**14/08/23 10.20 Dr Sarah Parry**
Patient describes fatigue, weight loss and fever over the previous 8-12 weeks. Upon further investigation, she also reported intermittent polyarticular stiffness and swelling of the first and second metacarpophalangeal joints on both hands which was most severe upon waking.

OE: Positive metacarpophalangeal squeeze test, difficulty forming and releasing a fist, swelling, warm to touch and tender area.
BP: 132/76

Referral to Rheumatologist – Flatplace hospital.

**09/10/23 08.30 Dr Sarah Parry**
Letter received from Flatplace hospital. Diagnosis – Rheumatoid arthritis

1. **Which symptoms described for Mrs BT contribute to the diagnosis of RA?**

Non-specific symptoms – fatigue, weight loss and fever.

Intermittent polyarticular stiffness and swelling of the first and second metacarpophalangeal joint. Symptoms most severe on waking (duration 30 mins to several hours usually reflects severity of joint inflammation)

'Suspected persistent synovitis of undetermined cause' – NICE NG100 Positive squeeze test
Difficulty forming and opening a fist

Swelling, warm to touch and tender areas.

2. **In addition to the symptoms reported by the patient and the signs on physical examination, what additional tests would contribute to a diagnosis of RA?**

Acute phase response – CRP, ESR
Rheumatoid factor (anti-CCP if Rheumatoid factor negative) X-ray

These (or some of them) may be done by the GP before the patient is seen by the rheumatologist. Anything not already done during diagnosis should be done afterwards to form a baseline for comparison in the future.
The functional ability of the patient should also be assessed with i.e. Health Assessment Questionnaire (HAQ).

3. **Based on the NICE NG 100, what is the recommended course of treatment for Mrs BT?**

Offer first line treatment with conventional disease-modifying anti-rheumatic drug (cDMARD) **MONOTHERAPY** using oral METHOTREXATE or LEFLUNOMIDE or SULFASALAZINE as soon as possible. (Hydroxychloroquine is a weak DMARD and can be used if mild symptoms/palindromic disease, although it is not as effective).

'Treat-to-target' aim for remission DAS <2.6.

Escalate dose as tolerated, aim for escalation to effective doses in 4 -6 weeks.

Consider short term bridging treatment with a corticosteroid. This will provide immediate reduction in joint inflammation and pain relief as the DMARD has a lag time until effects are seen. Steroids may not be required by all it depends on each individual patient. Corticosteroid use should be reviewed at every visit with the aim to remove it once cDMARD is active (generally by 3 months). Patients should not remain on corticosteroids due to the ADR risks.
Under EULAR the initial treatment is – 'Methotrexate as part of the first treatment strategy'. This means methotrexate should be tried first; by using the term 'strategy' it could mean it is used as mono or combined therapy, although monotherapy was considered in the recommendation to be most appropriate due to the reduced risk of side effects.

**4. What drug factors should be considered when deciding on the initial treatment for Mrs BT? (You should consider the precautions, cautions/contraindications, side effects, dosing and monitoring)**

**Patient preference / clinician preference.**

**There are currently no robust RCT's demonstrating differences in efficacy with these three agents. Therefore, choices are made based on patient characteristics (i.e. co-morbidities) and drug characteristics, see below:**

**Cautions / contraindications MTX:**

Active infection – because MTX can cause immunosuppressive effect and therefore reduce the efficacy of the immune system to fight infection.
Ascities / pleural effusion – MTX is distributed into the fluid, accumulates and can be re-excreted to prolong serum half-life increasing the risk of toxicity.
Immunodeficiency syndromes – it causes an immunosuppressive effect.
Significant hepatic impairment/liver disease – increased with concomitant hepatotoxic drugs. Alcoholism (increased risk of hepatotoxicity from MTX).
Severe renal impairment – MTX is renally cleared therefore impairment would lead to accumulation and increased risk of S/E – ensure adequate hydration. Dose should be reduced in renal impairment. Care required with NSAIDs (use under supervision of the rheumatologist and not OTC) due to the risk to renal function and MTX excretion.
Blood dyscrasias - Myelosuppression is a side effect therefore may worsen this.
Pregnancy – MTX is teratogenic. Contraception required in males and females during treatment and for 3-6 months afterwards.
Elderly – caution due to reduced folate reserves and reduced renal and hepatic function. Consider interactions - antifolate agents. Folate deficiency increases MTX toxicity.

**Sulfasalazine:**

Hypersensitivity to parent molecule (sulfasalazine), 5-aminosalicylic acid or sulfapyridine (sulphonamide abx or salicylates).
Impaired hepatic or renal function – responsible for metabolism and excretion.
Blood dyscrasias – it can inhibit absorption and metabolism of folic acid and can cause deficiency potentially resulting in blood disorders.
Asthma – see below.
Glucose-6-Phosphate Dehydrogenase deficiency – it can increase the risk of haemolytic anaemia.

**Leflunomide:**

Hypersensitivity
Liver impairment – the active metabolite is cleared by hepatic metabolism and biliary secretion, therefore impairment will increase the risk of accumulation.
Hypoproteinaemia – highly protein bound therefore plasma levels expected to be higher if protein low.
Immunodeficiency
Bone marrow impairment Serious infection
Moderate/severe renal impairment
Pregnancy – women of childbearing potential should use effective contraception during treatment and for up to 2 years after (if washout procedure not carried out).
Possible male mediated foetal toxicity, therefore effective contraception required during treatment and should undergo the washout procedure prior to conception.

**Side effects MTX:**

Generally, the frequency and severity is dependent on dose and duration. If adverse events occur, it is sometimes possible to hold treatment/ alter the dose and restart cautiously.
Folinic acid can sometimes be used to improve/correct toxic effect. Concomitant folic acid can be used to reduce S/E.
Common S/E – malaise, fatigue, chills, fever, dizziness, leucopenia, infection, N&V&D, alopecia. Hepatotoxicity (MTX is hepatotoxic) – changes may occur without prior signs of toxicity - monitor. Myelosuppression – MTX can suppress haematopoiesis. This can occur abruptly - monitor.
Respiratory effects (stop treatment and do not re-start). Patients should be aware of the signs to be aware of (dry cough, dyspnoea, thoracic pain) and HCP should monitor at each visit. They can occur acutely during any stage of therapy.
GI side effects – Diarrhoea and ulcerative stomatitis (toxic effects, requiring interruption of treatment). Therefore, caution in those with peptic ulcer or ulcerative colitis. General non-serious GI S/E often require dose reduction.
Skin reactions – these can be serious and should be reported immediately.
Patient to be able to identify and report signs of these S/E to allow appropriate investigations.

**Sulfasalazine:**

Common S/E: nausea, headache, rash, loss of appetite, raised temperature, insomnia, tinnitus. Blood disorders – leucopenia > thrombocytopenia and neutropenia. Generally reversible on cessation.
Cough, dyspnoea (therefore it is cautioned in patients with reduced pulmonary reserve, i.e. asthma).
Nausea – very common. Abdominal pain, diarrhoea, vomiting, stomatitis.
Pruritus. Arthralgia.
Proteinuria (also crystalluria and other renal effects). Need to ensure adequate fluid intake.

**Leflunomide:**

Common S/E: mild increased BP, mild allergic reactions, diarrhoea, N&V, abdominal pain, elevation of liver enzymes (may require dose adjustment), paraesthesia, headache, dizziness, increased hair loss, rash, itching dry skin.
Colitis – therefore need to investigate diarrhoea
Severe liver injury – if it is to occur it most commonly in the first 6 months (especially when co- treatment with other hepatotoxic drugs).
Blood disorders – mild leucopenia > anaemia and mild thrombocytopenia. Increased risk when given with other haematotoxic drugs.

**Special precautions MTX:**

Dehydration, impaired renal function and co-administration with medicines that may cause renal impairment (i.e. NSAIDs – close monitoring required) – due to these increasing the risk of MTX levels.
Alcohol use, hepatotoxic drugs (including hepatotoxic DMARDs i.e. leflunamide, close monitoring required if used together) – increase the risk of hepatotoxicity.
Concomitant use of haematotoxic drugs – myelosuppression is common, occurring without warning within the normal dosing range. Additional drugs increase the risk of this occurring. Patient should report any signs of infection.
Avoid additional antifolate drugs such as trimethoprim as these increase the risk of bone marrow suppression.
Use with folic acid once a week (increased to every day except methotrexate day) to reduce side effects.
Can be given by SC or IM if GI side effects intolerable (increased expense).

**Sulfasalazine:**
Safest for use in pregnancy (give with folic acid as folic acid absorption is inhibited). Enteric coated version licensed in RA. Do not crush or take with antacids.
NSAIDs can be taken.
Sulfasalazine may colour urine orange/yellow and stain contact lenses orange.
Can cause oligospermia and infertility in men – effects reversed in 2-3 months of stopping treatment.
Slow acetylator status – it is taken up and acetylated in the in the liver. This acetylated version of sulfapyridine is renally excreted, therefore slow acetylators can have accumulation of the drug.
Due to the similarity on structure, sulphonamide have caused hypoglycaemia – monitor. Myelosuppression, haemolysis or hepatoxicity have occurred – patients should report signs of bleeding, bruising, sore throat, fever, jaundice and malaise.

**Leflunomide:**
Concurrent hepatotoxic/haematotoxic drugs – increased risk of serious S/E.
Active metabolite (A771726) has a long half-life (1-4 weeks) meaning adverse reactions may occur even if treatment has stopped. If this needs to be removed from the body rapidly then the washout procedure should be followed.
Active metabolite of leflunamide is highly protein bound and cleared via hepatic and biliary metabolism – levels therefore expected to be higher in those with hypoproteinaemia or impaired liver function.
Patients with impaired bone marrow function or low cell red/white cell counts are at increased risk of haematological disorders. Due to its immunosuppressive effect it may increase susceptibility to infections.

**<u>Monitoring</u> MTX:**
FBC, LFT, renal function checked before initiations and weekly until stabilised. Then every 2-3 months. – This is because MTX can cause bone marrow suppression, pulmonary toxicity are potential risks of treatment/SE. A chest x-ray should be done prior to initiation – due to the risk of pulmonary effects.
MTX is renally cleared and therefore checked as impairment would increase the risk of S/E. Patient self-reporting signs of hepatic, pulmonary and blood disorders.
MTX book given to patient.

**Sulfasalazine:**
FBC and LFT before treatment, every other week (during the first three months of treatment) for 3 months, monthly for 3 months then every 3 months.
Renal function when beginning therapy (at initiation and monthly for the first 3 months).

**Leflunomide:**
LFT and FBC at initiation and every 2 weeks during the first 6 months and every 8 weeks thereafter.

**<u>Dosing</u> MTX:**
2.5mg-5mg (some references say up to 10mg) administered a week prior to initiation of therapy to detect any idiosyncratic adverse reactions.
Weekly (7.5mg to 20mg ONCE a WEEK – the dose is usually increased by 2.5mg to 5mg every 2- 6 weeks)
Effect seen in 6 weeks to 3 months
Dose can be adjusted based on side effects and response.
Day should be the same each week and specified on the prescription.
Only 2.5mg tablets should be used and multiples of these taken to make up the required dose.
**Sulfasalazine:**
Gradual increase in dose (1 tablet daily, increased by 1 tablet a day each week until on 1 QDS or 2 TDS – as tolerated) – this improved GI S/E.
Slow to effect, 6-8weeks to 3 months.
**Leflunomide:**
Loading dose can lead to more S/E. Without loading dose it has a longer time to effect. 100mg OD for 3 days then maintenance 10-20mg.
Therapeutic effect starts 4-6 and may further improve up to 4-6 months.

For all:
Live vaccines should not be used with any DMARD.
Patients should be up to date with their immunisation before initiation and should receive the influenza and pneumococcal vaccine each year.
Caution use of all three preparations in patients with inactive chronic infections where immune response is important or essential, i.e. TB and hepatitis B & C.
The consultant decides to start her on methotrexate; you receive her prescription in the hospital pharmacy:

Methotrexate 10mg tablets 20mg
once a WEEK Supply: 28

Folic acid 5mg tablets 5mg weekly
Supply 4 tablets

5. Would you want to discuss this prescription with the prescriber before dispensing it? If so, what would you want to discuss and why?

**YES.**

Strength of tablets it is available as 2.5mg, 10mg (10mg NOT used due to an NPSA safety alert). It is always important to check the dose with the patient and ensure they are taking them correctly. (There have been occasions where a patient has received a different strength but known they always take 'four' – so received 40mg instead of 10mg.)

Is 20mg an appropriate starting dose? BNF, Moderate/severe: 7.5mg WEEKLY adjusted according to response, max 20mg weekly. Start with 7.5mg weekly increase by 2.5mg -5mg to 20mg (maximum dose) or highest dose tolerated below the max.

May consider a test dose (2.5mg) initially to determine any idiosyncratic adverse reactions.

Is it appropriate to supply 28 tablets? Generally, you would only supply up to the next appointment to reduce the risk of taking them incorrectly (if dispensing from a larger pot). Otherwise, if in specially labelled original plaster packs, these should be dispensed complete to enable all of the information to be given to the patient.

Should folic acid be prescribed with MTX? Generally, only once a week (to begin with) on a different day to the MTX. This is given to reduce the incidence of antifolate side effects that are experienced with MTX.
Bridging course of corticosteroids - Due to the delay to DMARD effect (of up to 3 months). Prescribing depends on the patient (not everyone will have it). This may be in the form of an oral prednisolone course or one-off IM or IV methylprednisolone or intraarticular inj. These should only be used for a relatively short period of up to 3 months and stopped appropriately.
Day of the week for administration should be stated (information added to the label, mtx booklet checked).

MTX booklet.

6. In groups of 3, allocate a pharmacist, Mrs BT (the patient) and an observer.
Undertake a patient consultation for the new initiation of methotrexate. Use your pre-workshop task material to support your knowledge and enable you to play any of the roles.

***Role play the patient***
***Explain that you have been struggling to type and use a pen due to the swelling in your joints, you are anxious that you will have to give up your job***

***The doctor did give you some paracetamol and codeine –can you take these with the MTX?***

**What is it for?**
- Reduces over activity of the immune system, works by suppressing this over activity of the immune system. NOT pain relief.

**Dosage administration:** once WEEKLY dose, day of administration M – Monday for Methotrexate, (although it can take ANYDAY!!).

**What to do if you miss a dose** – take it the following day. Do not take the dose if you are three or more days late (a flare up is unlikely in this time). In both cases take your dose on the normal day on the following week.

**How long will it take to work?** 6 weeks to 3 months. Use of the corticosteroid will provide you more immediate relief to reduce pain and swelling until the MTX is fully effective. The corticosteroid will then be stopped – this is not a long-term therapy.

MTX is a cytotoxic drug (toxic to living cells) – therefore handle with care, keep out of reach of children, if female – appropriate contraceptive is necessary as it's teratogenic.

You will be given a booklet to record your blood test results, and any changes in dose. Carry this with you and ensure your doctors fill it in. Needs to be up to date. Show to any HCP you need to see.

You will need regular blood tests to monitor your therapy/adverse effects, this will reduce your risk of some adverse effects as intervention can be made prior to them occurring.

As with all medicines there can be side effects for example:
**Side effects:**
GI – nausea, diarrhoea (these normally settle-inform prescriber if they persist) and stomatitis (inflammation of mouth and lips) – need to inform prescriber so they can investigate whether this is a S/E or toxic effect requiring intervention.

CNS – headache, drowsiness and blurred vision – inform prescriber. Hair thinning – generally returns to normal upon stopping.

Advise patients to report any signs of infection – including sore throat – as they may be signs of immunosuppression. Yellowing of the whites of the eyes, N&V – as they may be signs of hepatic impairment. SOB, dry cough, fever – as they may be signs of pulmonary toxicity.

By informing the prescriber about observed effects, they can investigate the cause and make appropriate interventions to ensure safety and disease control. Dose alterations of MTX and folic acid may be required.

**Cautions -** You would want to investigate the following to see if they would impact on your patient: Alcohol in moderate, increased risk of liver impairment
Do not have contact with anyone with chicken pox (seek advice if you do), avoid any live vaccinations whilst on methotrexate
Avoid self-medicating with Ibuprofen OTC and possible drug interactions with other medicines.

Avoid non-pasteurised foods.

Appropriate contraceptives are required during treatment and for 3-6 months afterwards.

Inform practitioners of the MTX – would stop prior to surgery, interacts with medicines and can decrease ability to fight infection.

7. What tests and investigations should be done before and during methotrexate therapy?

LFT's, RF, FBC Chest X ray

Newly started patients: FBC and LFT's/RF before starting therapy and every 1-2 weeks until stabilised there after every 2-3 months. Local policies may vary.

FBC to check for - neutropenia, thrombocytopenia and lymphopenia, bone marrow suppression. This can occur abruptly or over time. RF to ensure MTX can be cleared and does not accumulate. LFT to ensure no underlying impairment as MTX is hepatotoxic. Chest X ray: pulmonary toxicity
Patient symptoms, ESR, CRP – to check for efficacy.

After regular drug monitoring and dose escalation to methotrexate 20mg weekly, Mrs BT's DAS28 was recorded as 2.1, (8 months after starting therapy).
After a stable couple of years, Mrs BT contacted her specialist nurse with a flare in her symptoms and is seen as a priority by the rheumatologist. She has increased stiffness on waking (lasting greater than 30 minutes and after resting, increased pain and swelling of her hands and with new symptoms in her ankles. She is also feeling generally unwell and tired. She reports difficulty with her everyday tasks such as brushing her teeth and typing at work. She is quite down and upset that her symptoms are worse again.

| | | |
|---|---|---|
| CRP | **40mg/L** | (<10mg/L) |
| WBC | **20.4** | (4-11x109/L |
| RBC | 4.9 | (4.6-6.5x1012/L) |
| Hb | **88** | (115-164g/L) |
| Platelets | 222 | (150-400x109/L) |
| Neutrophils | 7.2 | (2-7.50x109/L) |
| Lymphocytes | 1.5 | 1.10-3.50x109/L) |
| ESR | **65** | (1-15mm/h) |
| Bilirubin | 14 | (0-22µmol/L) |
| Albumin | 40 | (35-50g/L) |
| Alkaline Phosphate | 84 | (38-126U/L) |
| ALT | 40 | (0-50U/L) |
| GGT | 50 | (0-60U/L) |

| | | |
|---|---|---|
| Creatinine | 95 | (55-125mmol/L) |
| Sodium | 138 | (134-145mmol/L) |
| Potassium | 4.0 | (3.6-5.0mmol/L) |
| Urea | 6.0 | (1.7-7.1mmol/L) |

8. According to NICE NG 100, what is the next step in the treatment recommendation for Mrs BT?

As the MTX has already been optimised, the next step in therapy needs to be considered. 'Step-up strategy'.
Offer additional cDMARD (MTX, SSZ, LEF) in combination when the treatment target has not been reached. NICE does not specify which agent should be used. So, Mrs BT would receive MTX plus another cDMARD.

(Potentially consider bridging corticosteroids – ensure they are stopped appropriately). Potentially - symptomatic pain relief – i.e. NSAID with caution and close monitoring.
Optimise the new therapy. Increased monitoring until stabilised.

9. According to NICE NG100, what is the next step in the treatment recommendation for Mrs BT if the patients target is not reached?

Biologic or tDMARDS as discussed in the NICE TA, used for either moderate or severe disease,

i.e. anti-TNF agents, anti-IL-6 (sarilumab/tocilizumab), antibody blocking t-cell activation (co- stimulation modulator) (abatacept), anti-b-cell antibody (rituximab), or 'nibs(considering the drug characteristics/risks of each).

You would make the prescribing decision based on patient and drug characteristics, if there was no clear agent indicated the most cost effective should be chosen.
Can be used with MTX as no contraindication to this. Consider bridging corticosteroids.
Symptomatic pain relief. Optimise the new therapy.

**Case Study 2**

Mr TW is a 35 year old man who has been taking sulfasalazine and methotrexate combination therapy for the past 6 months after optimised methotrexate monotherapy failed to induce remission. On review he continues to have active symptoms of RA: pain and swelling in both knees and 5 joints of each hand, tenderness in 4 joints of each hand and morning stiffness of about 2 hours. He has detectable RF and ACPA. His DAS28 calculated to be 5.2 on review by the rheumatologist.

He has also been taking diclofenac 50mg tablets TDS and paracetamol 1g tablets QDS.

1. Mr TW is prescribed infliximab 300mg IV with MTX (sulfasalazine stopped). Based on the NICE NG 100 and EULAR 2022, comment on the appropriateness of this.

NICE NG 100 refers you to technology appraisals for the use of bDMARDs. TA 375 refers to anti- TNF agents in severe disease. It has also relatively recently (2021) been considered appropriate for moderate disease (DAS 3.2-5.1).

After failure of optimised combined cDMARD therapy, in severe disease (i.e. DAS28 >5.1) biological DMARD therapy should be considered. ***Mr TW fits this criteria***. (In practice, you are likely to see other anti-TNF agents given that can be administered outside the hospital setting (i.e. home) by the patient/carer).

EULAR comments upon this. Mr TW has poor prognostic factors – active disease after cDMARD treatment and after combination treatment, presence of RF and ACPA and a high DAS28.
According to EULAR the guidance is to add in a bDMARD or tDMARD-(only after risk has been assessed).

2. What is the mechanism of action of infliximab? Consider how you would explain the mechanism of action to a patient?

Monoclonal antibody made of IgG light (1) and heavy chains (2). Two FAB (Fragment of antigen binding) – TNF binding areas (3).
Linked to a Fc region (4) – this part dictates the antibodies capabilities, i.e. complement fixation and Fc receptor binding.

Infliximab is a tumour necrosis factor alpha (TNFα) inhibitor) and binds with high affinity to monomers and trimers of soluble TNF and transmembrane TNF and can form complexes of each. This prevents pro-inflammatory TNF from binding to either one of its receptors reducing its effect) and can also induce other outcomes that reduce TNFs effect on inflammation. Outcomes include reduced cytokine and chemokine production, reduced activation and proliferation, inflammatory cell apoptosis, reduced angiogenesis and reduced effects on bone.
It is a chimeric protein made of human and murine origin.

Explanation to patient:
Infliximab is a manufactured "antibody". Antibodies are normally produced by the body to fight against harmful bacteria. Tumour necrosis factor alpha or TNFα is a cytokine.

Cytokines are substances released by the body during inflammation. Inflammation is a normal process generated by the body to fight against harmful bacteria and viruses.

Normally, this inflammation is controlled and regulated. In rheumatoid arthritis this process breaks down, therefore the joints of patients with rheumatoid arthritis become inflamed, excessive production of TNFα can lead to inflammation and damage to joints. but infliximab has been designed to bind to TNFa and reduce it's effect on causing inflammation.

**3. What are the administration instructions for infliximab?**

Check that the patient has been weighed as the dose is 3mg/kg and the dose is based on 100kg. Doses given at 1, 2, 6 weeks and then every 8 weeks.
Ensure that it is diluted to 250mL with 0.9% NaCl
Give over a 2-hour period minimum and give slower if signs of reaction (or to reduce the risk of a reaction) – patients to be observed for 1-2 hour post infusion to monitor for acute infusion-related reactions (pre-treatment can reduce the risk of this).

**4. What clinical checks would you want to do before supplying the infliximab?**

Check that the patient has had pre-treatment testing for TB / heptatitis B / has no active infection / does not have HF / does not have a history or current malignancy or demyelinating disease or is due any surgery (due to further increased risk of infection).

Check that the patient has been prescribed paracetamol, antihistamines and potentially methylprednisolone prior to administration to reduce the risk of infusion reactions.

Check whether the patient is to be continued on methotrexate therapy as infliximab should be used in combination with methotrexate – this can reduce the production of antibodies against the infliximab and the likelihood of infusion reactions.

Check the patients was up to date with their vaccines. Ensure they were not due to have any live vaccines.

Manufacturer recommends adequate contraceptives during and for 6 months after therapy. The patient had been appropriately counselled, to include:

Drug used to control the disease progression of RA. It will control the inflammation and therefore control the pain and effects of the disease.

Dosing – every 2 weeks for 6 weeks then every 8 weeks. Dose may be altered according to response and blood test monitoring.

Methotrexate to continue as prescribed.

Infusion reactions – anaphylaxis and delayed hypersensitivity possible. Due to this a pre- treatment of antihistamine, hydrocortisone and paracetamol may be given.

Monitoring for infection – you will be closely monitored for infections. Treatment will not be given if you have a serious infection. Treatment can put you at risk of some serious opportunistic infections.

Monitoring for hepatobiliary events – LFT checks and signs/symptoms due to effects on the liver.

Vaccinations – Patient should be up to date when treatment is initiated.

Development of malignancy or lymphoproliferative disorders is a risk of treatment.

Patients should report signs of blood dyscraisias (fever, bruising, bleeding).

Undesirable effects – Viral infection, bacterial infection, neutropenia, leucopenia, anaemia, headache, nausea, tachycardia, flushing, depression, conjunctivitis, skin disorders.

Monitor disease for moderate improvement in RA, denoted by equal/greater than 1.2 to continue therapy.

Additional information from infliximab SPC Rheumatoid arthritis

3 mg/kg given as an intravenous infusion followed by additional 3 mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter.

Remicade must be given concomitantly with methotrexate.

Available data suggest that the clinical response is usually achieved within 12 weeks of treatment. Dose adjustments may occur if response is not adequate.

Antibodies to infliximab may develop and have been associated with an increased frequency of infusion reactions. A low proportion of the infusion reactions was serious allergic reactions. An association between development of antibodies to infliximab and reduced duration of response has also been observed. Concomitant administration of immunomodulators has been associated with lower incidence of antibodies to infliximab and a reduction in the frequency of infusion reactions. The effect of concomitant immunomodulator therapy was more profound in episodically- treated patients than in patients given maintenance therapy. Patients who discontinue immunosuppressants prior to or during Remicade treatment are at greater risk of developing these antibodies.

5. What monitoring requirements are necessary while the patient has the infliximab infusion?

Anaphylactic reactions can occur within seconds or within a few hours the infusion, therefore recommended that the patient is observed for 1-2 hours post administration.
If acute infusion reactions occur then stop the infusion, emergency treatment should be available such as adrenaline, antihistamines, corticosteroids and breathing apparatus.
Monitor for symptoms of delayed hypersensitivity if re-administered after a prolonged period

A month later Mr TW is admitted to hospital and diagnosed with a severe community acquired pneumonia. He is started on Co-amoxiclav IV and Clairthromycin IV. You review him on the ward.

**6. Would you advise that they continue or stop Mr TW's RA treatment? Please provide the rationale for your decision.**

We do not know how long this is after starting treatment with infliximab or how well controlled his RA is now. In either situation there is the need to review the infliximab and MTX in light of the serious infection (serious defined as requiring hospitalisation or IV abx). Both therapies can cause myelosuppression and reduce the effectiveness of the body to manage/clear infection. Continued use may mean the infection cannot be treated, may spread, become more severe and may be fatal.
It is important that the rheumatologist is involved.

You would want both the MTX and infliximab held until the abx treatment cleared the infection (or until IV to PO step down could occur / patient could be discharged, i.e. outside acute stage of infection, when, in severe RA cases they would cautiously restart treatment with close monitoring). Consider symptom control as RA treatments on hold.

**Lower GI (Constipation and Diarrhoea) Workshop**
**ANSWERS**

**Learning outcomes**

At the end of this session you should be able to:

- Utilise knowledge from lectures and the BNF to answer clinical based scenarios
- Consider responding to symptoms in relation to diarrhoea/constipation/other common lower GI conditions:
  - Ask appropriate questions to enable differential diagnosis
  - Recommend appropriate action
  - Provide appropriate pharmaceutical and non-pharmaceutical advice

**Part 1 Case studies (30 minutes)**

**Task 1**

Mrs Smith is a 40 year old lady and regular patient at your local community pharmacy. She wishes to purchase eye drops for her itchy, watery eyes-which you diagnose as dry eyes. She has no other eye conditions and has never experienced dry eyes before. You've ruled out any obvious causes of dry eye (based on age and environmental factors).
Her list of medication is below.

| **Prescription medication:** |
|---|
| • Gaviscon Advance Peppermint suspension (5-10ml after meals and at bedtime)<br>• Ispaghula Husk 3.5g sachets (ONE to be taken TWICE daily PRN)<br>• Loperamide 2mg capsules (TWO STAT, followed by ONE after each loose stool, maximum FOUR daily PRN) |
| **OTC medication:** |
| • Buscopan cramps (dose recently increased to 2 QDS due to abdominal discomfort) |

1. Are there any potential pharmacological cause(s) for Mrs Smith's dry eye (discuss the mechanism of this side effect)?

To do this, you need to know the mechanism of action of the drug!
The aim of this question is to get you to see the bigger picture.
Hyoscine (like other medications with antimuscarinic effects) binds to nicotinic acetylcholine receptors (nAChR) and prevents their activation by the natural ligand, Acetylcholine. Acetylcholine activation of these receptors promotes the parasympathetic system (rest and digest) which promotes tear production (lacrimation) AND peristalsis/related smooth muscle contractions which is why Hyoscine Butylbromide is useful for crampy IBS symptoms. When the nAChR is antagonised, tear production is reduced AND when muscarinic M3 receptors in GI tract are antagonised, smooth muscle contractions are reduced.

2. Mrs Smith has frequent abdominal cramping, altered bowel habit, bloating, flatulence, urgency to defecate, sometimes passing mucus in stools, abdominal pain is relieved by passing stools or wind, symptoms are worsened by eating (her blood test results and GI scans are all normal, no abdominal tenderness present on palpation).

   A. What conditions would you consider as part of a differential diagnosis?

IBS
IBD
Diverticular disease/diverticulitis
Coeliac disease
Lactose intolerance

   B. As part of a differential diagnosis, what key signs/symptoms would you expect her clinician to exclude?

Whilst many of these tests/signs/symptoms relate to GP/consultant roles, it is useful to have a basic knowledge of what is required as you may need it as while signposting/supporting patients.

- Blood test - ↑ WBC, ↑ platelets ↑ CRP (Diverticulitis/IBD), autoimmune antibodies (coeliac disease), blood sugars (as part of lactose intolerance test), ↓ iron (can indicate blood loss, e.g. IBD/diverticular disease, or malabsorption which could be caused by any of above conditions).
- Lactose exclusion diet (lactose intolerance).
- Endoscopy – signs of inflammation (IBD).
- Physical examination of abdomen to determine tenderness and pain (diverticular disease/diverticulitis, IBD).
- Body temp - >38 can indicate infection (diverticulitis).

   C. Based on the information provided – what would be the most likely diagnosis for this patient?

IBS

3. Mrs Smith recently submitted a 2-week diary of her stool types to her consultant using the Bristol stool chart and reported >25% of stools at type 6/7 and <25% at types 1/2. What diagnostic criteria was being used AND what classification of the condition would be assigned to the patient based on her stool diary?

The Rome IV criteria are sometimes used in secondary care to assign a classification to IBS, based on their stool type over at least the previous 2 weeks.

IBS-D subtype

4. Given her specific condition, is there anything about her medication regimen that you would like to discuss with the prescriber AND explain your reasoning based on the mechanism of action of the medication(s)?

For IBS-D, which predominates with diarrhoeal symptoms, it may seem unusual to take a laxative (Ispaghula Husk). Any other class of laxative such as osmotic, stimulant, stool softeners etc would be contra-indicated.

Bulk forming laxatives mechanism of action involves drawing water into the GI tract and stool, which bulks up the faecal mass and consequently stimulates peristalsis. This bulkier stool formation directly reduces diarrhoeal symptoms.

5. Regarding the potential pharmacological cause(s) for the dry eye, what evidence-based medication change would you recommend to their GP (please list your evidence source) ?

The most recent full NICE guide -Irritable Bowel Syndrome in adults: diagnosis and management (CG 61) from 2008 states that antispasmodics can be prescribed, but it doesn't make specific medicine recommendations.

NICE CKS for IBS was written in September 2022, so is more up to date. It states that antimuscarinics like Hyoscine Butylbromide and Dicycloverine are more likely to cause adverse antimuscarinic effects than direct acting intestinal smooth muscle relaxants such as Alverine Citrate, Mebeverine, Peppermint Oil.

Any of the above 3 are suitable substitutions.

6. Mrs Smith is going away for the weekend and wishes to bring along a more convenient product instead of her usual Ispaghula Husk sachets (which must be mixed with water). She has asked to purchase some Lactulose oral solution as a liquid is easier to take on the go. What is your response?

Answer to patient: Lactulose can increase gas production and worsen IBS symptoms. There are no liquid versions of bulk forming laxatives. The PIL for Ispaghula Husk also states that it must be taken straight away after reconstitution-so we cannot suggest an alternative. (NICE CKS 2022 recommends that Lactulose must never be used in IBS patients).

In addition, laxatives are typically only used in IBS-C. As discussed in question 4, her use of a laxative has nothing to do with increasing GI motility, but everything to do with bulking up stools. So using anything other than a bulk forming laxative will exacerbate her symptoms.

**Task 2**

Mr Harry Jacobs, a 65 year old male, complains of being constipated. He admits to being a bit of a 'salad dodger' and his current medication is:

84 Prochlorperazine 5mg tablets 1 TDS
28 Simvastatin 40mg tablets 1 OD
28 Lisinopril 20mg tablets 1 OM
60 MST Tablets 1 BD
28 Aspirin 75mg tablets dispersible 1 OM

A. What medicine(s) is/are likely to be causing the constipation?

- MST (opioid analgesic)
- Prochlorperazine (anti-muscarinic)
- Lisinopril (constipation SE of ACEI)

B. What treatment do you suggest? What are the advantages and disadvantages of each of these medicines?

Should not suggest bulk forming laxative; does not respond to opioid induced constipation!!
Recommend stimulant e.g. senna or bisacodyl
Advantages:

- relatively quick 12-hour action
- opposes the opioid induced reduction in GI motility

Disadvantages:

- Avoid long term use over concerns of weakening bowel.
- Effect can be strong in some patients (causing water and electrolyte loss)

Glycerol suppositories can be considered
Advantages:

- 30 minutes action
- Clears material already close to rectum, clearing passage for backed up material

Disadvantages:

- Patients may need help administering them
- Some patients don't like using them

Recommend a longer-term treatment alongside use of MST to prevent constipation. E.g. osmotic laxative (macrogol salts or lactulose).
Advantages:

- Safe for long term use because they do not act upon the bowel itself
- Generally have milder laxative effect than stimulants

Disadvantages:

- They take 1-3 days to work
- Relatively high doses may be needed to ensure GI motility
- Can also be high in sodium

C. What non-pharmacological advice could you give to prevent him getting constipated again?

- Water, fruit and exercise too!
- Increase his fluid intake; aim for at least 8 glasses of fluid daily (more if exercising/warm climate)
- Doesn't like salad, but explore other fruits and vegetable. Suggest dried fruits and fruit juices, and higher fibre cereals and breads
- Try to keep physically active; don't expect patient to join a gym, but try gentle walks, swimming if possible
- Target 30g dietary fibre per day (small changes and can easily be achieved within 3 meals per day).

**Task 3-(feedback at end of session if time).**

Clostridium difficile is a Gram positive, spore producing organism. People become infected by ingesting the spores either directly from infected individuals or from the environment highlighting the essential need for a clean environment. These infections may occur in a healthcare setting but can also occur at home without the patient ever going into hospital.
Infected individuals may demonstrate a spectrum of symptoms from mild self-limiting diarrhoea to severe colitis and toxic megacolon.
C. difficile infection is commonly precipitated by the use of broad-spectrum antibiotics, i.e. cephalosporins and quinolones. Older patients are most at risk especially those who are frail or with medical conditions.
Faecal specimens are tested for either glutamate dehydrogenase, an enzyme specific for carriage of C. difficile and one for the production of toxins A and B.

1. Mr P.Patterson, a 72 year old gentleman on your ward who has just had a positive result for Clostridium difficile. You can see from his stool chart that he has had 8 episodes of type 6 and 7 stools in the past 24 hours and is becoming dehydrated.

His current prescription is shown below:

- Dalteparin 5000 units OD
- Co-amoxiclav 625mg TDS – suspected UTI
- Lisinopril 10mg OD
- Aspirin 75mg OD
- Simvastatin 40mg ON
- Lansoprazole 30mg OD

A. What general considerations must you and the ward staff consider in the ongoing care of this patient?

- Inform the infection control team.
- Isolation within 2 hours of symptomatic diarrhoea.
- Sent to isolation ward – resolution of the episode and specific consideration of each case by the infection control team allows the patient to go back to the ward.
- Hand washing with soap/chlorhexidine and water – spiragel is ineffective.
- Gloves and aprons to be worn – barrier nursing.
- Visitors to wear PPE and undertake handwashing.
- Bowel chart.
- Sodium hyperchlorite 1:10 or Chlor-Clean followed by detergent anything that is not disposable, i.e. BP cuffs, moving and handling equipment and physio equipment.
- Hydrogen peroxide vapour treatment once area vacated.

B. What pharmacological treatment do you recommend for this patient?

Primary actions

- Stop PPI.
- Stop non-urgent antibiotics required for immediate patient management.
- Commence Vancomycin oral therapy – as patient suffering with severe diarrhoea (>6 motions/24hours), the recommended treatment is VANCOMYCIN 125mg PO 6-hourly for 10 days.

Optional discussion points

- Why is it possible to use IV metronidazole? – Metronidazole is excreted in the bile and by the inflamed colonic mucosa achieving faecal levels sufficient to treat C. Diff.
- What if the patient was unable to swallow or had an NG tube? – Use vancomycin injection diluted and administered down the tube or IV metronidazole. We often use the IV orally as the capsule coat takes time to dissolve and it GI transit is very quick the medication is not released appropriately.
- Why do we not use IV vancomycin? – IV vancomycin is not secreted into the GIT and is therefore ineffective against C.Diff infection.
- When would you expect to see improvement? – 48 hours with resolution by the 6th or 7th dose.

**Part 2 Responding to symptoms (1 hour)**

You will have prepared questions for the three patient scenarios labelled as patient 1, 2 or 3. We will role play these as a class to support your clinical decision making.
For each patient, consider what you may need to know to be able to help them. In the workshop, you will be given the answers from your 'patient' and you will need to make a decision. The workshop facilitators will act as your 'patient'.

**STEP 1 (15 mins) – in your groups create a list of questions you wish to ask ALL 3 'patients'. We will then work through patient 1,2,3 chronologically.**
**Patient 1:** Miss Sarah Green, 25 years, presents in pharmacy asking for something to help her go to the toilet.
(5 mins) – the groups will ask the 'patient' their questions (2 spokespeople per group).

(5 mins) – use the information garnered from step 2 to reach a group decision about the most appropriate treatment.

(5 mins) – spokespeople to state:
- Treatment choice (both pharmacological and non-pharmacological).
- Counselling points.
- Justification for your treatment choice.

**Constipation:** ignoring call to stool. Lifestyle advice and short-term laxative e.g. senna or lactulose dependent upon patient preference. Give patient pros and cons and reach a shared decision.
What would you do if you had young women repeatedly asking for senna? Professional decision making? How would they handle it? Why? Consider legal/ethical/clinical/professional.
Legal - short term/occasional use.
Ethical - duty of care to safeguard patients.
Clinical – can weaken bowel, can cause dehydration and electrolyte disturbances.
Professional – point out there is no evidence for weight loss with Senna, signpost to appropriate service.
**Patient 2:** Mr Joe Franks, 35 years, presents in pharmacy asking for something for diarrhoea.
(5 mins) – the groups will ask the 'patient' their questions (2 spokespeople per group).
(5 mins) – use the information garnered from step 2 to reach a group decision about the most appropriate treatment.
(5 mins) – spokespeople to state:
- Treatment choice (both pharmacological and non-pharmacological).
- Counselling points.
- Justification for your treatment choice.

**Diarrhoea:** diet induced: prevent dehydration, relieve symptoms and remove causation. If at risk of dehydration you can give ORS, but if eating and drinking normally not indicated. Can supply Loperamide for symptom management.
There has been conflicting evidence over the years as to whether we should 'let it run it's course'. Some have believed that slowing down GI motility can prolong the infection (and it is easy to see why!). This advice still stands for serious infections such as gastroenteritis or dysentery (unlike more common causes of diarrhoea, these conditions will also cause blood/mucus in stools, fever and should not be managed OTC). Understandably these conditions carry greater risk of dehydration with potential knock-on effects such as kidney impairment and electrolyte disturbances. Patients need more careful monitoring, may need antibiotic treatment and so we refer them.
It is now more commonly believed that for simple acute diarrhoea, it is the immune system acting on the causative agent that resolves the condition and has less to do with the cause 'working it's way through the GI system'. It is worth noting that NICE CKS for diarrhoea does not specifically recommend Loperamide (possibly because the data is quite conflicting over the benefit), yet Loperamide is licenced for the symptomatic relief of acute diarrhoea. So the best advice is to discuss the options with the patient, ascertain how urgent it is to reduce bowel movements-some patients will choose to have the medication so that they can return to work etc. In addition, treating with Loperamide will reduce the loss of water and electrolytes, so in the long run, in most instances, there will likely be a benefit to treating with Loperamide. They key is to identify the patient's preference, advise them of the pros and cons and reach a shared decision.

**Patient 3:** Mrs Helen Morgan, 34 years, presents in pharmacy asking to speak to the pharmacist about diarrhoea.
(5 mins) – the groups will ask the 'patient' their questions (2 spokespeople per group).

(5 mins) – use the information garnered from step 2 to reach a group decision about the most appropriate treatment.

(5 mins) – spokespeople to state:
- Treatment choice (both pharmacological and non-pharmacological).
- Counselling points.
- Justification for your treatment choice.

**Diarrhoea with warning symptoms:** Possible IBD. Refer to GP as a number of red flags are present.
- Unexplained blood in stool – this is a red flag symptom as per NICE CKS for diarrhoea. Bleeding — less likely to be a feature of irritable bowel syndrome or functional diarrhoea. Bleeding also indicates possible underlying inflammation.
- Severe diarrhoea is passing stool > 6 times per day (patient has passed 8 in 24 hours).
- Extreme tiredness also more indicative of IBD (? Anaemia).
- Rectal pain also suggests possible inflammation (patient has never had piles)
- Loperamide is only licenced for IBS-D attacks lasting up to 48 hours (patient has had symptoms 3 days, so we must refer).
- Patient has symptoms once or twice a month on an ongoing basis-suggesting that there has been an undiagnosed issue for some time.

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.

## 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)<br><br>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 | 38.2ºC |
| | Pulse | 98bpm |
| | Weight | 49kg (recent weight loss) |
| | Lungs | NAD |
| | Patient appears pale and exhausted.<br>Tender, red patches on both shins<br>Stool sample - negative<br>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**<br>Collection LAB<br>No Today 8904 | Potassium<br>**3.2*** <br>3.6-5.00<br>mmol/L | Sodium<br>**132*** <br>134-45<br>mmol/L | Urea<br>**9.8*** <br>1.7-7.1<br>mmol/L | Creatinine<br>**135*** <br>55-125<br>µmol/L | |
|---|---|---|---|---|---|
| | **ESR**<br>**50*** <br><10mm/h | **CRP**<br>**60*** <br><10mg/L | **Hb**<br>10.5* <br>13.0-18.0<br>g/dL | **WBC**<br>22* <br>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 Estin | | | 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.

## 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

## 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 | |

**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 | | | | | | | | | | |
| | 08:00 | ✓ | X | | | | | | | | |
| Dose: 400mg; Route: Po; Frequency: TDS | 12:00 | | | | | | | | | | |
| | 14:00 | ✓ | | | | | | | | | |
| Indication: | 18:00 | | | | | | | | | | |
| Pharm check: | 22:00 | ✓ | | | | | | | | | |
| Prescriber's signature: P Sven; 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 | | | | | | | | | | |
| 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 REQU RED DRUGS

CIH OK FA.GE 1 FOR ALLSRGY STATiUS

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Drug (a pproved 1!12J11e) r.?12m a | S1e111 d'ata *Dt19* 1.. | d | | | | | | | | | | |
| Dose Route *:S'OOmg-1,9* ! ,PO | Max Fr,eql!Jancy 4-6 g | ▪ | | | | | | | | | | |
| Indication --..,..,..1"§' " | Phannmeck | i | | | | | | | | | | |
| Fi'irescmEt"a 5lg,-a11.Jre **0rPS\!U1,c** | Slffl' | j | | | | | | | | | | |
| 2. Drug (Af1Pr<:il.l..d,a,) | Suanll d' " | j | | | | | | | | | | |
| Dose !Route | Max Fr,egl!lancy | ,c: | | | | | | | | | | |
| Indication | **F'hamlmeck** | / | | | | | | | | | | |
| Pirescd!&"a olg re | SUJ!f!fy- | J | | | | | | | | | | |
| 3. Drug (ap;proved 1!12J11e) | Slelll d'ata | .!I | | | | | | | | | | |
| Dose !Route | Max Fr,egl!lancy | | | | | | | | | | | |
| Indication | **Phann** ,c:hEd; | / | | | | | | | | | | |
| Fi'iresCJber'iS 5lg,-a11.Jre | SUJ!f!fy- | j | | | | | | | | | | |
| 4. Drug (ap;pf"lJ'El1l!l12J11e) | :ilelil data | IJ | | | | | | | | | | |
| Dose !Route | Max Fr,eql!Jancy | ,c: | | | | | | | | | | |
| Indication | **PharmfflE!Ck** | Du. / "' | | | | | | | | | | |
| l='iresrrih-«!a slg re | | J | | | | | | | | | | |
| 5. Drug (approved name) | S1elll d'ata | IJ | | | | | | | | | | |
| Dose !Route | Max Fr,egl!lancy | | | | | | | | | | | |
| Indication | **Phannml!Ck** | / | | | | | | | | | | |

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| Fi'r.escrbEt-'iS 5lg,ia11Jre | Suwfy | ..<br>"i' | | | | | | | | | | |
| CIHffiK FA.GE 1 FOR ALLSRGY 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 se ere 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 ,.go 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 diag11osis to CD) |
| | Strictures | As a result of scar tissue or inflai11111a tion | Unusual in UC, sometimes a sign of bowel cancer |
| | Fissures | Complication of perianal disease | Absent |
| | Extt-aintestinal 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)<br>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; VIE: 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)<br>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<br>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)<br>or<br>Erythrocyte sedimentation rate (ESR) | CRP <5mg/L<br>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<br>Bilirubin <19 µmol/L<br>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.<br>Levels in IBS are normal.<br>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?**

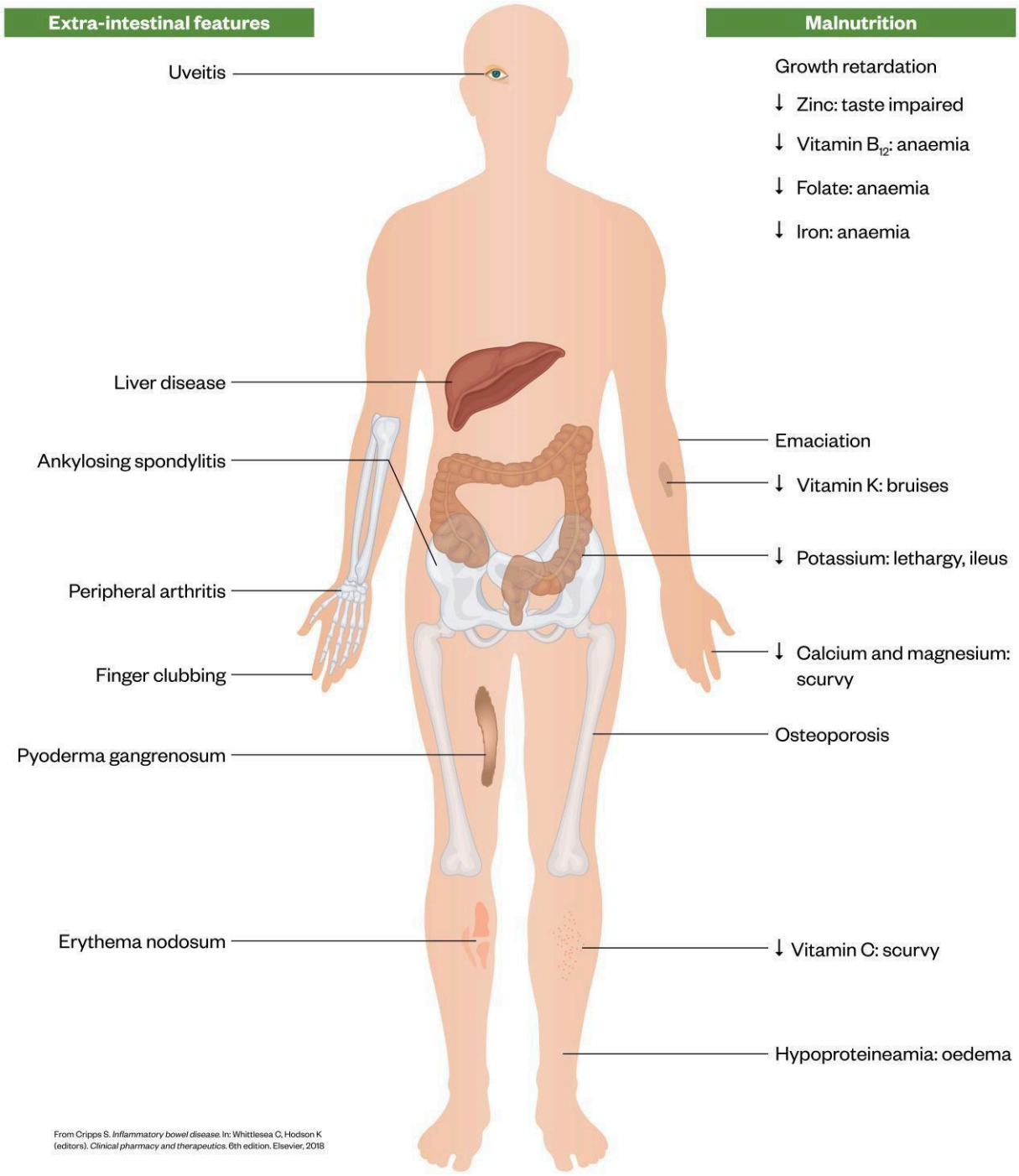
Erythema nodosum 2-3cm, more lower limbs, erupt over 1-several weeks tender red nodules of subcutaneous fat/adipose and can be accompanied by joint pain/swelling and fever – complication of IBD/inflammatory disease. Important to treat the underlying condition.

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

**Severe: (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?**

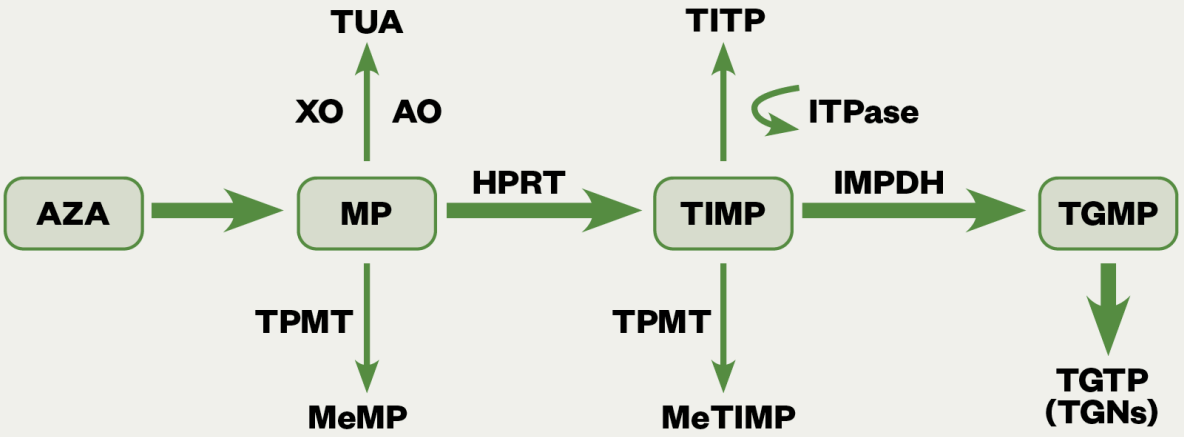
Therapeutic: Symptom control, CRP/ESR, reduce faecal calprotectin, endoscopy, Truelove and Witt score reduction.
Toxic: Differential WBC/FBC (myelosuppression), LFTs (deranged LFTs), Thiopurine Methyl-Transferase (TPMT), nausea (take with meals), presence of opportunistic infections, lymphoproliferative 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<br>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<br>NKDA | |
| **SH:** | Highway maintenance – shift work<br>Lives alone | |
| **Alcohol** | 8-14 units per week | |
| **Smoking Status** | Smoker – 5-10 cigarettes/day | |
| **OE** | BP | 122/75 |
| | Temp | 37.0$^{o}$C |
| | Pulse | 72bpm |
| | Weight | 64kg (recent weight loss) |
| | Lungs | NAD |
| | Stool sample - negative<br>Faecal calprotectin >140micrograms/g<br>Colonoscopy – Patchy inflammation of the terminal ileum and right ascending colon<br>HBI – 7<br>ESR, CRP - Raised<br>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