

Microbiology Nuts & Bolts

Key Concepts of
Microbiology & Infection

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About the Author

The author qualified from Southampton University Medical School in 1997 and gained his background knowledge from jobs in medicine, general surgery, emergency medicine and paediatrics. After 5 years of specialist training he gained his CCT in Microbiology in 2006. Now as a Consultant Clinical Microbiologist in an NHS hospital in the UK, he spends his days diagnosing, treating and managing infections.

It is becoming increasingly apparent that there is a lack of knowledge about microbiology and infections amongst doctors. Through a series of clinical teaching sessions for medical students and junior doctors on “key concepts of microbiology and infection”, the need for a clinically orientated microbiology book became obvious.

Having been asked repeatedly, which book should students read to learn more, he had to admit that he did not know of one? The student’s feedback was direct...get on and write one! This book and the accompanying website are an attempt to rectify the lack of clinically orientated information on microbiology.

www.microbiologynutsandbolts.co.uk

Introduction

Microbiology Nuts & Bolts has been written to provide doctors and healthcare staff with the ability to confidently identify the micro-organisms that are the cause of a patient's infection and how to treat them. The book is set out by condition rather than micro-organism allowing for quick reference in a clinical setting. However, it is not an all-encompassing reference text and has deliberately not been referenced extensively in order to keep its presentation simple. It is intended to be concise enough to be of use on a daily basis, be it on a ward or in a clinic, yet detailed enough to promote a thorough understanding of micro-organisms, their management and ultimately patient treatment.

The book is divided into six parts: Basic Concepts, Microbiology, Infection Control, Clinical Scenarios, Antibiotics and Emergencies. It is best to read Basic Concepts and Microbiology thoroughly first, as this will give the building blocks to understanding infections. After that, dipping into the Clinical Scenarios and Antibiotics sections will aid diagnosing and managing patients with specific infections. Emergencies have been separated into their own section to ensure they can be found quickly. Flowcharts help guide initial emergency treatment, which often needs to be implemented immediately in order to save lives, although they are not a replacement for experienced senior support. Infection Control does not go in to depth regarding policies and politics but gives practical advice about preventing the spread of infections and what to do when you have too many patients for the side rooms available.

The ultimate aim of the book is to empower doctors and healthcare staff to manage patients with infections better, if it achieves this then it will be a success.

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A clinically focused, no nonsense pocket book to the key elements of microbiology and infection. A must have guide to stop common and often unnecessary mistakes that occur in everyday medicine and antibiotic prescribing.

Dedication

To Jenny and the cat club who have helped and hindered in equal measure!

Disclaimer

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If you like this book, recommend it to someone else. If you don't, then tell me why at...

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Basic Concepts

Preview



What is Infection? Infection vs. Colonisation

Infection is the presence of micro-organisms causing damage to body tissues, usually in the presence of acute inflammation (pain, swelling, redness, heat and loss of function). For example *Staphylococcus aureus* on intact skin does not cause a problem; it is the normal flora for skin. However if you cut your skin, *Staphylococcus aureus* can cause infection in the cut.

Micro-organisms can also cause damage in the absence of inflammation but it is unusual, e.g. in neutropaenic patients with angio-invasive fungal infections causing tissue infarction.

Colonisation describes when bacteria grow on body sites exposed to the environment, without causing infection. This is a normal process. These bacteria may form part of the normal flora of the individual; however colonisation is not necessarily normal flora. Occasionally bacteria, which are not normally regarded as part of the normal flora can also colonise body areas e.g. *Pseudomonas* sp. in a wound is not normal flora of the skin or a wound but it is not actually causing tissue damage or infection it is just growing in the warm wet conditions of the wound. *Pseudomonas* sp. are the normal flora of warm wet places. Likewise some prosthetic devices can also become colonised with bacteria without causing infection e.g. urinary catheters.

Colonisation does not normally harm the patient and does not usually need treating with antibiotics e.g. *Neisseria meningitidis* can be found in up to 30% of the healthy population in their oropharynx. However, infection can result in harm and often needs treatment with antibiotics e.g. if *Neisseria meningitidis* enters the blood stream from the oropharynx to cause septicaemia, then it needs urgent treatment.

Examples of colonisation

Body Site or Prosthetic Device	Bacterial Colonisation
Pressure sores	<ul style="list-style-type: none">• Skin flora e.g. <i>Staphylococcus</i> sp.• Enteric flora e.g. <i>Escherichia coli</i>, <i>Pseudomonas</i> sp.
Breaks in the skin e.g. wounds	<ul style="list-style-type: none">• Skin flora e.g. <i>Staphylococcus</i> sp.• Enteric flora e.g. <i>Escherichia coli</i>, <i>Pseudomonas</i> sp.
Upper respiratory tract	<ul style="list-style-type: none">• Mixed enteric flora in patients given antibiotics or who have been in healthcare settings for more than 4 days e.g. <i>Escherichia coli</i>, <i>Pseudomonas</i> sp.
Urinary catheter	<ul style="list-style-type: none">• Enteric flora e.g. <i>Escherichia coli</i>, <i>Pseudomonas</i> sp.
Endotracheal tube OR Tracheostomy tube in a ventilated patient	<ul style="list-style-type: none">• Mixed enteric flora in patients given antibiotics or who have been in healthcare settings for more than 4 days e.g. <i>Escherichia coli</i>, <i>Pseudomonas</i> sp.

Warning

In the absence of good clinical information on request forms (see section – Microbiology, Why Bother Completing Request Forms?) microbiology laboratories are unable to distinguish between colonisation and infection and so will just report the presence of bacteria. It is then up to the clinician to decide if these bacteria are causing infection.

Better filled in request forms lead to better clinical advice from microbiology services.

Source of Infection: Endogenous vs. Exogenous

It is important to understand how infections arise in patients in order to manage them appropriately.

Endogenous infections are caused when the patient's own bacterial flora gets into a site it should not be in. This is responsible for about 85% of all infections. Knowledge of the patient's normal flora aids the management of these types of infection. For example, pneumonia tends to be caused by bacteria from the URT; knowing what the normal flora of the URT is allows prediction of the antibiotics necessary to treat pneumonia.

Exogenous infections are much less frequent than endogenous and occur when the patient acquires a micro-organism that directly invades and causes disease. Knowledge of methods of transmission aids the management of outbreaks of these types of infections. For example, knowing that *Norovirus* is transmitted by the faecal-oral route allows the precautions of hand hygiene, individual toilets, isolation of infected patients and environmental cleaning to be implemented to prevent transmission and control outbreaks.

What is Normal Flora and why is it Important?

Normal flora are the micro-organisms that live on another living organism (human or animal) or inanimate object without causing disease. The human body is not sterile; we become colonised by bacteria from the moment we are born. We are covered with, and contain within our intestines, approximately one hundred trillion (10^{14}) bacteria that form the normal flora of our bodies. This normal flora helps to prevent us becoming colonised with more dangerous bacteria, which might lead to infection.

Many circumstances can change normal flora, e.g. normal flora of the human body begins to change after admission to a hospital or long-term care facility. The process usually begins around day 4 of admission; this is why after 4 days of admission the antibiotics for hospital acquired infections change. It is not because the severity of the illness is different.

Knowledge of the normal flora of the human body allows:

- Prediction of the pathogens causing infection as bacteria tend to grow in specific body sites e.g. *Streptococcus pneumoniae* from the upper respiratory tract causing pneumonia or *Staphylococcus aureus* from the skin causing intravenous cannula infections.
- Investigation for underlying abnormalities in specific areas of the body when bacteria are isolated from normally sterile sites e.g. *Escherichia coli* isolation from blood cultures indicates probable intra-abdominal pathology because *Escherichia coli* is part of the normal gastrointestinal flora, or isolation of a Viridans *Streptococcus* in blood cultures may indicate infective endocarditis as a result of poor dentition as Viridans *Streptococcus* are part of the normal mouth flora.

Nothing is 100% accurate but it's a good place to start. Knowing where bacteria normally live can help you work out when they are in the wrong place. This knowledge allows the prediction of the likely causes of disease and hence the choice of a suitable antibiotic for empirical therapy.

Knowing what factors affect normal flora allows predictions to be made as to what the flora will become under the influence of those factors, e.g. exposure to antibiotics removes sensitive bacteria, so if a patient with a cut hand, and a sensitive *Staphylococcus aureus* (MSSA) in their normal flora, is given Flucloxacillin for the cut, a void will be left behind, which could be filled by a Flucloxacillin resistant bacteria such as Meticillin resistant *Staphylococcus aureus* (MRSA).

Myth

Bacteria have no place in our environment. **FALSE** - Bacteria are part of the normal environment. Almost everything has its own normal flora. Hospitals, the community, soil, animals, air conditioning units and swimming pools all have their own "normal flora". However certain things like surgical instruments and synovial fluid should be sterile. If something contains its normal flora it is normal, if it grows something else's normal flora e.g. synovial fluid grows skin flora, it is abnormal. Knowing where normal flora comes from allows you to identify the likely cause of infection or know where to investigate.

Bacterial Flora in a Normal Person in the Community

Below are body sites and their common normal flora, isolating these micro-organisms from their normal body site is normal and does not indicate infection. Knowing where micro-organisms are normally found helps identify a cause if they migrate from their normal body site into another body site. The micro-organisms listed below are also most likely to cause disease if they migrate to another body site. For example, *Escherichia coli* from the gastro-intestinal tract gets into the genital tract causing a UTI.

Upper Respiratory Tract

- *Staphylococcus* sp.
- *Streptococcus* sp.
 - *Streptococcus pneumoniae*
 - Viridans *Streptococcus*
- *Haemophilus* sp.
- Anaerobes

Skin

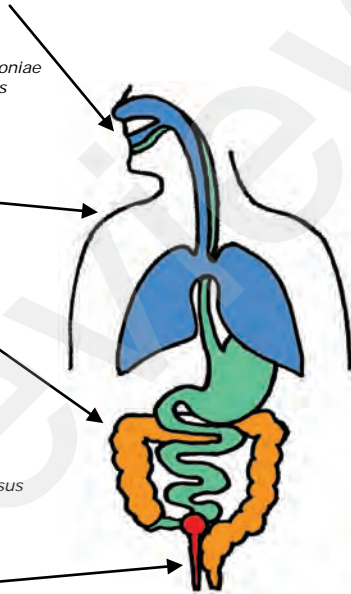
- *Staphylococcus* sp.
- Coryneform bacteria or "Diphtheroids"
- *Propionibacterium* sp.

Gastrointestinal Tract

- Anaerobes
- *Enterococcus* sp.
- Enterobacteriaceae
 - *Escherichia coli*
 - *Klebsiella* sp.
- *Streptococcus* sp.
 - *Streptococcus anginosus* (milleri) group
- *Lactobacillus* sp.
- *Candida* sp.

Genital Tract

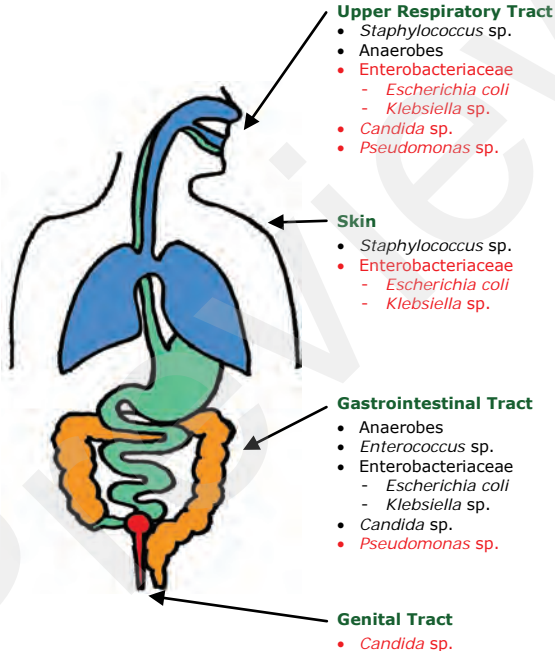
- *Lactobacillus* sp.
- *Streptococcus* sp.
 - *Streptococcus agalactiae*



In the community, normal flora is generally sensitive to antibiotics.

Bacterial Flora in a Normal Person in a Hospital or Long-term Care Facility

Below are body sites and their common normal flora for a hospital patient or a person in a long-term care facility. They are different to community normal flora because of exposure to different micro-organisms, physiological changes, immunosuppressants and selective pressures. Isolating these micro-organisms from their normal body site in hospitals or long-term care facilities is normal and does not indicate infection.



In hospital environments most of the normal flora remains sensitive to antibiotics but added to these are normal flora that are resistant to antibiotics and environmental factors, such as drying, alcohol hand scrubs or detergents (these more resistant micro-organisms are shown in red)

Diagnosing Infection: History

It may sound obvious but in order to manage a patient with an infection safely and effectively you first have to work out what is wrong with them. This is done through the dynamic process of formulating a differential diagnosis. The process begins the moment the patient is referred (e.g. you are told the patient has a cough) you narrow questioning to the respiratory system and a differential diagnosis that includes diseases like pneumonia, lung cancer, COPD etc). By taking a **history, examination** and requesting targeted **investigations** you narrow down the differential diagnosis until you get to a single diagnosis.

A differential diagnosis is a list of potential diseases or infections that a patient might have. The simplest and most effective method of formulating a differential diagnosis is:

- Immediately life threatening conditions e.g. meningitis, encephalitis, necrotising fasciitis
- Common conditions e.g. UTI, pneumonia, cellulitis, heart failure
- Uncommon conditions e.g. infective endocarditis

In the History the key infection related aspects to concentrate on are:

History	Examples of Significance
The patient's specific symptoms	<ul style="list-style-type: none">• Cough indicating chest or upper respiratory tract• Right upper quadrant pain indicating possible cholangitis
A chronological timeline of when and how symptoms developed	<ul style="list-style-type: none">• Chicken Pox followed by haemorrhagic skin lesions pointing towards invasive Group A Beta-haemolytic <i>Streptococcus</i> and necrotising fasciitis
Contact with people with infections OR symptoms	<ul style="list-style-type: none">• Tuberculosis contact
A list of recent travel (countries and regions)	<ul style="list-style-type: none">• Malaria endemic regions
The patient's vaccination history	<ul style="list-style-type: none">• Primary infant courses as well as travel related vaccines
The patient's current and former occupations	<ul style="list-style-type: none">• Healthcare staff and blood borne viruses• Plumber and exposure to <i>Legionella pneumophila</i>
The patient's pastimes and hobbies	<ul style="list-style-type: none">• Water sports and exposure to rats in leptospirosis
Any pets OR contact with animals	<ul style="list-style-type: none">• Zoonotic infections e.g. <i>Pasteurella multocida</i> and cat bites, <i>Chlamydia psittaci</i> and parrots
A sexual history	<ul style="list-style-type: none">• Sexually transmitted diseases and blood borne viruses
The patient's ethnic origin	<ul style="list-style-type: none">• Exposure to relatives with tropical infections
The patient's country of birth	<ul style="list-style-type: none">• Chronic tropical infections• Exposure to relatives with tropical infections

Microbiology



Preview

How to Take Microbiology Specimens

Aseptic Technique

Aseptic technique is a procedure that is performed under sterile conditions. Microbiology samples should be taken aseptically to prevent contamination with bacteria e.g. if you take blood cultures without aseptic technique it is likely that the result will be a skin contaminant rather than the cause of the infection.

Examples of techniques to minimise the risk of contamination:

- Blood cultures and CSF - clean the skin with 2% Chlorhexidine and wear gloves
- Midstream urine specimen - part the labia or retract the foreskin
- Wound swabs - remove slough from ulcers to reveal the fresh tissue beneath
- Sputum - ask patients to cough sputum immediately into the specimen container rather than holding it in the mouth whilst looking for a container

Sample Before Treatment

If safe to do so, take microbiology samples before starting antibiotics otherwise those antibiotics may inhibit the growth of bacteria, causing negative cultures.

Blood Cultures First

Always take blood cultures before any other blood samples because other blood sample collection bottles are not necessarily sterile and can therefore contaminate the blood culture collection kit. This will lead to contaminated blood cultures, known as pseudobacteraemia.

Aerobic Bottle First

Take the aerobic bottle before the anaerobic bottle in case there is not enough blood for both bottles e.g. if the needle comes out of the patient's arm. You are more likely to diagnose infection from the aerobic blood culture bottle because more pathogenic bacteria grow in this type of bottle than the anaerobic bottle.

Cerebrospinal Fluid

Do not forget to take samples for peripheral blood glucose, at the same time as CSF protein and CSF glucose. The glucose levels need to be compared and therefore done at the same time. As glucose levels vary, if peripheral blood glucose is forgotten you will not be able to take the sample later as the comparison will not be valid. The comparison allows a distinction to be made between bacterial meningitis and other causes of meningitis (see section – Emergencies, Meningitis).

Avoid a Quick Swab

If possible send pus or tissue rather than swabs because pus and tissue can be Gram stained allowing recognition of bacteria or fungi that are present but which have failed to grow on culture.

Hints and Tips

What's the difference between cultures and Gram stains? Microscopy includes any investigation using a microscope, including the Gram stain. Culture is whatever grows after incubation e.g. on the agar plate. They are not necessarily the same, antibiotics can inhibit growth in culture, micro-organisms may not grow fast enough or may have specific growth requirements that prevent them being cultured even though they can be seen on microscopy. Therefore microscopy may give a more complete view whereas culture may not. Culture, however, will give the micro-organisms names and provide antibiotic sensitivities.

For example: At the time of appendicectomy the patient is on Cefuroxime and Metronidazole. The intra-abdominal pus sample is sent to the laboratory, the result later shows:

Specimen	Pus
Appearance	-
Microscopy	Gram-positive cocci in chains Gram-negative bacilli Yeasts
Culture	<i>Enterococcus faecium</i> - Amoxicillin resistant - Vancomycin sensitive

The microscopy shows a mixture of bowel flora, but the *Enterococcus faecium* is the only bacteria that grows on culture because it is inherently resistant to Cefuroxime and Metronidazole. The yeast may not have had sufficient time to grow on culture. It would be a mistake to only treat the *Enterococcus faecium* as the microscopy clearly shows the presence of other bowel flora.

How to Interpret Microbiology Results - Bacteriology

There are methods to systematically read chest X-rays (see appendix 1), and a similar approach should be taken to laboratory results. They are multipart results and reading them in isolation means you will misinterpret the significance of the result. In order to correctly interpret a bacteriology report all three parts (if given) need to be considered in this order:

- **Appearance**
 - A description of the appearance of the sample e.g. purulent, blood stained, turbid, clear
 - Is there evidence of inflammation or disease e.g. purulent, pus or liquid stool
 - Is there evidence of contact with a non-sterile site or absence of disease e.g. salivary sputum, epithelial cells in urine, formed stool
- **Microscopy**
 - A list of the different appearances of micro-organism present e.g. the report states a Gram-positive coccus in chains seen on the Gram film
 - Is it consistent with the diagnosis e.g. the patient has symptoms of cough, SOB and fever, a possible diagnosis is pneumonia and pneumonia can be caused by a Gram-positive coccus in chains
- **Culture and sensitivity**
 - A list of the micro-organisms, which have grown
 - Is it consistent with the diagnosis e.g. *Streptococcus pneumoniae* is cultured from a patient with pneumonia
 - A list of antibiotics used to treat the bacteria that was cultured; it is not usually necessary to give every sensitive antibiotic listed
 - The list of antibiotics allows choices based around potential allergies to antibiotics
 - You may have to use combinations of antibiotics to treat mixed infections e.g. *Escherichia coli* and *Bacteroides* sp. with Cefuroxime and Metronidazole

Occasionally other tests are performed and reported separately as they do not fit the usual sequence of Appearance, Microscopy and Culture. They are performed when the clinical details alert the laboratory to the need for further or specific testing.

- **Antigen detection**
 - Clinical details state CAP e.g. the laboratory conducts the tests for urine Pneumococcal and Legionella antigens
 - Clinical details state an outbreak of diarrhoea and vomiting e.g. the laboratory conducts the tests for *Norovirus* and *Rotavirus* in stool
- **Molecular detection of nucleic acid or Polymerase Chain Reaction (PCR)**
 - Clinical details state meningitis e.g. the laboratory conducts the tests for *Neisseria meningitidis* and *Streptococcus pneumoniae* PCR in EDTA blood
- **Toxin detection**
 - Clinical details state diarrhoea after stating Ciprofloxacin e.g. the laboratory conducts the tests for *Clostridium difficile* toxin in stool

Basic Bacterial Identification by Microscopy

There are too many micro-organisms to remember therefore they need to be separated into groups with similar features. Microbiologists use a number of terms to describe the different appearances of bacteria; Gram-positive or Gram-negative, coccus or bacillus etc. For example, the Microbiologist might telephone with a result, saying "the cause is a Gram-negative bacillus growing both aerobically and anaerobically". This may appear to be pointless jargon but using a simple system of firstly identifying the staining method, then the shape of the micro-organism and finally the micro-organisms growth requirements, a doctor can begin to eliminate micro-organisms, like in a game of Cluedo®, in order to identify the most likely cause of the infection.

If a micro-organism is Gram-negative, it cannot be any of the Gram-positives or acid-fast bacilli and therefore these can be discarded. If the micro-organism is bacillus shaped then all of the cocci can be discarded. If the micro-organism is then described as growing anaerobically, the aerobes can be discarded; and if it is also described as growing aerobically as well as anaerobically the anaerobes can also be discarded. This identifies the micro-organism as a Gram-negative bacillus growing as a facultative anaerobe i.e. an Enterobacteriaceae, *Haemophilus* sp., *Eikenella* sp., *Pasteurella* sp. or *Capnocytophagus* sp. The clinical history can then narrow the list further because if the patient has CAP it is probably a *Haemophilus* sp., if they have a cat bite it is probably *Pasteurella* sp., and if they have pyelonephritis it will be one of the Enterobacteriaceae.

Identifying the staining method

Ziehl-Neelsen Stain	Acid-fast	Stains red using the ZN method, bacteria have mycolic acid in their cell wall
Gram's Stain	Gram-positive	Stains purple with Gram's method, bacteria have a thick cell wall and no cell membrane
	Gram-negative	Staining red with Gram's method, bacteria have a cell membrane outside a thin cell wall

Identifying the shape

Coccus	Shaped like a sphere
Bacillus	Shaped like a rod

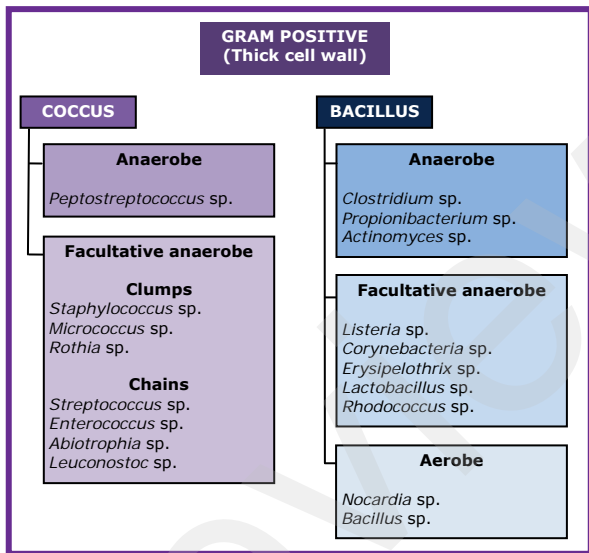
Identifying the growth requirements

Aerobic	Grows in the presence of oxygen
Anaerobic	Grows in the absence of oxygen
Facultative Anaerobe	Able to grow in the presence or absence of oxygen
Microaerophilic	Grows in the presence of oxygen at lower concentrations than in air

Knowledge of bacterial identification from the Gram film appearance helps predict the cause of an infection from the microscopy result up to 48 hours before the culture result is available. By using both the Basic Bacteria Identification diagrams and the Table of Bacterial Causes of Infection (following pages) you can identify the likely bacteria from the Gram film appearance on the microscopy result. For example:

- The patient clinically has meningitis; the Gram film of the CSF shows Gram-positive cocci in chains. Meningitis is caused by *Streptococcus pneumoniae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Haemophilus influenzae* and *Mycobacterium tuberculosis*. We know it is Gram-positive therefore ruling out *Neisseria meningitidis*, *Haemophilus influenzae*, which are Gram-negative and *Mycobacterium tuberculosis*, which is an acid-fast bacillus. The microscopy also states coccus, which rules out *Listeria monocytogenes* as this is a bacillus. This leaves *Streptococcus pneumoniae*, a chain forming Gram-positive coccus
- The patient clinically has septic arthritis; the Gram film of the synovial fluid shows Gram-positive cocci in clumps. Septic arthritis is caused by *Staphylococcus aureus*, Beta-haemolytic *Streptococcus*, *Escherichia coli* and Enterobacteriaceae. As it is Gram-positive this rules out *Escherichia coli* and Enterobacteriaceae, which are Gram-negative. The microscopy also states clumps, which rules out *Streptococcus* sp. as these form chains. This leaves *Staphylococcus aureus*, a clump forming Gram-positive coccus
- The patient clinically has peritonitis; the Gram film of the peritoneal fluid shows Gram-positive cocci in chains, Gram-positive bacilli and Gram-negative bacilli. Peritonitis is caused by bowel flora including: *Enterococcus* sp., *Clostridium* sp., *Bacteroides* sp., *Escherichia coli* and Enterobacteriaceae. The mixed Gram film appearance shows the presence of the entire bowel flora. This indicates the patient has probably perforated their bowel rather than developed spontaneous bacterial peritonitis. Even this result is helpful as it indicates there is a hole in the bowel. The patient needs surgery not just antibiotics, as no antibiotic tablet is large enough to plug the hole. Antibiotics will only help if the hole is surgically repaired

Basic Bacteria Identification



GRAM NEGATIVE
(Thin cell wall and cell membrane)

COCCUS

Facultative Anaerobe

Neisseria sp.
Moraxella sp.
Kingella sp.

Aerobe

Pseudomonas sp.
Stenotrophomonas sp.
Legionella sp.
Bordetella sp.
Aeromonas sp.
Vibrio sp.

Microaerophilic

Campylobacter sp.
Helicobacter sp.

BACILLUS

Facultative anaerobe

Enterobacteriaceae
- *Escherichia coli*
- *Klebsiella* sp.
- *Enterobacter* sp.
- *Citrobacter* sp.
- *Serratia marcesans*
- *Salmonella* sp.
- *Shigella* sp.
- *Acinetobacter* sp.
Haemophilus sp.
Eikenella sp.
Pasteurella sp.
Capnocytophagus sp.

Anaerobe

Bacteroides sp.
Fusobacterium sp.

ACID FAST BACILLI
(Mycolic acid in cell wall)

Mycobacteria sp.

NON-CULTURABLE
(No cell wall)

Mycoplasma sp.
Ureaplasma sp.
Chlamydia sp.

Table of Bacterial Causes of Infection

Key	✓ = Usually sensitive	= = Usually resistant or inappropriate therapy									
Clinical Scenarios	Gram-positive Bacteria									Anaerobes	
	Staphylococcus aureus (MSSA)	Staphylococcus aureus (MRSA)	Coagulase Negative Staphylococcus	Beta-haemolytic Streptococcus (A, B, C, G)	Enterococcus faecalis	Enterococcus faecium	Streptococcus pneumoniae	Listeria monocytogenes	Clostridium perfringens	Clostridium difficile	
Respiratory Infections											
Community Acquired Pneumonia (CAP)	✓	-	-	-	-	-	✓	-	-	-	
Hospital Acquired Pneumonia (HAP)	✓	✓	-	-	-	-	✓	-	-	-	
Ventilator Associated Pneumonia (VAP)	✓	✓	-	-	-	-	✓	-	-	-	
Aspiration Pneumonia	✓	-	-	-	-	-	✓	-	-	-	
Exacerbation of COPD	✓	-	-	-	-	-	✓	-	-	-	
Head and Neck Infections											
Otitis Media	-	-	-	-	-	-	✓	-	-	-	
Otitis Externa	✓	-	-	✓	-	-	✓	-	-	-	
Orbital Cellulitis	✓	-	-	-	-	-	✓	-	-	-	
Sinusitis	✓	-	-	✓	-	-	✓	-	-	-	
Urogenital Infections											
Urinary Tract Infection	-	-	-	-	-	-	-	-	-	-	
Prostatitis	-	-	-	-	-	-	-	-	-	-	
STDs	-	-	-	-	-	-	-	-	-	-	
Skin, Soft Tissue, Bone and Joint Infections											
Cellulitis	✓	✓	-	✓	-	-	-	-	-	-	
Cellulitis in Diabetes & vascular Insufficiency	✓	✓	-	✓	-	-	-	-	✓	-	
Bites	✓	-	-	✓	-	-	-	-	✓	-	
Burns, Skin Grafts and Post-Operative Wounds	✓	✓	-	✓	-	-	-	-	✓	-	
Intravenous Device Associated Infection	✓	✓	-	-	-	-	-	-	-	-	
Osteomyelitis	✓	✓	-	✓	-	-	-	-	-	-	
Septic Arthritis	✓	✓	-	✓	-	-	-	-	-	-	
Gastrointestinal Infections											
Peritonitis	-	-	-	-	✓	✓	-	-	✓	-	
Cholecystitis & Cholangitis	-	-	-	-	✓	✓	-	-	✓	-	
Other Infections											
Infective Endocarditis	✓	-	✓	-	✓	✓	-	-	-	-	
Emergencies											
Sepsis	✓	✓	-	✓	-	-	✓	✓	-	-	
Neonatal Sepsis	-	-	-	✓6	-	-	-	-	-	-	
Neutropaenic Sepsis	✓	✓	-	-	-	-	-	-	-	-	
Meningitis	-	-	-	-	-	-	✓	-	-	-	
Neonatal Meningitis	-	-	-	✓6	-	-	-	✓	-	-	
Epiglottitis	-	-	-	✓	-	-	-	-	-	-	
Epidural Abscess	✓	-	-	-	-	-	-	-	-	-	
Necrotising Fasciitis	-	-	-	✓	-	-	-	-	✓	-	
Toxic Shock Syndrome	✓	-	-	-	-	-	-	-	-	-	

- 1) *Escherichia coli* occasionally causes HAP in particularly debilitated patients
- 2) *Pseudomonas aeruginosa* can cause UTIs and prostatitis in patients with anatomically abnormal urinary tracts or catheters
- 3) Enterobacteriaceae and *Pseudomonas aeruginosa* can cause central venous catheter infections, particularly in the immunodeficient
- 4) *Escherichia coli* and Enterobacteriaceae can cause osteomyelitis and septic arthritis in the elderly, particularly following haematogenous seeding from UTIs

? = Variable sensitivity										P = Prophylaxis only		
Gram-negative Bacteria										Non-Culturable		
Bacteroides fragilis	Neisseria meningitidis	Neisseria gonorrhoea	Haemophilus influenzae	Escherichia coli	ESBL positive Escherichia coli	Enterobacteriaceae	Pseudomonas aeruginosa	Moraxella catarrhalis	Legionella pneumophila	Mycoplasma pneumoniae	Chlamydia sp.	
-	-	-	✓	-	-	-	-	-	✓	✓	✓	
-	-	-	✓	71	71	✓	✓	-	-	-	-	
-	-	-	✓	✓	✓	✓	✓	-	-	-	-	
✓	-	-	✓	✓	✓	✓	-	-	-	-	-	
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-	-	-	-	74	-	74	-	-	-	-	-	
✓	-	-	-	✓	75	✓	75	-	-	-	-	
✓	-	-	-	✓	75	✓	75	-	-	-	-	
-	-	-	-	-	-	-	-	-	-	-	-	
-	✓	-	-	✓	-	✓	✓	-	-	-	-	
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-	-	-	-	✓	-	77	-	-	-	-	-	
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-	-	-	-	✓	-	✓	-	-	-	-	-	
-	-	-	-	✓	-	✓	-	-	-	-	-	
-	-	-	-	-	-	-	-	-	-	-	-	

- 5) ESBL positive *Escherichia coli* and *Pseudomonas aeruginosa* are more common in intra-abdominal infections following surgery
6) Group B Beta-haemolytic *Streptococcus* is the most common cause of neonatal sepsis and meningitis
7) Enterobacteriaceae such as *Klebsiella* sp., *Salmonella* sp. and *Serratia marcescens* are unusual but severe causes of neonatal sepsis and meningitis

Examples of Bacteriology Requests, Results and Interpretations

Clinical Details on the request form:

Right upper quadrant pain, fever and jaundice

Result

Specimen	Blood culture
Appearance	-
Microscopy	Gram-negative bacilli
Culture	Escherichia coli - Amoxicillin sensitive - Gentamicin sensitive

How is this Interpreted?

The Gram-negative bacillus identifies as *E. coli*. *E. coli* is normal flora for the gut; finding it in a blood culture indicates a significant infection below the diaphragm, probably involving either the urinary tract or a gastrointestinal tract related structure. In the clinical details (above) the patient has Charcot's triad (fever, RUQ pain and jaundice) indicating a probable diagnosis of cholangitis (infection of the biliary tract). Appropriate antibiotics have been provided for treatment.

Clinical Details on the request form:

Cough and shortness of breath

Result

Specimen	Sputum
Appearance	Salivary
Microscopy	Gram-negative bacilli
Culture	Escherichia coli

How is this Interpreted?

The salivary appearance of the sample indicates that it has been held in the mouth and is likely to be contaminated with upper respiratory tract bacteria. The Gram-negative bacillus *E. coli* is not a common cause of LRTI, but is a common URT bacteria in hospitalised patients. This result therefore indicates URT contamination, not infection, and the *E. coli* does not need treating. No antibiotics have been released to discourage unnecessary prescribing.

Clinical Details on the request form:

Acute confusion in an elderly patient

Result

Specimen	Urine
Appearance	-
Microscopy	WBC $<10 \times 10^6/L$ Epithelial cells ++
Culture	<i>Pseudomonas aeruginosa</i>

How is this Interpreted?

The culture result cannot be interpreted without first assessing whether a UTI is likely from the microscopy. The absence of WBC ($<10 \times 10^6/L$) shows there is no evidence of inflammation in the urinary tract, however there is evidence that the urine has been in contact with the skin of the perineum (presence of epithelial cells). *Pseudomonas aeruginosa* represents contamination from the perineum and not infection. In addition, *Pseudomonas* sp. is not a common cause of UTI except in the presence of a urinary catheter. Another reason for the acute confusion should be sought.

Clinical Details on the request form:

Acutely hot, painful, swollen knee

Result

Specimen	Synovial fluid
Appearance	Turbid
Microscopy	Gram-positive coccus in clumps
Culture	Staphylococcus aureus - Flucloxacillin sensitive - Fusidic Acid sensitive

How is this Interpreted?

The presence of the Gram-positive coccus in clumps on microscopy is significant as synovial fluid should be sterile. The identification of *Staphylococcus aureus* confirms the diagnosis of septic arthritis. The patient should normally be treated with IV Flucloxacillin and PO Fusidic Acid.

Clinical Details on the request form:

Left iliac fossa pain, diverticular abscess found at laparotomy

Result

Specimen	Pus
Appearance	-
Microscopy	Gram-negative bacilli Gram-positive cocci in chains
Culture	Klebsiella pneumoniae - Amoxicillin resistant - Co-amoxiclav sensitive Enterococcus faecalis - Amoxicillin sensitive

How is this Interpreted?

The bacteria seen on microscopy are consistent with what has grown on culture, mixed bowel flora. This is in keeping with the diagnosis of diverticular abscess. There will be anaerobes present in a diverticular abscess because they are the most numerous bowel flora. However, they have not grown as they do not survive in air (anaerobes) and therefore are difficult to transport alive to the laboratory. This patient will need treatment with an antibiotic active against anaerobes, as well as the bacteria cultured.

Clinical Details on the request form:

Returned traveller, diarrhoea 2 weeks

Result

Specimen	Stool
Appearance	Liquid
Microscopy	Giardia lamblia oocysts seen
Culture	Salmonella, Shigella, Campylobacter and E. coli O157 not isolated

How is this Interpreted?

There has been no bacterial cause for the diarrhoea found. However, the history of travel has prompted the laboratory to look for parasites, which has diagnosed Giardiasis. There are no antibiotics given under culture as the micro-organism has been seen not grown (you cannot grow a parasite). The BNF advises that the treatment of Giardiasis is PO Metronidazole. If the travel history had not been mentioned, the diagnosis would not have been made.

Infection Control



Preview

Summary of Isolation Priority and Infection Control Precautions

"Help! I have 3 patients and only 2 side-rooms" is a common problem for an oncall Microbiologist. Below is the priority for use of side-rooms.

Micro-organism	Priority	Isolation
Influenza	1	Up to 7 days after onset, 14 days if immunodeficient
Open Pulmonary Tuberculosis	2	Until 2 weeks of completed antibiotic treatment OR until discharge
Measles	3	Until 5 days after onset of rash
<i>Varicella Zoster Virus</i> (VZV) Chicken Pox and Shingles	4	Until vesicles dry and crusted over
Meningitis	5	Bacterial meningitis only Until 24 hours after antibiotics started
<i>Clostridium difficile</i> Associated Disease (CDAD)	6	Until diarrhoea resolved for 48 hours
Diarrhoea and Vomiting	7	Until diarrhoea and vomiting resolved for 48 hours
Antibiotic Resistant Gram-negative Bacteria	8	Until discharge unless higher priority case requires isolation
MRSA	9	Until discharge unless higher priority case requires isolation
Glycopeptide resistant <i>Enterococcus</i> (GRE)	10	Until discharge unless higher priority case requires isolation
Group A Beta-haemolytic <i>Streptococcus</i>	11	Until 24 hours after antibiotics started
Cellulitis	12	Until 24 hours after antibiotics started

If there are more patients than side-rooms discuss the situation with the hospital Bed Manager, rather than a Microbiologist, as they will be able to help with up-to-date bed allocation and prioritisation.

PPE	Additional Information
Universal precautions	Surgical face mask, gloves and apron required if within 1 metre of patient OR when patient receiving nebulised medication. Gloves, gowns and FFP3 face protection for aerosol generating procedures
Universal precautions FFP2 face mask for aerosol generating procedures	FFP3 face mask if caring for patient with open pulmonary MDR-TB in negative pressure room
Universal precautions	Staff caring for patient must be immune
Universal precautions	Staff caring for patient must be immune
Universal precautions Face mask required for aerosol generating procedures	
Universal precautions	Separate toilet facilities Hand hygiene with soap and water
Universal precautions	Separate toilet facilities Hand hygiene with soap and water
Universal precautions	
Universal precautions	
Universal precautions	
Universal precautions	
Universal precautions	

Influenza

There are 3 types of *Influenza Virus*, which commonly affect patients, *A*, *B* and *C*. Although *Influenza B* and *C* can spread easily, from an infection control perspective *Influenza A* is of greater significance, as it can cause pandemics. *Influenza A* spreads readily in healthcare settings with a high mortality in at risk groups (see section – Clinical Scenarios, Influenza).

Influenza A can undergo antigenic drift and antigenic shift:

- **Drift** is due to small changes in the genetics of the virus, meaning people become infected but as they have experienced a similar virus their bodies can recognise a large element of the new virus. Relatively few people are infected and have milder symptoms. This is seasonal flu, which genetically changes slightly but continuously
- **Shift** occurs when the virus acquires new genes from a different *Influenza Virus*. This creates a new virus people have not been exposed to yet, capable of causing a pandemic. Pandemic “Swine Flu” and “Bird Flu” are examples of antigenic shift in an animal, e.g. the pig had both human and avian flu and genes swapped between them to create a new *Influenza Virus*. These pandemic viruses tend to become the “next” seasonal virus after the population has been exposed

Mode of Transmission

Transmission usually occurs via droplet and aerosols.

Incubation Period

1-4 days, although most infections occur within 2 days of exposure.

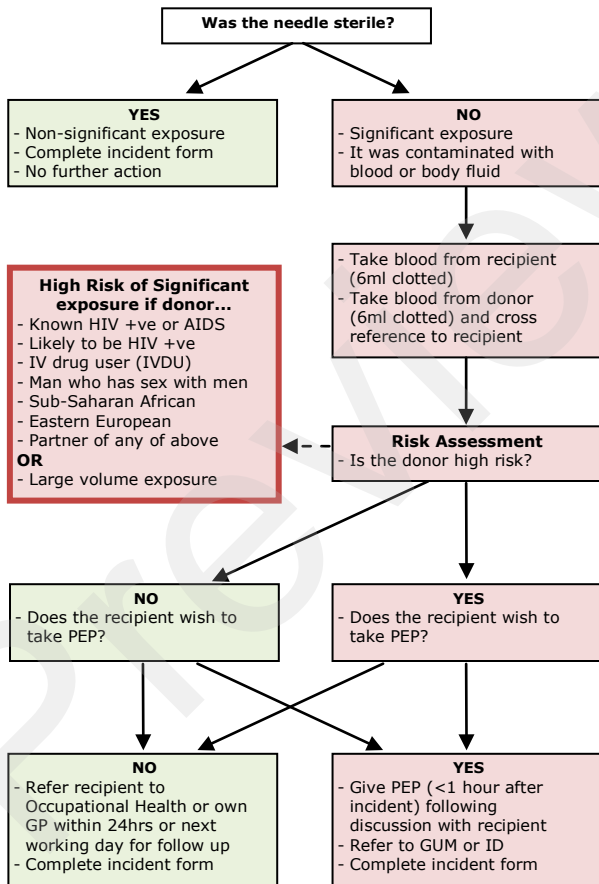
Period of Communicability

Potential cross infection can occur anytime the patient continues to shed virus from the upper respiratory tract. This is usually 3-5 days, although children and the immunodeficient can shed the virus for 10-14 days.

Best Practice Control Measures

Careful antibiotic prescribing	Oseltamivir or Zanamivir should be started as early as possible, ideally within 48 hours of the onset of symptoms
Hand Hygiene	With soap and water or alcohol hand gel
PPE	Surgical face mask, gloves and apron required if within 1 metre of patient or when patient receiving nebulised medication. Gloves, gowns and FFP3 face protection for aerosol generating procedures. Remove ALL PPE before leaving room
Isolation	Side-room with own toilet facility for 7 days or 14 days if immunodeficient Door to be kept closed
Environmental decontamination	Deep cleaning of the clinical area daily and after patient is discharged
Patient care	If patients require investigations in other departments inform those departments of patient's condition, in advance Patient should be last on a list and deep cleaning commence after patient's departure

Needlestick Injury HIV Post Exposure Prophylaxis (PEP) Flowchart



Clinical Scenarios

Preview



Community Acquired Pneumonia (CAP)

Community acquired pneumonia (CAP) is an acute infection of lung tissue with onset outside of hospital or within 48 hours of admission to hospital.

The British Thoracic Society Definitions for diagnosis are:

In community	<ul style="list-style-type: none">• Cough PLUS one other lower respiratory tract symptom• New focal chest signs on examination• One systemic symptom• No other explanation
In hospital (<48 hours)	<ul style="list-style-type: none">• Symptoms and signs consistent with pneumonia• New chest X-ray shadowing

Clinical Features

Respiratory symptoms and signs	Systemic symptoms
<ul style="list-style-type: none">• Cough• Shortness of breath• Purulent sputum• Chest pain• Chest signs of consolidation<ul style="list-style-type: none">- Reduced chest movement- Dull percussion- Bronchial breathing- Increased tactile vocal fremitus and vocal resonance	<ul style="list-style-type: none">• Fever• Sweats• Shivers• Aches• Pains

Children

- Fever
- Increased respiratory rate
- Cough
- Recession
- Chest pain or pain referred to abdomen

Common Mistake

Doctors diagnose pneumonia on the basis of hearing crackles on auscultation of the chest. **This is a mistake.** Crackles in the chest generally indicate heart failure or fibrosis but not pneumonia, especially in the elderly.

Assessment of Severity

C =	Confusion (new)
U =	Urea >7mmol/L
R =	Respiratory Rate >30/min
B =	Blood pressure <90mmHg systolic OR ≤ 60mmHg diastolic
65 =	Age >65 years

Score = 1 each per criteria e.g. **C + R + >65** = 3

CURB-65 = 0-1	Can often be discharged on oral antibiotics
CURB-65 = 2	Usually require observation in hospital
CURB-65 = 3-5	Usually require admission to hospital

Causes

Common	<ul style="list-style-type: none">• <i>Staphylococcus aureus</i>• <i>Streptococcus pneumoniae</i>• <i>Haemophilus influenzae</i>• <i>Mycoplasma pneumoniae</i>• <i>Legionella pneumophila</i> (especially if travelled)• <i>Chlamydia pneumoniae</i>• Viral e.g. <i>Influenza Virus</i>, <i>Parainfluenza Virus</i>, <i>Respiratory Syncytial Virus (RSV)</i>, <i>Adenovirus</i>
If history of COPD	As above plus: <ul style="list-style-type: none">• <i>Pseudomonas aeruginosa</i>
Aspiration	As above plus: <ul style="list-style-type: none">• Anaerobes e.g. <i>Bacteroides</i> sp., <i>Fusobacterium</i> sp.
Zoonotic	<ul style="list-style-type: none">• <i>Chlamydia psittaci</i> (from parrots and budgerigars)
Empyema	<ul style="list-style-type: none">• <i>Staphylococcus aureus</i>• <i>Streptococcus pneumoniae</i>• <i>Streptococcus anginosus</i> group

Warning

Two conditions, which are often missed and are not covered by the normal antibiotics used to treat community acquired pneumonia are: **Tuberculosis** – consider in patients from endemic countries, returned travellers or contacts of people with tuberculosis.

Pneumocystis Pneumonia (PCP) – consider in patients with HIV infection or those who have risk factors for HIV infection.

Myth

Doctors traditionally refer to “atypical pneumonia” however, **this is a poor term**. “Atypical pneumonia” is pneumonia caused by bacteria that cannot easily be grown in a microbiology laboratory e.g. *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. It was the Victorians that first coined the phrase as they could not identify these bacteria. However, with modern methods “atypical pneumonia” bacteria were identified and found to be common causes of pneumonia and hence the term “atypical” is highly misleading. Clinically there is no difference between how different bacterial pneumonias present. The conditions should be called *Mycoplasma pneumoniae* or *Chlamydia pneumoniae* etc just like we use *Staphylococcal pneumonia* or *Streptococcal pneumonia*.

“Atypical” as a term should really be abolished and “non-culturable”, for example, should be used. Non-culturable is used throughout this book.

Investigations

Sputum	<ul style="list-style-type: none"> • Low sensitivity approximately 50% • Will grow upper respiratory tract bacteria, which may or may not be the cause of CAP • Microscopy and culture for acid fast bacilli in tuberculosis
Blood cultures	<ul style="list-style-type: none"> • Positive in $\leq 25\%$ of cases
Urine antigens	<ul style="list-style-type: none"> • <i>Streptococcus pneumoniae</i> • <i>Legionella pneumophila</i> serogroup 1
Blood	<ul style="list-style-type: none"> • Serology in paired samples 10-14 days apart, complement fixation tests for <i>Chlamydia</i> sp., <i>Mycoplasma</i> sp., viruses
Bronchoalveolar Lavage (BAL)	<ul style="list-style-type: none"> • Bypasses upper respiratory tract flora • Can be directed or non-directed • Especially useful for tuberculosis and PCP
Tap pleural effusion	<ul style="list-style-type: none"> • For microscopy, culture and sensitivity • Empyema = pH < 7.2, glucose < 2.2mol/L, LDH > 1000IU/L

Treatment

If CURB-65 score 0-2	
1 st line	PO Amoxicillin PLUS PO Clarithromycin (if <i>Mycoplasma</i> sp. or <i>Chlamydia</i> sp. suspected)
2 nd line (if 1 st line contraindicated)	PO Doxycycline OR PO Levofloxacin

If CURB-65 score 3-5	
1 st line	IV Co-amoxiclav PLUS IV Clarithromycin
2 nd line (if 1 st line contraindicated)	IV Teicoplanin OR IV Vancomycin PLUS PO or IV Levofloxacin
If MRSA positive	ADD IV Teicoplanin OR IV Vancomycin

If history of COPD	
1 st line	IV Piptazobactam
2 nd line (if 1 st line contraindicated)	IV Meropenem
If MRSA positive	ADD IV Teicoplanin OR IV Vancomycin

If Aspiration pneumonia	
1 st line	IV Co-amoxiclav
2 nd line (if 1 st line contraindicated)	IV Teicoplanin OR IV Vancomycin PLUS IV Ciprofloxacin PLUS IV Metronidazole
If MRSA positive	ADD IV Teicoplanin OR IV Vancomycin

Myth

Some doctors believe that aspiration pneumonia requires treating with Metronidazole in addition to other antibiotics in order to cover anaerobic bacteria. **FALSE** - Co-amoxiclav, Piptazobactam and Meropenem all provide excellent anaerobic cover and do not require the addition of Metronidazole.

Children	
1 st line	PO or IV Co-amoxiclav
2 nd line (if 1 st line contraindicated)	PO or IV Clarithromycin
If MRSA positive	ADD IV Teicoplanin OR IV Vancomycin

Total Duration

7 days

Empyema requires drainage and 2-4 weeks total treatment

Dosing

See section - Antibiotics, Empirical Antibiotic Guidelines.

Prognosis and Complications

Mortality is dependent on CURB-65 score:

CURB-65	0-1	<3%
CURB-65	2	9%
CURB-65	3-5	15-40%

Up to 40% of patients with *Streptococcus pneumoniae* reactivate *Herpes Simplex Virus* (HSV) leading to cold sores.

Prophylaxis and Prevention

No roll for antibiotics to prevent recurrence.

Vaccine against *Streptococcus pneumoniae*

- 23 valent, for adults, covering approximately 96% of pneumonia strains but not active in <2 year olds
- 13 valent, for children, covering approximately 90% of pneumonia strains
- Vaccination of children reduces exposure and hence infection in adults by decreasing reservoir of bacteria in community

Antibiotics

Preview



The Daily Review of Antibiotic Therapy

Patients on antibiotics should be reviewed every day to ensure they are responding to treatment and that they are not getting any side effects.

Questions to ask:

Is the patient getting better?	<ul style="list-style-type: none">• Are they improving subjectively i.e. feeling better?• Are they improving objectively i.e. blood tests improving such as white blood cell count, CRP?• Is the diagnosis still correct? <p>If the patient is not feeling better follow the method for failing to respond to antibiotics (see section – Antibiotics, Reasons for Failing Antibiotic Therapy)</p>
Can the patient be converted from IV to oral antibiotics?	<ul style="list-style-type: none">• See section - Antibiotics, Intravenous to Oral Switching of Antibiotics
Can the antibiotics be narrowed down to a specific treatment?	<ul style="list-style-type: none">• Review the microbiology results• Empirical antibiotics cover all common causes of a particular type of infection, they are not specific• Narrowing down antibiotics reduces side effects and risks of complications such as CDAD
Are antibiotic levels required?	<ul style="list-style-type: none">• Have levels been taken?• Are they within acceptable ranges (see section – Antibiotics, Therapeutic Drug Monitoring)
Is the patient's renal and liver function stable?	<ul style="list-style-type: none">• If not, then dosage of antibiotic may require adjusting (see section – Antibiotics, Antibiotic Dosing in Adult Renal Impairment)
Is the patient experiencing side effects?	<ul style="list-style-type: none">• If side effects are severe the antibiotic may require changing (see section – Antibiotics, for individual antibiotic agents)• Consult the BNF• Do not forget to ask about symptoms of CDAD, for patients on Cephalosporins, Ciprofloxacin, Clindamycin and Co-amoxiclav
Have any other drugs been started that might interact with the antibiotics?	<ul style="list-style-type: none">• See section – Antibiotics, for individual antibiotic agents• Consult the BNF
Can the antibiotics be stopped?	<ul style="list-style-type: none">• Is there an indication?• Is there a stop date?• Has the patient received the correct duration of antibiotics for the infection?• Is the patient better? Not necessarily the same as back to normal, which may take longer

How is Antibiotic Resistance Tested in the Laboratory?

Antibiotic resistance is determined using four methods in the laboratory:

1. Implication of resistance from bacterial species identification
2. Disc diffusion using the British Society of Antimicrobial Chemotherapy (BSAC) method
3. Measurement of the minimum inhibitory concentration (MIC)
4. Measurement of the minimum bactericidal concentration (MBC)

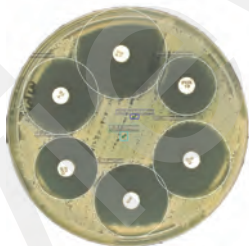
Bacterial Species Identification

Each bacteria has different patterns of sensitivity and resistance to the array of antibiotics available. Once a bacteria has been identified (Gram stain, ZN stain etc) resistance patterns can be implied, as certain bacteria are known to be consistently resistant to certain antibiotics (see section – Antibiotics, What is Antibiotic Resistance?)

Disc Diffusion

Antibiotic impregnated filter paper discs are placed on specific agar plates, which have been inoculated with the bacteria to be tested. If the micro-organism is sensitive to the antibiotic it will not be able to grow in a zone around the antibiotic, called the zone of inhibition. Resistant bacteria will be able to grow close to the disc. Because resistance is usually relative it is necessary to measure the zone diameter to see if it is large enough to correspond to physiologically achievable concentrations of antibiotic.

BSAC publish yearly updates to their method, which includes the zone sizes for bacteria and antibiotic combinations. This method takes 24-48 hours.

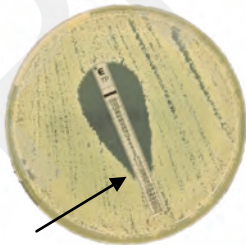


Disc diffusion testing of antibiotic sensitivity

Minimum Inhibitory Concentration (MIC)

The MIC is the least amount of antibiotic required to prevent a bacteria from multiplying. The bacteria may still be alive. It is only usually

performed in specific clinical scenarios under the instruction of a Microbiologist, e.g. infective endocarditis. The most common method employed in most UK laboratories is the Etest method whereby an antibiotic gradient impregnated strip is placed on an inoculated agar plate. The MIC is determined by how far up the strip the bacteria can grow. Low concentrations allow growth whereas higher concentrations inhibit the growth. The MIC is the point at which the growth meets the strip. This method takes 24-48 hours.



Etest for determining MIC

Minimum Bactericidal Concentration (MBC)

The MBC is the least amount of antibiotic required to kill a bacteria. It is very rarely performed. It is difficult to do and labour intensive. Different dilutions of antibiotic are prepared in liquid culture media from low concentration to high concentration. Bacteria are then inoculated into these tubes. After 24-48 hours the tubes where bacteria are growing become cloudy (green tubes in the diagram below); some tubes show no bacterial growth (clear tubes in the diagram below).

This test allows the laboratory to initially determine the MIC (the lowest concentration of antibiotic required to prevent a bacteria from multiplying). The first clear tube shows no growth and corresponds to the MIC.

The MBC is determined by plating out the liquid culture to agar. The first cloudy tube is known to have bacteria growing and is used as a positive control, while the clear tubes have either inhibited or killed bacteria in them. The agar does not contain antibiotic therefore any living bacteria will now not be inhibited and start to grow (tube A). Tube B is the MBC; the bacteria in the tube have not grown on the agar because they have been killed by the concentration of antibiotic that was in tube B.

Calculation of Minimum Bactericidal Concentration (MBC)

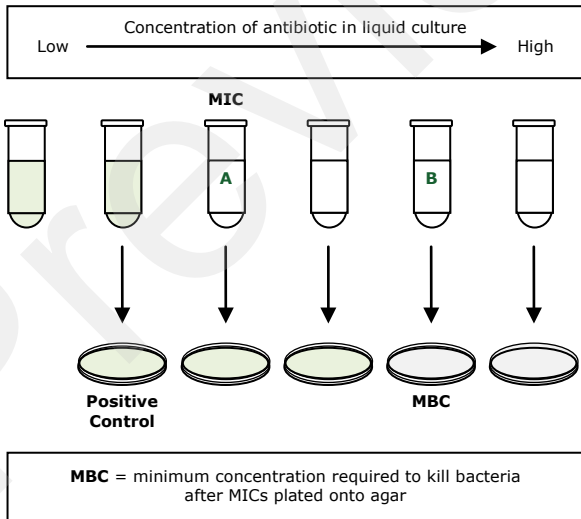


Table of Antibiotic Spectrum of Activity

Key	✓ = Usually sensitive		= Usually resistant or inappropriate therapy							
Antibiotic	Gram-positive								Anaerobe	
	Staphylococcus aureus (MSSA)	Staphylococcus aureus (MRSA)	Coagulase Negative Staphylococcus	Beta-haemolytic Streptococcus (A, B, C, G)	Enterococcus faecalis	Enterococcus faecium	Streptococcus pneumoniae	Listeria monocytogenes	Clostridium perfringens	Clostridium difficile
Penicillins										
Benzylpenicillin	-	-	-	✓	✓	-	✓	✓	✓	-
Amoxicillin	-	-	-	✓	✓	-	✓	✓	✓	-
Ampicillin	-	-	-	✓	✓	-	✓	✓	✓	-
Co-amoxiclav	✓	-	-	✓	✓	-	✓	✓	✓	-
Flucloxacillin	✓	-	?	✓	✓	-	✓	✓	✓	-
Piptazobactam	✓	-	-	✓	✓	-	✓	✓	✓	-
Cephalosporins										
Cefradine	✓	-	?	✓	-	-	✓	-	-	-
Cefalexin	✓	-	?	✓	-	-	✓	-	-	-
Cefuroxime	✓	-	?	✓	-	-	✓	-	-	-
Ceftriaxone	✓	-	-	✓	-	-	✓	-	-	-
Cefotaxime	✓	-	-	✓	-	-	✓	-	-	-
Ceftazidime	-	-	-	-	-	-	-	-	-	-
Carbapenems										
Ertapenem	✓	-	-	✓	-	-	✓	-	✓	-
Meropenem	✓	-	-	✓	✓	-	✓	-	✓	-
Diaminopyrimidines										
Trimethoprim	?	?	-	-	-	-	-	-	-	-
Macrolides and Lincosamides										
Erythromycin	✓	?	-	✓	-	-	✓	-	-	-
Clarithromycin	✓	?	-	✓	-	-	✓	-	-	-
Azithromycin	✓	-	-	✓	-	-	✓	-	-	-
Clindamycin	✓	?	-	✓	-	-	✓	-	✓	-
Aminoglycosides										
Gentamicin	✓	✓	-	-	-	-	-	-	-	-
Amikacin	✓	✓	-	-	-	-	-	-	-	-
Quinolones										
Ciprofloxacin	✓	-	-	-	-	-	✓	-	-	-
Levofloxacin	✓	-	-	-	-	-	✓	-	-	-
Glycopeptides and Lipopeptides										
Vancomycin IV	✓	✓	✓	✓	✓	✓	✓	✓	✓	-
Teicoplanin	✓	✓	✓	✓	✓	✓	✓	✓	✓	-
Vancomycin PO	-	-	-	-	-	-	-	-	-	✓
Daptomycin	✓	✓	✓	✓	✓	✓	✓	✓	✓	-
Nitroimidazoles										
Metronidazole	-	-	-	-	-	-	-	-	✓	✓
Tetracyclines and Glycylcyclines										
Doxycycline	✓	✓	-	?	-	-	✓	-	-	-
Tigecycline	✓	✓	✓	✓	✓	✓	✓	-	-	-
Oxazolidinones										
Linezolid	✓	✓	✓	✓	✓	✓	✓	✓	✓	-
Other										
Rifampicin	✓S	✓S	✓S	-	-	-	-	-	-	-
Fusidic Acid	✓S	✓S	✓S	-	-	-	-	-	-	-
Colistin	-	-	-	-	-	-	-	-	-	-
Chloramphenicol	?	?	?	?	-	-	✓	?	-	-

1) May not be active against bacteria producing AmpC e.g. *Enterobacter cloacae*, *Serratia marcescens*, *Citrobacter freundii*

2) Not active against bacteria producing AmpC e.g. *Enterobacter cloacae*, *Serratia marcescens*, *Citrobacter freundii*

? = Variable sensitivity										P = Prophylaxis only		
Gram-negative										Non-Culturable		
Bacteroides fragilis	Neisseria meningitidis	Neisseria gonorrhoea	Haemophilus influenzae	Escherichia coli	ESBL positive Escherichia coli	Enterobacteriaceae	Pseudomonas aeruginosa	Moraxella catarrhalis	Legionella pneumophila	Mycoplasma pneumoniae	Chlamydia sp.	
-	✓	?	-	-	-	-	-	-	-	-	-	
-	-	?	?	?	-	-	-	-	-	-	-	
✓	-	-	-	✓	-	✓	✓	-	-	-	-	
-	-	-	-	✓	-	-	-	-	-	-	-	
-	✓	✓	✓	✓	-	?	-	-	-	-	-	
-	-	✓	✓	✓	-	✓	✓	✓	-	-	-	
-	-	-	✓	✓	-	✓	✓	✓	-	-	-	
✓	-	-	-	✓	✓	✓	✓	-	-	-	-	
✓	✓	-	✓	✓	✓	✓	✓	✓	-	-	-	
-	-	-	?	✓	-	✓	-	-	-	-	-	
-	-	-	-	-	-	-	-	-	✓	✓	✓	
-	-	-	-	-	-	-	-	-	✓	✓	✓	
✓	-	-	-	-	-	-	-	-	✓	✓	✓	
-	-	-	-	✓	?	✓	✓	✓	-	-	-	
-	-	-	-	✓	?	✓	✓	✓	-	-	-	
-	P	?	✓	✓	?	✓	✓	✓	✓	✓	✓	
-	-	-	✓	✓	-	✓	✓	✓	✓	✓	✓	
-	-	-	-	-	-	-	-	-	-	-	-	
-	-	-	-	-	-	-	-	-	-	-	-	
-	-	-	-	-	-	-	-	-	-	-	-	
✓	-	-	-	-	-	-	-	-	-	-	-	
-	-	?	✓	-	-	-	-	✓	✓	✓	✓	
-	-	-	✓	✓	✓	?	-	✓	-	-	-	
-	-	-	-	-	-	-	-	-	-	-	-	
-	P	-	-	-	-	-	-	-	-	-	-	
-	-	-	-	-	-	-	-	-	-	-	-	
✓	-	-	-	✓	✓	✓	✓	-	-	-	-	
-	✓	-	✓	?	-	-	-	?	-	-	-	

3) Most ESBL positive *Escherichia coli* clones are resistant to Gentamicin and Ciprofloxacin, but this is unpredictable

4) Not active in the urinary tract or against *Proteus* sp.

5) Should not be used as single therapy, should only be used as adjuncts to other anti-Staphylococcal antibiotics

Gentamicin, Amikacin and Tobramycin

Gentamicin, Amikacin and Tobramycin are aminoglycoside antibiotics.

Mechanism of Action

- Bactericidal
- Antibiotic binds to the ribosome causing a shape change that interferes with mRNA translation thereby preventing protein synthesis
- Aminoglycosides are taken up into bacterial cells by an energy dependent mechanism (not concentration dependent), which results in very high intracellular levels. This is responsible for the “post-antibiotic effect” seen with these drugs (continued potent antibacterial activity despite sub-therapeutic levels in blood), because the level in the bacteria remains therapeutic

Mechanisms of Resistance

- Reduced entry of antibiotic into anaerobic bacteria because these lack an energy dependent transport mechanism
- Mutation of the active site therefore antibiotic does not bind
- Production of aminoglycoside modifying enzymes, which breakdown the antibiotic before it reaches the active site. This is usually specific to each individual antibiotic so other aminoglycosides often remain active
- Antibiotic is removed from the bacteria before it is able to act, by an efflux pump, often leading to resistance to all aminoglycosides

Pharmacology and Pharmacodynamics

- Intravenous and topical only
- Aminoglycosides display concentration dependent killing, i.e. more bacteria are killed at higher peak concentrations. Once daily dosing gives higher peak concentrations and is therefore preferable to conventional TDS dosing
- 99% excreted unchanged in urine
- Bile levels achieve 30% of serum level
- Aminoglycosides are often used in combination with cell wall active agents (e.g. Beta-lactams) as this leads to synergy, i.e. the combination of the antibiotics is more effective than the sum of both agents used alone

Spectrum of Activity of Gentamicin, Amikacin and Tobramycin

Gram-positive	<ul style="list-style-type: none">• <i>Staphylococcus aureus</i> (including MRSA)
Gram-negative	<ul style="list-style-type: none">• Enterobacteriaceae e.g. <i>Escherichia coli</i>, <i>Klebsiella</i> sp., <i>Enterobacter</i> sp., <i>Salmonella</i> sp.• <i>Pseudomonas</i> sp.

Cautions and Contraindications

- See BNF for full details
- Renal failure (reduce dose in severe renal failure or do not use)
- Avoid in pregnancy unless benefit outweighs risk
- Myasthenia gravis (aminoglycosides are contraindicated in myasthenia gravis as they can precipitate a myasthenic crisis)
- Drugs
 - Increased ototoxicity when used in conjunction with Furosemide
 - Increased renal toxicity if used with other nephrotoxic agents e.g. Colistin, Vancomycin, Cyclosporin, Tacrolimus

Side Effects

Side effects tend to be related to concentration in blood therefore doses should be calculated for ideal body weight in renal failure (for IBW calculation see section – Antibiotics, Antibiotic Dosing in Adult Renal Impairment) and serum levels must be monitored.

- Nephrotoxic
- Ototoxic

Monitoring

- Monitor serum levels on the 3rd - 4th dose, then weekly or more frequently if renal function changes
- For peak and trough levels (see section – Antibiotics, Therapeutic Drug Monitoring)
- Warn patients to report hearing and balance disturbances, and review daily for symptoms
- At least twice weekly urea and electrolytes monitoring

Emergencies

Preview



Sepsis

Sepsis is infection with evidence of the systemic response to that infection e.g. hypoxia, oliguria, confusion. It is a clinical diagnosis not a laboratory diagnosis.

Severe sepsis is sepsis associated with organ dysfunction, hypoperfusion or hypotension.

Clinical Features

1. Does the patient have a potential source of infection?

- Pneumonia
- Empyema
- UTI
- Acute abdomen
- Meningitis
- Infective endocarditis
- Skin/soft tissue infection
- Bone or joint infection
- Wound infection
- CVC infection
- Other

2. Does the patient have new signs or symptoms of infection? TWO or more of the following:

- Hyperthermia $>38.3^{\circ}\text{C}$
- Hypothermia $<36^{\circ}\text{C}$
- Tachycardia $>90\text{bpm}$
- Tachypnoea $>20\text{ bpm}$
- Leucopaenia $<4 \times 10^9/\text{L}$
- Leucocytosis $>12 \times 10^9/\text{L}$
- Altered mental state
- Hyperglycaemia $>6.5\text{mmol/L}$

3. Does the patient have evidence of organ dysfunction remote to the site of infection?

- Systolic blood pressure $<90\text{mmHg}$
OR Mean arterial pressure $<65\text{mmHg}$
- Systolic blood pressure $>40\text{mmHg}$ below baseline
- Bilateral pulmonary infiltrates
PLUS O_2 required to keep O_2 saturations $>90\%$
- Bilateral pulmonary infiltrates
PLUS $\text{PaO}_2/\text{FiO}_2$ ratio $<300^*$
- Bilirubin $>34\text{ mmol/L}$
- Creatinine $>175\text{mmol/L}$
OR urine output $<0.5\text{ml/kg/hour}$ for more than 2 hours
- Coagulopathy INR >1.5
OR APTT >60 seconds
- Platelet count $<100 \times 10^9/\text{L}$
- Lactate $>2\text{mmol/L}$

* PaO_2 measured in mmHg ($1\text{kPa} = 7.5\text{mmHg}$), FiO_2 as % converted into a decimal e.g. $32\% = 0.32$

If YES to questions 1, 2 and 3 then patient meets the criteria for SEVERE SEPSIS

Adapted from: Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock www.survivingsepsis.org

Causes

Common	<ul style="list-style-type: none">• <i>Staphylococcus aureus</i>• Enterobacteriaceae e.g. <i>Escherichia coli</i>, <i>Klebsiella</i> sp., <i>Enterobacter</i> sp.,• <i>Pseudomonas</i> sp.• <i>Neisseria meningitidis</i>
--------	--

Investigations

- Blood cultures
- Urine for microscopy, culture and sensitivity if able
- Do not unduly delay treatment as mortality increases

Treatment

Antibiotics should be given within 1 hour of the diagnosis of sepsis (see section – Emergencies, Adult Sepsis “Golden-Hour” Management Flowchart)

Adults	
1st line	IV Piptazobactam PLUS IV Gentamicin
2nd line (if 1 st line contraindicated)	IV Teicoplanin OR IV Vancomycin PLUS IV Gentamicin PLUS IV Metronidazole
If previous ESBL OR AmpC positive bacteria	IV Meropenem PLUS IV Gentamicin
If MRSA positive	ADD IV Teicoplanin OR IV Vancomycin

For Children (see section – Emergencies, Initial Management of Meningococcal Sepsis in Children)

Paediatrics	
1st line	IV Cefotaxime PLUS IV Gentamicin
2nd line (if 1 st line contraindicated)	IV Chloramphenicol PLUS IV Gentamicin

Total Duration

7-10 days

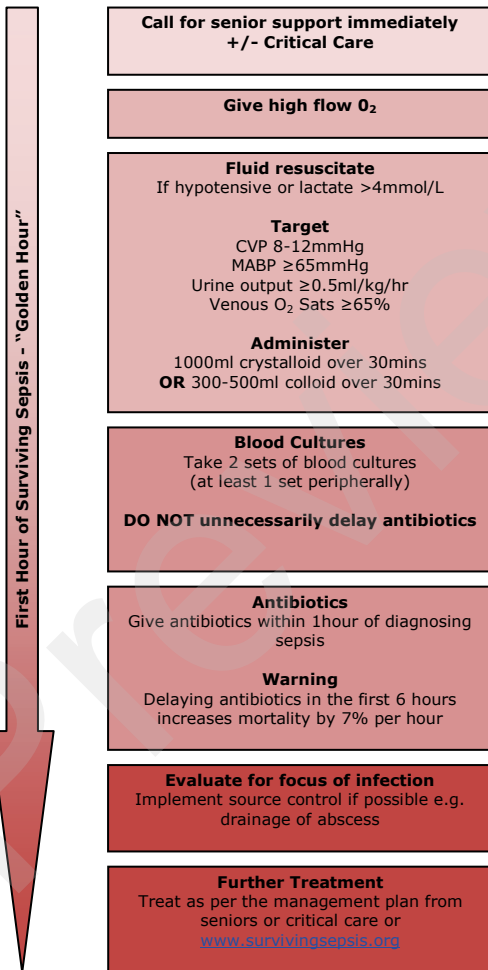
Dosing

See section - Antibiotics, Empirical Antibiotic Guidelines Emergencies.

Warning - Prognosis and Complications

Mortality increases by 7% per hour for the first 6 hours that treatment is not adequate, up to 42%.

Adult Sepsis "Golden-Hour" Management Flowchart



Glossary

Preview



Acid-fast	Staining red using the Ziehl-Neelsen method, used to identify bacteria with mycolic acid in their cell wall
Aerobic	Grows in the presence of oxygen
Anaerobic	Grows in the absence of oxygen
Bacillus	Shaped like a rod
Bacteraemia	Presence of bacteria in blood
Bactericidal	Kills bacteria
Bacteriostatic	Stops bacteria growing without killing it
Biofilm	Collection of bacteria sticking to a surface
Blanching	Redness, which disappears with pressure
Blood Borne Virus	Virus, which can be transmitted between people via blood
Bullae	Large fluid-filled blister >5mm diameter
Clone	Genetically indistinguishable bacteria
Coccus	Spherical shape
Communicability	Able to be transmitted between people
Critical Care Unit	A department looking after a mixture of High Dependency and Intensive Care Unit patients
Culture	Micro-organisms grown under laboratory conditions
Decontamination	Free from any micro-organism or substance that may harm health
Donor	A person who is the source of a body fluid in a needlestick injury
Empirical Antibiotics	Antibiotics that treat the most common causes of infection before the actual cause is known
Endemic	Present in the population all the time
Epidemic	An outbreak of an infectious disease that exceeds the normal background rate of that disease within a population
Erythema	Redness of the skin
Facultative Anaerobe	Grows in the presence or absence of oxygen
Flora	Bacteria living in a specific place
Fomite	An inanimate object capable of transferring micro-organisms
Fungaemia	Presence of fungi in blood
Genotype	Classification of viruses based on their genetic material
Gram-negative	Staining red with Gram's method, cell membrane outside of a thin cell wall
Gram-positive	Staining purple with Gram's method, thick cell wall with no cell membrane
Incident form	Method of recording adverse events in healthcare settings in order to monitor trends and implement corrective changes
Incubation period	Time from when exposed to a micro-organism until the development of symptoms of infection
In vitro	In the laboratory, literally means "in glass"
Lysing	Killing a cell by breaking the cellular membrane
Macules	Area of red skin <5mm diameter

Microaerophilic	Grows in the presence of oxygen at lower concentrations than in air
Mode of transmission	The process by which a micro-organism transfers between people
Morbidity	Ill health
Mortality	Death
Nephrotoxicogenic	Bacteria produces toxins that damage the kidney
Non-blanching	Redness, which does not disappear with pressure
Nucleic Acid	The main constituents of human genes
Opportunist	A micro-organism causing infection, which does not normally cause an infection
Out-of-hours	The time period of medical care when staffing levels are reduced, usually from 5pm-9am and at weekends
Pandemic	An outbreak of an infectious disease across a large geographical area, e.g. multiple continents
Papules	Raised area of skin <5mm diameter
Pathogen	A micro-organism causing disease
Petechiae	Haemorrhage <3mm diameter
Predisposing	A criteria that comes before the acquisition of a disease
Prosthetic	An artificial device or material, which replaces part of the human body
Purpura	Haemorrhage >3mm diameter
Purulent	The presence of white blood cells forming pus
Pyuria	The presence of white blood cells in urine
Recipient	A person who receives the body fluid in a needlestick injury
Seasonal	Occurring at a particular time of year
Sensitivity	A test's ability to identify positive results
Slough	Dead tissue overlying healthy tissue
Specificity	A test's ability to identify negative results
Spore	An asexual form of a micro-organism, which is able to survive for prolonged periods in unfavourable conditions
Sterile	Free from any living micro-organisms
Toxin	A poisonous substance produced in a micro-organism
Transposon	A mobile genetic element
Turnaround time	The time taken from a laboratory receiving a sample to when the laboratory releases the result of any tests performed on that sample
Vacutainer	A glass tube containing a vacuum used to collect blood samples from patients
Vesicle	Small fluid-filled blister <5mm diameter
Vesico-ureteric Reflux	Abnormal movement of urine from the bladder into the ureters
Virulence	The ability of a micro-organism to cause disease
Wildtype	The naturally occurring form of a micro-organism
Zoonotic	Derived from animals


Appendix 1 Systematic Assessment of a Chest X-ray

A simple method to systematically read chest X-rays:

A	Airways and lung fields
B	Bones
C	Cardiac outline and blood vessels
D	Diaphragm, air under the diaphragm, effusions etc
E	Everything else. CVCs, pacemakers, stents and heart valves, sternal wires and surgical staples, ET tubes, NG tubes, ECG lines, piercings

Appendix 2 Bristol Stool Chart

Diarrhoea is stool loose enough to take the shape of the container (types 5-7 on the Bristol Stool Chart below:

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on the surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

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Numbers & Notes

Preview

Useful Telephone Numbers

FY1/HO	
FY2/SHO	
Registrar	
Consultant	
Outreach Team	
Critical Care/ITU	
Microbiology Lab	
Biochemistry Lab	
Haematology Lab	
Transfusion	
Radiology	
Pharmacy	

Please feel free to alert me to items you feel this book misses and that are needed via www.microbiologynutsandbolts.co.uk. They will be considered for future editions.

Sources of Information and Further Reading

1. Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. Gould K, Denning D, Elliott T *et al.* J Antimicrob Chemother 2012; 67: 269–289
2. British Society for Antimicrobial Chemotherapy Methods for Antimicrobial Susceptibility Testing. Wootton M, 2013
3. British National Formulary (BNF) www.bnf.org
4. British National Formulary for Children (cBNF)
5. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 7th edition. Churchill Livingstone, 2009
6. The Renal Drug Handbook, 3rd edition. Ashley C, Currie A. Radcliffe Publishing Ltd, 2008
7. Control of Communicable Diseases Manual, 19th edition. Heymann D. American Public Health Association, 2008
8. Immunisation Against Infectious Disease, Salisbury D, Ramsay M. Department of Health, 2006
9. The Flesh and Bones of Medical Microbiology. Guyot A, Schelenz S, Myint S, Mosby, 2010

Useful websites

1. Infectious Diseases Society of America, www.idsociety.org
2. British Society for Antimicrobial Chemotherapy, www.bsac.org.uk
3. The Hospital Infection Society, www.his.org.uk
4. British Infection Association www.britishinfection.org
5. Learn Infection (British Infection Association) www.learninfection.org.uk
6. Surviving Sepsis Campaign www.survivingsepsis.org
7. Meningitis Research Foundation www.meningitis.org
8. National Institute for Health and Care Excellence www.nice.org.uk

Commonly Used 1st Line Antibiotics

The list below is not exhaustive and may be used when there is no access to local guidelines. See sections – Antibiotics, Adult Empirical Antibiotic Guidelines for 2nd line antibiotics and Paediatrics Guidelines for children.

Infections	1st Line Antibiotic
Community Acquired Pneumonia (CAP) (CURB 0-2)	PO Amoxicillin 500mg-1g TDS PLUS PO Clarithromycin 500mg BD (If Nil By Mouth use IV)
Community Acquired Pneumonia (CAP) (CURB 3-5)	IV Co-amoxiclav 1.2g TDS PLUS IV Clarithromycin 500mg BD If MRSA ADD IV Teicoplanin 400mg BD for 3 doses THEN OD (OR 6mg/kg if >70kg)
Hospital Acquired Pneumonia (HAP) Onset 2-4 days after admission	IV Co-amoxiclav 1.2g TDS If MRSA ADD IV Teicoplanin 400mg BD for 3 doses THEN OD (OR 6mg/kg if >70kg)
Hospital Acquired Pneumonia (HAP) Onset ≥4 days after admission	IV Piptazobactam 4.5g TDS If MRSA ADD IV Teicoplanin 400mg BD for 3 doses THEN OD (OR 6mg/kg if >70kg)
Infective Exacerbation of COPD	PO Amoxicillin 500mg TDS
Pyelonephritis	IV Co-amoxiclav 1.2g TDS PLUS IV Gentamicin as per renal function
Cellulitis	IV Flucloxacillin 1-2g QDS
Cellulitis (if MRSA positive)	IV Teicoplanin 400mg BD for 3 doses THEN OD (OR 6mg/kg if >70kg)
Osteomyelitis OR Septic Arthritis	IV Flucloxacillin 1-2g QDS PLUS PO Fusidic Acid 500mg TDS
Prosthetic Joint OR Osteomyelitis* OR Septic Arthritis* (*if MRSA positive)	IV Teicoplanin 400mg BD for 3 doses THEN OD (OR 6mg/kg if >70kg) PLUS PO Fusidic Acid 500mg TDS
<i>Clostridium difficile</i> Associated Disease	PO Metronidazole 400mg TDS
Emergencies	
Sepsis	IV Piptazobactam 4.5g TDS PLUS IV Gentamicin as per renal function If MRSA ADD IV Teicoplanin 400mg BD for 3 doses THEN OD (OR 6mg/kg if >70kg)
Meningitis	IV Cefotaxime 2g QDS OR IV Ceftriaxone 2g BD
Meningitis (if Listeria suspected)	IV Cefotaxime 2g QDS OR IV Ceftriaxone 2g BD PLUS IV Amoxicillin 2g 4 hourly

Adult Sepsis "Golden-Hour" Management Flowchart

First Hour of Surviving Sepsis - "Golden Hour"

Call for senior support immediately
+/- Critical Care

Give high flow O₂

Fluid resuscitate
If hypotensive or lactate >4mmol/L

Target

CVP 8-12mmHg
MABP ≥65mmHg
Urine output ≥0.5ml/kg/hr
Venous O₂ Sats ≥65%

Administer

1000ml crystalloid over 30mins
OR 300-500ml colloid over 30mins

Blood Cultures

Take 2 sets of blood cultures
(at least 1 set peripherally)

DO NOT unnecessarily delay antibiotics

Antibiotics

Give antibiotics within 1 hour of diagnosing sepsis

Warning

Delaying antibiotics in the first 6 hours
increases mortality by 7% per hour

Evaluate for focus of infection

Implement source control if possible e.g.
drainage of abscess

Further Treatment

Treat as per the management plan from
seniors or critical care or
www.survivingsepsis.org

Preview