ANTI-MICROBIAL STEWARDSHIP

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HEALTHCARE TRAINING

WORKBOOK

LEARNING OUTCOMES

SESSION OVERVIEW

It's is estimated that over 50% of antibiotic prescribing is inappropriate. This is especially worrying as it is the most frequently prescribed class of drug. This session will introduce you to the basic principles when prescribing antibiotics.

OBJECTIVES

This audio course will:

- Explore some of the current prescribing practices and legislature around prescribing.
- Provides an overview of guidelines around treating infections presenting in primary care.
- Demonstrates the principles and application of appropriate antimicrobial use.
- Understand the importance of using local guidelines and an evidence based approach for antimicrobial stewardship in your practice setting.

RECOMMENDED READINGS

Cervoni, E and K. Leech (2017)ENT in Primary Care: A Concise Guide Paperback – Springer; 1st ed. 2017 edition (21 April 2017)

- ISBN-10: 3319519867
- ISBN-13: 978-3319519869

Robb, P. and A. Watson (2007)ENT in Primary Care Rila Publications Ltd (31 Jan. 2007)

- ISBN-10: 1899839070
- ISBN-13: 978-1899839070

Penicillin's https://www.osmosis.org/learn/Cell_wall_synthesis_inhibitors:_Penicillins
Cephalosporins https://www.osmosis.org/learn/Cell_wall_synthesis_inhibitors:_Cephalosporins
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Videos by Armando Hasudungan

Antibiotics Mode of Action https://www.youtube.com/watch?v=IVBCrzjOl40
Antibiotic Resistance https://www.youtube.com/watch?v=057phDG4mKU

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DIFFERENT TYPES OF BACTERIA

In this section we will focus on bacteria and bacterial infection although it must be remembered that infection can also be caused by viruses, parasites and fungi too.
There are four main groups of bacteria (according to sensitivity)
1 Gram positive
2 Gram negative
3 Anaerobes
4 Atypical

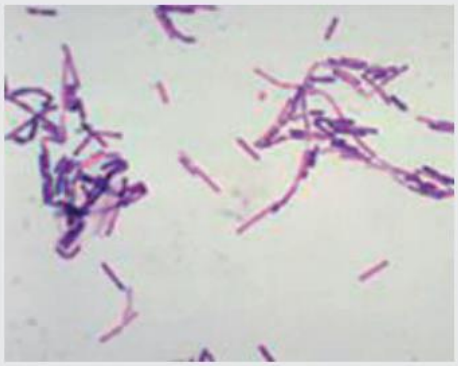
Gram staining:
Gram staining, although pioneered many years ago, remains as first step in identifying bacteria. Gram stains are carried out on most samples that are sent to the laboratory and can quickly and easily provide essential information to direct empirical treatment of potentially serious infections.
This technique is particularly useful in blood cultures.

Gram negative (-ve) (pink/red)

Thin peptidoglycan cell wall does not retain primary stain but does retain red safranin stain

Gram positive (+ve) (blue/ purple)

Thick peptidoglycan cell wall retains primary crystal violet stain



Gram stain (colour observed when the bacteria are treated with Gram stain involving initial purple crystal violet followed by red safranin).

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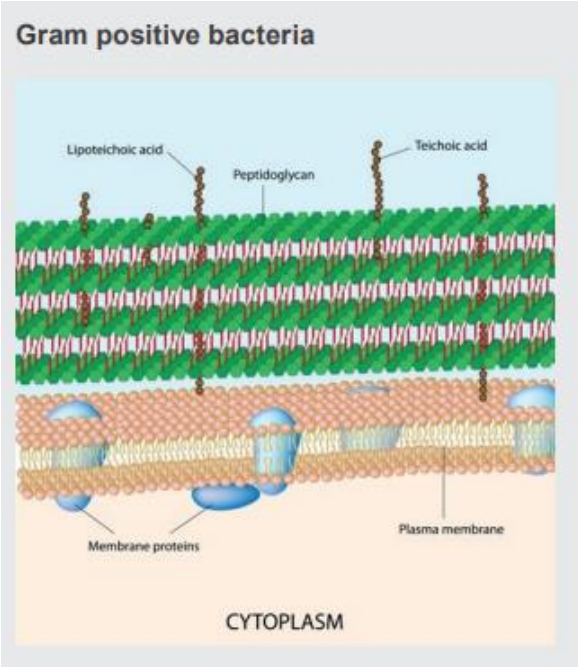
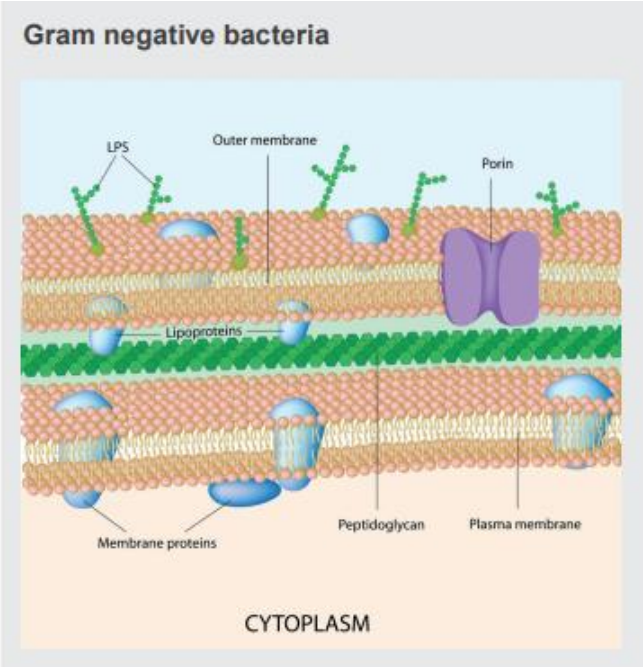
DIFFERENT TYPES OF BACTERIA





The thicker peptidoglycan cell wall of the Gram-positive bacterium retains the primary blue/purple stain and looks blue/purple under a microscope.

The thinner peptidoglycan cell wall of the Gram-negative bacterium does not retain the primary Gram stain so the bacteria will look pink under a microscope

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DIFFERENT TYPES OF BACTERIA

Common bacteria that cause Gram positive infection:

Staphylococcus aureus – methicillin sensitive Staphylococcus aureus (MSSA) & methicillin resistant Staphylococcus aureus (MRSA)

- Where is it found? Skin
- Infections: cellulitis, wound infections, blood stream infections

Streptococcus pneumoniae

- Where is it found? Respiratory tract
- Infections: otitis media, pneumonia, meningitis

Common bacteria that cause Gram negative infection:

Escherichia coli

- Where is it found? Colon
- Infections: GI infections, UTI

Haemophilus influenzae

- Where is it found? Respiratory tract
- Infections: otitis media, sinusitis, pneumonia

Moraxella catarrhalis

- Where is it found? Respiratory tract
- Infections: COPD exacerbation

Common Anaerobes

Anaerobic bacteria are bacteria that grow in the absence of oxygen.

Clostridium perfringens(Gram +ve)

Where is it found? GI tract

Infections: tissue necrosis and gas gangrene

Clostridium difficile (Gram +ve)

Where is it found? GI tract

Infections: C. difficile associated disease causing diarrhoea and pseudomembranous colitis

DIFFERENT TYPES OF BACTERIA

Bacterioides fragilis (Gram -ve)
• Where is it found? GI tract
• Infections: tonsillitis, peritonitis

Common Atypicals
Atypical bacteria do not have any peptidoglycan in their cell walls so do not show any colour when treated with Gram stain.

Mycoplasma pneumoniae
- Where is it found? Respiratory tract
- Infections: pneumonia

WHERE DO WE FIND MICROBES AND MICROBIAL INFECTION?

When a microbe encounters a potential host, in order for it to survive it must be able to adhere to either the host's skin/mucous membrane or other bacteria already attached. Having formed an attachment it must then be able to grow and colonise its host. A major factor that affects the adherence, growth and colonisation of bacteria is the normal bacterial flora.

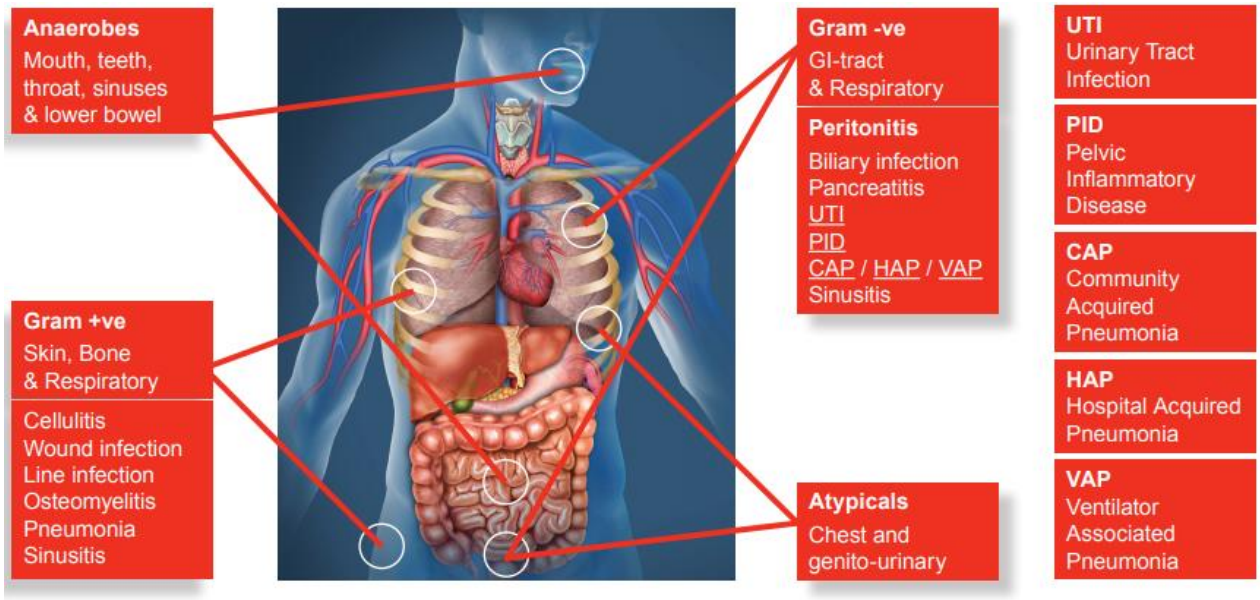
The normal flora are a collection of bacterial species that have adapted to a co-existence with the conditions found at various sites within and on the human body. The normal flora is acquired rapidly during and shortly after birth and it fluctuates continually throughout life. Specific organisms tend to be found in specific areas of the body.

This knowledge allows infections to be treated empirically (without prior microbiological identification) if the site of infection is known.

If the site of infection is unknown then a broad spectrum agent or a combination or two or more narrow spectrum agents may be required.

WHERE DO WE FIND MICROBES AND MICROBIAL INFECTION?

The diagram provides some guidance on where different types of bacteria tend to thrive and cause infection.



ACTIVITY

Find an individual in your care environment who has an infection and has had microbiology specimens taken.

Where was the site of infection?

_____

What samples were taken?

_____

Did the results (if available) show that bacteria has been isolated in the specimen?

_____

Which bacterial infection was found (if results available)

_____

Achieved: ☐ Yes ☐ No

ANTIMICROBIAL RESISTANCE (AMR)

DEFINITION:
Antimicrobial resistance is the ability of a microorganism to stop an antimicrobial from working against it. As a result, treatments become ineffective, infections persist and may spread to others.

Resistance is not a new problem
Sir Alexander Fleming (1881–1955), the discoverer of penicillin wrote:
“The microbes are educated to resist penicillin and a host of penicillin fast organisms is bred out which can be passed on to other individuals and perhaps from there to someone else and to others until they reach someone with a pneumonia which penicillin cannot save.
“I hope this evil can be averted.”

HOW DOES ANTIMICROBIAL RESISTANCE (AMR) DEVELOP?

The development of AMR is a natural phenomenon but certain human actions accelerate the emergence and spread of AMR.
Development of resistance may take the form of a spontaneous or induced genetic mutation, or the acquisition of resistance genes from other bacterial species.
Exposure to an antibiotic naturally selects for the survival of the organisms with the genes for resistance. In this way, a gene for antibiotic resistance may readily spread through an ecosystem of bacteria. Bacteria can become resistant to antibiotics by the methods shown in the diagram opposite and some bacteria can use more than one method. Once a bacterium has become resistant it can pass on its DNA to other types of bacteria to spread resistance.

What can we do about antimicrobial resistance (AMR)?
1. USE ANTIBIOTICS MORE WISELY
2. STOP unnecessary use and use appropriate choice, dose, route and duration when antibiotics are required
3. MINIMISE use of broad spectrum antibiotics like co-amoxiclav, piperacillin/tazobactam, meropenem

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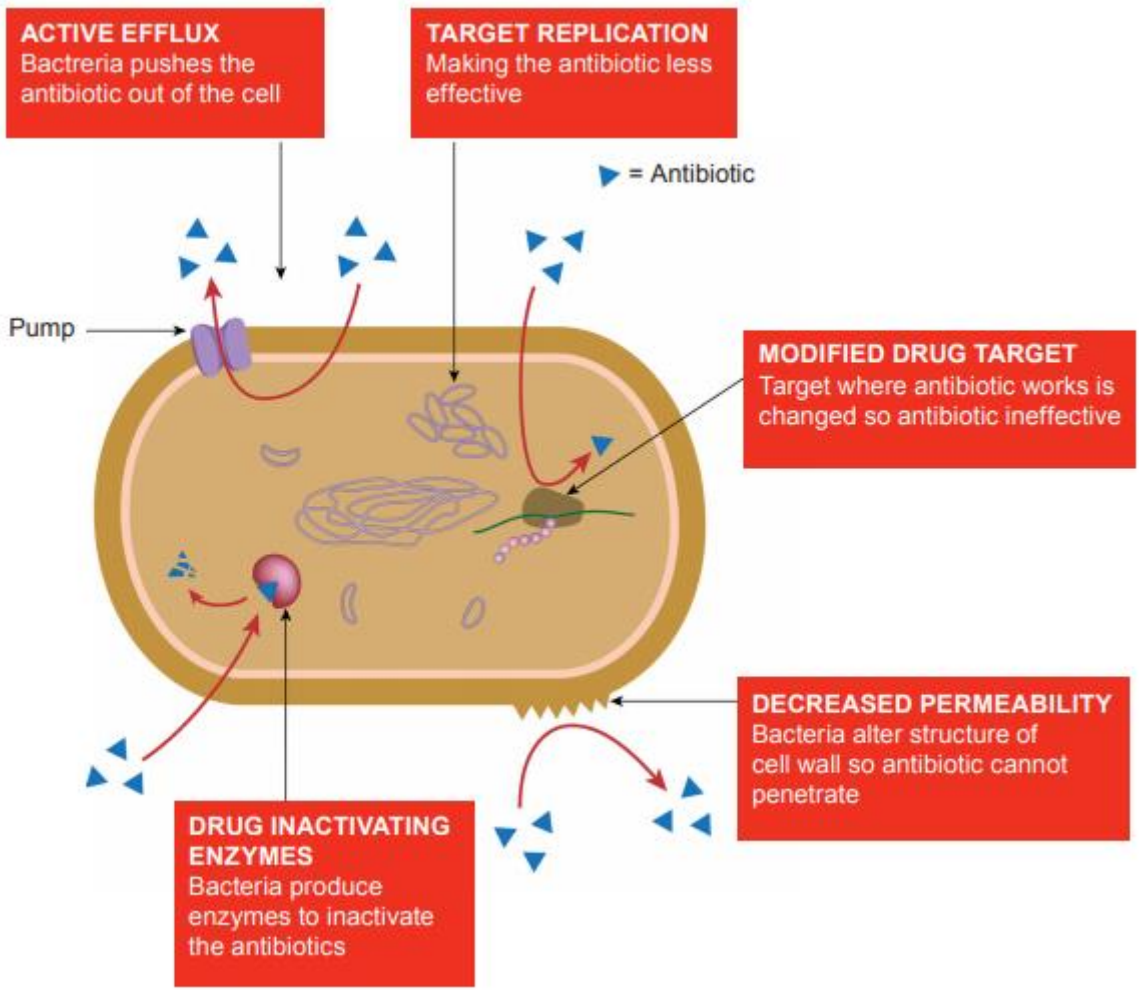
MECHANISMS OF RESISTANCE



ANTIBIOTICS AND HOW THEY WORK

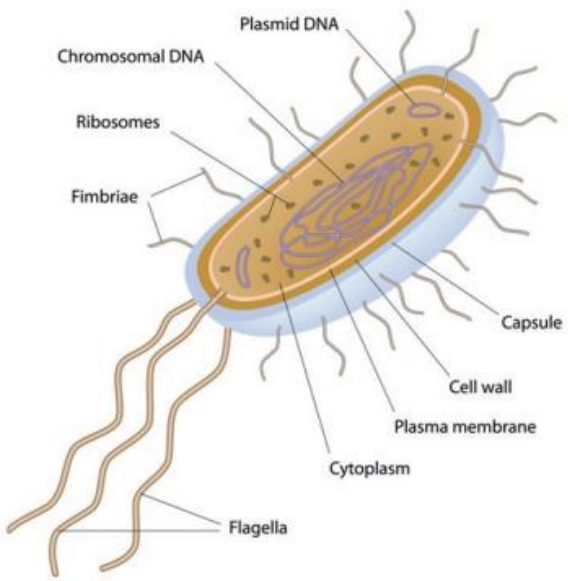
Antibiotic use
Antibiotics exert their action on bacteria in different ways. Some inhibit the development of the bacterial cell wall and so kill the bacteria that way. Others bind with and damage various mechanisms within the bacterial cell thus preventing cell replecation.

Antibiotics may kill Gram positive bacteria or Gram negative bacteria. Some antibiotics can kill both Gram positive and Gram negative bacteria, these are called broad spectrum because they kill a wide range of organisms.

When choosing an antibiotic prescribers will consider the site of infection and the type of bacteria likely to cause an infection at this site.

Where possible, a narrow spectrum antibiotic will be used i.e. one that only kills Gram positive or only kills Gram negative bacteria. However in some infections a broad spectrum antibiotic may be required.

STRUCTURE OF A BACTERIAL CELL



Inhibition of...
Cell wall synthesis
Penicillins
Cephalosporins
Carbapenems
Daptomycin
Glycopeptides
DNA synthesis
Fluoroquinolones
RNA synthesis
Rifampin
Protein synthesis
Macrolides
Chloramphenicol
Tetracycline
Aminoglycosides
Oxazolidonones
Folic acid synthesis
Sulfonamides
Trimethoprim

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ANTIBIOTICS AND HOW THEY WORK

Antibiotics for Gram positive infections (Staphs and Streps)
Commonly used policy antibiotics
- Benzylpenicillin (IV penicillin)*, No S. aureus cover
- Phenoxymethylpenicillin (oral penicillin V)*
- Flucloxacillin
- Erythromycin, Clarithromycin (macrolides)

Restricted use antibiotics
- Clindamycin
- Fusidic acid
- Rifampicin
- Teicoplanin, (glycopeptide)
- Daptomycin
- Linezolid

Antibiotics for Gram negative infections
(Pseudomonas, E-coli)
- Gentamicin, Tobramycin, Amikacin (aminoglycosides)
- Ceftazidime (anti-pseudomonal cephalosporin)
- Aztreonam
- Colistin
- Fosfomycin
- Ciprofloxacin (quinolone – restricted due to C. diff risk)

Broad spectrum antibiotics
Gram +ve and Gram -ve cover
- Clarithromycin, Azithromycin (macrolides)
- Trimethoprim, Nitrofurantoin (used specifically for UTI)
- Amoxicillin, Co-amoxiclav (amoxicillin/ clavulanate)
- Minocycline, Doxycycline, Oxytetracycline (tetracyclines)
- Moxifloxacin, Levofloxacin (quinolones – restricted due to C. diff risk)
- Cefalexin, Cefuroxime, Ceftriaxone, Cefotaxime (cephalosporins – restricted due to C. diff risk)
- Tazocin (piperacillin/tazobactam)
- Ertapenem, Imipenem, Meropenem (carbapenems)

ANTIBIOTICS AND HOW THEY WORK

Common side effects:
GENERAL
(with most antibiotocs): Nausea, vomiting, diarrhoea, rashes, Candida infections

Penicillins in general:
hypersensitivity/skin reactions

Flucloxacillin & co-amoxiclav:
cholestatic jaundice

Clindamycin, cephalosporins (e.g. cefuroxime) & quinolones (e.g. ciprofloxacin):
C. difficile infection

Macrolides (e.g. erythromycin):
GI disturbances, hepatitis, Q-T interval (cardiac problems)

Quinolones (e.g. ciprofloxacin):
Q-T interval (cardiac problems), convulsions, tendonitis

Aminoglycosides (e.g. gentamicin)/ glycopeptides (e.g. vancomycin):
damage to kidneys and hearing

Vancomycin:
'red man' syndrome

ACTIVITY

Select 3 antibiotics that you commonly see prescribed in your clinical area and find out the following:

- What is it usually used to treat?
- What is usual dose and frequency?
- What is usual course length?
- Are there any precautions or contraindications to using it?
- What are common side effects?
- What are common interactions?

Name of antibiotic: _____	Name of antibiotic: _____	Name of antibiotic: _____
Used to treat: _____	Used to treat: _____	Used to treat: _____
Dose & frequency: _____	Dose & frequency: _____	Dose & frequency: _____
Length of course: _____	Length of course: _____	Length of course: _____
Precautions/contraindications: _____	Precautions/contraindications: _____	Precautions/contraindications: _____
Common side effects: _____	Common side effects: _____	Common side effects: _____
Common drug or food interactions: _____	Common drug or food interactions: _____	Common drug or food interactions: _____
		Achieved: YES NO

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MICROBIOLOGY INVESTIGATIONS

Importance of microbiology samples

Any tissue or bodily fluid can undergo microbiological investigation. Microbiology samples are integral in the diagnosis and management of infection as they identify causative organisms and effective antimicrobial therapy.

There are costs associated with microbiology sampling and should therefore only be obtained where there is a clinical indication that will assist in the diagnosis, treatment and on going management of a patient.

Transmission based precautions should be taken at the time samples are obtained and not when results are known to prevent the spread of infection i.e. consideration of isolation of patients with diarrhoea.

Many methods are used within microbiology to identify organisms and within this section we will provide a brief overview of the techniques that are used for the most frequently requested samples.

Sample collection

Microbiology samples are taken to assist in the diagnosis of infection and to provide information on the appropriate antimicrobial treatment. Microbiology samples should NOT be taken as a matter of routine on admission to a ward or department and should be taken within the context of a patient's illness and presenting symptoms.

Remember:

1. Where possible, samples should be taken before antimicrobial therapy starts
2. If the patient is already on antibiotics then blood cultures should be taken immediately before the next dose (with the exception of paediatric patients)
3. Use appropriate sample containers. Using inappropriate containers may result in the delay of diagnosis and subsequent treatment
4. Adhere to Standard Infection Control Procedures (SICPs) when collecting samples taking care not to contaminate samples
5. Only take samples when it is appropriate to do so.

MICROBIOLOGY INVESTIGATIONS

Within your clinical area think about which of the following investigations are routinely carried out then read below to find out if it is appropriate to do these routinely.
Tick each one you perform routinely in your area.

A. MRSA screen _____
B. Urinalysis _____
C. Urine Sample _____
D. Sputum sample _____
E. Wound swab _____
F. Stool sample _____
G. Blood culture _____

Key points to consider on appropriate sample collection:

A. MRSA Screen

There is no requirement to screen every patient that is admitted to hospital. By following Health Protection Scotland's MRSA Clinical Risk Assessment, only individuals who are at a higher risk of MRSA acquisition/infection are required to be screened.

B. Urinalysis

Urine should not be tested indiscriminately, but tested within the context of a patient's illness or to assist in the management of a condition.
Urinalysis should not be used in the diagnosis of UTI in the over 65s or for those with indwelling urinary catheters. Individuals over the age of 65 and those with urinary catheters are likely to have asymptomatic bacteriuria which will be highlighted through the presence of leucocytes and nitrites (by-products of bacteria) in a urinalysis. The diagnosis of UTI in both patient groups should be made based on signs and symptoms as detailed in the SAPG management guides.

C. Urine Sample

Urine samples should not be routinely obtained unless there is a clinical indication for the sample.

D. Sputum Sample

Sputum samples should only be obtained where there is clinical indication. Sputum samples should not be taken as a matter of routine practice.

E. Wound swab
Wound swabs should only be taken where there is evidence of local or systemic infection. Many wounds are colonised with bacteria but are NOT infected. Refer to local wound management policy.

F. Stool sample
Unless clinically indicated stool samples should not be taken as a matter of routine.

G. Blood cultures
Blood cultures should only be taken where there is clinical indication.
Microbiology samples should not be taken as a matter of routine or without thinking about why the samples are being obtained.

REVIEW OF ANTIMICROBIAL PRESCRIPTIONS

Key components of the review of antimicrobial prescriptions:

- Please ensure good antimicrobial stewardship with each antimicrobial prescription.
- Always check the medicines record chart and think:
    - Is antimicrobial needed?
    - Right drug? Right route?
    - Right dose? Right time?

Antimicrobial stewardship encompasses review of the following:

- Is an antibiotic required to treat the patient?
- If so, does the choice of antibiotic follow local antibiotic prescribing guidelines?
- Have the correct microbiology samples been take?
- Is the antibiotic being given by the correct route, for the correct duration and at the correct dose? (Right drug by right route at the right dose for the right time)
- Is the antibiotic being reviewed on a daily basis to assess whether it can be stepped down to oral (if IV) and/or stopped?

ACTIVITY

Locate a copy of your local antimicrobial prescribing guidelines
Find a medicines record chart where a patient is receiving an IV antimicrobial*
*If nobody is on an IV antimicrobial then choose an oral antimicrobial

Is the choice of antimicrobial and route of administration appropriate?

_____

Did you need further information to complete your prescription review?

_____

What was it?

_____

Where did you find it?

_____

Achieved: Yes No

THE SEPSIS SIX

The Sepsis Six is a set of interventions which can be delivered by any junior healthcare professional working as part of a team. All you need to deliver the Sepsis Six is a patient with suspected sepsis, a qualified prescriber, basic healthcare equipment and the will to make it happen!
Just by doing these six simple things in the first hour after suspected sepsis has been diagnosed, you can double your patient's chance of survival!

Apply Sepsis six criteria within 1 hour

- Administer high flow oxygen
- Take blood cultures
- Give broad spectrum antibiotics
- Give intravenous fluid challenges
- Measure serum lactate and haemoglobin
- Measure accurate hourly urine output (insert urinary catheter if necessary)

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List of Common Adverse Antimicrobial Reactions

Drug Class	Class Member	Common Adverse Reaction
Penicillins +/- Beta-Lactamase inhibitors	Ampicillin, Ampicillin-Sulbactam, Amoxicillin, Amoxicillin-Clavulanate, Cloxacillin, Dicloxacillin, Nafcillin, Oxacillin, Penicillin, Piperacillin-Tazobactam	Nausea, vomiting, diarrhea, C difficile infection, allergic reactions (including rash, hemolytic anemia), elevated serum creatinine, bone marrow suppression with long-term use, phlebitis with IV therapy
Cephalosporins +/- Beta-Lactamase Inhibitors	Cefaclor, Cefazolin, Cefdinir, Cefditoren, Cefepime, Cefixime, Cefotetan, Cefoxitin, Cefpodoxime, Cefprozil, Ceftaroline, Ceftazidime, Ceftazidime-Avibactam, Ceftibuten, Ceftolozane-Tazobactam, Ceftriaxone, Cefuroxime, Cephadroxil, Cephalexin	Nausea, vomiting diarrhea, C difficile infection, allergic reactions (including rash, serum sickness), altered mental status
Carbapenems	Doripenem, Ertapenem, Imipenem-Cilastatin, Meropenem	Nausea, vomiting, diarrhea, C difficile infection, seizure
Fluoroquinolones	Ciprofloxacin, Delafloxacin Levofloxacin, Moxifloxacin	Disorientation, delirium, agitation, seizure, hypo- or hyper-glycemia, peripheral neuropathy, tendon rupture, QT prolongation, nausea, vomiting, C difficile infection, increased in liver function tests, aortic dissection
Macrolides	Azithromycin, Clarithromycin, Erythromycin	Nausea, vomiting, elevation in liver function tests, reversible tinnitus or deafness, taste alteration, phlebitis with IV therapy
Tetracyclines	Doxycycline, Minocycline, Tetracycline	Nausea, vomiting, sunburn, esophageal ulcer, phlebitis with IV therapy, teeth discoloration
Sulfonamides	Sulfamethoxazole-Trimethoprim	Allergic reactions (rash, hives, drug fever, Steven Johnson Syndrome), headache, sunburn, hyperkalemia, worsen renal functions, bone marrow suppression, hemolytic anemia, hypoglycemia (especially with sulfonylureas)
Glycopeptides	Telavancin, Vancomycin IV	Redman syndrome (flushing, itching, hypotension), worsened renal functions
Others	Clindamycin, Metronidazole, Nitrofurantoin	All: Nausea, vomiting; Clindamycin: diarrhea, C difficile infection, taste alteration; Metronidazole: disulfiram reaction after alcohol (flushing, dyspnea), taste alteration, peripheral neuropathy, confusion; Nitrofurantoin: interstitial pneumonitis especially with chronic use, hemolytic anemia

The above list does not include all antimicrobials or all adverse drug reactions. Consult drug references and published literature for additional information if an adverse drug reaction not listed above is suspected.

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Interpretation of Probability Categories

Category	Score Range	Interpretation
Definite	≥ 9	Reaction 1) followed a reasonable temporal sequence after a drug or in which a toxic drug level had been established in body fluids or tissues; 2) followed a recognized response to the suspected drug; and 3) was confirmed by withdrawal but not by exposure to the drug
Probably	5 – 8	Reaction 1) followed a reasonable temporal sequence after a drug; 2) followed a recognized response to the suspected drug; 3) was confirmed by withdrawal but not by exposure to the drug; 4) could not be reasonably explained by the known characteristics of the patient's clinical state
Possible	1 – 4	Reaction 1) followed a temporal sequence after a drug; 2) possibly followed a recognized pattern to the suspected drug; 3) could be explained by characteristics of the patient's disease
Doubtful	0	Reaction was likely related to factors other than a drug

Reference
Naranjo CA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981:30:239-45.

CASE STUDY 1

40year old male presents with a cough and feeling sick for the past 3 weeks. He has had a bit of shortness of breath with green sputum. He wants an antibiotic because his neighbour was also coughing for a week and it turned out he has pneumonia. On examination T: 37.7, P:88, RR20. Mild bilateral wheeze. No crackles. Speaking full sentences.

How would you treat?

_____

_____

_____

CASE STUDY 2

Lucy is a 12 year old girl who attends the surgery complaining of a sore throat and cough. She has had some hoarseness in her voice for a few days but no fever. Has a history of seasonal allergies for which she takes cetirizine. She has sore throat but no runny nose, sinuses not painful and no headache. T: 37.2 – 38. Chest exam nad. Throat red but otherwise nad. RAS test negative.

How would you manage this patient?

_____

_____

_____

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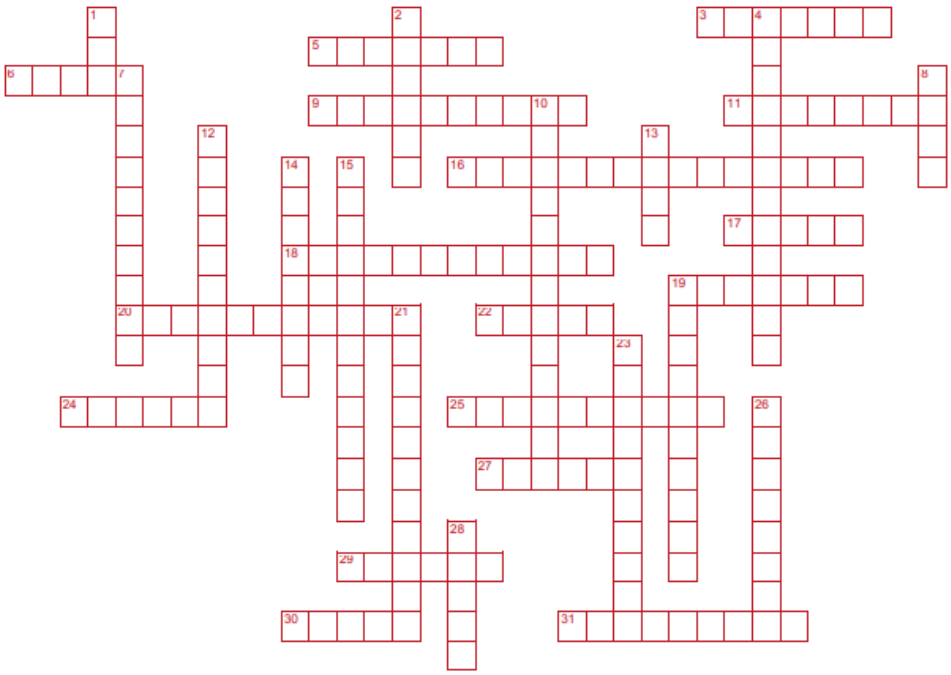
ANTIBIOTIC GUARDIAN CHALLENGE CROSSWORD



ACROSS

3 Veterinarians may prescribe antibiotics to these (7)
5 Antibiotics will most commonly be given to adults in these forms (7)
6 This type infectious agent will cause the common cold, coughs and the flu (5)
9 Medicine used to help treat fungal infections (10)
11 As an Antibiotic _11_, my actions help _19_ antibiotics for
19 the children of tomorrow (8,7)
16 The main immune system cells for defending against bacterial infections (3 words: 5,5,5)
17 Antibiotics will most commonly be given to children in this form (5)
18 You require one of these for antibiotics (12)
20 These medicines should be used as prescribed and only when needed for bacterial infections (11)
22 Main professional group that administer and may prescribe antibiotics (5)
24 This infectious agent includes yeasts and moulds (6)
25 When the antimicrobials are no longer effective the microbes have developed this (10)
27 You often generate more of this when you have a cough, cold or flu and ranges in colour from yellow to green (6)
29 Professional who may prescribe antibiotics for humans (6)
30 Clean your hands to prevent the spread of these (5)
31 Medicine used to treat viral infections (9)

DOWN

1 You can get a vaccination jab against this viral seasonal illness (3)
2 When you have a viral illness you should consume lots of this (6)
4 Your body's natural defense system against infections (2 words 6,6)
7 A common symptom of coughs, colds and flus (2 words: 4,5)
8 Runs from your nose, especially when sick with a viral infection (4)
10 This term covers antibiotics, antivirals and antifungals (13)
12 When you are ill and can make others ill with the same bug you are _____ (10)
13 A viral infection that causes sore throat and runny nose (4)
14 When you have a cough, cold or flu you should ask your pharmacist how to treat your _____(8)
15 Professional who may prescribe antibiotics for animals (12)
19 The first antibiotic discovered (10)
21 Taking antibiotics unnecessarily can lead to _____ such as diarrhoea (2 words: 4,7)
23 Ask this healthcare professional which over-the-counter medicines are best to treat your symptoms (10)
26 Misuse of antibiotics allows _____ to develop resistance (8)
28 Often a symptom of a respiratory tract infections caused by viruses (5)

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