University of East Anglia

PHA 6020Y

Person centered medicine from bench to bedside

Inflammatory Bowel Disease (IBD) Workshop

Learning Outcomes

- Critique the prescribing of medication for the treatment of Inflammatory Bowel Disease (IBD) in line with NICE NG 129, NICE NG 130 and British Society of Gastroenterology 2019 guidance.
- Identify signs and symptoms used in the differential diagnosis of IBD.
- Identify considerations required when starting therapy in IBD patients.
- Clinically assess prescriptions to identify actual/potential prescribing and pharmaceutical care issues for patients with IBD.
- Provide appropriate solutions to identified issues.
- Identify monitoring parameters pharmacists must review to maintain the safety and ensure efficacy for patients on medication for the treatment of IBD.

NM/CLH 2023-24

Case Study 1

You are the pharmacist on the ward seeing CS for the first time. Their medical notes, blood tests results and drug chart are below:

Patient:	CS	
Hospital number:	895623	
DoB:	2.3.93	
Gender:	F	
Address:	8a Garden Lane, Flatplace	
PC:	Frequent diarrhoea (>6 stools/day) with blood and mucus in her stool)	
HPC:	1 week history of increasing stool frequency/urgency and cramping pain before passing a stool. Generally, feels unwell and fatigued	
PMH:	UC left sided, distal colitis (2014) (affecting descending colon, sigmoid and rectum)	
DH:	Mesalazine 400mg TDS (Asacol MR) NKDA	
SH:	Primary school teacher, lives with partner	
Alcohol	3-6 units per week	
Smoking Status	Ex-smoker – stopped when diagnosed with UC	
OE	BP	105/65
	Temp	38.2°C
	Pulse	98bpm
	Weight	49kg (recent weight loss)
	Lungs	NAD
	Patient appears pale and exhausted. Tender, red patches on both shins Stool sample - negative Faecal calprotectin >250micrograms/g	
Diagnosis:	Acute severe exacerbation of UC	
	Dr P Sven **Bleep 5893**	

Her blood test results on admission are as follows:

PATHOLOGY DEPARTMENT		Consultant/GP: Dr P Ross		PATIENT LOCATION
Patient Name: CS			NHS No: 00897241	***Gastro***
Hosp no: 895623		Sex: F	Age: 30 Yr	Pathology
Patient Address: 8a Garden Lane Flatplace				
Lab Episode No:	7564		Date/Time Collection: Today	
Address for Report: Flatplace Hospital				

BIOCHEMISTRY Collection LAB No Today 8904	Potassium **3.2*** 3.6-5.00 mmol/L	Sodium **132*** 134-45 mmol/L	Urea **9.8*** 1.7-7.1 mmol/L	Creatinine **135*** 55-125 µmol/L	
	ESR **50*** <10mm/h	**CRP** **60*** <10mg/L	**Hb** 10.5* 13.0-18.0 g/dL	**WBC** 22* 4-11 x 10^9/L	

UEA Training Prescription Chart

Number of drug charts in use: 1

Date	Surname	Forename	Sex	D/O/B	Hosptial No.	Weight (kg)	Height (cm)	Surface Area (m^2)	SAM?
Day 1	**S**	**C**	F	2/3/93	882113	49 Estimate / **Actual**			Yes / **No**

Ward/ward change:	**Admissions**	**Patient address:**	
Consultant(s)	**Dr P Sven**	8a Garden Lane	

DRUG SENSITIVITIES/ALLERGIES MUST BE ENTERED. If no allergies/sensitivites you must write 'NKDA' and sign and date.

Medicine/Substance	Description of allergy/sensitivity	Signature	Date
	NKDA	*P Sven*	*Day 1*

PRE-MEDICATION AND ONCE ONLY DRUGS

Pharm	Date	Drug (approved name)	Dose	Directions/ route/ other	Time to be given	Signature	Administered by	
							Initials	Date

			Thromboprophylaxis Risk Assessment					
Drug thromboprophyaxis recommended								
Drug thromboprophlaxis NOT recommende								

Prescribing

- Write clearly in black, indelible ink.
- Use approved drug names.
- All prescriptions must be signed and dated.
- If a drug is to be intentionally omitted by a prescriber or pharmacist, indicate this with an 'X' in the drug administration box.
- If a drug is being stopped, or a dose altered, draw a line through the whole prescription, sign and date.
- Doctors to re-write charts as required. Start dates should be transferred to new chart. Include cross-reference to drugs on other charts.

Drug omissions

If a drug is omitted, one of the below codes must be entered into the drug administration box.

1. Nil by mouth
2. Not required
3. Patient refused
4. Drug unavailable
5. Vomiting/nausea
6. Patient off ward
7. No IV access
9. Contra-indicated
8. Other - reason must be recorded in notes

Self administration of medicines (SAM)

If a patient is suitable for SAM they can initial in the relevant drug administration box or a nurse can write 'SAM' in the box.

Prescribers

Signature	*Dr P Sven*
Bleep no.	**5893**
Print name	**Doctor P Sven**
Signature	
Bleep no.	
Print name	
Signature	
Bleep no.	
Print name	
Signature	
Bleep no.	
Print name	
Signature	
Bleep no.	
Print name	

Pharmacy codes

Pharm: Signature confirms checked/date

TTO ✔ = from locker; **H** = at home; **R** = relabel; ★ = new supply at discharge

Supply: S = ward stock; **T** = dispensing, see date and quantity; **P** = POD, see date and quantity

Version 001-19

REGULAR MEDICINES 1

CHECK PAGE 1 FOR ALLERGY STATUS

Tick box to indicate time of admission or add other times ↓	Date →	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
2. Drug (approved name): Mesalazine; Start date: Day 1; End date:	06:00										
Dose: 400mg; Route: Po; Frequency: TDS	08:00	✓	X								
Indication:	12:00										
Pharm check	14:00	✓									
Prescriber's signature: P Sven; Supply	18:00										
	22:00	✓									
	00:00										
3. Drug (approved name): Start date: End date:	06:00										
	08:00										
Dose: Route: Frequency:	12:00										
	14:00										
Indication: Pharm check	18:00										
	22:00										
Prescriber's signature: Supply	00:00										
3. Drug (approved name): Start date: End date:	06:00										
	08:00										
Dose: Route: Frequency:	12:00										
	14:00										
Indication: Pharm check	18:00										
	22:00										
Prescriber's signature: Supply	00:00										
4. Drug (approved name): Start date: End date:	06:00										
	08:00										
Dose: Route: Frequency:	12:00										
	14:00										
Indication: Pharm check	18:00										
	22:00										
Prescriber's signature: Supply	00:00										
5. Drug (approved name): Start date: End date:	06:00										
	08:00										
Dose: Route: Frequency:	12:00										
	14:00										
Indication: Pharm check	18:00										
	22:00										
Prescriber's signature: Supply	00:00										

CHECK PAGE 1 FOR ALLERGY STATUS

AS REQUIRED DRUGS

CHECK PAGE 1 FOR ALLERGY STATUS

1. Drug (approved name) *Paracetamol*		Start date *Day 1*	Date											
Dose *500mg-1g*	Route *PO*	Max Frequency *4-6hrly*	Time											
Indication *Pain/pyrexia*		Pharm check	Dose											
			Route											
Prescriber's signature *Dr P Sven*		Supply	Given by											
2. Drug (approved name)		Start date	Date											
Dose	Route	Max Frequency	Time											
Indication		Pharm check	Dose											
			Route											
Prescriber's signature		Supply	Given by											
3. Drug (approved name)		Start date	Date											
Dose	Route	Max Frequency	Time											
Indication		Pharm check	Dose											
			Route											
Prescriber's signature		Supply	Given by											
4. Drug (approved name)		Start date	Date											
Dose	Route	Max Frequency	Time											
Indication		Pharm check	Dose											
			Route											
Prescriber's signature		Supply	Given by											
5. Drug (approved name)		Start date	Date											
Dose	Route	Max Frequency	Time											
Indication		Pharm check	Dose											
			Route											
Prescriber's signature		Supply	Given by											

CHECK PAGE 1 FOR ALLERGY STATUS

1. **Which signs and symptoms described for patient CS, contribute to the diagnosis of severe flare of UC? How would these differ if the patient had Crohn's Disease?**

- Frequent diarrhoea (>6 stools/day) with urgency – blood and mucus in stool (CD not always mixed with blood/mucus, stools may be dark in colour, indicating a bleed in the proximal bowel)
- Cramping pain before passing stool (CD- abdominal pain + abdominal mass common)
- Symptoms of being generally unwell, feverish and fatigued
- Tachycardia – pulse >90bpm => severe UC
- Pyrexia – temp >37.8^{o}C => severe UC
- Anaemia => complication of UC/CD
- Raised CRP and ESR => disease flare
- Dehydration – raised Ur/Cr reduced sodium/potassium => due to dehydration from diarrhoea
- PMH: UC

Overview:
Chronic inflammation of the GIT. Lifelong, with considerable ongoing morbidity and psychological wellbeing.

Disease is at different sites, UC = COLON; CD = GIT mouth to anus.

There are different disease phenotype classifications, i.e. the Montreal classification (as described in the screencast for UC, but which also exists for CD but is more complex in also including age, location and behaviour (i.e. structuring/penetrating)).

Location – UC – continuous mucosal inflammation beginning in the rectum and extending proximally. Mucosal inflammation (surface). Degree of involvement – PROCTITIS – rectum only; PROCTOSIGMOIDITIS – rectum and sigmoid colon; LEFT SIDED/DISTAL COLITIS – distal to the splenic flexure; EXTENSIVE – any extent beyond the splenic flexure; PANCOLITIS – entire colon.

CD – Can affect any area but most commonly the ILEOCAECAL – terminal ileum and proximal colon. Patchy/skip lesions with normal appearing bowel between. TRANSMURAL – extends through the gut wall => fibrosis, strictures causing obstruction and fistulae.

Symptoms of CD and UC – Relapsing and remitting. See table below from PJ article.

Assessment tools used to define disease, score helps to define activity and severity:
Harvey Bradshaw Index (HBI) – CD - table at the end of workshop document. May also see the Crohn's Disease Activity Score (CDAI).
CDAI < 150 and HBI <4 suggests remission
CDAI ≥ 300 and HBI >8 suggests severe active disease

Truelove and Witts' criteria – UC – Table at back of workshop document.

Table 1: Similarities and differences between Crohn's disease and ulcerative colitis (adapted from GIP 2019)			
Feature		**Crohn's disease**	**Ulcerative colitis**
Symptoms	Fever	Some people may feel generally unwell, feverish, with raised temperature	
		Suggests severe disease with systemic toxicity	Temperature >37.8°C indicative of severe UC
	Diarrhoea	Sometimes mixed with mucus, pus, or blood	Often with blood and mucus, and an urgent need to rush to the toilet
	Abdominal pain	Common	Cramping pain, often before passing a stool
	Abdominal mass	Common	Absent
	Tachycardia	Suggests severe disease with systemic toxicity	Pulse rate >90 bpm suggests severe UC
	Other	Hair loss (owing to nutritional deficiencies e.g. B12 and iron), mouth ulcers (50% CD), fatigue, anaemia, weight loss, loss of appetite, and growth impairment in children and young people	
Complications	Fistulae	Often perianal, occurs in around 25–33% of cases	Rare, more likely in those who have had pouch surgery (may prompt consideration of change of diagnosis to CD)
	Strictures	As a result of scar tissue or inflammation	Unusual in UC, sometimes a sign of bowel cancer
	Fissures	Complication of perianal disease	Absent
	Extraintestinal manifestations	More common when disease affects the colon; can affect the joints, skin, bone, eyes, liver, and biliary tree and are mostly (but not exclusively) associated with active disease (refer to Figure 4) Thromboembolic complications occur in 1–2% of patients; this risk is higher in acute cases resulting in hospitalisation, but this is low due to routine use of VTE prophylaxis	

UC: ulcerative colitis; CD: Chron's disease; GI: gastrointestinal; VTE: venous thromboembolism

Table 2: Key tests used in IBD				
Common blood tests	**Normal adult reference values**	**Result**	**Associated with**	**Comments**
Haemoglobin	13–18.0g/dL (males) 11.5–16.5 g/dL (women)	Reduced	GI Inflammation	
White cell count	4.0–11.0 x 10^8/L	Raised	Infections, corticosteroid use	Unreliable marker of inflammation
		Reduced	Immunomodulator toxicity (e.g. thiopurine, methotrexate)	
Platelets	150–450 x 10^8/L	Raised	GI Inflammation	
Ferritin	Males: 20–300 µg/L Females: 10–200 µg/L	Raised	GI Inflammation	
		<100 µg/L	Iron-deficiency	IDA affects up to 25% of IBD patients.
C-reactive protein (CRP) or Erythrocyte sedimentation rate (ESR)	CRP ≤ 5mg/L ESR <10 mm/h	Raised	GI Inflammation	UC patients, with disease confined to the mucosa may not develop an elevated CRP even in the context of disease flare.
Albumin	34–50 g/L	Reduced	GI inflammation and/or malabsorption	Negative acute phase protein. Malabsorption tends to occur in CD rather than UC as it involves the small intestine.

Table 2: Key tests used in IBD				
Common blood tests	**Normal adult reference values**	**Result**	**Associated with**	**Comments**
Other blood tests				
Potassium	3.5–5.2 mmol/L	Reduced	Diarrhoea, corticosteroids	
Sodium	135–145 mmol/L	Reduced	Diarrhoea	
Creatinine	75–155 micromol/L	Raised	5-ASA / ciclosporin toxicity, dehydration	
Urea	3.1–7.9 mmol/L	Raised	Dehydration	
Magnesium	0.70–1.0 mmol/L	Reduced	Diarrhoea	
Liver function tests	ALT <45 U/L Bilirubin <19 µmol/L Alkaline phosphatase 35–120 U/L	Raised	Sepsis, inflammation, liver disease (e.g. PSC, CMV), gallstones, immunomodulator toxicity (e.g. thiopurine, methotrexate)	
Vitamin B12	170–700 ng/L	Reduced	Terminal ileal CD	Site of B12 absorption.
Folate	3.0–20.0 µg/L		Malabsorption and poor nutritional state	Malabsorption/ nutritional deficits tend to occur in CD and not UC as it involves the small intestine.
Vitamin D	>50 nmol/L	Reduced	Poor bone health and use of recurrent corticosteroids, inflammation	May require bone density scan.
Other micronutrients: iron, vitamin K, selenium, zinc, vitamin B1, B6	Various	Reduced	Malabsorption and inflammation	More common in CD than UC, and in active disease.

Table 2: Key tests used in IBD				
Common blood tests	**Normal adult reference values**	**Result**	**Associated with**	**Comments**
Stool				
Microbiology, culture and sensitivities (and other microbiological techniques)		Pathogen identified	Potential precipitate for flare in symptoms; exclude clinical mimic for IBD	Presence of red & white blood cells in fresh stools; infective cells such as amoeba; PCR for bacterial species.
Clostridioides difficile toxin		Positive toxin	Potential precipitate for flare in symptoms	Higher prevalence in IBD patients and is associated with increased mortality.
Faecal calprotectin	<50 µg/g (but <250 µg/g indicative of remission)	Raised	GI inflammation	Suggestive of mucosal inflammation and can be used to assess disease response over time. Useful when unclear if symptoms are due to inflammation or other non-inflammatory causes such as bile acid malabsorption, functional bowel disorders or short bowel. Levels in IBS are normal. Proton pump inhibitors and NSAIDS may be associated with elevated calprotectin values so this should be accounted for when interpreting results.

Abbreviations: GI = gastrointestinal, IDA =iron deficiency anaemia, 5-ASA = 5-aminosalicylic acid, PSC = primary sclerosing cholangitis, CMV = cytomegalovirus.

2. What is the significance of the tender, red patches on both shins?

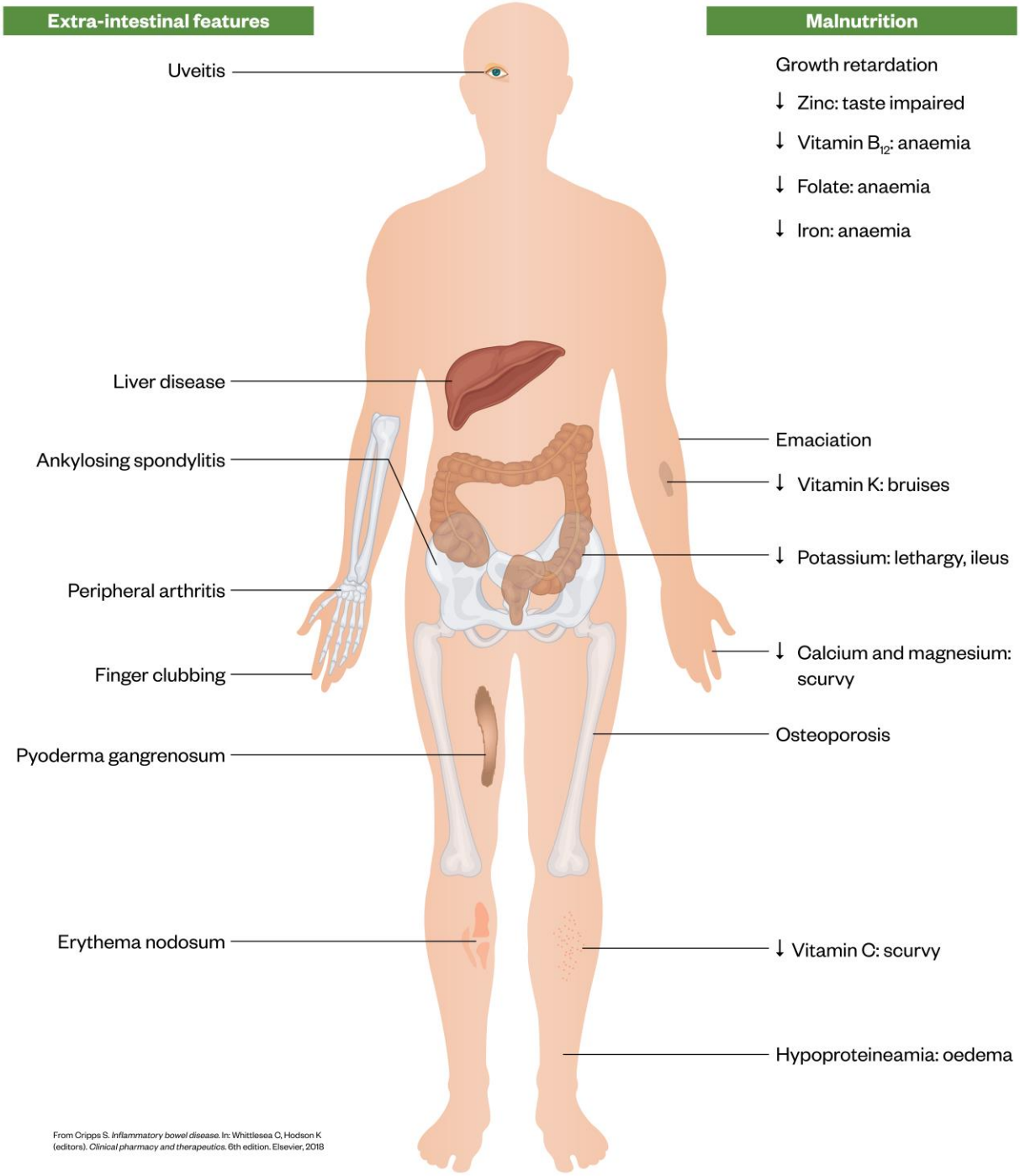
Erythema nodosum 2-3cm, more lower limbs, erupt over 1-several weeks tender red nodules of subcutaneous fat/adipose and can be accompanied by joint pain/swelling and fever – complication of IBD/inflammatory disease. Important to treat the underlying condition.

3. What extraintestinal complications of UC should be checked for in patient CS?

50% of IBD patients have at least one.

Joints – ankylosing spondylitis, arthritis
Skin – pyoderma gangrenosum
Eye – uveitis
Bone – osteoporosis
Liver and biliary tree
Malnutrition – weight loss, anaemia, vitamins (all more common in CD as it involves small intestine)

Thromboembolic risk – needs VTE prophylaxis (see below)



Pharmaceutical journal

4. **Based on the NICE NG 130, what is the recommended course of treatment for patient CS?**

Patient in hospital

<u>Severe:</u> (appropriate for patient CS)

- Multidisciplinary approach
- Mesalazine usually stopped at this point
- IV hydrocortisone 100mg tds/qds or methylprednisolone 60mg OD (sometimes 40mg BD) for 5 days – expect to see results by day 3 (no benefit after 7-10 days with increased risk of dependence) for severe.
- Convert to oral 40mg OD and reduce over 4-6 weeks (>40mg OD ⇒↑ side-effects & no ↑ benefit). Reducing schedule usually 2.5-10mg/week to stop but will be tailored to disease severity and patient tolerance. Reduction helps to prevent acute adrenal insufficiency and early relapse.
- Consider ciclosporin or surgery if little or no improvement within 72 hours, as per NICE guidance.

- Infliximab only if ciclosporin is contraindicated/clinically inappropriate, as per NICE guidance.

Other considerations:

- Fluids, stool culture, nutritional support, removing drugs that can cause colonic dilatation/ppt or potentially worsen a flare – i.e NSAIDs, opiates, anticholinergic drugs, anti-diarrhoeal drugs.
- VTE prophylaxis.

5. In general terms, what factors affect the choice and route of UC treatment?

Depends on site/ extent/ severity / treatment history/ compliance/ preparations available/ patient choice.

To start therapy -
Anus/rectum/left colon => use topical (direct to site & reduce side effects) – additional steps when these are not effective (see screencast).
Diffuse disease => combination oral/topical (e.g. Pentasa tablets and retention enema)
Acute severe + hospitalized => IV

Overview – based on NICE guidance:
Inducing remission in other mild-moderate UC phenotypes: (mesalazine = aminosalicylate)

Proctitis – topical mesalazine (i.e. 1g/day supp) BEST OPTION => if remission not seen in 4 weeks add oral mesalazine 2-4.8mg/day (2-3g usually sufficient) => further treatment if needed, Po (i.e. pred 40mg OD, reducing schedule over 4-8 weeks) or PR (i.e. pred 5mg BD) corticosteroid

Procrosigmoiditis/left sided – Topical mesalazine (i.e. enema 1g/day) => if remission not seen in 4 weeks consider high dose oral mesalazine or switching to high dose oral mesalazine and time limited topical steroid => if further Tx required consider switching to oral mesalazine and time limited Po steroid

Extensive – Topical mesalazine PLUS high dose oral mesalazine => if remission not seen add time limited oral corticosteroid

Moderate to severe – oral corticosteroid.

NB: COMPLIANCE ISSUES WITH TOPICAL – suppository helpful tips – wet the tip in warm water or water based lubricant, use a bedtime to reduce leakage and increase contact time, try not to go to the toilet for an hour after insertion, place a towel on the bed to minimise disruption caused by leakage, if it comes out within 10 mins, insert another. Enema and foam helpful tips – before bed, stand leg raised or lay on side for insertion, pillow under bottom can prevent leakage. Try to stay in a position that prevents leakage.

Involve patient in decision making. There are options if they do not want topical treatment but may not be as effective alone in some UC phenotypes.

Topical preparations:

- Proctitis => suppositories
- Rectum/sigmoid colon (proctosigmoiditis) => foam enemas
- Extensive => splenic flexure => liquid enemas

Often need combination (e.g. >90% liquid and some foam preparations bypasses rectum > use suppositories)

6. When considering oral aminosalicylates, what factors affect the choice of therapy?

Need to confirm **BRAND** of mesalazine to assess appropriateness – this will allow understanding of the formulation.

Sulfasalazine, mesalazine, olsalazine, balsalazide => all deliver mesalazine (5-aminosalicylic acid – 5-ASA) to gut lumen – induce & maintain remission (esp UC – less evidence for Crohn's) Maintenance => reduce risk of colorectal cancer by 75%

Formulations – there is a difference in the site of release:

Unstable in acid medium => different formulations:

Jejunum = pH 6-7
Ileum/colon - >7

1. Mesalazine tablet coated with pH dependent acrylic resin
E.g.: Asacol and Octasa – Eudragit S methyl acrylate copolymer coating - dissolves at pH >7 => release in terminal ileum & colon
Salofalk – Eudragit L - dissolves at pH >6 and above => release in jejunum & ileum to colon

Mezevant XL- multi-matrix, mesalazine incorporated not lipophilic matrix and enterically coated, swells and releases slowly - dissolves at pH >7 => release in terminal ileum & colon (once daily dosing possible, even at 4.8g/day)

2. Ethylcellulose coated mesalazine granules
Eg: Pentasa - disintegration time dependent not dependent on pH – microspheres of mesalazine encapsulated in ethylcellulose semi-permeable membrane = slow dissolution rate – released gradually in stomach, duodenum, ileum & colon

3. Diazotization of mesalazine itself or to carrier compound
Eg: Olsalazine (Dipentum□) – dimer of mesalazine – bacterial cleavage in colon
Balsalazide (Colazide□) – mesalazine + 4-aminobenzoyl beta- alanine

Sulphasalazine: (Sulfapyridine + mesalazine): (rarely used now)
- *broken down by bacterial azoreductase in colon*
- *Sulphapyridine absorbed in colon, metabolised by hepatic acetylation or hydroxylation then glucuronidation & excreted in urine*
- *Depends on acetylation phenotype – slow causes inc. s/e*
- *S/e (30%) – Dose related: N&V, abdo pain, diarrhoea, headache, metallic taste, haem. anaemia. Not dose related: rashes, aplastic anaemia, agranulocytosis, pancreatitis, pulmonary, hepatic*
- *Metabolites => yellow coloration of body fluids & staining of contacts*
- *COUNSELLING*

PRESCRIBE BY BRAND – some patients may notice a difference in their treatment with inadvertent brand swaps.

EFFECTIVENESS – BNF – there is no evidence to show that one mesalazine preparation is more effective than another.

Oral preparations - main role is in maintaining remission in UC but can be used for active disease

7. Based on NICE NG 130, what is recommended for maintaining remission of UC in patient CS?

Patient already on a low maintenance dose of mesalazine and suffered with a **severe acute episode of UC requiring hospitalisation**. Maintenance therapy – azathioprine (2-2.5mg/kg daily) or mercaptopurine (1-1.5mg/kg daily).

Review (maintenance based on NICE guidance):
Proctitis and proctosigmoiditis – Patient preference – topical mesalazine (daily or intermittent or in proctitis at the onset of symptoms) or oral mesalazine plus topical (daily or intermittent) or oral alone (may not be as effective)
Left sided and extensive – Low maintenance dose of oral mesalazine

All extents – 2 or more exacerbations or remission not maintained on mesalazine – Aza or mercap

8. What are the monitoring parameters for azathioprine therapy?

Therapeutic: Symptom control, CRP/ESR, reduce faecal calprotectin, endoscopy, Truelove and Witt score reduction.
Toxic: Differential WBC/FBC (myelosuppression), LFTs (deranged LFTs), Thiopurine Methyl-Transferase (TPMT), nausea (take with meals), presence of opportunistic infections, lymphoproliferative disease (cervical screening), U&E, renal function (may result in slower elimination).

Pre-screening/history for viral infections – HBV, HCV, HIV, HSV, VZV

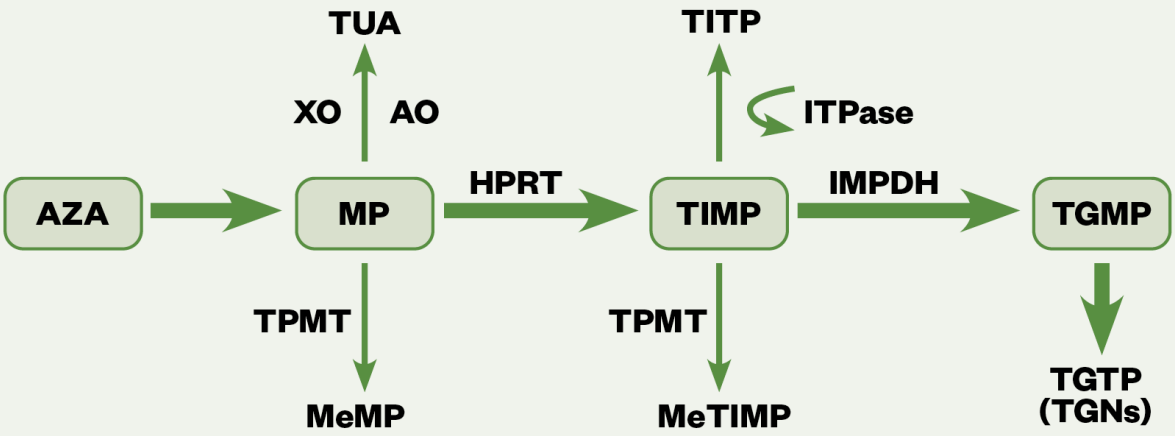
Overview:
Metabolised to 6-mercaptopurine in liver, steroid sparing, 2-2.5mg/kg/day, adjust to patient response/tolerance/WBC/Plts, can take several weeks to have an effect (& therefore allow reduce steroids)

Check TPMT prior to starting. If level absent or low patient will experience life-threatening bone-marrow suppression so it must be avoided. Doses will need to be reduced if the patient has reduced activity.

The therapeutic efficacy of thiopurine is achieved by the enzyme HPRT (Hypoxanthine-guanine phosphoribosyl transferase) converting the drug to active, cytotoxic metabolites, including 6-thioguanine nucleotides (6-TGNs) which are incorporated into DNA.
Accumulation of high levels of 6-TGNs are responsible for the side-effects of thiopurine drugs and leucopenia.

The metabolism of mercaptopurine (MP) involves three competing pathways: the first is degradation to thiouric acid (TUA) which is then excreted, the second is methylation by thiopurine S-methyltransferase (TPMT) into methylmercaptopurine (MeMP), and the third is breakdown of MP into thioinosine monophosphate (TIMP) catalysed by hypoxanthine phosphoribosyltransferase (HPRT).

TIMP is then further metabolised via inosine monophosphate dehydrogenase (IMPDH) into thioguanine monophosphate (TGMP). Kinases convert this into the thioguanine nucleotides (TGNs). Approximately 15–20% of patients with inflammatory bowel disease (IBD) demonstrate hypermethylation when treated with thiopurines. This means that during thiopurine metabolism, methylated thiopurine metabolites are preferentially produced instead of TGNs.



AO: aldehyde oxidase; **AZA**: azathioprine; **ITPase**: inosine triphosphatase; **MeTIMP**: methylthioinosine monophosphate; **TGTP**: thioguanine triphosphate; **TITP**: thioinosine triphosphate; **XO**: xanthine oxidase.

9. During your review of this patient, document any other actual/potential pharmaceutical care issues and action required for this patient.

Issue	Action required
Paracetamol dose in a patient weighing <50kg. Use with caution.	Monitor requirement (currently unclear how much the patient requires). If regular doses required ,speak to the prescriber and get dose reduced (15mg/Kg).
Monitoring parameters	
Therapeutic	**Toxic**

Issue	Action required
VTE assessment needs completion +/- Low molecular weight heparin prescribed. IBD patients have an increased risk of VTE.	Request addition of LMWH, i.e. dalteparin injection 5000units od (weight<50kg – in practise you may see 2500 units for low weight patients) (seems confusing with GI bleeding, but 3x normal risk of VTE during a flare of IBD and bleeding should be controlled when flare controlled).
Monitoring parameters	
Therapeutic	**Toxic**
No venous thromboembolism	Hb, signs of bleeding, platelets, U&E (K), renal function

Issue	Action required
Low Hb indicates anaemia.	Highlight bloods to the team. Check ferritin. Discuss with dietician for dietary advice. +/- IV iron replacement. Po potentially for ongoing issues when in remission up to 100mg OD.
Monitoring parameters	
Therapeutic	**Toxic**
Increased Hb, reduction in symptoms	PO – GI disturbance, darkened stools IV – dizziness, flushing, hypo/hyper-tension, nausea, skin reactions, skin reactions

Issue	Action required
Electrolyte imbalance, potassium low.	Recommend potassium replacement, i.e sando K 2 tabs TDS for 2 days and review.
Monitoring parameters	
Therapeutic	**Toxic**
Increase in serum potassium (3.6-5.0 mmol/L)	Hyperkalaemia, GI disturbance

Issue	Action required
Patient showing signs of dehydration – reduced renal function, increased urea, reduced sodium (due to fluid and electrolyte loss - diarrhoea).	Discuss with the team. Treat the underlying condition and provide supportive therapies, i.e. sodium chloride 0.9% 1 L over 4-8 hours.
Monitoring parameters	
Therapeutic	**Toxic**
Improvement in signs and symptoms, decreased urea, sodium and creatinine, fluid balance	Fluid balance, U&E (K&Na).

Issue	Action required
Check patient vaccination status.	Clarify with patient and follow-up with

	medical team if needed. Ensure annual influenza vaccine given, Covid-19 vaccine received and booster if appropriate, pneumococcal.
Monitoring parameters	
Therapeutic	**Toxic**

Issue	**Action required**
Counselling and education	All new drugs – counsel on indication, dose, frequency and side effects. SPECIFIC DETAIL – nausea with azathioprine, GIT adverse effects with iron.
Monitoring parameters	
Therapeutic	**Toxic**

10. Document your assessment of key pharmaceutical care issues, alongside your recommendations in the patient's medical notes, using the SBAR tool.

Situation / Background / Assessment / Recommendation

In this workshop, this entry in the medical notes only relates to the additional pharmaceutical care issues identified in the grid above (Q8), as the previously posed questions discuss different treatments for acute and maintenance therapy. It does, however, show you another example of how to set out your medical notes entries.

Date & Time

Pharmacist N. Surname

I reviewed inpatient CS (DoB: 2/3/93; 895323) admitted with an acute severe exacerbation of UC.

PMHx – Mesalazine 400mg TDS (Asacol MR)

BP 105/65
Weight 49kg
K 3.2
Hb 10.5
Urea 9.8
Na 132

VTE risk assessment not complete and no prophylaxis prescribed. PR bleed managed with UC treatment and risk of VTE increased due to UC.

HPC - rectal bleeding and Hb 10.5 patient anaemic.

Potassium levels low.

Increased urea and decreased sodium due to diarrhoea (dehydration).

Based on my review, I would recommend the following:

- Complete VTE risk assessment. Prescribe a low molecular weight heparin, e.g dalteparin 5000 units OD – monitor weight, Plt, Hb and CrCl.
- Check patients ferritin. Prescribe IV iron during the flare with oral during remission to maintain iron levels if required.
- Replace potassium. Start a short course of Sando-K 1 TDS for two day and monitor serum potassium levels.
- Replace fluids and encourage oral intake. Prescribe 1L sodium chloride 0.9% over 4-6 hours.

Name Surname (contact details)

Case Study 2

You are the pharmacist on the ward seeing RT for the first time. Their medical notes are below:

Patient:	RT	
Hospital number:	897867	
DoB:	9.7.75	
Gender:	M	
Address:	6 Skylark, Flatplace	
PC:	Frequent diarrhoea (3 stools/day), tired, abdominal pain	
HPC:	Weight loss over the past month. Loss of appetite and fatigue requiring time off work. Change to bowel habits.	
PMH:	Nil	
DH:	Nil NKDA	
SH:	Highway maintenance – shift work Lives alone	
Alcohol	8-14 units per week	
Smoking Status	Smoker – 5-10 cigarettes/day	
OE	BP	122/75
	Temp	37.0ºC
	Pulse	72bpm
	Weight	64kg (recent weight loss)
	Lungs	NAD
	Stool sample - negative Faecal calprotectin >140micrograms/g Colonoscopy – Patchy inflammation of the terminal ileum and right ascending colon HBI – 7 ESR, CRP - Raised Cr, U&E LFT, FBC - NAD	
Diagnosis:	Crohn's disease (ileocecal disease)	
	Dr D Goran Bleep 0093	

1. **Based on NICE 129 guidance, what is the recommended induction and maintenance treatment for patient RT?**

Induction - Monotherapy with conventional glucocorticosteroid (prednisolone 40mg OD or methylprednisolone or hydrocortisone 100mg QDS). Reducing schedule (i.e. 5mg every week but will be tailored to the individual patient, to stopping). Tapering helps to prevent adrenal suppression and early relapse.

Overview, based on NICE guidance for additional therapy:
Potential for add on therapy (when 2 or more exacerbations in 12 months or when the steroids can not be tapered) – azathioprine, mercaptopurine (or methotrexate).

Severe disease, when the disease has not responded to conventional therapy – infliximab,

adalimumab, ustekinumab, vedolizumab.

Maintenance – Treatment or no treatment.
Treatment – azathioprine or mercaptopurine (or methotrexate when needed at induction) (or infliximab, adalimumab, ustekinumab or vedolizumab when refractory to immunomodulators or when required at induction).

RT experiences 10 months of remission without maintenance therapy, but then suffers two flares in his condition (within 7 months of each other) that require treatment. RT is very concerned about how the disease is taking over his life and stopping him going to work or having any social life outside of work.

2. What treatment would you expect to see for patient RT?

Treatment – azathioprine (2-2.5mg/kg/day) or mercaptopurine (1-1.5mg/kg/day)

After a period of sustained remission (3 years), RT is admitted with an acute severe exacerbation of Crohn's Disease (CD). He has frequent diarrhoea (>10 stools/day) with severe abdominal pain, bloody stools and some vomiting. He has lost more than 10% of his body weight, he is unable to work and his CD is diffuse. RT's consultant and the colorectal surgeons do not want to consider surgery at the moment and consider starting him on vedolizumab therapy.

3. Does patient RT meet the current NICE guidelines for the use of vedolizumab in Crohn's Disease?

No
Vedolizumab is a human monoclonal antibody that acts as a cytokine inhibitor and is usually reserved for patients who have had an inadequate response to conventional treatment or TNF alpha inhibitors such as Infliximab or adalimumab.

Infliximab or adalimumab may be a preferable treatment option as Mr PR has severe active Crohn's disease (CDAI >300 or Harvey Bradshaw Index of 8/9), his condition has proved to be refractory to treatment with immunomodulating drugs.

4. Patient RT develops multiple fistulas requiring a total colectomy with ileostomy formation. Ten days after the surgery, patient RT experiences high volume output from his stoma exceeding 2.5 litres per day. How could this be managed?

Exclude and manage other causes/contributing factors such as C.Diff infection, drug treatment etc.

Monitor U&Es. Correct sodium/water imbalance, and ensure magnesium brought into range.

Replace fluid lost with IV sodium chloride 0.9% 2-4 litres/day if marked sodium and water depletion.

Gradually replace IV sodium chloride with restricted intake of oral fluids. Both hypotonic and hypertonic solutions may be problematic. Oral rehydration solutions such as St Marks Solution may

be used. Strict fluid balance required to maintain urine output.

Antimotility drugs

- Loperamide (dose 4–16 mg four times daily), or,
- Codeine phosphate (dose 30–60 mg four times daily)

The effect may be greater if both are taken together

Antisecretory drugs

- Omeprazole (40 mg once or twice daily), or,
- Octreotide (50 mcg twice daily as subcutaneous injection)

Nutritional considerations
Is TPN or enteral feeding required? Consider absorption, areas of the GIT removed and what is absorbed there.

5. **During your review of this patient, document any other actual/potential pharmaceutical care issues and action required for this patient.**

VTE – assessment and prophylaxis required in patients with acute severe exacerbations (but all patients in hospital will be assessed).

Counselling and education – new drug counselling (i.e. azathioprine or mercaptopurine), monitoring required, signs to look out for

Lifestyle – smoking cessation and the importance of stopping smoking due to the link of increased severity and treatment required for CD in patients that smoke (including all of the other health reasons to not smoke), reduce alcohol intake.

Truelove and Witts – PJ. IBD: Symptoms and diagnosis. August 2021

Table 4: Truelove and Witts severity index for ulcerative colitis			
Parameter	**Mild**	**Moderate**	**Severe**
Bowel movements (number per day)	<4	4 – 6	≥6 plus at least one of the features of systemic upset (marked with *below)
Blood in stool	No more than small amounts of blood	Between mild and severe	Visible blood
Pyrexia (temperature greater than 37.8°C*	No	No	Yes
Pulse greater than 90 bpm*	No	No	Yes
Anaemia*	No	No	Yes
Erythrocyte sedimentation rate*	30 or below	30 or below	Above 30

Table 4 Truelove and Witts severity index for ulcerative colitis

Harvey-Bradshaw Index - A five point score is based on:

A	General well-being	0=very well; 1=slightly below par; 2= poor; 3+very poor; 4=terrible
B	Abdominal pain	0+none; 1=mild; 2=moderate; 3=severe
C	Number of liquid stools per day	
D	Abdominal mass	0=none; 1=dubious; 2=definite; 3=definite and tender
E	Complications	Score 1 for each of arthralgia, uveitis, erythema nodosum, pyoderma gangrenosum, apthous ulcers, anal fissure, new fistula, abscess

[2]Harvey RF, Bradshaw JM. A simple index of Crohn's disease activity. Lancet 1980;I:514