University of Brighton
School of Applied Sciences

Foundation Year EXAMiner

Edition 4, November 2021

Contents

1.Calculations; Density and Displacement Values

Principles/Equations/Question types	Examples
Density The weight per volume of a liquid expressed in g per ml. Something with a high density has a large mass in a small volume, whereas something with a small density has a small mass in a large volume. Density= Mass(weight)(g) / Volume (ml) If we know the density of a liquid, we can then convert a volume to a weight or vice versa. Mass = Density x Volume Volume = Mass / Density	**Example 1; Liquid X has a density of 0.75g/ml. Convert 30mls of liquid X to its equivalent weight.** Answer; We know that 1ml weighs 0.75g We want to know how much 30mls weighs, so we multiply 0.75 by 30 = 22.5g We can also solve this by using proportional sets; Weight (g) | 0.75 | y Volume (ml) | 1 | 30 Y = 0.75 so Y=0.75x30 =22.5g 30 1 1 Link to video Density example 1 **Example 2;** Or a question may ask you to convert the weight into a volume. **Using the same figures from above, the question may ask you to convert 22.5g of liquid X into mls where you know the density to be 0.75g/ml.** You could take the final weight (22.5g) and divide by the density (0.75)= 30mls. Or if you prefer to use proportional sets; Weight (g) | 0.75 | 22.5 Volume (ml) | 1 | y Y=1x22.5=30mls 0.75 Link to Density Example 2 video Sometimes the need to convert from weight to volume or vice versa is needed as a stage to answering a question in order to get all the ingredients expressed in the same units. **Example 3.**

You are asked to make 250g of an ointment using the following formula;

Liquid paraffin 50ml
White soft paraffin (WSP) to 250g

The density of liquid paraffin is 0.88g/ml. How many g of WSP do you need to use?
Answer;
Note that the amount of liquid paraffin is expressed in mls not g, so the answer is not 250-50=200g!
We need to know how many g 50mls of liquid paraffin weighs, and to do this we need to know its density. (You would be told the density in this type of question).

As the density of Liq. Paraffin is 0.88, each 1ml weighs 0.88g, and we need 50mls, i.e. we need 0.88x50=44g of liquid paraffin
The final weight needed is 250g, of which 44g is liquid paraffin. So the amount of WSP needed is 250-44=206g
If you prefer to work this out using proportional sets;

Wt. of liquid paraffin	0.88	X
Vol of liquid paraffin	1	50

X=50x0.88=44g of liquid paraffin needed,
1 so amount of WSP=250-44=206g

Link to Density example 3 video

Displacement Volume

This is the volume which a solid takes up when it is added to a solvent.

E.g. **a displacement volume of 0.8 means 1g of a solid takes up 0.8ml of space.** We need to know this so we can work out how much solvent to add to a known amount of solid in order to make an exact volume of solution. Examples include antibiotic solutions.

Example 1.
A powder contains Drug Y.
73mL of water needs to be added to the powder to produce 100mL of a mixture containing 200mg of drug Y in every 5ml dose. Calculate the displacement volume for a quantity of powder equivalent to the 200mg dose of drug Y

Answer;

You can practice this type of question at work; Next time you dispense an antibiotic liquid, look at how much water you are instructed to add, and from this work out the displacement value of the powder. You will notice that the amount of water you need to add to different antibiotics to make 100mls is very variable; from 60mls for some through to 90mls for co-amoxiclav. The reason for this difference is that the antibiotic powders you are reconstituting have different displacement volumes.
This will help you to visualise displacement volumes in practice

Method 1;

If there is 73mls of water in 100ml, then the powder containing of Drug Y must be taking up 100-73=27ml.
The question is asking for the displacement volume for each 5ml dose.
100ml contains 100/5=20 doses, so the powder needed for 20 doses is displacing 27mls, so the amount of powder needed for one 5ml dose is displacing
27/20=1.35mls

Method 2;
Using proportional sets;

Volume (ml)	27	X
Drug Y(doses)	20	1

$\frac{X}{1} = \frac{27}{20} = 1.35$

i.e. 1.35mls water is displaced by the powder needed for each 5ml dose
Link to displacement vol example 1 video

Example 2;
The displacement value of diamorphine 5mg is 0.06. What volume of water for injections (WFI) would you need to prepare 5 x 1ml diamorphine 10mg injections?
Answer;
The displacement volume is 0.06 for 5mg
i.e. 5mg diamorphine occupies 0.06ml.
Therefore 10mg diamorphine must occupy
2 x 0.06 = 0.12mls
So in each 1ml injection, we need 1ml-0.12mls= 0.88mls WFI
We need to make 5 injections;
5 x 0.88 = 4.4mls
Displacement vol example 2 video

Displacement value

Similar to displacement volume but used when a solid is added into another solid e.g. when making a suppository.

Definition; the number of parts, by weight, of a medication that will displace one part of suppository base.

Total base(g)=
(No.of supps x mould size)-Total Drug
DV

A displacement value (DV)of 2 means that 2g of a solid will displace 1g of the base to which it is added. i.e. 2g of drug will occupy the same space in the suppository mould as 1g of base We need to know this so we can work out for example how much suppository base we need to add to the known amount of active ingredient to make an exact size of suppository.

Displacement value is dependent on density;

Lead has a higher density than feathers so 1kg of lead would clearly take up a much smaller volume than 1kg of feathers, i.e. the feathers would have a much larger displacement volume.
Similarly, different pharmaceutical ingredients have different densities and will therefore displace different volumes/weights when added to other liquids or solids

I'm going to use 2 variants of the same example because I want to demonstrate a way of checking your answer in the exam (See Tip in red below the examples)

Example (a)

You have been asked to make 40 suppositories each weighing 3g. The suppositories are each to contain 150mg active ingredient, and the displacement value of the active ingredient is 3.2.

Calculate the total quantity of suppository base to be used.

Answer; Use the formula;

Total base(g)=
(No.of supps x mould size)-Total Drug
DV

$$\text{Total base} = (40 \times 3) - \frac{(0.150 \times 40)}{3.2} = 120 - \frac{6}{3.2}$$

= 120-1.875= 118.125g total weight of base

Or you could use proportional sets;

Example (a)		In 40 supps
Wt. of ingredients (g)	3.2	6
Base displaced (g)	1	x

$\frac{x}{6} = \frac{1}{3.2}$ so $x = \frac{6}{3.2} = 1.875$

i.e. 6g of ingredient (the total needed for 40 supps) will displace 1.875g of suppository base, so the total amount of base needed is 120-1.875=118.125g

Displacement value example 1 video

⚠

TIP;

Check your answers in the exam; if the DV is more than 1 the total amount of ingredients used (Active + Base) should be more than the number of suppos x the mould size.

If the DV is less than 1 the total amount of ingredients used should be less than the number of moulds x the mould size

Example 2;
I'd like now to use **the same example but for an active ingredient with a displacement value of 0.6**

So the question now becomes; **you need to make 40 suppositories each weighing 3g. Each suppository needs to contain 150mg of active ingredient, and the displacement value of the active ingredient is 0.6.**

Calculate the total quantity of suppository base to be used.

Have a go at doing this yourself using the method in example (a)

Answer;

Total base= (40x3)- $\frac{(0.15x40)}{0.6}$=120-$\frac{6.0}{0.6}$=
=110g

Or using proportional sets-again, have a go yourself!

Example(b)		
Wt. of ingredient (g)	0.6	6
Base displaced (g)	1	y

Answer; Total g base displaced (y)= (1x6) = 10 i.e. 6g of ingredient (the amount needed for 40 supps) will displace 10g of suppository base, so the total amount of base needed is 120-10=110g

Displacement value example 2 video
Why have I done 2 examples?

So, you can see that **the ingredient with the larger displacement value displaces LESS base** i.e.. more base is needed than

	with the ingredient with the smaller displacement volume. If we look at example (a), where the DV is 3.2, the total weight of ingredients used is 6g (active ingred) + 118.75g(base)=124.75g total, which is more than the total mould size (3gx40=120g). This is because less base is displaced In example (b)where the DV is 0.6 the total amount of ingredients is less than the total mould size ie.6g+110g=116g. This is because more base is displaced

2. High Risk drugs; Drugs with a Narrow Therapeutic Index

I have written about some of the drugs with a narrow TI and provided you with a template so that you can use this if you wish for other drugs with a narrow TI. I've also provided some links to some excellent resources; please do check these out; **the Propharmace guide and the OSCE stop revision chart look particularly good**

Which drugs does this cover?

Suggestions are:

Aminophylline
Amiodarone
Carbamazepine
Ciclosporin
Digoxin
Gentamicin
Lithium
Methotrexate (covered in August edition of newsletter)
Phenobarbital
Phenytoin
Tacrolimus
Theophylline
Vancomycin
Warfarin

Key:

Covered in this newsletter

Covered in other newsletters

Suggested drugs to revise which aren't covered in newsletters

Suggested reading/revision aids

Propharmace High Risk Drugs guide (includes narrow TI but also other high risk drugs)

https://www.resourcepharm.com/pre-reg-pharmacist/therapeutic-drug-monitoring.html

OSCE stop revision chart

C&D article counselling-patients-prescribed-drugs-with-a-narrow-therapeutic-window

Prereg shortcuts video high risk drugs

Prereg shortcuts video Drug Ranges

Digoxin

Digoxin is a cardiac glycoside. It helps in heart failure by increasing the force of myocardial contraction (positive inotropism) and in AF by reducing conductivity within the AV node

Used for/dose

Dose adjustments needed when switching formulations; oral dose may need to be 20-33% more than the IV dose. 62.5mcg tablet = 50mcg solution

Adults:

Digoxin has a long half life so only needs once daily dosing. Doses may be divided to reduce nausea

Rapid digitalisation for atrial fibrillation or flutter

- 0.75-1.5mg over 24 hours in divided doses

Emergency loading dose for atrial fibrillation or flutter

- Initially by IV infusion; 0.75-1mg over at least 2 hours then maintenance by mouth starting on the day following the LD

Maintenance therapy for AF or atrial flutter:

- 125-250mcg daily. Adjust dose according to renal function and loading dose. Dose usually determined by ventricular weight at rest (should not persistently be below 60bpm)

Heart failure and patient in sinus rhythm:

- 62.5-125mcg once daily. No loading dose required if in sinus rhythm

Reduce dose in the elderly or in renal impairment. Reduce dose if has had digoxin or other cardiac glycoside within the last fortnight

Cautions

Hypokalaemia can be managed by use of a potassium-sparing diuretic or a potassium supplement

- Hypercalcaemia (risk of toxicity)
- Hypokalaemia (risk of toxicity)
- Hypomagnesaemia (risk of toxicity)
- Hypoxia (risk of toxicity)
- Recent MI
- Severe respiratory disease
- Sick sinus syndrome
- Thyroid disease
- Renal impairment (monitor)
- Elderly (reduce dose)

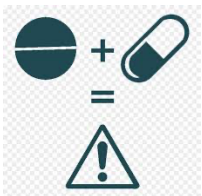
Electrolyte disturbance is a risk for toxicity, e.g., due to vomiting, diarrhoea, excessive sweating or medications

The BNF has useful tables in Appendix 1;
Table 16; drugs which increase potassium
Table 17; drugs which decrease potassium
Table 18; drugs which decrease sodium

Contraindications

- Constrictive pericarditis (unless to control AF or improve systolic function but use with caution)
- Hypertrophic cardiomyopathy (unless concomitant AF and heart failure but use with caution)
- Intermittent complete heart block
- Myocarditis
- Second degree AV block
- Supraventricular arrythmias associated with accessory conducting pathways e.g. Wolff-Parkinson-White syndrome

Ventricular tachycardia or fibrillation

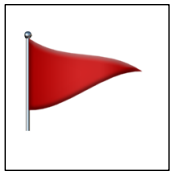


Important interactions

See BNF or Stockley for full list of interactions

- Digoxin doses should be halved with concurrent use of **amiodarone, dronedarone and quinine**
- Digoxin levels affected by **anything which causes electrolyte disturbances, also anything else causing bradycardia** (e.g. beta blockers, diltiazem, verapamil, other antiarrythmics; See appendix 1, tables 6,16,17,18
- In particular, drugs causing hypokalaemia increase the risk of digoxin toxicity e.g. thiazide diuretics, loop diuretics, corticosteroids
- Calcium; increases digoxin levels

Sympathomimetics (increased risk of cardiac arrythmias and hypokalaemia)



Red flags/important side effects

The risk of toxicity increases progressively through the range 1.5 to 3mcg/ litre (1.5 to 3 nanograms/ml)
Normal range usually 0.5-2.0 nanograms/ml

Signs of Digoxin toxicity

- **Irregular heartbeat**
- **Heart rate change—may be rapid in chronic toxicity or slow in acute toxicity**
- **Nausea and vomiting**
- **Fatigue**
- **Weakness**
- **Weight loss, lack of appetite**
- **Confusion**
- **Vision problems, such as blurred vision, how colours look and flashing lights**

Link to BNF; treatment of digoxin toxicity

- Signs of toxicity can easily be overlooked e.g. irregular heartbeat could be misinterpreted as AF being undertreated
- Treatment of toxicity; withdraw digoxin, specialist management needed, severe may need administration of digoxin-specific antibody

Toxicity may occur at lower levels, especially in the elderly or those with hypokalaemia

Counselling

- Counsel patients on the use of the pipette provided with the elixir
- Warn about signs of toxicity
- Warn about risks of toxicity if experience vomiting, diarrhoea, profuse sweating

Monitoring

- Regular monitoring not necessary during maintenance therapy unless problems suspected
- Monitoring required in renal impairment
- Plasma-digoxin concentration assay; blood should be taken at least 6 hours after a dose
- Monitor serum electrolytes and renal function (toxicity increased by electrolyte disturbances)

Renal impairment

Dose reduction may be necessary
Monitor plasma-digoxin concentration

Liver impairment

Pregnancy

May need dose adjustment

 **Breastfeeding**	Amount too small to be harmful
 **References/suggested reading**	The attached guidance is also useful for other drugs where switching formulations needs care/dose adjustment; Guidance on switching-between-liquid-and-tablet-capsule-formulations-which-medicines-require-extra-care/ https://www.medicines.org.uk/emc/search?q=digoxin SPCs and PILs https://preregshortcuts.com/videos-revision/ Pre-reg Shortcuts video on digoxin https://bnf.nice.org.uk/drug/digoxin.html **Switching between digoxin formulations** • From IV to oral route; may need to increase dose by 20-33% to maintain same plasma levels • One 62.5mcg digoxin tablet is equivalent to 50 mcg in liquid form as the liquid has a higher bioavailability. The attached guidance is also useful for other drugs where switching formulations needs care/dose adjustment; Guidance on switching-between-liquid-and-tablet-capsule-formulations-which-medicines-require-extra-care/

Lithium

Lithium is an important medication used in conditions such as mania and bipolar disorder and is very effective at reducing the risk of suicide (by about 80% in bipolar). It requires careful monitoring of Li^+ levels due to its narrow TI, and also of other parameters which it can affect such as thyroid, parathyroid and renal

Used for/dose

Lithium should be prescribed by brand, not generically

Treatment and prophylaxis of;

- Mania
- Bipolar disorder
- Recurrent depression
- Aggressive or self-harming behaviour

Doses adjusted according to serum lithium concentrations. Initially doses are split throughout the day, but **once stable it is given as a once daily dose**.

Patients should always be given the same brand, as bioavailability varies greatly. If they change brand, they must be monitored as closely as they are during initiation

Changes between dose form e.g. tablets to liquid or vice-versa requires dose conversion.

Solid dose forms contain lithium carbonate, whilst liquid dose forms contain lithium citrate

Priadel liquid contains lithium citrate tetrahydrate 520mg/5ml; 520mg is equivalent to 204mg lithium carbonate

Li-liquid contains either 509mg/5ml or 1018mg/5ml lithium citrate tetrahydrate. 509mg is equivalent to 200mg lithium carbonate

Cautions

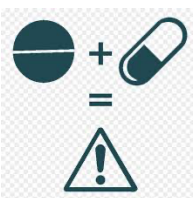
- Avoid abrupt withdrawal
- Cardiac disease
- Concurrent ECT (may lower seizure threshold)
- Diuretics (risk of toxicity) especially with thiazides
- Elderly (reduce dose)
- Epilepsy (may lower seizure threshold)
- Myasthenia gravis
- Psoriasis (risk of exacerbation)
- QT interval prolongation
- Review dose as necessary in diarrhoea, vomiting or current infection (especially if sweating profusely) **i.e. whenever dehydration is a risk**

Surgery

Contraindications

- Addison's disease
- Cardiac insufficiency
- Dehydration
- Family or personal history of Brugada syndrome
- Low sodium diets
- Rhythm disorder

Untreated hypothyroidism



There are many; **see BNF for full list,** also BNF appendix 1 Table 9 (QT prolongation),Table 13 (serotonin syndrome),and Table 18 (hyponatraemia)

The following may **increase** lithium concentrations;

- Diuretics (but potassium-sparing diuretics increase the clearance)
- NSAIDs
- ACEIs/Angiotensin-II antagonists

The following may **increase the risk of neurotoxicity;**

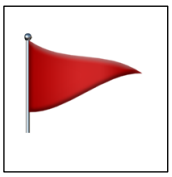
- Antidepressants which cause hyponatraemia e.g. amitriptilline

Important interactions

Lithium levels are affected by changes in sodium concentration & by drugs which alter renal blood flow & sodium balance

- Carbamazepine
- Aminophylline theophilline

Amiodarone- AVOID (prolonged QT interval)



Red flags/important side effects

Side effects are mostly dose related

Symptoms of toxicity requiring immediate referral to A&E:

Nausea/vomiting	blurred vision	severe hand shake (coarse tremor*)
Drowsiness	seizures	muscle weakness
Confusion	being unsteady on feet	

*A fine hand tremor is a common side effect but a severe or worsening tremor affecting other parts of the body is a sign of toxicity

Any sickness and diarrhoea for more than two days as dehydration may lead to toxicity

Symptoms of renal failure (tiredness, oedema, shortness of breath, itchy skin, nausea)

Common side effects	Recommended action
Tremor	A fine hand tremor is a common side effect of lithium and is not dangerous but can affect daily tasks. A worsening tremor affecting other parts of the body is a sign of toxicity and requires urgent referral.
Nausea/GI disturbance	Mild gastro-intestinal upset can occur. If it persists for more than one day, refer to prescriber.
Polydipsia	Drink water or low calorie drinks in moderation. Suck sugar free boiled sweets.
Polyuria	Avoid excess alcohol, discuss with prescriber if problem persists.
Metallic taste	This should wear off after a few weeks. If it persists discuss with prescriber.
Weight gain	Give lifestyle advice and refer to prescriber if not tolerated. Weight monitoring is important.
Hypothyroidism	Discuss with prescriber
Fluid retention/ankle oedema	Discuss with prescriber if troublesome.

Counselling

Give lithium treatment pack

https://www.sps.nhs.uk/wp-content/uploads/2018/02/2009-NRLS-0921-Lithium-patientet-2009.12.01-v1.pdf

Report signs and symptoms of:

- toxicity,
- hypothyroidism,
- renal dysfunction (including polyuria & polydipsia)
- Benign intracranial hypertension (persistent headache and visual disturbance

Maintain adequate fluid intake

Avoid changes to sodium intake in diet or medication (e.g. Gaviscon)

May affect ability to drive or operate machinery

 **Monitoring** Raised Ca^{++} may be a sign that Li^{+} has caused hyperparathyroidism. Li^{+} may cause hypothyroidism & reduced GFR	**Serum concentrations- Weekly after initiation & after each dose change** until stable **then every 3 months**. Additional tests should be taken if patient develops significant intercurrent disease or if a significant change in sodium or fluid intake. Take levels 12 hours after the dose. Levels should be 0.6 to 1mmol/litre, but an optimum range needs to be determined for each individual patient • Aim for lower end of the range for maintenance and elderly patients • Aim for 0.8 to 1mmol/litre for acute mania episodes or patients who have previously relapsed or have sub-syndromal symptoms **Body weight or BMI, serum electrolytes, eGFR & thyroid function every 6 months** (more often if impaired renal or thyroid function or raised calcium) **Cardiac function**- 'regularly' **Before initiation;** renal, cardiac & thyroid function, Body weight or BMI, serum electrolytes, FBC. ECG for patients with CV disease or CV risk factors
 **Renal impairment**	Severe impairment- AVOID Mild to moderate; CAUTION and monitor closely
 **Liver impairment**	No cautions
 **Pregnancy**	Avoid, if possible, particularly in first trimester. Women of childbearing potential should use effective contraception during treatment
 **Breastfeeding**	Present in milk and risk of toxicity in infant; AVOID

References / suggested reading	https://www.sps.nhs.uk/wp-content/uploads/2018/02/2009-NRLS-0921-Lithium-patientet-2009.12.01-v1.pdf Lithium treatment pack https://bnf.nice.org.uk/drug/lithium-carbonate.html https://bnf.nice.org.uk/drug/lithium-citrate.html BNF entry lithium carbonate and lithium citrate https://webarchive.nationalarchives.gov.uk/20100312174238/http://www.nrls.npsa.nhs.uk/resources/search-by-audience/community-pharmacy-staff/?entryid45=65426&cid=898358&p=1 NPSA Safer Lithium guidance https://www.cppe.ac.uk/learningdocuments/pdfs/murrisk/lithium.pdf Lithium MUR guide; may require CPPE login https://www.medicines.org.uk/emc/search?q=lithium SPCs and PILs https://www.resourcepharm.com/pre-reg-articles/drug-induced-hyponatraemia.pdf Drugs which can lower sodium levels and therefore affect lithium levels https://www.resourcepharm.com/pre-reg-articles/drug-induced-hypernatraemia.pdf Drugs which can raise sodium levels and therefore affect lithium levels

Phenytoin

Mechanism of action; sodium channel blocker. As well as having a narrow therapeutic index leading to the risk of toxicity or subtherapeutic levels (risk of loss of seizure control), phenytoin is also an enzyme inducer so has many drug interactions. When looking at drug interactions I recommend you separate them out into those which affect the phenytoin levels and those where phenytoin affects the levels of the other medication

Used for/dose

These doses are from the BNF; manufacturers doses for IV may differ
Preparations containing phenytoin sodium are not bioequivalent with preparations containing phenytoin base
100mg phenytoin sodium=92mg phenytoin base in therapeutic effect.
Monitoring is required when switching formulations

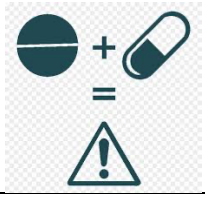
Taken from BNF edition 80	Tonic-clonic seizures, Focal Seizures	Prevention & treatment of seizures during or following neurosurgery or head injury	Status epilepticus/acute symptomatic seizures associated with head injury or neurosurgery
Adults	Initially 3-4mg/kg daily, or 150-300mg daily in 1 or 2 divided doses, usual maintenance 200-500mg daily Higher doses may be needed	Initially 3-4mg/kg daily, or 150-300mg daily in 1 or 2 divided doses, usual maintenance 200-500mg daily Higher doses may be needed	Loading dose 20mg/kg (max 2g per dose) then (by IV infusion, slow IV injection or mouth) maintenance of 100mg every 6-8hours, adjusted according to plasma concentration
Child 1month-11years	Initially 1.5-2.5mg/kg twice daily then adjusted according to response and plasma-phenytoin concentration to 2.5-5mg/kg twice daily (max 7.5mg/kg twice daily).Max 300mg daily	Initially 2.5mg/kg twice daily then adjusted according to response and plasma-phenytoin concentration to 4 to 8mg/kg daily. Max 300mg daily	Loading dose 20mg/kg then (by IV infusion or slow IV injection 2.5-5mg/kg twice daily
Child 12-17 years	Initially 75-150mg twice daily then adjusted according to response and plasma-phenytoin concentration to 150-200mg twice daily (max 300mg twice daily)	Initially 2.5mg/kg twice daily then adjusted according to response and plasma-phenytoin concentration to 4 to 8mg/kg daily. Max 300mg daily	Loading dose 20mg/kg then (by IV infusion or slow IV injection up to 100mg 3 to 4 times a day

Cautions

Enteral feeding (interrupt feeding for 2 hours before and after each dose; more frequent monitoring may be needed)
With IV use; Heart failure, hypotension, injection solutions alkaline (irritant to tissues), respiratory depression, resuscitation facilities must be available
Consider Vitamin D supplement in patients at risk e.g. immobile, inadequate sun exposure, poor dietary intake of Vitamin D
Do not give by IM route

Contraindications

Acute porphyrias
Patients of Han Chinese or Thai origin should have a test for HLAB*1502 allele (risk of Stevens-Johnson syndrome); AVOID unless essential
Cross sensitivity with carbamazepine
With IV use; second- and third-degree heart block, sino-atrial block, sinus bradycardia, Stokes-Adams syndrome



Numerous! I recommend using the BNF app rather than the paper BNF as the paper BNF clumps all antiepileptic interactions together. A few of note are;
Amiodarone; increases phenytoin levels; monitor & adjust dose.
Apixaban, dabigatran, edoxaban, rivaroxaban :phenytoin reduces levels; caution or AVOID
Carbamazepine Levels of both drugs affected (carbamazepine reduced); monitor & adjust
Cimetidine increases phenytoin levels; monitor & adjust dose
COCs, POCs, HRT, EHC; Phenytoin can reduce efficacy

Important interactions

See FSRH guidance on contraceptive choice with phenytoin https://www.fsrh.org/documents/ceu-clinical-guidance-drug-interactions-with-hormonal/

Warfarin: warfarin levels may be affected; monitor & adjust dose

Some **calcium channel blockers** e.g. **Amlodipine, felodipine, lacidipine, lercanidipine** are reduced by phenytoin. **Diltiazem & verapamil** levels may be reduced & they may increase phenytoin levels

Significant potential OTC interactions: St John's Wort (avoid), NSAIDs, theophylline, some PPIs. Antihistamines can make seizures more likely in all epilepsy patients.

Some more examples of significant interactions taken from:
https://www.nhstaysideadtc.scot.nhs.uk/approved/guidance/Phenytoin%20Prescribing%20and%20Monitoring%20Guidline.pdf

- I have highlighted interactions which increase phenytoin levels in red
- Interactions which decrease phenytoin levels are in blue
- Interactions affecting the levels of the other medication are in black

Drug	Nature of interaction
Amiodarone	Increased phenytoin concentrations (metabolism of phenytoin inhibited by amiodarone)-monitor and adjust dose
Ciclosporin	Phenytoin induces metabolism of ciclosporin (reduced concentration of ciclosporin)
Aripiprazole	Phenytoin possibly reduces plasma concentration of aripiprazole and an increased dose of aripiprazole may be required
Antiretrovirals	Plasma concentration of boceprevir possibly reduced by phenytoin – manufacturer advised avoiding concomitant use
Corticosteroids	Phenytoin accelerates metabolism of corticosteroids (reduced effect, Prednisolone most affected, hydrocortisone less so)
Digoxin	Phenytoin possibly reduces digoxin levels
Diltiazem	Plasma concentration of phenytoin increased by diltiazem and effect of diltiazem also reduced
Doxycycline	Phenytoin accelerates doxycycline metabolism and levels may be reduced below MIC
Dronedarone, Eplerenone	Phenytoin reduces concentration of these drugs - avoid concomitant use
Fluconazole	Plasma concentration of phenytoin increased by fluconazole (consider reducing dose of phenytoin)
Itraconazole	Phenytoin reduces plasma concentration of itraconazole (avoid concomitant use)
Ketoconazole, Posaconazole	Phenytoin reduces plasma concentration of these drugs
Miconazole	Increases anticonvulsant effects of phenytoin by increasing concentrations of phenytoin
Rifampicin	Phenytoin metabolism accelerated by rifampicin – reduced plasma concentrations of phenytoin
Sucralfate	Reduced absorption of phenytoin
Tacrolimus	Phenytoin may reduce levels of tacrolimus, phenytoin levels may be increased.
Theophylline	Phenytoin may reduce levels of tacrolimus, phenytoin levels may be increased.

Trimethoprim / Co-trimoxazole	**Phenytoin concentrations increased, also increased antifolate effect**
Voriconazole	**Phenytoin plasma concentration increased by voriconazole and phenytoin reduces plasma concentrations of voriconazole (increase dose of voriconazole and monitor of phenytoin toxicity)**
Warfarin	**Phenytoin accelerates metabolism of warfarin (effect of warfarin may be reduced, but increased effect also reported)-monitor and adjust dose**

This list is not exhaustive; see the BNF or Stockley for full list
There are also good tables in the SPC;
https://www.medicines.org.uk/emc/product/4225/smpc

Red flags/important side effects

See BNF for full list.

Signs of leucopenia e.g. fever, mouth ulcers, bruising or bleeding
Rash; discontinue. If mild re-introduce but discontinue immediately if recurs
Signs of toxicity:

- **Nystagmus**
- **Diplopia**
- **Slurred speech**
- **Ataxia**
- **Confusion**
- **Hyperglycaemia**

Risk of death and severe harm from error with injectable phenytoin e.g., respiratory arrest, cardiac arrest, particularly if injection too rapid

Oral use can cause electrolyte imbalance, pneumonitis & Vitamin D deficiency
Serious skin reactions e.g., DRESS, Stevens-Johnson syndrome
Has been known to cause suicidal thoughts

Counselling

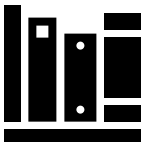
Patient should always be prescribed the same preparation. Monitoring is required if they are switched as bioavailability varies.
Teach patient or carer how to recognise signs of blood or skin disorders and **seek immediate medical attention if symptoms such as fever, rash, mouth ulcers, bruising or bleeding develop.**
Maintain good oral hygiene (may cause gingival hyperplasia-gum overgrowth)
Counsel patient or carer on the signs of toxicity (see above)

Monitoring

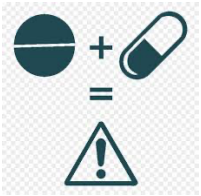
Patient should always be prescribed the same preparation. Monitoring is required if they are switched as bioavailability varies.
Teach patient or carer how to recognise signs of blood or skin disorders and **Seek immediate medical attention if symptoms such as fever, rash, mouth ulcers, bruising or bleeding develop.**
Maintain good oral hygiene (may cause gingival hyperplasia-gum overgrowth)
Counsel patient or carer on the signs of toxicity (see above)

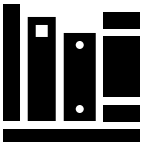
Renal impairment

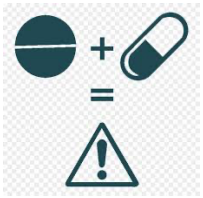
No cautions in use as phenytoin is metabolised by the liver. Interpretation of blood levels may be affected though as phenytoin is highly protein-bound

 **Liver impairment**	Caution (increased risk of accumulation and toxicity due to decreased protein binding.) Dose reduction may be needed
 **Pregnancy**	Monitoring in pregnancy difficult as plasma-protein binding changes. Risk of teratogenicity. Refer for specialist advice. Drug withdrawal may be considered if threat of seizure/seizure type not severe. Folic acid should be taken.
 **Breastfeeding**	Small amounts in milk but not known to be harmful
 **References**	http://ubmidrupalcandd.s3.amazonaws.com/public/CD%20Document%20Library/Update%20PDFs/C%2BD-update-module-1818-v3.pdfCase studies on enzyme inducers and inhibitors https://www.resourcepharm.com/pre-reg-articles/substrates-inhibitors-and-inducers-of-the-major-CYP450-enzyme.pdf https://bnf.nice.org.uk/drug/phenytoin.html https://www.fsrh.org/documents/ceu-clinical-guidance-drug-interactions-with-hormonal/ Interactions with hormonal contraception

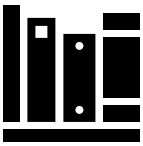
Theophylline

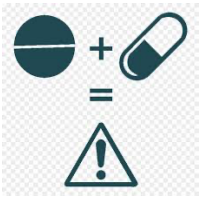
 **Used for/dose**	**Chronic asthma; 2-11yrs;** 9 mg/kg every 12hrs (max per dose 200mg). In children with chronic asthma dose may be increased to 10-16 mg/kg every 12hrs (max 400mg per dose). Can give larger evening or morning dose to achieve maximum benefit when symptoms most severe. **12-17 yrs & adults;** 200 mg every 12 hrs, adjusted according to response to 400 mg every 12 hrs. Can give larger evening or morning dose to achieve maximum benefit when symptoms most severe Also used at same dose for reversible airways obstruction or severe acute asthma in adults Dose adjustments may be necessary if smoking started or stopped during treatment Initiation: Total daily requirements may be added as single evening or morning dose if night or day symptoms persist
 **Cautions**	Always supply same brand Cardiac arrhythmias or other cardiac disease (levels are increased in heart failure) Elderly (increased plasma concentrations). Epilepsy Fever Hypertension Peptic ulcer Risk of hypokalaemia Thyroid disorder
 **Contraindications**	Elderly; Potentially inappropriate as monotherapy for COPD
 **Important interactions**	Concentrations increased by viral infection Concentrations decreased by smoking and alcohol Any medications which reduce serum potassium (BNF 80 p.1450 table 17) e.g. corticosteroids, diuretics Click here for link to BNF interactions; BNF Theophylline interactions Interactions which the BNF marks as severe include Aciclovir, beta-blockers, esketamine, cimetidine, isoniazid, erythromycin, fluvoxamine, St John's Wort, Valacoclovir
 **Red flags/important side effects**	Side effects; Anxiety, arrhythmias, diarrhoea, dizziness, GI discomfort, GORD, headache, hyperuricaemia, nausea, palpitations, seizures, skin reactions, sleep disorders,tremor,urinary disorders, vomiting Signs of toxicity; • Vomiting (may be severe and intractable), Agitation, Restlessness, Dilated pupils, Sinus tachycardia, Hyperglycaemia Serious effects: Haematemesis, convulsions, supraventricular and ventricular arrhythmias, rapid development of severe hypokalaemia especially when given alongside beta-agonist therapy

 **Counselling**	Make sure you are always given the same brand Levels may change if you start or stop smoking, or drink more or less alcohol than usual Warn about signs of toxicity and monitoring requirements
 **Monitoring**	Usual levels required for control; 10-20 mg/Litre (55-110 micromol/Litre) but 5-15 mg/Litre may be effective. Adverse effects can occur at 10-20mg/litre. Frequency and severity increase at levels above 20mg/litre Measure concentrations 5 days after starting oral therapy and at least 3 days after any dose adjustment. Blood sample taken 4-6 hours after oral dose of a MR preparation
 **Renal impairment**	
 **Liver impairment**	Caution (risk of increased exposure) Consider dose reduction
 **Pregnancy**	Neonatal irritability and apnoea reported. Can be taken as normal as important to have good asthma control in pregnancy
 **Breastfeeding**	Present in milk-irritability in infant reported; MR preparations preferrable. Can be taken as normal
 **References**	https://bnf.nice.org.uk/drug/theophylline.html https://cks.nice.org.uk/topics/asthma/prescribing-information/theophylline/ https://pharmaceutical-journal.com/article/ld/theophylline-interactions

Carbamazepine	
 **Used for/dose**	**Focal & 2° generalised tonic-clonic seizures/1° generalised tonic-clonic seizures** **Trigeminal neuralgia** **Prophylaxis of bipolar disorder unresponsive to lithium** **Adjunct in acute alcohol withdrawal (unlicensed)** **Diabetic neuropathy (unlicensed)** **Focal & generalised tonic-clonic seizures** Doses Varies according to indication and preparation; click here for link to BNF doses; Carbamazepine indications and doses
 **Cautions**	Cardiac disease History of haematological reactions to other drugs May exacerbate absence and myoclonic seizures Skin reactions Susceptibility to angle-closure glaucoma Consider Vit D for patients who are immobilised for long periods or do not get enough sun exposure or dietary calcium Blood, hepatic or skin disorders; withdraw immediately in cases of aggravated liver dysfunction or acute liver disease. Leucopenia that is severe, progressive or associated with clinical symptoms requires withdrawal (if necessary under cover of a suitable alternative)
 **Contraindications**	Acute porphyrias AV conduction abnormalities (unless paced) History of bone-marrow depression
 **Important interactions**	Carbamazepine is an enzyme inducer and therefore has numerous interactions; click here for the BNF list of interactions; BNF carbamazepine interactions This link gives guidance on contraceptive choice in women on carbamazepine and other enzyme inducers; Contraceptive choice with enzyme inducers See also the FSRH guidance I gave you earlier when discussing phenytoin
	**Blood, hepatic and skin disorders;** Seek urgent medical attention if develop fever, rash, mouth ulcers, bruising or bleeding develop Antiepileptic hypersensitivity syndrome*. Cross-sensitivity with oxcarbazepine and phenytoin. Rare but potentially fatal

Red flags/important side effects *usually occurs after 1-8 weeks. Fever, rash, lymphadenopathy, also renal, haematological hepatic, & pulmonary abnormalities, vasculitis & multi organ failure. Withdraw drug immediately, seek urgent advice	Side effects which are dose-related, more common at start of treatment and in the elderly; headache, ataxia, drowsiness, nausea, vomiting, blurred vision, dizziness, allergic skin reactions
 **Counselling**	**Warn patients to look out for signs of blood, hepatic or skin disorders;** Seek urgent medical attention if develop fever, rash, mouth ulcers, bruising or bleeding develop **Make sure they are always given the same brand**
 **Monitoring**	Blood counts, hepatic, and renal function tests Plasma concentration for optimal response 4-12mg/litre (20-50 micromol/litre) measured after 1-2 weeks Before treatment; Test for HLA-B*1502 allele in Han Chinese or Thai origin (risk of Stevens-Johnson syndrome; avoid if possible) Treatment cessation: When used for bipolar disorder, reduce dose gradually over at least 4 weeks
 **Renal impairment**	Use with caution
 **Liver impairment**	Caution and close monitoring
 **Pregnancy**	Teratogenic. If used, monitor and adjust dose according to plasma levels See BNF advice on epilepsy and pregnancy Link; Epilepsy and pregnancy

 **Breastfeeding**	Amount too small to be harmful but monitor infant for possible ADRs
 **References**	https://bnf.nice.org.uk/drug/carbamazepine.html

Gentamicin	
 **Used for/dose**	https://bnf.nice.org.uk/drug/gentamicin.html#indicationsAndDoses It is usually active against most strains of the following organisms: *Escherichia coli*, *Klebsiella spp.*, *Proteus spp.* (indole positive and indole negative), *Pseudomonas aeruginosa*, *Staphylococci, Enterobacter spp.*, *Citrobacter spp.* and *Providencia spp.*
 **Cautions**	Auditory disorder: care must be taken with dosage (the main side-effects of the aminoglycosides are dose-related) conditions characterised by muscular weakness (aminoglycosides may impair neuromuscular transmission) If possible, dehydration should be corrected before starting an aminoglycoside Vestibular disorder: whenever possible, parenteral treatment should not exceed 7 days
 **Contraindications**	Myasthenia gravis **When used by ear**-patent grommet, perforated tympanic membrane
 **Important interactions**	systemic absorption can follow topical application, so there is the possibility of interactions with topical **gentamicin** **Interacts with anything else that can cause ototoxicity or nephrotoxicity** https://bnf.nice.org.uk/interaction/gentamicin-2.html
 **Red flags/important side effects**	Ototoxicity and nephrotoxicity

Counselling

Monitoring

Make sure you can interpret the Hartford Nomogram; this can crop up as a resource pack question in the assessment

Learn this- may come up in exam as a resource question

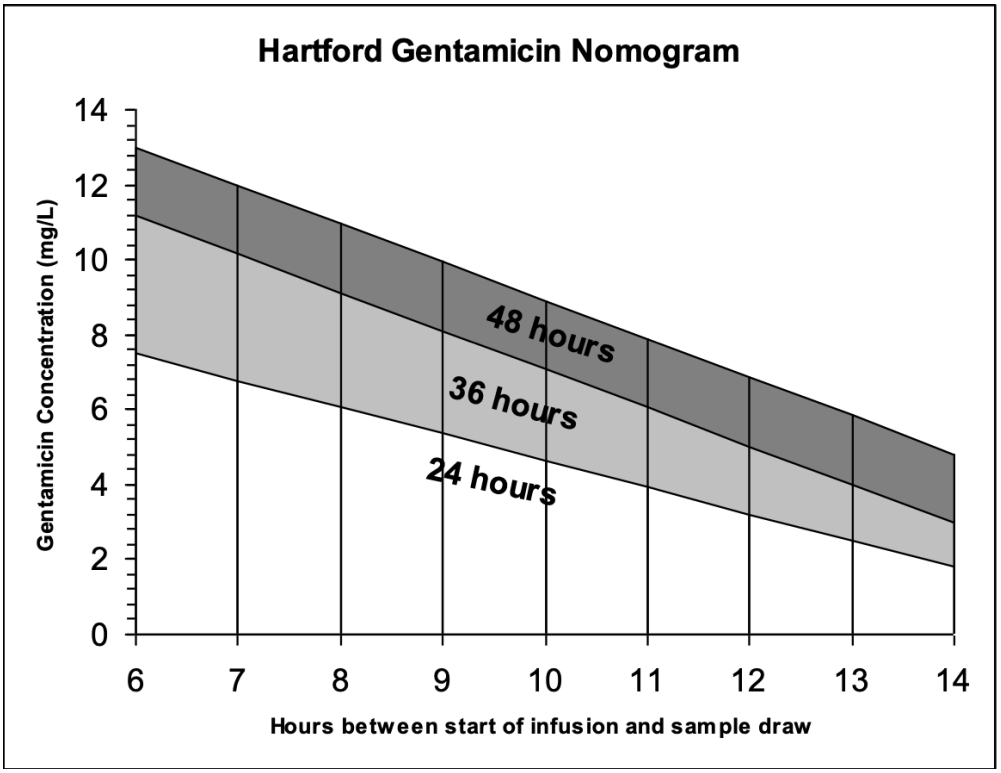
Renal function should be assessed before starting an aminoglycoside and during treatment.

Auditory and vestibular function should also be monitored during treatment

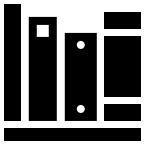
Therapeutic Drug Monitoring (TDM)- see BNF. There are target peak and trough concentrations, and charts are used to determine the dosage and dose interval (Hartford Nomogram) http://www.leedsformulary.nhs.uk/docs/RxGentamicinHartford.pdf

If given during pregnancy, serum-aminoglycoside concentration monitoring is essential

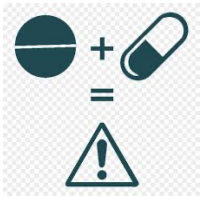
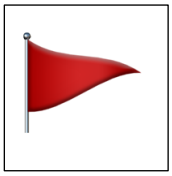
Gentamicin Therapeutic Drug monitoring: The Hartford Nomogram

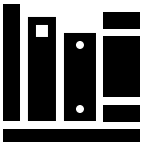


- Take a 10mL blood sample 6 – 14 hours after the 1st infusion
- Record the resulting level on the nomogram.
- If the level falls in the area designated 24hours, 36hours or 48hours, the dosing interval is 24, 36 or 48-hourly respectively.
- If the level is above the 48-hour line then STOP the treatment. If gentamicin is to be continued take daily levels, but do not give any more gentamicin until the level falls below 2mg/L.
- Check U & E's and creatinine daily to monitor renal function.

	• Gentamicin may be reported in micrograms/mL rather than mg/L. These units are equivalent. Example: a sample is taken 10 hours after the 1st infusion, and the gentamicin levels are 8mg/L. This tells us that the dosing interval needs to be 36 hours http://www.leedsformulary.nhs.uk/docs/RxGentamicinHartford.pdf
 **Renal impairment**	accumulation can occur in renal impairment (increased risk of ototoxicity and nephrotoxicity) concentrations **must** be frequently monitored
 **Liver impairment**	
 **Pregnancy**	risk of auditory or vestibular nerve damage in the infant when aminoglycosides are used in the second and third trimesters of pregnancy. The risk is greatest with streptomycin. The risk is probably very small with gentamicin and tobramycin, but their use should be avoided unless essential.
 **Breastfeeding**	the amount of gentamicin ingested from the milk is unlikely to result in significant blood levels in breast-fed infants.
 **References**	https://bnf.nice.org.uk/drug/gentamicin.html#indicationsAndDoses http://www.leedsformulary.nhs.uk/docs/RxGentamicinHartford.pdf

Template

Drug name	
 **Used for/dose**	
 **Cautions**	
 **Contraindications**	
 **Important interactions**	
 **Red flags/important side effects**	

 **Counselling**	
 **Monitoring**	
 **Renal impairment**	
 **Liver impairment**	
 **Pregnancy**	
 **Breastfeeding**	
 **References**	

3.
BNF notes: Chapter 1 (Gastro-intestinal system)

University of Brighton

Pre-registration assessment BNF revision notes by chapter NB these notes were made from BNF edition 80 and the BNF online; you should always check for the most up to date information

Chapter 1- Gastro-intestinal system

Coeliac disease

- Gluten-free products for coeliac disease are **borderline substances** (ACBS)
- Coeliac patients should not self-medicate with vitamins and supplements-supplementation needs should be through healthcare team
- Prednisolone may be used in refractory coeliac disease whilst awaiting specialist advice

Diverticular disease and diverticulitis

- Diverticulosis or diverticular disease managed by gradually increasing fibre in diet. Bulk forming laxatives may be given e.g. ispaghula
- Diverticular disease – use paracetamol for pain, avoid NSAIDs and opioids as may increase risk of diverticular perforation. Antispasmodics may be used for abdominal cramps
- Uncomplicated acute diverticulitis- Paracetamol. Antibiotics may not be needed. Co-amoxiclav first choice. In penicillin allergy use cefalexin (caution with penicillin allergy) with metronidazole or trimethoprim with metronidazole. Complicated acute diverticulitis- (all IV) co-amoxiclav, or cefuroxime with metronidazole, or amoxicillin with gentamicin and metronidazole

Crohn's disease

- Acute Crohn's disease- corticosteroids e.g. prednisolone, methylprednisolone or IV hydrocortisone. Budesonide less effective but less systemic side effects. Aminosalicylates are an alternative but less effective. Azathioprine or mercaptopurine (unlicensed) may be added on. Adalinumab or infliximab may be used in severe active disease
- Crohn's maintenance treatments- azathioprine or mercaptopurine (both unlicensed), or MTX. Corticosteroids or budesonide should not be used
- Loperamide or codeine can be used for diarrhoea in Crohn's if no colitis. They can cause toxic megacolon if used in acute ulcerative colitis so should only be used in ulcerative colitis on specialist advice. Colestyramine can be used for diarrhoea in Crohn's

Ulcerative colitis

- Aminosalicylates or corticosteroids (rectal administration if inflammation is distal, systemic if inflammation is extended). Aminosalicylates used for maintenance therapy, corticosteroids unsuitable for maintenance therapy
- Single doses of aminosalicylates may be more effective at maintaining remission in ulcerative colitis but may cause more side effects. Azathioprine or mercaptopurine (both unlicensed) may be used to maintain remission if 2 or more exacerbations in 12 months. MTX often used but no evidence to support this.

Aminosalicylates

- renal function should be monitored before starting, at 3 months then annually.
- Advise patients to report any unexplained bleeding, bruising, purpura, sore throat, fever or malaise (risk of agranulocytosis, bone marrow disorders, neutropenia)
- sulfasalazine can cause sulphonamide-related side effects but this doesn't occur with mesalazine, balsalazide and olsalazide. Blood disorders and lupus-like syndrome can occur with all these (all contain 5-aminosalicylic acid)
- Maintain on same brand of mesalazine-if switch brand patient should report changes in symptoms
- Granule formulations of mesalazine are placed on tongue and washed down without chewing
- Olsalazine capsules may be opened and sprinkled on food
- Sulfasalazine needs monitoring- FBC (including differential white cell count and platelet count) initially then monthly for 3 months, monthly LFTs for first 3 months

Drug treatment of IBS

- Antispasmodics e.g. alverine, mebeverine, peppermint oil
- Laxatives if constipated but not lactulose
- Linaclotide if no response to laxatives and constipation for 12 months
- Loperamide first choice for diarrhoea
- Low dose TCA 2nd line for abdominal pain or discomfort if no response to antispasmodics, anti-motility drugs or laxatives. SSRIs if TCAs don't work/not suitable

Short bowel syndrome e.g. due to large surgical resection, with or without stoma

- Vitamin and mineral supplementation
- Diarrhoea is common-oral rehydration salts, loperamide, or codeine. High doses of loperamide may be needed.
- Loperamide preferred as less sedative, and doesn't cause dependence or fat malabsorption (steatorrhoea)
- Colestyramine binds unabsorbed bile salts and reduces diarrhoea
- Drugs to reduce gastric acid secretion e.g. omeprazole, cimetidine
- Drug absorption may be incomplete so larger oral doses of drugs may be needed or may need to give IV.
- Avoid GR/modified-release formulations.
- Soluble forms should be used, or uncoated tabs or liquids (but care over the excipients in liquid formulations)
- Depends on how much intestine has been removed

Constipation

Laxatives

- Bulk-forming e.g. bran, ispaghula, methylcellulose, sterculia
  - Onset up to 2 hrs
  - Must maintain adequate fluids to avoid intestinal obstruction
  - Can cause flatulence, bloating, cramping
- Stimulant e.g. bisacodyl, sodium picosulfate, senna, co-danthramer, co-danthrusate
  - Increase motility
    - Avoid in intestinal obstruction
  - Can cause abdominal cramps
  - Co-danthramer and co-danthrusate reserved for use in terminally ill (concerns over carcinogenicity and genotoxicity)
  - Docusate is a faecal softener which also has stimulant effect
  - Glycerin suppositories are lubricant and also rectal stimulant
- Faecal softeners e.g. docusate, glycerin suppositories
  - Reduce surface tension, increase penetration of fluid into the faecal mass
  - Also arachis oil enemas, liquid paraffin (use with caution-risk of ADRs such as anal seepage, granulomatous disease of the GI tract or lipoid pneumonia on aspiration)
- Osmotic e.g. lactulose, macrogols
  - Draw in extra fluid to the colon or retain the fluid they were administered with
  - Lactulose is not absorbed from the GI tract
- Other drugs used in constipation
  - Linaclotide- in IBS, increases intestinal fluid secretion and transit, decreases visceral pain
  - Prucalopride- selective serotonin 5HT-4 agonist, prokinetic-licensed in chronic constipation where other laxatives have failed

Management of short-term constipation

- Dietary measures. If ineffective-
- Bulk-forming laxative plus plenty of fluid. If stool remain hard-
- Add or switch to osmotic laxative. If stools soft but difficult to pass or inadequate emptying-
- Add stimulant laxative

Opioid-induced constipation

- Osmotic laxative or docusate plus a stimulant laxative
- Avoid bulk-forming laxatives
- Naloxegol or methylnaltrexone(as an adjunct to other treatment)when other laxatives ineffective

Faecal impaction

- Hard stools-high dose of oral macrogol
- Soft stools or hard stools after a few days treatment with a macrogol-add oral stimulant laxative
- If response inadequate, for soft stools add bisacodyl suppositories, and for hard stools add glycerin suppositories alone or with bisacodyl. Alternatively a docusate or sodium citrate enema
- If response still inadequate, a phosphate or arachis oil enema

Chronic constipation

- Bulk-forming laxative plus plenty of fluids
- If stools remain hard add or change to osmotic laxative e.g. macrogol(lactulose if not effective or not tolerated)
- If an inadequate response add a stimulant laxative

- If at least 2 laxatives have been tried at max tolerated doses for at least 6 months, prucalopride can be used (women only)

Constipation in Pregnancy

- Dietary and lifestyle changes
- Fibre supplements e.g. bran, wheat
- Bulk-forming laxative
- Osmotic laxatives e.g. lactulose can also be used
- Use bisacodyl or senna if stimulant needed but avoid senna near term or history of unstable pregnancy
- Docusate and glycerin suppositories can also be used

Constipation in Breastfeeding

- Bulk-forming laxative
- Lactulose or macrogol if stools remain hard
- Short term course of bisacodyl or senna can be used

Constipation in Children

- First-line- dietary modification, fluids, exercise plus laxative plus behavioural intervention
- Unprocessed bran NOT recommended
- Macrogol first choice
- If inadequate add or switch to a stimulant laxative
- Stimulant laxatives cannot be sold OTC under the age of 12 (age 12-17 under supervision of a pharmacist, GSL products 18 years and over, new pack size restrictions)
- If stools remain hard add lactulose or docusate

Diarrhoea

- Acute diarrhoea-less than 14 days
- Symptoms usually improve in 2-4 days
- **Red flag symptoms**- unexplained weight loss, rectal bleeding, persistent diarrhoea, systemic illness, received recent hospital treatment or antibiotic treatment, foreign travel (other than Western Europe, Northern America, Australia or New Zealand
- **Mostly doesn't need treatment**
- **Oral rehydration therapy**
- Hospitalisation for urgent IV fluids if severe dehydration
- **Loperamide** for rapid symptom control. Suitable for mild to moderate travellers' diarrhoea but **avoid in bloody or suspected inflammatory diarrhoea** and in **significant abdominal pain**
- Loperamide first choice in faecal incontinence
- Ciprofloxacin sometimes used for prophylaxis against travellers' diarrhoea, but **routine use is not recommended**
- **Loperamide contraindications**- active ulcerative colitis, antibiotic-associated colitis, bacterial enterocolitis, abdominal distension, where inhibition of peristalsis should be avoided
- Serious cardiac ADRS with large doses of loperamide-naloxone can be used as antidote

Dyspepsia

- Test for *H.pylori*
- Drugs which cause dyspepsia- alpha-blockers, antimuscarinics, aspirin, benzodiazepines, beta-blockers, bisphosphonates, calcium-channel blockers, corticosteroids, nitrates, NSAIDs, theophyllines, TCAs
- **Continuous long-term use of antacids and/or alginates not recommended**
- Reduce NSAID doses and use long-term gastro protection, or switch from NSAID to paracetamol or COX- inhibitor
- Consider switching from aspirin to another antiplatelet
- Annual review for patients with dyspepsia
- Antacids-liquids more effective than tablets
    - Bismuth-containing antacids apart from chelates not recommended (neurotoxic, cause encephalopathy)
    - Calcium-containing antacids can cause rebound acid secretion. Prolonged high doses can cause hypercalcaemia and alkalosis
    - Magnesium can be laxative, aluminium can constipate-may be combined in a product
    - Simethicone relieves flatulence and can relieve hiccups in palliative care
    - Alginates help reflux symptoms by forming a raft

Peptic ulcer disease

- Most common causes NSAIDs and *H.pylori*
- Review and stop drugs which can induce peptic ulcers (NSAIDs, aspirin, bisphosphonates, immunosuppressants e.g. corticosteroids, potassium chloride, SSRIs, crack cocaine)

- Patients at high risk of GI complications with an NSAID- Age over 65yrs, high dose NSAIDs, other drugs increasing the risk e.g. anticoagulants, bisphosphonates, SSRIs, serious comorbidity e.g. CVD, hypertension, diabetes, renal or hepatic impairment, heavy smoker, excessive alcohol consumption, previous ADR to NSAID, prolonged use of NSAID. Stress is also a risk
- Test for *H.pylori*
- Eradicate *H.pylori*
- If *H.pylori* present and ulcer associated with NSAID, use PPI or H2-antagonist for 8 weeks then *H.pylori* eradication
- If *H.pylori* present and ulcer no history with NSAID, eradicate *H.pylori*
- If test negative for *H.pylori* and no history of NSAID use, PPI or H2-antahonist for 4-8 weeks
- Review 6-8 weeks after *H.pylori* eradication
- ***H.pylori* eradication;**
    - Triple therapy BD for 7 days -PPI plus 2 antibacterials. PPI= 20mg Esomeprazole, 30mg lansoprazole, 20-40mg omeprazole, 40mg pantoprazole or 20mg rabeprazole
    - 1st line PPI plus amoxicillin and either clarithromycin or metronidazole. **Take into account previous treatment with clarithromycin or metronidazole**
    - if allergy to penicillin PPI plus clarithromycin and metronidazole.
      If previously treated with clarithromycin, PPI plus bismuth subsalicylate plus metronidazole and tetracycline
    - 2nd line for 7 days if symptomatic after 1st line treatment PPI plus amoxicillin and either clarithromycin or metronidazole **(whichever was not used first).**
      PPI plus amoxicillin and tetracycline or levofloxacin **if patient has had previous treatment with both clarithromycin and metronidazole**
    - **if allergy to penicillin** PPI plus metronidazole and levofloxacin
    - **if allergy to penicillin and previous exposure to fluoroquinolone,** PPI plus bismuth plus metronidazole and tetracycline

Proton Pump inhibitors

- Safety information- very low risk of subacute cutaneous lupus erythematosus (SCLE)
- Increased risk of fractures
- Increased risk of GI infections e.g. *C.diff*
- May mask symptoms of gastric cancer
- Patients at risk of osteoporosis
- Esomeprazole and omeprazole decrease efficacy of clopidogrel

GORD

- **Exacerbated by** alpha-blockers, antimuscarinics, aspirin, benzodiazepines, beta-blockers, bisphosphonates, calcium-channel blockers, corticosteroids, nitrates, NSAIDs, theophyllines, TCAs
- PPI for 4-8 weeks. If no response, H2-antagonist
- In pregnancy- dietary and lifestyle changes. If fails, antacid or alginate. If ineffective, omeprazole or ranitidine (unlicensed)

Antispasmodics

- Useful in IBS
- Antimuscarinics e.g. dicycloverine, hyoscine. Antimuscarinic side effects
- Direct relaxants e.g. alverine, mebeverine, peppermint oil. No serious ADRs
- All should be avoided in paralytic ileus

Obesity

- Consider underlying causes e.g. hypothyroidism, **medicines known to cause weight gain**- atypical antipsychotics, beta-blockers, insulin (when used in type 2 DM), lithium, sodium valproate, sulphonylureas, pioglitazone, TCAs
- Orlistat- Used when BMI of 30kg/m^2 or more or 28kg/m2 or more with risk factors e.g. type 2 DM, hypertension or hypercholesterolaemia. Reduces absorption of dietary fat
    - Used in conjunction with mildly hypocaloric diet
    - Patient should restrict fat intake to reduce GI side effects
    - May impair absorption of fat-soluble vitamins (may need supplementation, especially of Vit D)

Anal fissures

- Ensure soft stools-bulk-forming laxative or osmotic laxative
- Short-term use topical anaesthetic e.g. lidocaine, or paracetamol or ibuprofen for prolonged burning pain after defaecation

- Refer for specialist treatment if these are inadequate
- Diltiazem cream may be prescribed

Haemorrhoids

- Keep stools soft
- Paracetamol for pain. Avoid opioids (constipating). Avoid NSAIDs if any rectal bleeding
- No evidence any topical preparation is better than any other
- Topical local anaesthetics can cause contact sensitisation if used more than a few days. Theoretical risk of side effects as can absorb through mucosa
- Topical steroids limited to 7 days. Exclude infection. Risk of systemic effects with continuous use, and thinning of perianal skin
- Pregnancy-bulk-forming laxatives. No topical products are licensed in pregnancy

Exocrine pancreatic insufficiency

- Pancreatin preparations contain a mixture of protease, amylase and lipase
- Administer with meals and snacks
- Total dosed in cystic fibrosis not to exceed 10 000 units a day (risk of fibrosing colonopathy)
- Assess levels of fat-soluble vitamins and micronutrients e.g. zinc, selenium and supplement if necessary
- Acid suppression may improve effects of pancreatin. PPIs may be trialled in patients who are symptomatic despite high doses of pancreatin
- Patients should avoid food that is hard to digest e.g. peas, beans, lentils, and high-fibre foods. Alcohol should be avoided.
- Food intake should be split between 3 main meals per day plus 2 or 3 snacks

Stoma care

- Troublesome drugs- opioids (constipation), NSAIDs (gastric irritation and bleeding), magnesium- or aluminium-containing antacids, (diarrhoea and constipation), iron (loose stools and sore skin)
- patients on digoxin at risk of hypokalaemia (give potassium supplements or potassium-sparing diuretic). Caution over diuretic use with ileostomy or urostomy (potassium-sparing preferred). Avoid laxatives in ileostomy. If colostomy patients need a laxative, use bulk-forming laxatives, or a small dose of a stimulant laxative.
- PPIs can be used to decrease stoma output, also octreotide and lanreotide
- Loperamide or codeine decrease water and sodium output from an ileostomy

Part 1 (Calculations)

1. You need to make a batch of 30 Diamorphine 30 mg in 1ml injections. The displacement volume for diamorphine is 0.06 for 5mg

How much water for injections do you need to make this batch?
Give your answer to one decimal place

You may use this space for rough working. Transfer your answer to your answer sheet

2. You have to add 82 ml water to a powder to make 100 ml of 125 mg/ 5 ml Amoxicillin solution.

What is the displacement volume for the powder needed for a 5ml dose? Give your answer to one decimal place

You may use this space for rough working. Transfer your answer to your answer sheet

3. You are working in a specials manufacturing unit. An order has come if for 20 suppositories, each weighing 4 g and containing 200 mg of active ingredient which has a displacement value of 1.7.

How much base do you need to use to make this batch? Give your answer in grams to 2 decimal places

You may use this space for rough working. Transfer your answer to your answer sheet

4. You have a vial containing 600 mg benzylpenicillin and are required to reconstitute it with WFI such that you end up with a 300mg/ mL injection. The displacement value for the benzylpenicillin powder is 0.4.

How much WFI do you need to add? Give your answer to the nearest whole number/to given number of decimal places

You may use this space for rough working. Transfer your answer to your answer sheet

5. You need to make a batch of 8 codeine suppositories. Each suppository is to contain 30 mg codeine phosphate, which has a displacement value of 1.1 and the mould size is 3g.

How much base do you need to make this batch? Give your answer in grams to 2 decimal places.

You may use this space for rough working. Transfer your answer to your answer sheet

Part 2 paper; Single Best Answer

Directions for questions 1 to 5. Each of the questions in this section is followed by five suggested answers. Select the single best answer in each case.

1. 1. Miss S is 8-years-old and has otitis externa which is suspected to be caused by Pseudomonas aeruginosa.

Which would be the first choice treatment for Miss S?

A Amoxicillin capsules 500mg TDS for 7 days

B Chloramphenicol ear drops 2-3 drops three times a day

C Ciprofloxacin ear drops 0.25 % 0.25 mls BD for 7 days

D Flucloxacillin capsules 500mg QDS for 7 days

E Otomize spray (Dexamethasone/acetic acid/neomycin) 1 spray TDS

2. A middle-aged man asks to speak to the pharmacist. He has been struggling to find a pharmacy with Modrasone cream in stock. You know that there is a supply problem with this product and so ring the surgery to suggest a prescription for an alternative.

Which product do you suggest?

A Betnovate 0.1 % cream

B Cutivate cream

C Dermovate cream

D Eumovate cream

E Mildison cream

3. Mrs H has a replacement mechanical aortic valve for which she takes warfarin, and attends your INR clinic regularly. Her target INR is 3.0-4.0 but today her INR is just 1.8. You notice on her record that she has an allergy to tinzaparin.

What should be given as additional anticoagulant cover until her INR is above 2.0?

A Enoxaparin

B Fondaparinux

C Heparin

D Phenindione

E Warfarin 10mg booster dose

4. You are actioning a Class 3 Drug recall.

What action do you need to take?

A Be cautious in using the product

B Quarantine stock immediately even out of hours, contact patients

C Quarantine stock within 24 hours

D Quarantine stock within 48 hours

E Quarantine stock within 5 days

5. Miss M, aged 18-years, has been prescribed an antiepileptic. You advise the GP that this must always be prescribed by brand.

Which antiepileptic drug has she been prescribed?

A Carbamazepine

B Lamotrigine

C Levetiracetam

D Sodium valproate

E Topiramate

Directions for questions 6-10. For each question in this section select one answer from the list of eight options above it. Each option may be used once, more than once, or not at all

Theme; Antiepileptic drugs

A Carbamazepine
B Ethosuximide
C Gabapentin
D Lamotrigine
E Phenobarbital
F Phenytoin
G Primidone
H Sodium valproate

For the situations described, select the most suitable antiepileptic drug from the list above. Each option may be used once, more than once, or not at all

1. Female patients of reproductive age must be enrolled on a pregnancy prevention programme

2. Patients on this drug may be at increased risk of severe respiratory depression

3. If being prescribed for epilepsy a 5-day emergency supply of this drug may be made

4. This drug is the first line choice in absence seizures in premenopausal women

5. This drug is largely converted to phenobarbital in the body

Part 1 Answer sheet (calculations)

1.

						.			mL

2.

						.			mL

3.

						.			9

4.

						.			mL

5.

						.			g

	A	B	C	D	E
1	[A]	[B]	[C]	[D]	[E]
2	[A]	[B]	[C]	[D]	[E]
3	[A]	[B]	[C]	[D]	[E]
4	[A]	[B]	[C]	[D]	[E]
5	[A]	[B]	[C]	[D]	[E]
6	[A]	[B]	[C]	[D]	[E]
7	[A]	[B]	[C]	[D]	[E]
8	[A]	[B]	[C]	[D]	[E]
9	[A]	[B]	[C]	[D]	[E]
0	[A]	[B]	[C]	[D]	[E]