the lower right quadrant • perianal disease: e.g. Skin tags or ulcers if the patient has sepsis secondary to a perianal abscess, due to underlying Crohn’s disease. The priority is to delineate the extent of the abscess and potential fistula by an urgent pelvis MRI before draining it via Examination under anaesthesia (EUA). the next best investigation to guide further management Immediate MRI pelvis CT is inferior to MRI in detecting perianal pathology • An abdominal mass is often palpable in the presence of small bowel disease which can lead to Vitamin K malabsorption. • extra-intestinal features are more common in patients with colitis or perianal disease Extra-intestinal manifestations of IBD A PIE SAC: • Aphthous ulcers
• Pyoderma gangrenosum
• Iritis
• Erythema nodosum
• Sclerosing cholangitis
• Arthritis
• Clubbing of fingertips

Chapter 3

Gastroenterology

Questions regarding the 'extra-intestinal' features of inflammatory bowel disease are common: Common to both Crohn's disease (CD) and Ulcerative colitis (UC) Notes Related to disease activity
• Aphthous oral ulcers
• Arthritis: pauciarticular, asymmetric • Erythema nodosum • Episcleritis • Osteoporosis Unrelated to disease activity • Arthritis: polyarticular, symmetric • Uveitis • Pyoderma gangrenosum •

Clubbing • Primary sclerosing cholangitis

Smoking in IBD • Smoking associated with earlier age of onset of disease and more frequent need for immunosuppression among women with Crohn's disease but not men. • Smoking cessation is associated with an increased risk of ulcerative colitis. Investigation Bloods • C-reactive protein correlates well with disease activity Faecal calprotectin • Calprotectin is a protein belonging to the S100 family and occurring in large amounts in neutrophil granulocytes • Increased faecal calprotectin indicates increased migration of neutrophils to intestinal mucosa • ↑↑ Calprotectin in stool is the direct consequence of neutrophil degranulation due to mucosal damage.
Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

• the most common extra-intestinal feature in both CD and UC
 Arthritis
• more common in CD
 Episcleritis Interstitial lung disease
• more common in UC
 Primary sclerosing cholangitis
 Uveitis

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

• The logical next step in excluding inflammatory bowel disease • Recommended by NICE to distinguish between inflammatory bowel diseases and noninflammatory bowel diseases, such as irritable bowel syndrome in people presenting with any of the following lower gastrointestinal symptoms for at least 6 weeks: abdominal pain or discomfort, bloating, or change in bowel habit.
• ↑↑ when there is any intestinal inflammation Crohn’s disease or ulcerative colitis.
• normal value is approximately 25 mg/kg. • in IBS values may be slightly higher than those of healthy subjects , but in IBD significantly ↑↑ • Calprotectin exceeding 50 mg/kg should be considered positive do endoscopy to confirm IBD • Non-invasive screen for IBD • Normal faecal calprotectin makes IBD unlikely
• ↑↑ faecal calprotectin drive further imaging
Stool culture • should be performed first • Even if the presentation is highly suggestive of inflammatory bowel disease. However, it is unforgivable not to do a stool culture in a case of diarrhoea and that should be the starting point before considering the other investigations
Endoscopy • colonoscopy is the investigation of choice Crohn's disease most typically affects the terminal ileum and proximal colon, therefore the investigation of choice would be ileo-colonoscopy.
 A flexible sigmoidoscopy may not identify any areas of disease.
• features suggest of Crohn's include deep ulcers, skip lesions Histology • inflammation in all layers from mucosa to serosa • goblet cells • granulomas • Patchy inflammation Small bowel enema • high sensitivity and specificity for examination of the terminal ileum • strictures: 'Kantor's string sign' • proximal bowel dilation • 'rose thorn' ulcers • fistulae

Chapter 3

Gastroenterology

Barium study is shown from a patient with worsening Crohn's disease. Long segment of narrowed terminal ileum in a 'string like' configuration in keeping with a long stricture segment. Termed 'Kantor's string sign'. Thumb printing
• thumb printing is a predominantly radiological finding due to inflamed, oedematous folds of bowel as a result of mucosal oedema caused by inflammation. Thumb printing may be seen in either Crohn's disease or ulcerative colitis. Management (NICE 2012)

CD UC Inducing remission

1st line • conventional glucocorticosteroids (oral, topical or I.V) , OR
• Budesonide (less effective and less side effect): (for mild to moderate + distal ileal, ileocaecal or right-sided colonic disease + conventional glucocorticosteroids are contraindicated, or not tolerated) OR • enteral nutrition (If any concern about growth SE of steroids e.g. in children) OR • aminosalicylate (less effective and less side effect): (for mild to moderate + conventional glucocorticosteroids are contraindicated, or not tolerated) Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

The picture shows the typical 'cobblestone mucosa' of Crohn's disease with isolated areas of normal mucosa surrounded by deep ulceration (ulcerative colitis does not result in such deep ulceration). Mild & moderate UC 1st line: • Rectal & distal colitis rectal (topical) Aminosalicylates is superior to rectal steroids • Proximal colitis oral Aminosalicylates Sever UC hospital 1st line (I.V steroid)

2nd line adding azathioprine or mercaptopurine to a conventional glucocorticosteroid or budesonide (if: • there are 2 or more inflammatory exacerbations in a 12-month period or • the glucocorticosteroid dose cannot be tapered. 3rd line: add methotrexate to a conventional glucocorticosteroid or budesonide (If azathioprine or mercaptopurine not tolerated , or in whom TPMT activity is deficient),

Severe form 1st line : conventional glucocorticosteroids 2nd line: (not responded to conventional therapy (including immunosuppressive and/or corticosteroid treatments) Infliximab or adalimumab

(severe active Crohn's disease is defined as very poor general health and one or more symptoms such as weight loss, fever, severe abdominal pain and usually frequent (3 to 4 or more) diarrhoeal stools daily.)

Maintaining remission Stop smoking 1st line azathioprine or mercaptopurine (or methotrexate ONLY if needed to induce remission) 2nd line (if azathioprine or mercaptopurine not tolerated or not appropriate) methotrexate post-surgery azathioprine in combination with up to 3 months' postoperative metronidazole, OR azathioprine alone for people who cannot tolerate metronidazole

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad

2nd line oral prednisolone

• oral 5-ASA e.g. mesalazine • azathioprine and mercaptopurine (methotrexate is NOT recommended for UC)