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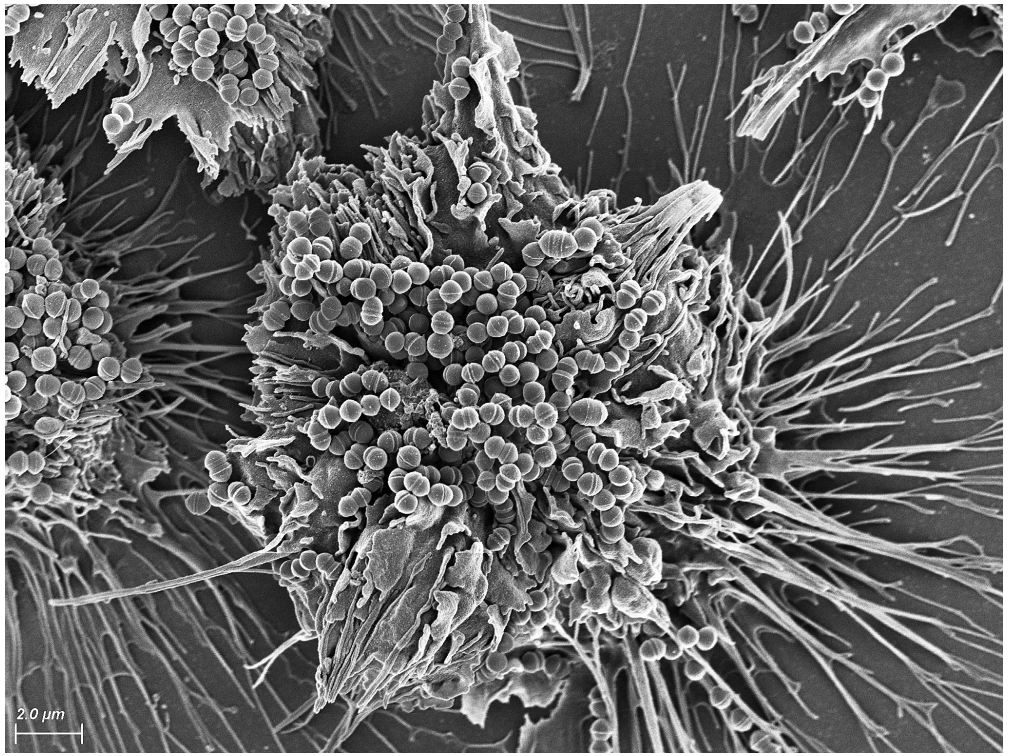

Aciclovir 2014-2-C

Stem: . We are now moving to pharmacology. Treatment is commenced with Acyclovir			
Question 4 Acyclovir (pp 862-864) **Subject:** Pharm LOA: 2	1. What are the indications for acyclovir in the ED?	**HSV – encephalitis**; VZV, patients with HIV, genital herpes	**Bold**
	2. Describe the mechanism of action of acyclovir.	**Inhibition of viral DNA synthesis** • Irreversible binding to viral DNA polymerase. • Incorporation in to viral DNA with termination Specificity for virus-infected cell (virus-specific thymidine kinase).	**Bold**
	3. Describe the pharmacokinetics of acyclovir?	**Short half life 2.5 hrs** (5xdaily dosing oral); low oral bioavailability; mostly excreted unchanged in urine; CSF 20-50% of plasma; wide distribution	**Bold + 1 other**
	4. Name some side effects of acyclovir	Nausea, vomiting, diarrhoea, headache, reversible renal toxicity Neuro – tremor, delirium, seizures	**2 to pass**

Aciclovir 2011-1

Aciclovir	What are the indications for acyclovir in the ED?	**HSV – encephalitis**; VZV, patients with HIV	Bold
	To which class of antiviral drugs does acyclovir belong? Prompt: Describe the mechanism of action of acyclovir.	**DNA polymerase inhibitors** (Specificity for virus-infected cell (virus-specific thymidine synthase). Inhibition of viral DNA synthesis (irreversible binding to viral DNA polymerase)	Bold
	Describe the pharmacokinetics of acyclovir?	**Short half life 2.5 hrs** (5times daily dosing oral); low oral bioavailability; **mostly excreted unchanged in urine**; CSF 50% of plasma; wide distribution	Bold

Aciclovir 2009-1

Question 4 Acyclovir	1. Describe the mechanism of action of acyclovir.	a. Converted to monophosphate by virus-specific thymidine kinase (infected cell specific) b. Converted to di- and tri- phosphates by host cell enzymes c. Inhibits viral DNA synthesis by irreversible binding to viral DNA polymerase, and chain termination	Pass: virus-infected cell specificity and inhibition of viral DNA synthesis (without detail)
	2. What are the indications for acyclovir?	Oral: initial or recurrent genital HSV2 infection Varicella-Zoster – within 24 h of varicella and 72 h or zoster (higher doses required) IV: HSV encephalitis, neonatal HSV, serious HSV or VZV	Pass: Use in HSV or VZV, plus encephalitis.

Anti influenza drugs 2012-2

Question 5 Anti-influenza agents LOA: 2	List some anti-influenza agents What is the mechanism of action of zanamivir (relenza) and oseltamivir (tamiflu)? What are the indications for their use? What is the relevance of these agents to emergency medicine practice? PROMPT: what about during the recent flu pandemic?	Zanamivir, Oseltamivir, Amantadine, Rimantadine Neuraminidase (a glycoprotein) inhibitors: disrupt viral replication and release Active against both influenza A and B; Approved for treatment of uncomplicated influenza; 5 day course of therapy within 36 – 48 hrs of symptom onset shortens severity and duration of illness; may decrease incidence of respiratory complications May be of use to **higher risk groups** eg indigenous, pregnant women, older people and immunocompromised, however primary prevention by **vaccination is preferred**. Used preferably at **early phase of pandemic** to limit spread and numbers infected, and limit severity of disease in those infected.	1 to pass Some concept 1 to pass One of bold

Antibiotics for Staph 2009-1

Question 4: Antibiotics for Staphylococcal infections	1. What classes of antibiotics are used in the treatment of **Staphylococcal** infections?	Beta-lactamase negative staph Penicillin 1st Generation Cephalosporins Beta-lactamase positive staph Beta-lactamase resistant penicillins – Methicillin / Naficillin, Isoxazolyl Penicillins (dicloxacillin, flucloxacillin etc) 1st Generation Cephalosporin Beta-lactamase inhibitor with penicillin combination – clavulinic acid, sulbactam, tazobactam Vancomycin Aminogycosides Macrolides	Pass: 3 classes
	2. What is the mechanism of **resistance** in Methicillin Resistant Staph Aureus?	Beta-lactam antibiotics normally bind to PBP's (Penicillin Binding Proteins) causing inhibition of transpeptidation, thus blocking cell wall synthesis and lead to cell wall death MRSA produce PBP's that have a low affinity for binding beta-lactam antibiotics and hence render then ineffective May be overcome if used in high enough concentrations, but not clinically achievable	Must demonstrate understanding of PBP's binding to pass
	3. What are the adverse effects of **Vancomycin**?	Local phlebitis Chills & fever Flushing due to histamine release (Red Man) Ototoxicity / nephrotoxicity if administered with aminoglycoside	Must get 1 to pass

Antituberculosis drugs 2011-1

Drugs used in Tuberculosis	a) In treatment of a new case of Tuberculosis, what are the important principles of drug use? Prompt: How might the problem of drug resistance influence your therapy?	1. **Multiple drugs used initially** (usually 4) ensures efficacy 2. Prolonged course, usually 6 months 3. Close supervision to ensure compliance and detect adverse effects	Suggested pass criteria: Bold to pass
	b) Describe the pharmacology of Rifampicin	1. **Well absorbed orally** 2. **Highly lipid soluble** - widely distributed in tissues 3. **Metabolism in liver**, excreted in faeces 4. **Induces P450 enzymes** – many drug interactions **5. Discolouration (orange) of body fluids** **6. Can be used prophylaxis**	2/6 bold to pass

Azithromycin 2017-2-B

Stem: Moving onto Pharmacology. He is commenced on antibiotics, one of which is azithromycin.			
Question 3 **Subject:** Pharm Katzung 13th Edition page 793. LOA:	1. What class of antibiotic is azithromycin	1. **Macrolides**	Bold to pass
	2. What is its mechanism of action?	2. **Inhibits protein synthesis** by binding to the ribosomal RNA. It is bactericidal at high concentrations.	Bold to pass
	3. What organisms does azithromycin cover?	3. • Haemophilus influenza • Chlamydia species. • Mycobacterium avium complex • Staph • Strep • Mycoplasma • Legionella	3 to pass
	4. What is an important cardiac side effect?	4. Prolonged QT interval.	Bonus question

Azithromycin 2016-1-C

Stem: Moving onto Pharmacology. Her chest X-ray shows consolidation and she is commenced on Azithromycin			
Question 3 Azithromycin (Macrolides) **Subject:** Pharm LOA: 2	1. What class of antibiotic is Azithromycin	**Macrolide**	**Bold to pass**
	2. Describe the mechanism of action of azithromycin?	**Inhibition of bacterial protein synthesis** by binding 50S ribosomal RNA, blocking aminoacyl translocation and formation of initiation complexes (transpeptidation), may be inhibitory or bactericidal (esp at higher concentrations)	**Bold to pass**
	3. Against which micro-organisms is azithromycin effective?	Gm+ pneumococci,strep,staph,corynebact Mycoplasma legionella chlamydia sp, listeria Some mycobacteria Gm- Neis sp, Bordatella pert, Trep pall. Campylobacter sp, Bartonella	**3 to pass** but must include one atypical
	4. How does Azithromycin differ from other macrolides? *(Prompt eg Compared to erythromycin & clarithromycin)*	Higher tissue penetration (tissue conc >>>>serum conc) **Long elimination T1/2** (2-4 days) vs 2-5 hr **Single daily dosing** More effective against haemophillus m.catarr. neiss Highly effective against chlamydia sp Less active against staph & strep Excreted unchanged in urine Absorption impeded by food Doesn't inhibit hepatic cytochrome P450 so drug interactions are uncommon	**Bold** plus one other

Ceftriaxone 2016-2-C

Stem: A 50-year-old woman is given Ceftriaxone for septic shock. Starting with Pharmacology.			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Ceftriaxone **Subject:** Pharm LOA: 1	What kind of antibiotic is ceftriaxone? [What group?]	**Third generation cephalosporin.** **Beta lactam antibiotic.**	2 to pass
	What is the mechanism of action of ceftriaxone? [What is its site of action?]	**Bacteriocidal antibiotic.** Only kills growing bacterium. **Inhibits** transpeptidation reaction of **bacterial cell wall synthesis**. Halts peptidoglycan synthesis, leading to inhibition of bacterial growth, and ultimately cell death.	2 bold to pass
	Explain the microbiological spectrum of activity of ceftriaxone [Is there anything it is not active against?]	**Not usually degraded by bacterial beta-lactamases,** therefore broader spectrum of activity. **Expanded gram-negative** cover and crosses the blood brain barrier. Effective against many B-lactamase producing **Haemophilus** and **Neisseria** and penicillin-resistant pneumococcus. **Not active against pseudomonas**	3 of 5 bolded
	What is ceftriaxone's plasma half life? [How is this relevant clinically?]	Half life of 7 to 8 hours, meaning it may be administered once daily at 15 to 50mg/kg	Bonus

Ceftriaxone 2015-1-A

Stem: We will now move to Pharmacology. He is given ceftriaxone.			
Question 2	What type of antibiotic is ceftriaxone?	**Third generation cephalosporin. Beta lactam**	1/2 bold
Ceftriaxone (pp 799-800) Subject: Pharm LOA: 1	Describe the pharmacodynamics of ceftriaxone	**Inhibits** transpeptidation reaction of **bacterial cell wall synthesis.** Halts peptidoglycan synthesis, leading to inhibition of growth, and ultimately **cell death (Bacteriocidal)**	Bold
	Explain the microbiological spectrum of activity of ceftriaxone	**Stable to bacterial beta-lactamases**, therefore broader spectrum of activity. **Expanded gram-negative cover** and crosses the blood brain barrier. Effective against B-lactamase producing **Haemophilus and Neisseria**	Bold
	What is the clinical relevance of ceftriaxone's half-life?	**Half life of 7 to 8 hours**, meaning it **may be administered once daily** at 15 to 50mg/kg	Bold

Cephalosporins 2013-2-B

Question 3 PHARMACOLOGY LOA: 1	*"Moving on. He is treated with a cephalosporin."* 1. What is the mechanism of action of cephalosporins? 2. What class of antibiotics do they belong to? 3. How are they classified and give an example of each class ?	1. **Inhibit bacterial cell wall synthesis**, cell division and growth (similar to penicillins) Bactericidal Work best in rapidly dividing cells 2. Beta-lactams 3. Generations – First through Fourth 4. **1st Generation**: very active against GPC, E. coli, K. pneumoniae, Proteus OK but Pseudomonas not. Anaerobic cocci sensitive. Cephalexin, Cephazolin	1. Bold to pass 2. **Beta-lactams** 3. **4 Generations** 4. Concept of increasing activity against gram –ves and example of 2 classes
	Prompt: How does the spectrum of microbiological activity differ between the different generations?	**2nd Generation**: active against those by 1st generation but added GN coverage – Klebsiella, some anaerobe cover. NO Pseudomonas. Cefaclor, Cefuroxime **3rd Generation:** expanded GN coverage and cross BBB. Less active vs Staph. Effective against against B- lactamase producing Haemophilus and Neisseria. Ceftazadime works vs Pseudomonas. Ceftriaxone, Ceftazidine, Cefotaxime. **4th Generation:** more resistant to B- lactamases, extended coverage against enteric GNR, pseudomonas, enterobacteriaceae, S pneumonia, S aureus, Haemophilus and Neisseria. Cross BBB. Cefipime.	

Cephalosporins 2013-1

Question 3 **CEPHALOSPORINS** LOA:1	What is the mechanism of action of cephalosporins?	**Inhibit bacterial cell wall synthesis** , cell division and growth (similar to penicillins) Bacteriocidal Work best in rapidly dividing cells	**Bolded to pass**
	How does the spectrum of microbiological activity differ between the cephalosporin generations?	**1st generation: very active against GPC**, Ecoli, K.pneumoniae, proteus ok but Pseudomonas not. Anaerobic cocci sensitive **2nd generation:** active against those by 1st generation but **added GN coverage** -klebsiella Some anaerobe cover NO Pseudomonas **3rd generation expanded GN coverage and cross BBB**. Less active re staph . Work against B-lactamase Haemophilis and Neissria. Ceftazadime works re Pseudomonas 4th generation more resistant to B- lactamases, extended coverage against enteric GNR-pseudomonas, enterobacteriaceae, S pneumonia, S aureus, Haemophilis and Neisseria. Cross BBB	**Understand the principles of the 1st, 2nd and 3rd generations**

Cephalosporins 2010-2

3. a. What is the mechanism of action of cephalosporins	**Inhibit bacterial cell wall synthesis**, cell division and growth (similar to penicillins) **Bactericidal** Most effective in rapidly dividing cells.	Bolded material
How does the spectrum of microbiological activity for the 4th generation cephalosporins compare to that of earlier generations?	**Gram negative** as for 3rd generation e.g. E Coli, H Influenza, Klebsiella **Some gm positive** (S Pneumonia) but less than 1st generation **More resistant to B Lactamases** than earlier generations	Bolded material
What is the relationship between penicillin allergy and cephalosporin allergy.	5-15% possibility of cross-reaction with penicillin allergy.	Aware of cross-reactivity

Cephalosporins 2010-1

Question 2: Antibiotics in CNS infections P737-40, 751-2, 790-5, 835	1. How are cephalosporins classified? *What are the differences between the classes?* 2. Why are 3rd generation cephalosporins used in CNS infection? 3. Are there any bacteria responsible for CNS infection that cephalosporins do not cover?	1- GPs; 2- + haemophilus & kleb; 3-GP + GN; 4- pseudomonas Expanded GN activity & cross the BBB; penetrate body fluids well; good toxicity profile Listeria Resistant pneumococci may need vancomycin Resistant E Coli; use with aminoglycoside to cover Pseudom	1-4 with increasing GN spectrum activity; less GP activity Spectrum activity & penetration CNS 1 example
Question 3:	1. Describe the mechanism of Paracetamol	In normal dose	

Cephalosporins 2008-2

Question 2: Cephalosporins	1. How are the cephalosporins classified and give examples? *Prompt:* *What are the different antimicrobial spectrums of the generations?*	1st-gen: (cephalexin, cephazolin, cephalothin) **very active against GPC** (pneumococci, strep, and staph). **GN org** (*E coli, K pneumoniae, & Proteus mirabilis*) **often sensitive**, but not against GN aerobes (*P aeruginosa,* indole-positive proteus, enterobacter, *Serratia marcescens,* citrobacter), & acinetobacter. 2nd-gen: (cefaclor, cefamandole, cefuroxime) **active against organisms inhibited by 1st-gen drugs,** but have **extended GN coverage.** Klebsiellae are usually sensitive. Some anaerobic 3rd-gen agents (cefotaxime, ceftazidime, ceftriaxone) have **expanded GN coverage & X BBB.** Less active against staphyl than earlier cephalosporins but are active against citrobacter, *S marcescens,* & providencia. Also **effective against β-lactamase-producing strains of haemophilus & neisseria.** Some anaerobic None above active against MRSA, enterococci or *P aeruginosa.* 4th see next column	**Know there are 4 generations, and understand principles of 3 of these** 4th-gen: (Cefepime) **extended spectrum of activity covering the majority of the enteric GNRs, including *Pseudomonas* and Enterobacter. Also active against *S aureus,* &*S pneumoniae*.** More resistant to hydrolysis by chromosomal β-lactamases (eg, those produced by enterobacter).
	2. What are the adverse effects of the Cephalosporins?	**Hypersens reactions identical to penicillins: anaphylaxis, fever, skin rashes, nephritis, granulocytopenia, & hemolytic anemia**. Some individuals with a history of penicillin allergy may tolerate cephalosporins. **Frequency of cross-allergenicity** uncertain, probably around **5–10%.** Severe pain IMI. Thrombophlebitis IVI. **Renal toxicity: interstitial nephritis & ATN**. Cephalosporins with a methylthiotetrazole group (eg, cefamandole, cefotetan) may **cause: hypoprothrombinemia, bleeding** (preventable with Vit K_1 10 mg twice weekly) and severe disulfiram-**like reactions** with alcohol.	Essential penicillin cross reactivity + 2 others

Cephalosporins 2004-2

Cephalosporins	How do you classify cephalosporins ? (could you expand on that in terms of their spectrum of activity ?)	1 to 4 based on spectrum of activity Increasing gram negative cover from 1 to 4, less gram positve 1 to 3, 4 a bit of both	

Chloramphenicol 2007-1

3.4 Chloramphenicol	What are the adverse effects of chloramphenicol	GIT: nausea, vomiting and diarrhoea **Bone marrow suppression**: reversible RBC suppression, idiosyncratic aplastic anaemia: 1/24000 – 1/40000 Newborn: gray baby syndrome Drug interaction: Phenytoin, chlorpropamide ,warfarin prolongs half life and raises concentration **(must get 2)**	
	Which bacteria does it affect:	Aerobic and anaerobic gram pos and neg; rickettsia but not Chlamydia	
	What is mechanism of action?	Potent inhibitor of microbial protein synthesis-binds to 50S subunit of bacterial ribosome by inhibiting peptidyl transferase. Bacteriostatic	/1

Chlorhexidine 2007-1

3.5 Anti-sepsis: Chlorhexidine	What is an antiseptic?	A **chemical** disinfectant applied to living tissue (skin, mucous membranes and wounds) which decreases the number of organisms by **killing, removing, diluting** and has generally **low toxicity to tissues**	
	Describe the actions and uses of chlorhexidine	low skin sensitising or irritating capacity; oral toxicity low (poorly absorbed from the alimentary tract); -active against bacteria (most effective against G pos cocci), mycobacteria, moderate against fungi & viruses -not inhibited by blood or organic products	
	When is chlorhexidine contraindicated	middle ear surgery (causes sensorineural deafness), neurosurgery as neural toxicity allergy	/1

Ciprofloxacin 2016-1-D

Stem: Moving onto Pharmacology. Cultures grow an organism which is sensitive to ciprofloxacin			
Question 4 Ciprofloxacin- route of administration, dose and mechanism of action **Subject:** Pharm LOA: 2	Describe the pharmacokinetics of ciprofloxacin PROMPT: Which patients will need a dose adjustment? Describe its mechanism of action What is its antimicrobial spectrum?	**PO or IV**. PO bioavailability > 80% 20-40% protein bound **Elimination half-life 3-5 hours** PO 250 - 500mg bd (max 1.5gm) IV 200 – 300 mg bd (max 1.2 gm) **Renal elimination** – dose adjustment if Cr Cr < 50ml/min **Blocks DNA synthesis** by inhibiting bacterial topoisomerase II (DNA gyrase) and IV- prevents normal transcription and replication **Excellent Gram neg activity, moderate Gram pos activity**. S Aureus, Mycoplasma, Chlamydia, Legionella, Pseudomonas, Mycobacterium and Anthrax.	Bold to pass

Doxycycline 2016-2-C

Stem: Moving onto Pharmacology. She has been taking doxycycline for malaria prophylaxis			
Question 4 Doxycycline Pharmacodynamics **Subject:** Pharm: LOA: 2	1. What is the mechanism of action of doxycycline? [in general?]	**Protein synthesis inhibitor -** Binds reversibly to 30s subunit of ribosome (bacteriostatic) In malaria inhibits protein synthesis Active against erythrocytic schizonts of all malaria parasites Used for prophylaxis. Not used as single agent in treatment – slow and not active against liver stages	Bold
	2. What are the side effects of doxycycline? [Specifically for doxycycline?]	GI – nausea and vomiting Photosensitivity Candidal vaginitis Hepatotoxicity Discolouration teeth & bones (binds to calcium in newly forming bone/teeth - in pregnancy & children <8 years old) Intracranial hypertension	3 of list to pass including 1 of photosensitivity and teeth
	3. Other than malaria what are the other indications for doxycycline?	Respiratory tract infections STI's (eg Chalmydia, syphilis) Skin infections (eg acne) Rickettsia (eg. Q fever) Vibrio species (eg. Cholera) Antihelminthic Anthrax Gram negatives (rarely)	2 to pass

Erythromycin 2010-2

3. a. What is the mechanism of action of erythromycin?	**Inhibits** RNA-dependent **protein synthesis** by binding to the 50S ribosomal subunit. **Bacteriostatic** (at high conc with selected organisms can be bactericidal)	Protein synthesis inhibitor Bacteriostatic
b. What is the mechanism for the drug interactions associated with erythromycin & give some examples?	**Inhibits hepatic CYP3A4.** Usually inhibits metabolism of other drugs metabolism causing increased activity. Examples: benzodiazepines, carbamazepine, cisapride (cardiotoxicity), digoxin, warfarin, theophylline, cyclosporine, tacrolimus	Inhibit hepatic metabolism One example
c. What are the adverse effects of erythromycin?	Common: **GIT**: abdo cramp, diarrhoea, N&V, candida (oral,vag) Rare: hypersensitivity, hearing loss, pancreatitis, hepatotoxicity Rapid iv may cause ventric arrhythmias.	GIT plus another

Flucloxacillin 2016-2-D

Stem: A 70yo man presents with left leg cellulitis. He has been treated with Flucloxacillin. Starting with Pharmacology.			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Flucloxacillin **Subject:** Pharm LOA: 1	a. What is the mechanism of action of flucloxacillin?	Beta lactam Inhibits bacterial growth by binding to active site of **penicillin binding proteins (PBP), interfering with transpeptidation of bacterial cell wall synthesis** → cell death (bactericidal)	Bold
	b. What microorganisms are susceptible to flucloxacillin?	**Staphylococcal** (including beta lactamase producing) **Streptococci** Not active against MRSA, enterococci, anaerobes, gram negatives	Bold
	c. What are the important side effects of flucloxacillin?	**Allergy/anaphylaxis**, GIT upset (n/v), **Hepatic (cholestasis),** Renal (interstitial nephritis) , Haematological (neutropenia/thrombocytopenia), Serum sickness	Bold + 1

Flucloxacillin 2015-2-B

Stem: Moving onto Pharmacology. Prior to surgery for debridement, Flucloxacillin is administered			
Question 4 Flucloxacillin **Subject:** Pharm LOA: 1	(a) What micro-organisms are susceptible to flucloxacillin Prompt: is fluclox active against all Staph?	**Staphylococci** (including B lactamase producing**), streptococci** (not active against enterococci, anaerobes, Gram negatives, MRSA)	Bold
	(b) What is the mechanism of action of flucloxacillin Prompt : how does penicillin work	Inhibits bacterial growth by binding to active site of PBPs, **interfering with transpeptidation of bacterial cell wall synthesis** → cell death **(bactericidal)**	Bold
	(c) Why is oral flucloxacillin given before meals	It is acid labile (inactivated by gastric acid), and binds to food proteins (decreasing absorption)	1 out of 2
	(d) What are the important side effects of flucloxacillin?	**Liver (cholestasis),** GI upset (Nausea, vomiting, etc), renal interstitial nephritis, neutropenia/thrombocytopenia, **allergy/anaphylaxis**, serum sickness.	Both bold to pass
	Extra question: What is the frequency of cross allergenicity between flucloxacillin and cephalosporins	Around 5-10%	Any % in range to pass

Fluoroquinolones 2008-1

Fluoroquinolones	What is the mechanism of action of fluoroquinolones ? What are the mechanisms of resistance to fluoroquinolones ? What are the clinical uses ciprofloxacin ?	DNA gyrase inhibitor/blocks protein production Resistance is due to one or more point mutations in the quinolone binding region of the target enzyme or to a change in the permeability of the organism. UTI Bacterial diarrhoea caused by Shigella, Salmonella, toxigenic *E coli,* Campylobacter Soft tissue, bone, joint, intra-abdominal and respiratory tract infections Treatment against multidrug-resistant organisms (pseudomonas and enterobacter) Prophylaxis and treatment against anthrax Gonococcal infection Chlamydial urethritis or cervicitis TB and atypical mycobacterial infections Eradication of meningococcal carrier state Prophylaxis in neutropenic patients Pass – DNA gyrase inhibition, 3 organ system uses	

Fluoroquinolones 2004-2

Quinolones	What is the mechanism of action of quinolones ? Describe the antibacterial spectrum of the quinolones What are the possible adverse effects of the quinolones in children	Inhibits bacterial synthesis of DNA Mixed, broad spectrum, newer increasingly broad Cartilage type effect	

Fluoroquinolones, Ciprofloxaxin 2014-2-B

Stem: We will now move on to Pharmacology. Treatment with Ciprofloxacin is commenced.			
Question 3 Fluoroquinolones (Chp 46) **Subject:** Pharm LOA: 2	1. What class of drug is Ciprofloxacin?	**Fluoroquinolone**	Bold to pass
	2. What is its mechanism of action?	**Blocks DNA synthesis** by inhibiting bacterial topoisomerase II and IV	Bold to pass
	3. What is its antimicrobial spectrum?	**Excellent Gram neg activity and moderate Gram positive activity.** Methicillin susceptible strains of S *Aureus* are susceptible, but methicillin resistant Staphylococci are resistant. Also active against agents of atypical pneumonia – Mycoplasma and Chlamydiae Intracellular pathogens such as Legionella and Mycobacterium. Ciprofloxacin the drug of choice for anthrax.	Bold + 1 to pass MIC for Gram neg are 1-2 mcg/mL.
	4. What are the potential adverse effects of Fluoroquinolones?	• **Prolonged QT** (with some), • Nausea, vomiting, diarrhoea (inc. C difficile) • Rash • Abnormal LFTs • Photosensitivity • Hyperglycemia in diabetics, • Growing cartilage damage (not routinely recommended for < 18 yo or pregnancies) • Tendonitis • Allergy	Bold + 2 dot points

Fluoroquinolones, Ciprofloxaxin 2003-1

FIRST QUESTION	What is the mechanism of action of ciprofloxacin ?	
	Synthetic fluorinated analogs of nalidixic acid - earlier forms not systemic antibacterial levels - fluorinated derivates improved serum activity **Block bacterial DNA synthesis by inhibiting** bacterial topoisomerase II **(DNA gyrase)** (prevent relaxation of positively supercoiled DNA needed for normal transcription and replication) and topoisomerase IV (interferes with separation of replicated chromosomal DNA into daughter cells during cell division)	
THIRD QUESTION	What are the uses of this drug	
	UTIs – norflox, cipro, oflox Bact.diarrhea –shigella, salmonella, Ecoli, Campyl ST,bone, joint, intraabdom, resp.infection GC (cipro, oxflox), chlamydia (cipro)	2 answers
THIRD QUESTION	What are the adverse effects of ciprofloxacin	
	Well tolerated Nausea, vomiting, diarrhea> h/ache, dizzy, insomnia, rash, LFT abnormalities May damage growing cartilage, cause arthropathy not <18 yrs Tendinitis in adults – risk of tendon rupture Avoid during pregnancy and lactation	

Fluoroquinolones, Norfloxacin 2013-1

Question 3 **NORFLOXACIN** LOA: 1	Describe the mechanism of action of norfloxacin.	Fluoroquinolone. Bacteriocidal. a. **Inhibition topoisomerase II /DNA Gyrase** → interferes with relaxation of supercoiled DNA, required for normal transcription and replication b. Inhibition topoisomerase IV → interferes with separation of replicated chromosomal DNA	**Bold to pass**
	Describe the anti-bacterial activity of norfloxacin	**Gram negative bacteria** Organisms of atypical pneumonia: mycoplasma, chlamydia Limited gram positive activity	**Bold to pass**
	How does the anti-bacterial activity of norfloxacin compare to that of ciprofloxacin?	**Ciprofloxacin has greater activity** (4-8 times lower MICs) against gram negatives and much greater activity against gram positives	**Bold to pass**

Gentamicin 2017-1-A

Stem: Moving onto Pharmacology. He is treated with Gentamicin.			
Question 4 Gentamicin **Subject:** Pharm LOA: 1	a) What class of antibiotic is Gentamicin? b) What is its mechanism of action? c) Please describe the pharmacokinetics of Gentamicin? d) What are the advantages of single daily dosing regimen for Gentamicin e) What are its adverse effects?	a) **Aminoglycoside** b) It acts by **binding to the 30S ribosomal proteins** - inhibiting protein synthesis in the bacteria. Bactericidal **–** gram neg. Concentration dependent killing. Post antibiotic effect. c) Route: parenteral (IV or IM), inhalation, topical Distrib: Small Vd because < 10% protein bound Metab: not metabolised. Elim: **renal dependent**. Glomerular filtration. T1/2 = 2-3 hours, typically given once daily d) **↓toxicity time** and **concentration dependent killing –** once daily results in less time above toxic threshold concentration**.** OP therapy, Cost effective e) **Nephrotoxic** **Ototoxic** Prolongs NM blockade	**Bold** **Bold** **Bold plus 2** others **Bold** **Bold**

Gentamicin 2015-2-A

Stem: Moving onto Pharmacology. She is treated with Gentamicin			
Question 4 Gentamicin **Subject:** Pharm LOA: 1	1. Describe the mechanism of action of gentamicin	**Irreversible inhibitor of protein synthesis.** **Binds** 30S **ribosome** & inhibits protein synthesis by: 1) interfering with initiation complex of peptide formation 2) Inducing misreading of mRNA thus producing non functional protein; 3) causing break up of polysomes into non-functional monosomes *Additional information*: Enters cell by passive diffusion via porin channels across outer membrane, then enters cytoplasm by o2 dependant active transport process (transport coupled to a proton pump the transmembrane electrochem gradient supplies the energy) Low ecf pH & anaerobic conditions inhibit transport as reduces gradient; transport enhanced by cell wall active drugs eg penicillin, vancomycin.	Bold to pass
	2. What are the benefits of once daily dosing of gentamicin? *Prompt how does this improve clinical effectiveness?*	**Concentration dependant killing** (at increased conc kill increased no of bacteria at a more rapid rate); Post antibiotic effect (effect lasts longer than detectable serum levels); **Reduced toxicity** (as toxicity is time & conc dependant –time above critical level will be longer with multi dose than single dose schedule); less nursing time; OPD therapy possible; convenience	Bold to pass
	3. What micro-organisms is it effective against? Prompt: What group of organisms	**Gram –ve bacteria** – E. coli, Pseudomonas, Proteus, Klebsiella, Serratia Gram +ve- Staph, Strep- with beta lactams, vancomycin No anaerobic activity	Bold + 3 organisms

Gentamicin 2010-1

Question 2: Antibiotics in urinary sepsis P 732, 755-61, 765-6	1. Describe the mechanism of action of gentamicin ?	Irreversible inhibitor of protein synthesis-possible mechanism: 1. Passive diffusion via porin channels across outer memb, then active transport into cytoplasm by an O2 dependant process. . 2. Binds 30S ribosome & inhibits protein synthesis by 1) Inducing misreading of mRNA thus producing toxic or nonfunctional protein; 2) interfere with initiation complex of peptide formation; 3) cause break up of polysomes into non-functional monosomes.	Irreversible protein synth inhibitor. Binds ribosomes
	2. What are the benefits of once daily dosing ? *Prompt how does this improve clinical effectiveness*	1. *Concentration- dependant killing* (at increased conc kill increased no of bacteria at a more rapid rate; 2. *Postantiobiotic effect*- activity lasts longer than detectable serum levels; 3. *Reduced toxicity* – time above critical level will be longer with multi dose than single dose schedule); 4. Less nursing time; OPD therapy possible; 5. Drug level not required unless >3 day therapy.	Conc dependant kill + 2 others.
	3. How do penicillins enhance the efficacy of gentamicin? *Optional question*	Low ECF pH & anaerobic conditions inhibits transport Transport enhanced by cell wall active drugs eg. penicillin	

Gentamicin 2008-2

Question 2: Gentamicin	1. Describe the mechanism of action of gentamicin? 2. What are the benefits of once daily dosing? *Prompt how does this improve clinical effectiveness?*	Irreversible inhibitor of protein synthesis. Passive diffusion via porin channels across outer memb, then active transport into cytoplasm by O2 dependant process; transmemebrane electrochem gradient supplies the E, transport coupled ti proton pump. Low ecf pH & anaerobic conditions inhibits transport as reduces gradient; transport enhanced by cell wall active drugs eg penicillin. Binds 30S ribosome & inhibits protein synthesis by simultaneously: 1). Inducing misreading of mRNA thus producing non toxic protein; 2) interfere with initiation complex of peptide formation; 3) cause break up of polysomes into non-functional monosomes Concentration dependant killing (at increased conc kill increased no of bacteria at a more rapid rate; post antibiotic effect (effect lasts longer than detectable serum levels); reduced toxicity (as toxicity is time & conc dependant –time above critical level will be longer with multi dose than single dose schedule); less nursing time; OPD therapy possible; convenience	Irreversible protein synth inhibitor A ribosome inhibitor Conc dependent kill + 1 other

Gentamicin 2007-1

1.3 Gentamicin	Why is once-daily dosing advocated for gentamicin?	**(1) Concentration-dependent killing + post-antibiotic effect vs toxicity proportional to time over threshold concentration** **Prompt (if needed):** "*What are the toxic effects of gentamicin (ototoxic and nephrotoxic)?*" (2) Practical advantages.	
	Why is gentamicin usually used in combination with another antibiotic?	Usually combined with a cell-wall active drug that enhances gentamicin transport into the cell, e.g. β-lactam or vancomycin	
	What is the mechanisms of action of gentamicin and how does resistance develop	Aminoglycoside that binds to specific ribosomal proteins and **inhibits protein synthesis** Resistance by i) transferase that inactivates drug, carried by plasmids ii) impaired cell entry (cell wall) iii) altering ribosomal receptor protein **(must get at least 1)**	/2

Gentamicin 2003-2

Gentamicin pp787-790	1.Regarding gentamicin, outline its pharmacokinetic properties.	Poor oral absorption Well absorbed IM and usually given IV Highly polar and thus does not enter cells well; Water soluble CSF –20% plasma levels Bile –30% plasma level Pleural/synovial 50-90% Most tissues low except renal cortex Not metabolised May be inactivated by bacteria Cleared by the kidney Half life –2-3 hours 40-60% removed by HD Dosage adjustment needed for renal impairment	To pass: must know very high renal excretion, no metabolism and poor oral absorption.	
	2.What are the reasons for once daily dosing of gentamicin?	**Concentration dependent killing** **Post antibiotic killing effect** Toxicity is both time and concentration dependent. **Numerous clinical studies suggest once daily dosing is just as effective and no more [possibly less] toxic.** More convenient. Outpatient administration possible No need to obtain serum levels unless > 4-5 days	To pass: must get 2/3 bold items	

Macrolides 2012-2

Question 3 Macrolides LOA: 2	Name some macrolide antibiotics?	Erythromycin, roxithromycin, azithromycin, clarithromycin.	**Pass = 2**
	Describe the mechanism of action of macrolides?	**Inhibits bacterial protein synthesis** by binding to 50S ribosomal RNA, which blocks the aminoacyl translocation reaction and formation of initiation complexes (transpeptidation). May be inhibitory or bactericidal, particularly at higher concentrations.	**Pass = bold**
	What organisms are macrolides effective against?	Gram + orgs: pneumococci, streptococci, staphylococci, corynebacteria Mycoplasma, Legionella, Chlamydia sp, listeria, some mycobacteria Gram – orgs: Neisseria sp, Bordatella pertussis, Treponema pallidum, Campylobacter sp, bartonella (Haemophillus less susceptible)	**Pass = 3**

Macrolides 2011-2

Question 4 Macrolides	a) Give some examples of macrolide antibiotics b) What is their mechanism of action? c) What are the adverse effects of erythromycin? *(prompt if has not mentioned in question1: " Erythromycin is a macrolide antibiotic. Do you know any adverse effects of erythromycin?")*	a) **erythromycin (prototype drug), roxithromycin, azithromycin, clarithromycin,** b) **inhibit protein synthesis by binding to 50S ribosomal RNA** which blocks aminoacyl translocation reaction and formation of initiation complexes. Erythromycin may be inhibitory or bacteriocidal at higher concentrations c) 1. **gastrointestinal** (anorexia, nausea, vomiting, diarrhoea) 2. liver toxicity (acute cholestatic hepatitis, particularly with estolate) 3. allergic reaction (fever, eosinophilia, rash) 4. drug interactions (inhibits cyt P450)	Must give at least 2 examples Pass = bold Bold + one other

Macrolides 2009-1

Question 4: Macrolides	1. Name some macrolide antibiotics?	Erythromycin, azithromycin ,clarithromycin, roxithromycin	Pass: 2 examples
	2. What is their mechanism of action?	Inhibits protein synthesis via binding to 50S ribosomal RNA and blocks aminoacyl translocation and the formation of initiation complexes	Pass: Protein synthesis and ribosomes
	3. What organisms are usually sensitive to macrolides?	Gram positive: eg pneumococci, staphylococcus Mycoplasma, legionella, chyamydia and some mycobacteria Gram negative : neisseria, bordatella pertussis, bartonella, campylobacter Treponema pallidum	At least 3

Mechanisms of Resistance 2005-2

TOPIC: MECHANISMS OF ANTIBIOTIC RESISTANCE _____ NUMBER: 4

OPENING QUESTION	**By what mechanisms can bacteria be resistant to β lactam antibiotics?**	**COMMENTS**
POINTS REQUIRED	1. Inactivation by β lactamase (commonest mechanism)	This + one other to pass
	2. Modification of target proteins (PBPs- Penicillin-binding proteins) (MRSA, pneumococci, enterococci)	
	3. Impaired penetration through cell wall to PBPs (gram negatives only- outer cell wall membrane)- which enhances efficacy or β lactamase enzymes within the cell.	
	4. Efflux pump (gram negatives only)	
PROMPTS		
SECOND QUESTION (if needed)	**What circumstances encourage the development of bacterial resistance to antimicrobial agents?**	
POINTS REQUIRED	Resistance is an example of natural selection, and arises through spontaneous mutations or DNA exchange between different species of bacteria (either directly by plasmids or via bacteriophages). Therefore resistance is promoted by:	Understands at least one mechanism well
	1. Dirty hospital environments with multiple species of bacteria co-existing and "exchanging" between environment, patients and staff	
	2. A course of antibiotics that only partially treats a target population (inadequate potency, dose or duration)	
	(Thus, paradoxically, both under-use and overuse of antibiotics plays a role in the development of resistance!)	
	Overall, however, total consumption of antibiotics within a human population is the critical factor in development of resistant strains	

Metronidazole 2017-2-B

Stem: Moving on to Pharmacology. The patient has aspirated. He is treated with antibiotics, one of which is metronidazole.			
Question 5 Metronidazole **Subject**: Pharm LOA: 1	(a)Describe the pharmacokinetics of Metronidazole. (b)What are the adverse effects of metronidazole?	Absorption - Well absorbed orally; Oral/IV/suppository (99% oral bio-availability); Metabolised in liver (can accumulate in hepatic insufficiency) Excreted via kidney; Low protein binding (10-20%); Half-life 7.5 hours - GIT: Nausea, diarrhoea, dry mouth, metallic taste - Neuro: Headache, paraesthesia, dizziness - thrombophlebitis - Disulfiram-like effect, hence avoid alcohol	3 pharmacokinetic parameters (Absorption / Metabolism / Excretion /protein binding/half-life) 2 systems side effects

Metronidazole 2008-2

Question 2: Metronidazole	1. Describe the pharmacokinetics of metronidazole	(Class: Nitroimidazole antiprotozoal drug.) Pharmacokinetics: Well absorbed orally; Oral/IV/suppository (99% oral bio-availability); Metabolised in liver (can accumulate in hepatic insufficiency) and excreted in kidney; Low protein binding (10-20%); Dosage: 500mg tds or single dose of 2g for vaginitis; Half life 7.5 hours	Need 3 out of 6 PK
	2. What are the adverse effects of metronidazole?	Nausea, diarrhoea, dry mouth, hairy black tongue Headache, paraesthesia, dizziness, insomnia Dysuria, dark urine, Disulfiram-like effect, hence avoid alcohol Potentiate the effect of coumarin anticoagulants, Lithium Teratogenic effect on mice, but not proven in human	Need 3 out of 6 categories

Penicillin 2012-1

Question 2 LOA: 2 **PENICILLINS**	Describe the mechanism of action of penicillins	**Inhibition of cell wall synthesis.** Interfere with transpeptidation. Covalently binding to PBP. Important in the cross linkage. Bacteriocidal,. Only kills growing cells.	
	How does resistance to penicillins occur?	a. Inactivation by beta lactamases b. Modification of target PBPs (Pneumo/entrococci) c. Impaired penetration of drug to PBP; impact on porin channels. Gram negatives d. Efflux pump (gram neg)	**At least 2 including beta-lactamases** **At least 3 bacteria**
	In general, what is the anti-microbial spectrum of penicillin G? *Prompt: Could you be specific*	Streptococci, meningococci, enterococci, some pneumococci, treponema pallidum, clostridia, non-betalactamase producing staphylococci	

Penicillin 2011-2

Question 3 Penicillin	a) What is the mechanism of action of penicillins? b) What are the important mechanisms of resistance to pencillins?	a)B-lactam antibiotic. **Inhibits bacterial cell wall synthesis by** interfering with trans-peptidation reaction of bacterial cell wall synthesis; bacteriocidal Structural analogue of D-Ala-D-Ala substrate present in cell wall. Covalently binds to the active site **of Penicillin-binding protein (PBP)** b) 1. inactivation by **B-lactamase** 2. modification of target PBPs (eg MRSA) 3. Reduced penetration (Gram neg organisms) 4. Efflux pump (Gram neg organisms)	Bold to pass bold + one other

Penicillin 2008-1

Beta Lactams	How does Penicillin exert its action ?	Inteferes in bacterial cell wall synthesis by binding to penicillin-binding-protein and preventing removal of terminal d-alanyl-d-alanine from peptides preventing crosslinking and formation of peptidoglycan.	Inhibits bacterial cell wall synthesis to pass.
	What are the mechanisms of resistance to B Lactam antibiotics ?	(1) Inactivation by B-lactamase (2) Modification of target PBPs (3) Impaired penetration of durg to target PBPs (4) Presence of efflux pumps	Inactivation of B-lactamase and one other to pass

Penicillin 2006-2

4. Penicillin	**Describe the mechanism of action of Penicillin?** **What are the important mechanisms of resistance to pencillins?** **Describe the pharmacokinetics of penicillin?**	**PBP binding, block peptidoglycan / cell wall synthesis** **B-lactamase, altered PBPs, reduce penetration, efflux pump (3 of 4)** **Oral absorption food impaired, wide distribution, renal excretion and tubal secretion**	

Penicillin 2005-1

Penicillin – allergy and side effects	What are the clinical manifestations of penicillin allergy?	**Anaphylaxis** **Fever** **Skin (Maculopapular rash, Urticarial skin rash , Exfoliative dermatitis)** **Serum sickness** **Steven Johnson Syndrome** **(2 of 4)**	Serum sickness nephritis, pseudomembranous colitis
	What other side effects of penicillin treatment do you know of?	**Renal failure, seizures at high doses, GI disturbance, Candidal infections, Hepatitis (fluclox/oxacillin),** **(3 of 5)**	

Penicillin 2003-2

Penicillins	1.Regarding penicillins, what is their mechanism of action?	Interfere with bacterial wall synthesis High intracellular osmotic pressure bursts weakened cell wall Inhibits transpeptidase reaction –thus inhibits cross linkage	To pass: 2/3	
	2. How do bacteria become resistant to penicillins?	Beta lactamase Modification of PBPs Impaired penetration Efflux pump	2/4 including beta lactamase	
	3. How are penicillins eliminated? Supplementary question: How does probenicid alter the elimination of some penicillins?	Renal excretion and secretion Biliary secretion Inhibits secretion of weak acids from the proximal tubule.	Must get renal	

Sulphonamides 2005-1

Sulphonamides	Describe the mechanism of antimicrobial activity of the sulphonamides.	**Reversibly block folic acid synthesis thus inhibiting growth.**	Structural analogs of PABA that competitively inhibit dihydropteroate synthetase. Usually bacteriostatic
	Why is trimethoprim commonly administered in combination with sulfamethoxazole?	**Antibacterial synergism. Block sequential steps in folic acid dependent purine synthesis**	The combination is frequently bacteriocidal

Tetracyclines 2003-2

Tetracyclines	1. How do tetracyclines exert their antimicrobial activity?	**Bacteriostatic.** Enter cells by diffusion and active transport. **Bind** irreversibly **to** 30S sub-unit of the **ribosome.** Block binding of tRNA to mRNA – ribosome complex. Stop addition of amino-acids to peptide.	**To pass must know that they bind to ribosome and stop protein synthesis.**	
	2. Describe the pharmacokinetics of the tetracyclines.	Variable oral absorption depending on which drug. **Generally greater than 60% absorbed.** Absorption occurs mainly in upper small intestine. **Food, calcium, dairy products and alkaline pH impair absorption.** **40-80% protein bound.** **Distributed widely to tissues except CSF.** Cross placenta. **Chelate to Ca and are bound to growing teeth and bones.** **Excreted in bile and in urine.** Concentrated in bile (up to 10x serum conc.) **Undergo enterohepatic circulation.** Depending on drug 10-50% urine or biliary excretion. Doxycycline is the exception. No renal elimination.	**Need to know 4 out of 7 bold items to pass.**	
	Prompt: Are their any group of patients where tetracyclines are contraindicated and why?	Pregnancy, children < 8 yrs, breast feeding,		

Tetracyclines -doxycycline 2003-1

QUEST 4. Tetracyclines

FIRST QUESTION	What the mechanism of action of doxycycline?	
	Broad spectrum antibiotic **inhibiting protein synthesis** Bacteriostatic for G+, G- (anerobes, rickettsiae, chlamydia, mycoplams, L forms) Enter by passive diffusion, energy dependent active transport Inside cell, **bind reversibly to 30S subunit** of bacterial ribosome, preventing addition of amino acids to growing peptide	
SECOND QUESTION	How does resistance to doxycycline develop?	
	a. Decreased intracellular accumulation – impaired influx, **increased efflux** by active transport protein pump – **encoded on plasmid** – commonly encode resistance genes for other Drugs: AG, sulfonamides, CAM etc b. Ribosome protection – proteins interfere with tetracycline binding to ribosome c. Enzymatic inactivation of tetracyclines	
THIRD QUESTION	What are the clinical uses of doxycyline?	
	Atypical RTI STDs H pylori infections Acne	Essential + one other

Trimethoprim 2013-1

Question 3 **TRIMETHOPRIM** LOA: 2	Describe the mechanism of action of trimethoprim.	Selectively **inhibits bacterial enzyme (**dihydrofolic acid reductase) which is required in the conversion of dihydrofolic acid to tetrafolic acid. **Hence inhibits** purine and **DNA synthesis.** Less efficient in inhibiting mammalian dihydrofolic acid reductase	**Inhibits bacterial enzyme Resulting in Inhibition DNA synthesis**
	What is the rationale for combining trimethoprim with sulphonamides?	**Enhanced effect** - sulphonamides **inhibit sequential steps (** acts step before triprim). Inhibits dihydropteroate synthase involved in conversion PABA to dihydrofolic acid As sequential steps are blocked in folate synthesis usually bacteriocidial c.f bacteriostatic of 1 alone.	**Bold**

Trimethoprim 2012-1

Question 2 LOA: 1 **TRIMETHOPRIM**	Describe the mechanism of action of trimethoprim Can you explain why trimethoprim and sulphonamides when used together are synergistic? How does resistance to trimethoprim occur?	**Inhibition of DNA synthesis.** Selective inhibition of bacterial dihydofolic acid reductase which is required from the step dihydrofolic acid to tetrahydrofolic acid. Much less efficient at inhibiting mammalian enzyme. **Inhibition of** sequential **steps in same pathway.** Sulphonamides inhibit dihydropteroate synthetase (PABA to DHFA), the step before that at which trimethoprim acts Reduced cell permeability Increased production of enzyme DHF reductase Alteration in the enzyme with reduced binding of drug	Any 1 of 3

Trimethoprim 2006-2

4. Trimethoprim	**What is the mechanism of action of trimethoprim?** **Why are sulphonamides synergistic with trimethoprim?** **What are mechanisms of bacterial resistance to trimethoprim?** (2/3 FOR PASS)	**Inhibits bacterial dihydrofolic acid reductase** **Converts dihydrofolic acid to tetrahydrofolic acid (→ purine synthesis & DNA)** **Sulphonamides are a structural analog of p-aminobenzoic acid (PABA)** **Inhibit synthesis of dihydrofolic acid therefore sequential blocking of sequence** **Reduced cell permeability, increased production of dihydrofolic reductase or alteration in dihydrofolic acid reductase with reducing binding**	

Vancomycin 2017-1-D

Stem: Moving onto Pharmacology. He is being treated with Vancomycin.			
Question 3 Vancomycin **Subject:** Pharm LOA: 2	a) What is the mechanism of action of vancomycin?	**Inhibits cell wall synthesis** by binding to peptidoglycan pentopeptide. This inhibits transglycosylase preventing crosslinking and weakening cell wall/membrane **Bactericidal**	Bold to pass
	b) What are the target organisms for vancomycin?	**Gram +ve** (**Staph** incl MRSA, **Enterococci**), G +ve anaerobes (**C. difficile**)	Any 2 to pass
	c) What clinical condition requires dose adjustment?	Renal impairment, Morbid obesity	Either