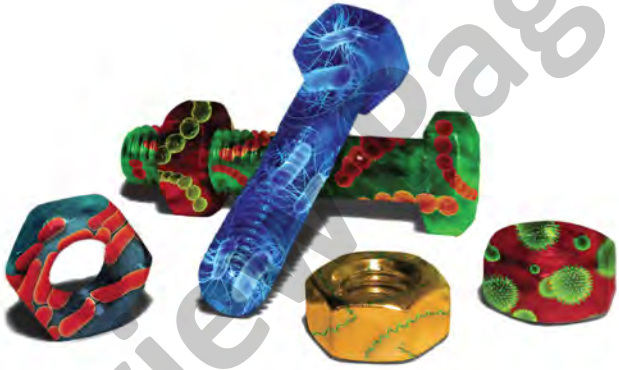
# Microbiology Nuts & Bolts



## Key Concepts of Microbiology & Infection

**3rd Edition**

Dr David Garner
BM MSc MRCPCH FRCPath

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**Table of Contents**

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**Hard work, artwork and front cover:** J Garner
**Editor Chief in Charge:** J Garner

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 are still helping and hindering in equal measure and using inappropriate terms in an untimely manner such as “that should be straight-forward” and “it will be simple”!



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

www.microbiologynutsandbolts.co.uk

## Introduction

Microbiology Nuts & Bolts helps doctors and healthcare staff to confidently identify the microorganisms causing an infection and understand how to treat them. The book is set out by condition rather than microorganism allowing for quick reference in a clinical setting. Readers regularly comment just how amazing it is that so much information has been packed into such a small book. It is not an all-encompassing reference text and is deliberately not referenced extensively in order to keep its presentation simple. It is 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 microorganisms, their management and the treatment of patients. It has received fantastic feedback in reviews by the Royal College of Physicians, the Royal College of Pathologists, the Royal Pharmaceutical Society, the Hospital Infection Society, the British Society for Antimicrobial Chemotherapy, the Institute of Biomedical Science and the Society for Applied Microbiology.

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 first, as this gives the building blocks to understanding infection. After that, the Clinical Scenarios and Antibiotics sections aid diagnosis and management of 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 into 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 previous editions were well received by doctors and healthcare staff and as always their valuable feedback has been instrumental in shaping this, the latest edition. Existing sections have been fully updated and new sections have been added for acute bronchitis, necrotising pancreatitis and Lyme disease as well as new antibiotics and updates for the management of sexually transmitted infections and infection control precautions for viral haemorrhagic fevers. The Emergencies section has undergone extensive revision to take into account changes in UK national guidelines for the management of sepsis, meningitis, encephalitis and malaria. The size has also changed to accommodate larger text but we hope it still remains small enough to be your go to pocket book.

We have been asked many times why is there no App for Microbiology Nuts & Bolts? The short answer is that Apps are great at giving answers but less able to “teach”, leading to healthcare staff blindly following algorithms and proformas instead of understanding the fundamental principles of medicine…so no, there is no App!

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 is a success.

**P.S.** Don’t forget to write a review on Amazon and like us on FaceBook where you’ll find the latest edition of the Bug Blog.

## About the Author

The author has been described as a gifted teacher and educator, who has an exceptional level of microbiology and infectious diseases knowledge, with an even greater ability to translate that knowledge so that others can also understand this often complicated subject. His award-winning teaching is the highlight of many medical students' clinical attachments and as a result of his dedication to the subject, many junior colleagues have been motivated and inspired to enter a career in Microbiology.

He qualified from Southampton University Medical School in 1997 and has worked in diverse areas of medicine, general surgery, emergency medicine and paediatrics. Now, as a Consultant Clinical Microbiologist in a United Kingdom NHS hospital, he spends his days diagnosing, treating and managing infections as well as teaching others how to do this safely and effectively.

Microbiology textbooks often considered by students to be dull and contain long lists of boring bacterial names; they appear to have little relevance to clinical medicine. The author recognised there was a need for a clinically-orientated no-nonsense microbiology book, so he decided to get on and write one. The feedback has been amazing, with both the first and second editions of Nuts & Bolts regularly making the list of top 3 microbiology textbooks on Amazon.co.uk. The website and accompanying Bug Blog are read worldwide by thousands of interested people every week and it is clear that many of you out there really value "Nuts & Bolts".

The author is ever grateful for your continuing support.

**www.microbiologynutsandbolts.co.uk**

## What is Infection? Infection vs. Colonisation vs. Contamination

**Infection** is the presence of microorganisms 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 with associated inflammation and tissue damage.

Microorganisms 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* spp. 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* spp. 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 bloodstream from the oropharynx to cause septicaemia, then it needs urgent treatment.

### Examples of colonisation

| **Body Site or Prosthetic Device** | **Bacterial Colonisation** |
|---|---|
| Pressure sores | • Skin flora e.g. *Staphylococcus* spp.<br>• Enteric flora e.g. *Enterococcus* spp., *Escherichia coli*, *Pseudomonas* spp. |
| Breaks in the skin e.g. wounds | • Skin flora e.g. *Staphylococcus* spp.<br>• Enteric flora e.g. *Enterococcus* spp., *Escherichia coli*, *Pseudomonas* spp. |
| Upper respiratory tract | • Mixed enteric flora in patients given antibiotics or who have been in healthcare settings for more than 4 days e.g. *Enterococcus* spp., *Escherichia coli*, *Pseudomonas* spp. |
| Urinary catheter | • Enteric flora e.g. *Enterococcus* spp., *Escherichia coli*, *Pseudomonas* spp. |
| Endotracheal tube **OR** Tracheostomy tube in a ventilated patient | • Mixed enteric flora in patients given antibiotics or who have been in healthcare settings for more than 4 days e.g. *Enterococcus* spp., *Escherichia coli*, *Pseudomonas* spp. |

**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.

**Contamination** is the presence of a microorganism that has been introduced into a microbiology sample from an external source e.g. poor technique when taking the sample, a swab touching a surface before being used, sneezing over a patient whilst they provide a sputum sample. Contamination can also occur when a sample is not collected correctly and the patients "normal flora" (microorganisms growing in their normal environment) gets into the sample e.g. urine taken incorrectly can contact perineal skin and pick up the "normal microorganisms" which then grow in the laboratory (the presence of epithelial cells in the urine sample indicates definite contact with skin and therefore a risk of contamination).

## 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 infections. 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 microorganism 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.

## Bacteraemia vs. Septicaemia

Many healthcare professionals use the terms bacteraemia and septicaemia to mean the same thing, however they are different. **Bacteraemia** is the presence of bacteria in blood. **Septicaemia** is the presence of bacteria in blood **PLUS** clinical features of sepsis e.g. temperature >38.3°C or <36°C, heart rate >90bpm, respiratory rate >20 bpm, WBC $<4x10^9$/L or $>12x10^9$/L, blood glucose >7.7mmol/L or altered mental state (see section – Emergencies, Sepsis). **WARNING:** patients can be septic without being septicaemic if they have the clinical features of sepsis but do not have bacteria in their blood.

A patient can be bacteraemic without being septicaemic **BUT** cannot be septicaemic without being bacteraemic.

Bacteraemia may be:

- **Significant** causing the patients infection or indicating where the infection is occurring e.g. *E. coli* in pyelonephritis, *Staphylococcus aureus* in cellulitis or Alpha-haemolytic *Streptococcus* spp. in infective endocarditis
- **Non-significant** a contaminant in the specimen (e.g. coagulase-negative *Staphylococcus* spp. from skin) or temporarily in the blood from another site, known as "translocation" e.g. bacteria can be pushed into blood by simply brushing your teeth (Alpha-haemolytic *Streptococcus* spp.), grazing your leg (coryneform bacteria) or squeezing a big spot (*Staphylococcus aureus*). None of these are a "problem" as the body "deals" with them and "clears" the blood

**BUT** the examples use the same bacteria! How do you know if they are significant or not? Answer: do they have the clinical features of the infection? E.g. *Staphylococcus aureus* in cellulitis presents with a hot, red, swollen leg whereas non-significant bacteraemia has no symptoms or signs, the test was just done at an opportune moment to "catch" the presence of, or be contaminated by, the bacteria.

## Types of Infectious Microorganisms

### Bacteria

Bacteria are free-living single cell microorganisms with no cell nucleus. Their genes are found on chromosomes, free within the cell cytoplasm. They reproduce by cell division to create identical daughter cells (clonal expansion). Bacteria are widely spread throughout the environment with only a small number causing human disease. There are approximately 15,000 times more bacteria on 1 human, than humans on the earth. You can see them with a light microscope in a laboratory. Examples: *Staphylococcus aureus*, *Escherichia coli*, *Listeria monocytogenes*.

### Viruses

Viruses are small microorganisms consisting of genetic elements surrounded by a protein coat. They cannot self-replicate. Viruses invade other cells and use their host's reproductive mechanism to replicate. They are too small to be seen with a light microscope and can only be seen with an electron microscope. Examples: *Varicella Zoster Virus* (VZV), *Influenza Virus*, *Rhinovirus*.

### Parasites

Parasites are organisms that grow on, feed off and are sheltered by another living organism but which contribute nothing to the survival of that organism. They are often multi-cellular and relatively large compared to bacteria and viruses. All are visible with a light microscope but some are large enough to see with the naked eye. A female *Ascaris* roundworm can be up to 30cm long. They usually reproduce by sexual reproduction. Examples: *Plasmodium falciparum* (malaria), *Giardia lamblia*, *Ascaris lumbricoides*.

### Fungi

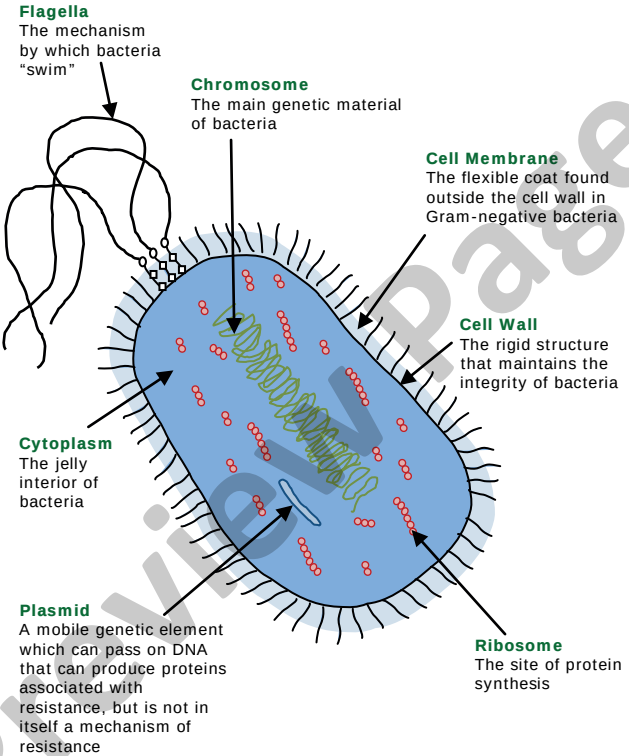
Fungi are multi-cellular organisms with eukaryotic DNA and a chitinous cell wall. They feed on organic matter and produce spores which can survive for long periods of time in the environment. These spores aid the spread of the fungi. Fungi are usually bigger than bacteria and are visible with a light microscope and occasionally with the naked eye. They usually reproduce by sexual reproduction. Examples: *Candida albicans*, *Aspergillus* spp., *Mucor* spp. (Zygomycetes).

### Prions

Prions are infectious proteins folded in an abnormal way. When they enter another cell they cause all the similar proteins to refold in the abnormal fashion resulting in disease. They are very rare and not considered further in this book. Examples: Creutzfeldt Jakob Disease (CJD), Kuru, Bovine Spongiform Encephalopathy (BSE).

## The Anatomy of a Bacterium

Bacteria are the most common microorganisms treated with specific antibiotics. Antibiotics have different mechanisms of action related to which part of the bacterium they act upon; therefore it is helpful to know the basic anatomy of a bacterium.



## What is Normal Flora and why is it Important?

Normal flora is the community of microorganisms that live on another living organism (human or animal) or inanimate object without causing disease. The human body is not sterile; we become colonised with 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 prevent us being colonised with dangerous bacteria, which might lead to infection.

**Microbiome** is the term for a community of normal microorganisms.
**Dysbiosis** is the term for the disruption of the microbiome, removing normal microorganisms or the growth of abnormal microorganisms.

Many circumstances can change normal flora. For example, the 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 as *E. coli* is part of the normal gastrointestinal flora, or growth of an Alpha-haemolytic *Streptococcus* sp. in blood cultures may indicate infective endocarditis as a result of poor dentition as Alpha-haemolytic *Streptococcus* spp. are part of the normal mouth flora

Nothing is 100% accurate but knowing where bacteria normally live can help work out when they are in the wrong place. This allows predictions of the likely causes of disease and hence the choice of suitable antibiotics for empirical therapy. Knowing which 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 bacterium 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.

## How to Take Microbiology Specimens

### Aseptic Technique

Aseptic technique is a procedure that is designed to minimise contamination. 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 (MSU) - part the labia or retract the foreskin, void the first part of the urine stream (10-20mls at least) and then collect the next portion (approx. 10-20mls)
- Wound swabs - remove slough (which is dead and detached tissue and is not a sign of infection), debride the wound to reveal the fresh tissue beneath, swab the fresh tissue
- 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 a sample 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, microorganisms 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 microorganisms names and provide antibiotic **sensitivities**. Microscopy, Culture and Sensitivities are often abbreviated to MC&S.

**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:

**Result**

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

The microscopy shows a mixture of bowel flora, but the *Enterococcus faecium* is the only bacterium 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.

## A to Z of Microbiology Tests by Microorganism or Condition

Information is based upon a District General Hospital laboratory service.

| Microorganism or Condition | Test | Sample | Container |
|---|---|---|---|
| *Adenovirus* | PCR | NPA<br>Sputum<br>BAL<br>Stool | See Tests by Specimen Type Table |
| *Aspergillus* spp. | Galacto-mannan | Serum | Red or yellow vacutainer |
| | (1,3)-Beta-d-glucan | Serum | Red or yellow vacutainer |
| *Bartonella* spp. | IgM<br>IgG | Serum | Red or yellow vacutainer |
| *Bordetella pertussis* (Whooping cough) | IgG | Serum | Red or yellow vacutainer |
| | Culture | Pernasal swab | Pernasal swab |
| | PCR | NPA | Sterile universal |
| *Borrelia burgdorferi* (Lyme disease) | PCR | CSF | Sterile universal |
| | ELISA | Serum | Red or yellow vacutainer |
| *Brucella* spp. | IgM<br>IgG | Serum | Red or yellow vacutainer |
| *Candida* spp. | (1,3)-Beta-d-glucan | Serum | Red or yellow vacutainer |
| *Clostridium difficile* toxin | Toxin | Stool | Blue stool container |
| *Chlamydia* spp. | PCR | Swab | Red/Orange Chlamydia swab |
| *Coxiella burnetii* (Q fever) | IgM<br>IgG | Serum | Red or yellow vacutainer |

Laboratories may vary slightly, if in doubt check with your local service.

| Minimum Volume Required | Turnaround Time from Lab Receipt |
|---|---|
| See Tests by Specimen Type Table | 10 days |
| 1 tube | 7 days |
| 1 tube | 7 days |
| 1 tube | 14 days |
| 1 tube | 10 days |
| 1 swab | Up to 7 days |
| 2-5mls | 7 days<br>**Note:** all +ves are phoned out |
| 0.5-1ml | 2-5 days<br>**Note:** all +ves are phoned out |
| 1 tube | 3 days<br>(+ve samples sent to Ref Lab for confirmation) |
| 1 tube | 10 days |
| 1 tube | 7 days |
| 5ml | 1 day |
| Eyes - 2 swabs (1 per eye)<br>Genital - 1 swab | 3 days |
| 1 tube | 21 days |

## 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<br>- Amoxicillin sensitive<br>- 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 bacterium 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:**
Acutely hot, painful, swollen knee

**Result**

| | |
|---|---|
| Specimen | Synovial fluid |
| Appearance | Turbid |
| Microscopy | Gram-positive cocci in clumps |
| Culture | Staphylococcus aureus<br>- Flucloxacillin sensitive<br>- Fusidic Acid sensitive |

**How is this Interpreted?**
The presence of Gram-positive cocci 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:**
Acute confusion in an elderly patient
**Result**

| | |
|---|---|
| Specimen | Urine |
| Appearance | - |
| Microscopy | WBCs $<10x10^6$/L<br>Epithelial cells ++ |
| Culture | Pseudomonas aeruginosa |

**How is this Interpreted?**
The culture result cannot be interpreted without first assessing whether a UTI is likely from the microscopy. The absence of white blood cells ($<10x10^6$/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* spp. are not common causes of UTI except in the presence of a urinary catheter. Seek another reason for the confusion.

**Clinical Details on the request form:**
Left iliac fossa pain, diverticular abscess found at laparotomy
**Result**

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

**How is this Interpreted?**
The bacteria seen on microscopy are consistent with what has grown on culture, mixed bowel flora, and in keeping with the diagnosis of a diverticular abscess. There will be anaerobes present in a diverticular abscess because they make up most of the 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?**
No bacterial cause for the diarrhoea has been 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 microorganism has been seen not grown (you cannot grow a parasite). The treatment of giardiasis is PO Metronidazole. If the travel history had not been mentioned, the diagnosis would not have been made.

## Table of Bacterial Causes of Infection

✓ = Common Cause  – = Not a Common cause

| Clinical Scenarios | Gram-positive Bacteria | | | | | | | | Anaero- | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 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) | ✓1 | – | – | – | – | – | ✓ | – | – | – |
| Hospital Acquired Pneumonia (HAP) | ✓ | ✓ | – | – | – | – | ✓ | – | – | – |
| Ventilator Associated Pneumonia (VAP) | ✓ | ✓ | – | – | – | – | ✓ | – | – | – |
| Aspiration Pneumonia | ✓ | – | – | – | – | – | ✓ | – | – | – |
| Exacerbation of COPD | ✓ | – | – | – | – | – | ✓ | – | – | – |
| Acute Bronchitis | – | – | – | – | – | – | – | – | – | – |
| **Head and Neck Infections** | | | | | | | | | | |
| Otitis Media | – | – | – | – | – | – | ✓ | – | – | – |
| Otitis Externa | ✓ | – | – | ✓ | – | – | – | – | – | – |
| Orbital Cellulitis | ✓ | – | – | ✓ | – | – | ✓ | – | – | – |
| Sinusitis | ✓ | – | – | ✓ | – | – | ✓ | – | – | – |
| **Urogenital Infections** | | | | | | | | | | |
| Urinary Tract Infection (UTI) | – | – | – | – | – | – | – | – | – | – |
| Prostatitis | – | – | – | – | – | – | – | – | – | – |
| STDs | – | – | – | – | – | – | – | – | – | – |
| **Skin, Soft Tissue, Bone and Joint Infections** | | | | | | | | | | |
| Cellulitis | ✓ | ✓ | – | ✓ | – | – | – | – | – | – |
| Cellulitis in Diabetes & Vascular Insufficiency | ✓ | ✓ | – | ✓ | – | – | – | – | ✓ | – |
| Bites | ✓ | – | – | ✓ | – | – | – | – | ✓ | – |
| Burns, Skin Grafts, Post-Operative | ✓ | ✓ | – | ✓ | – | – | – | – | ✓ | – |
| Intravenous Device Associated Infection | ✓ | ✓ | – | – | – | – | – | – | – | – |
| Osteomyelitis | ✓ | ✓ | – | ✓ | – | – | – | – | – | – |
| Septic Arthritis | ✓ | ✓ | – | ✓ | – | – | – | – | – | – |

**?** = Uncommon Cause **OR** only under specific circumstances (see notes)

| **Gram-negative Bacteria** | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **bes** | | | | | | | | | **Non-Culturable** | | |
| Bacteroides fragilis | Neisseria meningitidis | Neisseria gonorrhoeae | Haemophilus influenzae | Escherichia coli | ESBL-positive Escherichia coli | Enterobacteriaceae | Pseudomonas aeruginosa | Moraxella catarrhalis | Legionella pneumophila | Mycoplasma pneumoniae | Chlamydia spp. |
| | | | | | | | | | | | |
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| – | – | – | – | – | – | ?4 | ?4 | – | – | – | – |
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## *Clostridium difficile* Associated Disease (CDAD)

The bacterium *Clostridium difficile* was reclassified in 2016 to *Clostridioides difficile* but as this has not yet become mainstream this book will continue to use the old name. It is the most common cause of antibiotic associated diarrhoea. It spreads very readily in the hospital environment unless infection control measures are put in place. Clinical features of *Clostridium difficile* Associated Disease (CDAD) range from asymptomatic carriage through to diarrhoea, toxic megacolon and death.

### Mode of Transmission

- Faecal-oral spread
- *Clostridium difficile* can survive for long periods of time in the environment as spores which, if not removed, can then infect new patients

### Incubation Period

- Unknown
- Symptoms can occur at any time after prescribing antibiotics, however usually 5-10 days

### Period of Communicability

- Patients should remain in isolation until 48 hours after symptoms resolve

### Best Practice Control Measures

| | |
|---|---|
| Careful antibiotic prescribing | Where possible avoid the use of antibiotics which are regarded as particularly predisposing to CDAD – the "**4Cs**"<br>• **C**ephalosporins<br>• **C**iprofloxacin and other quinolones<br>• **C**lindamycin<br>• **C**o-amoxiclav<br>Reduced Ciprofloxacin usage was the main driver for decreasing CDAD in the UK |
| Hand hygiene | With soap and water, alcohol gel is **NOT** effective |
| PPE | See section – Infection Control, Personal Protective Equipment<br>Remove **ALL** PPE before leaving room |
| Isolation | Side room preferably with own toilet facility |
| Environmental decontamination | Deep cleaning of the clinical area daily and after patient is discharged |
| Patient care | Accurate recording of symptoms<br>Stool sample for *Clostridium difficile* toxin testing<br>Do not prescribe anti-motility agents<br>If patients require investigations in other departments, inform those departments of patient's condition in advance<br>Patient should be last on a list and deep cleaning commence after patient's departure |

**Myth**
Antibiotics cause CDAD. **FALSE** - Antibiotics do not cause CDAD they only predispose to CDAD. If a patient does not come into contact with *Clostridium difficile* bacteria the patient will not get CDAD even if they have many predisposing factors (e.g. over 65 years old, cancer, bowel surgery, previous antibiotics, nasojejunal tubes, Proton Pump Inhibitors, hospitalisation or living in a long-term care facility). Eradicating *Clostridium difficile* from the environment by good cleaning practices is of fundamental importance in the control of CDAD.

The attitude that certain antibiotics should be avoided at all cost so as to avoid CDAD **is potentially dangerous**. The correct antibiotic for the infection should be given whilst being aware of the risk of predisposing to CDAD. For example, an elderly patient with urosepsis who is allergic to Penicillin, the doctors don't want to use Ciprofloxacin as it predisposes to CDAD and don't like using Gentamicin because it can cause renal failure. As a result they choose a seemingly random antibiotic such as Teicoplanin…Why? This is like putting diesel in a petrol car…it is simply wrong. The antibiotic needs to be active against the causative microorganism and able to penetrate the infected site.

Teicoplanin is probably the worst possible choice because it has no activity against the common causes of urosepsis and therefore the patient may die as a result of avoiding the use of Ciprofloxacin for fear of causing CDAD infection. Interestingly, doctors don't worry about prescribing Ceftriaxone for meningitis even though this antibiotic also predisposes to CDAD.

**Don't select the wrong antibiotic for the infection the patient currently has because you are worried they may acquire another infection in the future.**

**Warning**
In order to try and reduce the incidence of CDAD, hospitals are restricting the use of high risk predisposing antibiotics. As a result there is an increasing reliance on a small pool of antibiotics to treat a broad range of infections. The heavy use of these antibiotics is leading to increasing bacterial resistance. For example, an empirical guideline that uses a lot of Beta-lactam-Beta-lactamase inhibitor combinations (Co-amoxiclav and Piptazobactam) leads to increased numbers of infections with AmpC and ESBL-positive bacteria.

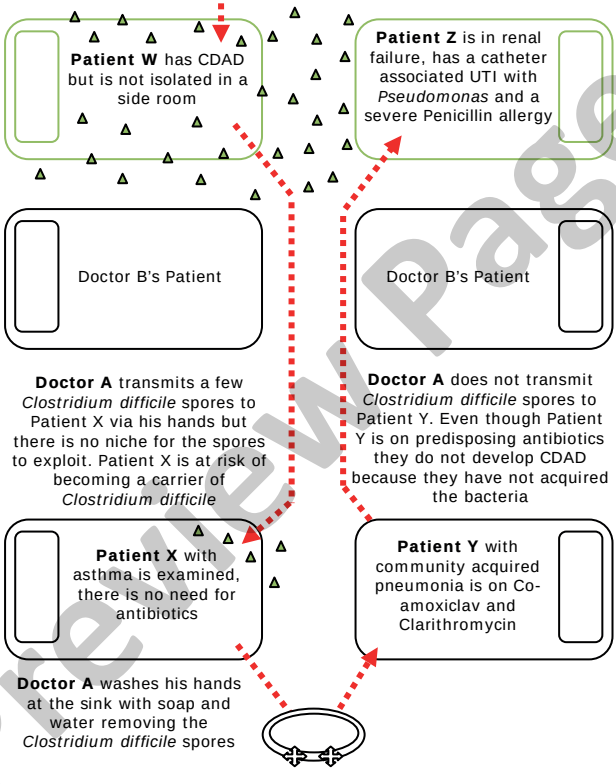
The increased rates of resistant bacteria mean an over reliance on carbapenem antibiotics (e.g. Meropenem); this has led to a rapid rise in carbapenemase producing Enterobacteriaceae. Not only are there no new antibiotics becoming available to treat these resistant bacteria, carbapenems also predispose to CDAD. Ultimately CDAD rates will increase while our ability to treat resistant infections decreases.

The current strategy of restricting antibiotics is storing up a problem for the future. Restrictive antibiotic guidelines put a strong selective pressure on bacteria that are far better at evolving than humans. Controlling CDAD in the environment may be a better long-term solution even though this proves harder to implement.

## How *Clostridium difficile* can Spread in a Ward Environment

**Doctor A** examines Patient W and diagnoses CDAD. He wrongly uses alcohol gel to clean his hands (alcohol gel does not kill spores △). Doctor A should have used soap and water and isolated patient W

**Doctor A** correctly gives Ciprofloxacin to Patient Z. Patient Z acquires *Clostridium difficile* spores from the environment, which exploit the niche left by Ciprofloxacin leading to Patient Z developing CDAD




The development of CDAD is often multi-factorial and there are many predisposing factors but ultimately the patient has to acquire the bacterium *Clostridium difficile* before they can develop CDAD or become a carrier of *Clostridium difficile*.

**The root cause for CDAD in Patient Z is failure to isolate Patient W in a side room NOT the antibiotic Ciprofloxacin**

## Diarrhoea and Vomiting (D&V)

Diarrhoea and vomiting is not a common cause of mortality amongst most people, however the old and frail or immunodeficient can die. The microorganisms that cause diarrhoea and vomiting are so infectious they easily spread around healthcare settings unless precautions are taken. The majority of cases are caused by viruses such as *Norovirus* and *Rotavirus*.

### Mode of Transmission

- Faecal-oral spread. In a patient with *Norovirus* each gram of stool contains approximately 10-100 million infectious doses of virus

### Incubation Period

- *Norovirus* - 24-48 hours
- *Rotavirus* - 24-72 hours

### Period of Communicability

- Up to 48 hours after symptoms resolve
- Virus is often still detectable at low levels in stool after symptoms resolve, so ongoing effective hand hygiene is essential

### Best Practice Control Measures

| | |
|---|---|
| Hand hygiene | With soap and water, alcohol gel is **NOT** effective |
| PPE | See section – Infection Control, Personal Protective Equipment<br>Remove **ALL** PPE before leaving room |
| Isolation | Side room preferably with own toilet facility |
| Ward closure | Only after advice from the Infection Control Team (ICT) and only if insufficient number of side rooms to isolate cases |
| Staffing | If ward closed, access to ward for essential staff only<br>Symptomatic staff must not return to work until 48 hours after last episode of diarrhoea or vomiting |
| Environmental decontamination | Deep cleaning of the clinical area daily and after patient is discharged |
| Patient care | Accurate recording of symptoms<br>Stool sample for testing under advice from ICT<br>Do not prescribe anti-motility agents<br>If patients require investigations in other departments, inform those departments of patient's condition in advance<br>Patient should be last on a list and deep cleaning commence after patient's departure |

**Hints and Tips**

Even with the very best cleaning regimens, a patient with diarrhoea will put their normal gastrointestinal flora into the environment whatever the cause of their diarrhoea. This can include Enterobacteriaceae, *Enterococcus* spp. and *Pseudomonas* spp. even though these are not causes of diarrhoea. If patients with diarrhoea due to the same cause (e.g. *Norovirus* or CDAD) were kept together in the same clinical area (cohorted) transfer of normal gastrointestinal flora will occur between patients. If one patient has antibiotic resistant bacteria in their normal flora e.g. GRE, then all cohorted patients will eventually acquire the antibiotic resistant bacteria. Therefore cohorting patients should be avoided, source isolation is best practice.

## Ventilator Associated Pneumonia (VAP)

Ventilator associated pneumonia (VAP) is pneumonia developing >48 hours after implementing endotracheal intubation or mechanical ventilation, which was not present before intubation.

### Clinical Features

- Patient mechanically ventilated for ≥ 48 hours **PLUS**
- New or worsening pulmonary infiltrates on chest X-ray **PLUS**
- Raised WBC **PLUS**
- Growth of a pathogenic bacterium at significant levels from a lower respiratory tract sample (aspiration or BAL)

### Causes

| | |
|---|---|
| Common | • *Staphylococcus aureus* (MSSA and MRSA)<br>• *Streptococcus pneumoniae*<br>• *Haemophilus influenzae*<br>• *Pseudomonas* spp.<br>• Enterobacteriaceae e.g. *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp., *Serratia marcescens* |

### Investigations

- Endotracheal secretions – culture and sensitivity indicates what a patient is colonised with, not necessarily what is causing the infection
- Bronchoalveolar lavage (BAL) - either directed or non-directed, bypassing upper respiratory tract flora, sampling directly from the lung
- Blood cultures – if systemic signs of infection

### Treatment

| | |
|---|---|
| 1st line | IV Piptazobactam |
| 2nd line (if 1st line contraindicated) | IV Teicoplanin **OR** IV Vancomycin<br>**PLUS**<br>IV Ciprofloxacin |
| If MRSA positive | **ADD** IV Teicoplanin **OR** IV Vancomycin |

### Total Duration

5-7 days

### Dosing

See section - Antibiotics, Empirical Antibiotic Guidelines.

**Warning**

Critical Care Units may have problems with specific bacteria, e.g. *Acinetobacter* spp., so be aware of your own unit's guidelines.

### Prognosis and Complications

25-75% mortality depending on underlying co-morbidities and infection with antibiotic resistant bacteria.

### Prophylaxis and Prevention

- Regular suctioning of pooled secretions in upper respiratory tract
- Sterile water for mouth washes
- Effective hand hygiene

## Infective Exacerbation of COPD

Infective exacerbation of COPD is the term used for worsening respiratory function in patients known to have chronic obstructive pulmonary disease (COPD).

### Clinical Features

- Increasing shortness of breath
- Increasingly purulent sputum
- Increasing amount of sputum
- Chest X-ray **DOES NOT** show changes indicative of pneumonia; if it does then treat for pneumonia not infective exacerbation of COPD

### Causes

| | |
|---|---|
| Viral | • *Respiratory Syncytial Virus* (RSV)<br>• *Rhinovirus*<br>• *Influenza Virus*<br>• *Parainfluenza Virus*<br>• *Adenovirus* |
| Bacterial | • *Streptococcus pneumoniae*<br>• *Staphylococcus aureus*<br>• *Haemophilus influenzae*<br>• *Moraxella catarrhalis* |

### Investigations

- Sputum culture may help identify the causative microorganism, but may only isolate upper respiratory tract normal flora

### Treatment

| | |
|---|---|
| 1st line | PO Amoxicillin |
| 2nd line (if 1st line contraindicated) | PO Clarithromycin **OR** PO Doxycycline |

### Total Duration

5-7 days

### Dosing

See section - Antibiotics, Empirical Antibiotic Guidelines.

### Prognosis and Complications

Most patients get better with treatment.

### Prophylaxis and Prevention

Prophylactic antibiotics should be avoided; although they may reduce the frequency of exacerbations ultimately they tend to lead to increasingly resistant bacteria within the patient's normal flora. This results in increasingly difficult-to-treat infections with a higher mortality.

## Antimicrobial Stewardship

It is widely acknowledged that 50% of antibiotic prescriptions are inappropriate; meaning that the antibiotic is incorrect for the condition, the dose is wrong or infection is not the actual diagnosis, therefore antibiotics are not the correct management. Global antibiotic resistance is becoming increasingly prevalent and worryingly the world faces a post-antibiotic era where there are no longer antibiotics to treat common infections.

Antimicrobial stewardship is the response to the increasing misuse of antibiotics. It promotes the use of the right antibiotic, at the right dose, route and duration, for the right infection at the right time in order to improve patient care whilst reducing antibiotic resistance. At the forefront of this fight are Antimicrobial Pharmacists; specialist clinical pharmacists who help optimise antibiotic use within hospitals and the community.

**Common Mistakes in prescribing antibiotics**

- Using antibiotics that do not cover the causes of the infection
- Unnecessary use of broad-spectrum (or narrow-spectrum) antibiotics
- Prescribing antibiotics where there is no evidence of infection
- Unnecessarily long courses of antibiotics
- Incorrect dosing
- Overuse of intravenous antibiotics
- Delaying antibiotics in the critically ill
- Failing to modify antibiotic treatments when microbiology results are available

**The Role of the Antimicrobial Pharmacist involves:**

- Expert advice regarding antibiotic usage in specific individual patients in conjunction with Microbiologists or Infectious Diseases Physicians
- Participation in Route Cause Analysis (RCA) for cases of Healthcare Associated Infections e.g. *Clostridium difficile* Associated Disease and MRSA bacteraemias
- Educating healthcare staff about prudent antibiotic usage
- Developing evidence-based guidelines for:
  - Empirical antibiotic treatment and surgical prophylaxis
  - Restricted antibiotics which specifically require the approval of a Microbiologist or Infectious Diseases Physician before their use
  - Intravenous to oral switching to reduce the unnecessary use of IV antibiotics
  - Stop and review to reduce unnecessarily long courses of antibiotics
- Providing clinical tools such as antibiotic drug charts to facilitate compliance with guidelines
- Surveillance and audit of antibiotic usage to ensure compliance with guidelines
- Antibiotic formulary decision-making and horizon-scanning for information about new antibiotics
- Representation at Infection Prevention and Control Committees and Antibiotic Steering Groups (sub-committees of Hospital Drug and Therapeutic Committees)

## How Antibiotics Work - Mechanisms of Action

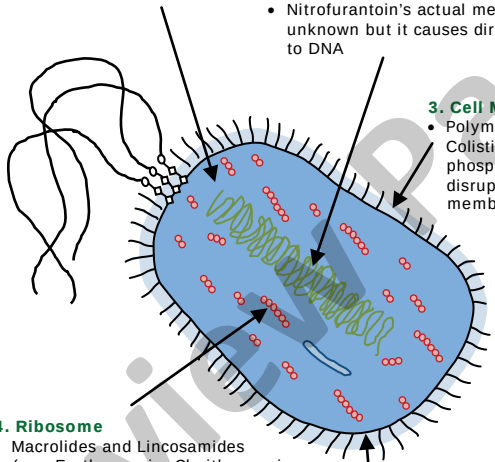
Essentially there are only 5 basic mechanisms of action or sites where the antibiotic works, either in the bacterium's cytoplasm, on its chromosome, at its cell membrane, on its ribosome or its cell wall. The flagella and plasmid have no role in antibiotic mechanisms of action.

**1. Cytoplasm**

- Nitroimidazoles (e.g. Metronidazole) produce oxygen free radicals which damage proteins and DNA
- Lipopeptides (e.g. Daptomycin) depolarise cell membranes inside the cell

**2. Chromosome**

- Diaminopyramidines (e.g. Trimethoprim) interfere with folic acid synthesis
- Quinolones (e.g. Ciprofloxacin, Levofloxacin) inhibit DNA coiling
- Rifampicin and Fidaxomicin inhibit RNA polymerase
- Nitrofurantoin's actual mechanism is unknown but it causes direct damage to DNA



**3. Cell Membrane**

- Polymyxin (e.g. Colistin) binds to phospholipids disrupting the cell membrane

**4. Ribosome**

- Macrolides and Lincosamides (e.g. Erythromycin, Clarithromycin, Azithromycin, Clindamycin) prevent protein elongation and inhibit ribosome formation
- Aminoglycosides (e.g. Gentamicin, Amikacin, Tobramycin) interfere with translation and protein formation
- Tetracyclines and Glycylcyclines (e.g. Doxycycline, Tigecycline) prevent protein synthesis
- Oxazolidinones (e.g. Linezolid) prevent ribosome formation
- Fusidic Acid blocks elongation factor G, preventing protein formation
- Chloramphenicol inhibits protein synthesis
- Nitrofurantoin's actual mechanism is unknown but it interferes with translation

**5. Cell Wall**

- Beta-Lactams (e.g. Penicillins, Cephalosporins, Carbapenems) inhibit cell wall formation
- Glycopeptides (Vancomycin, Teicoplanin) prevent peptidoglycan cross-linkage
- Fosfomycin blocks peptidoglycan synthesis

## How to Choose an Antibiotic

Before deciding whether to prescribe an antibiotic there are a number of things to consider and questions to ask. Firstly:

- Make sure you know normal flora and the causes of common infections
- Know your speciality's serious and common infections, the microorganisms that cause these and the usual treatments for them
- Use the British National Formulary (BNF) for interactions, cautions and contraindications as well as dosing information
- Discuss patients with your own senior team members and Consultant
- Know your own hospital's empirical antibiotic guidelines for your specialty

Empirical antibiotic guidelines are established by answering many of the questions below. It is essential to understand the relevance of these questions and the effect of the answers. Relying on empirical antibiotic guidelines without knowing why or how these guidelines are produced can be dangerous and is poor practice.

### Questions to ask:

| | |
|---|---|
| Does the patient have an infection? | There are many non-infectious reasons for "signs of infections"<br>• Fever caused by drugs, malignancy, connective tissue disorders<br>• Increased CRP caused by inflammation, malignancy, connective tissue disorders<br>• Chest crackles caused by heart failure, pulmonary fibrosis<br>• Pyuria caused by appendicitis, connective tissue disorders, malignancy |
| If the patient has an infection what is the likely source? | Urine, respiratory tract, skin, bone, joint, heart, CNS etc.... |
| What are the likely causative microorganisms? | Viruses, bacteria, fungi, parasites |
| Does the patient need an antibiotic or is the infection self-limiting? | • Viral infections are usually self-limiting<br>• Urethral syndrome and gastroenteritis do not usually require antibiotics |
| Does the patient need urgent treatment or is there time to make a diagnosis? | There is often time to make a diagnosis before starting treatment **HOWEVER** certain infections require immediate management without waiting for investigations:<br>• Sepsis<br>• Neutropaenic sepsis<br>• Meningitis<br>• Meningococcal sepsis<br>• Encephalitis<br>• Epiglottitis<br>• Spinal epidural abscess<br>• Necrotising fasciitis<br>• Toxic shock syndrome |
| Is the antibiotic active against the microorganisms? | See section<br>- Antibiotics, Table of Antibiotic Spectrum of Activity |

| | |
|---|---|
| Does the antibiotic get into the site of infection? | See section<br>- Antibiotics, Table of Antibiotic Tissue Penetration |
| Does the patient need a bactericidal antibiotic or is bacteriostatic adequate? | Immunodeficient patients require bactericidal antibiotics because they are unable to fight infections themselves |
| What route of administration should be used? | • **DO NOT** use oral antibiotics to treat systemic infections if patients are unable to absorb from the gastrointestinal tract<br>• Antibiotics with good oral bioavailability rarely need to be given intravenously (see section – Antibiotics, for individual antibiotic agents) |
| How much antibiotic should be prescribed? | • Patients in renal failure may need doses of antibiotics reducing<br>• Patients over 60-70kg may need increased doses of antibiotics as normal doses are calculated for previously normal body size (see section – Antibiotics, Antibiotic Dosing in Obesity) |
| Are there any contraindications or cautions for prescribing this antibiotic? | • **DO NOT** use any Beta-lactam antibiotics if the patient has a history of severe penicillin allergy<br>• Many antibiotics interact with Methotrexate e.g. Trimethoprim, Ciprofloxacin, Doxycycline<br>• Many antibiotics are contraindicated in myasthenia gravis e.g. macrolides, quinolones, aminoglycosides, Colistin<br>• Always check the BNF for interactions, cautions and contraindications as well as dosing information |
| What are the side effects of this antibiotic? | See section<br>- Antibiotics, for individual antibiotic agents<br>• Always check the BNF for side effects |
| When should the patient be reviewed? | • Septic patients should be reviewed within 1 hour of starting treatment<br>• Daily review of **ALL** patients on antibiotics<br>• Don't forget "stop and review" dates as these help prevent over-treatment and CDAD |
| When can I switch from IV to oral, and how long should I treat the patient for? | See sections<br>- Clinical Scenarios, for individual conditions<br>- Antibiotics, IV to Oral Switching of Antibiotics |
| Do the results of the microbiology investigations identify a specific causative microorganism? | Once the cause is known, antibiotics should be narrowed down to cover the specific microorganisms identified e.g. CAP caused by *Streptococcus pneumoniae* can be treated with Penicillin rather than Co-amoxiclav and Clarithromycin |

## Table of Antibiotic Spectrum of Activity

✓ = Usually sensitive  – = usually resistant **OR** inappropriate therapy

| Antibiotic | Gram-positive Bacteria | | | | | | | | Anaero- | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 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 | ✓ | – | ? | ✓ | – | – | ✓ | – | – | – |
| Temocillin | – | – | – | – | – | – | – | – | – | – |
| Pivmecillinam Hydrochloride | – | – | – | – | – | – | – | – | – | – |
| Piptazobactam | ✓ | – | – | ✓ | ✓ | – | ✓ | – | ✓ | – |
| **Cephalosporins** | | | | | | | | | | |
| Cefradine | ✓ | – | ? | ✓ | – | – | ✓ | – | – | – |
| Cefalexin | ✓ | – | ? | ✓ | – | – | ✓ | – | – | – |
| Cefuroxime | ✓ | – | ? | ✓ | – | – | ✓ | – | – | – |
| Ceftriaxone / Cefotaxime | ✓ | – | – | ✓ | – | – | ✓ | – | – | – |
| Ceftazidime | – | – | – | – | – | – | – | – | – | – |
| Ceftazidime + Avibactam | – | – | – | – | – | – | – | – | – | – |
| Ceftolozane + Tazobactam | – | – | – | – | – | – | – | – | – | – |
| Ceftaroline | ✓ | ✓ | ✓ | ✓ | – | – | ✓ | – | ✓ | – |
| **Carbapenems** | | | | | | | | | | |
| Ertapenem | ✓ | – | – | ✓ | ✓ | – | ✓ | – | ✓ | – |
| Meropenem | ✓ | – | – | ✓ | ✓ | – | ✓ | ✓ | ✓ | – |
| **Diaminopyramidines** | | | | | | | | | | |
| Trimethoprim | ? | ? | – | – | – | – | – | – | – | – |
| **Macrolides and Lincosamides** | | | | | | | | | | |
| Erythromycin | ✓ | ? | – | ✓ | – | – | ✓ | – | – | – |
| Clarithromycin | ✓ | ? | – | ✓ | – | – | ✓ | – | – | – |
| Azithromycin | ✓ | – | – | ✓ | – | – | ✓ | – | – | – |
| Clindamycin | ✓ | ? | – | ✓ | – | – | ✓ | – | ✓ | – |

**?** = Variable sensitivity **P** = Prophylaxis only

| Gram-negative Bacteria | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **bes** | | | | | | | | | **Non-Culturable** | | |
| Bacteroides fragilis | Neisseria meningitidis | Neisseria gonorrhoeae | Haemophilus influenzae | Escherichia coli | ESBL-positive Escherichia coli | Enterobacteriaceae | Pseudomonas aeruginosa | Moraxella catarrhalis | Legionella pneumophila | Mycoplasma pneumoniae | Chlamydia spp. |
| | | | | | | | | | | | |
| – | ✓ | ? | – | – | – | – | – | – | – | – | – |
| – | ✓ | ? | ? | ? | – | – | – | – | – | – | – |
| ✓ | – | ? | ✓ | ✓ | – | ?1 | – | ✓ | – | – | – |
| – | – | – | – | – | – | – | – | – | – | – | – |
| – | – | – | ✓ | ✓ | ✓ | ✓ | – | ✓ | – | – | – |
| – | – | – | – | ✓ | ✓ | ✓ | – | – | – | – | – |
| ✓ | – | – | ✓ | ✓ | – | ✓1 | ✓ | ✓ | – | – | – |
| | | | | | | | | | | | |
| – | – | – | – | ✓ | – | – | – | – | – | – | – |
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| – | – | – | ✓ | ✓ | – | ? | – | ✓ | – | – | – |
| – | ✓ | ✓ | ✓ | ✓ | – | ✓2 | – | ✓ | – | – | – |
| – | – | – | ✓ | ✓ | – | ✓2 | ✓ | ✓ | – | – | – |
| – | – | – | ✓ | ✓6 | ✓6 | ✓6 | ✓6 | ✓ | – | – | – |
| – | – | – | ✓ | ✓ | ✓ | – | ✓ | ✓ | – | – | – |
| – | – | – | ✓ | ✓ | – | ✓2 | – | ✓ | – | – | – |
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| – | – | – | – | – | – | – | – | ✓ | ✓ | ✓ | ✓ |
| – | – | – | – | – | – | – | – | ✓ | ✓ | ✓ | ✓ |
| – | – | – | – | – | – | – | – | ✓ | ✓ | ✓ | ✓ |
| ✓ | – | – | – | – | – | – | – | ✓ | – | – | – |

## Adult Empirical Antibiotic Guidelines

| Respiratory Infections | 1st Line Antibiotic |
|---|---|
| Community Acquired Pneumonia (CAP) (CURB-65 score 0-2) | PO Amoxicillin 500mg-1g TDS<br>**PLUS**<br>PO Clarithromycin 500mg BD<br>(If Nil By Mouth use IV) |
| Community Acquired Pneumonia (CAP) (CURB-65 score 3-5) | IV Co-amoxiclav 1.2g TDS<br>**PLUS**<br>IV Clarithromycin 500mg BD<br><br>If MRSA **ADD** IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) |
| Community Acquired Aspiration Pneumonia | IV Co-amoxiclav 1.2g TDS<br><br>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<br><br>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<br><br>If MRSA **ADD** IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) |
| Hospital Acquired Aspiration Pneumonia | IV Piptazobactam 4.5g TDS<br><br>If MRSA **ADD** IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) |
| Ventilator Associated Pneumonia (VAP) | IV Piptazobactam 4.5g TDS<br><br>If MRSA **ADD** IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) |

| **2nd line Antibiotic** (if 1st line contraindicated) | **Oral Treatment** (when appropriate) | **Duration** |
|---|---|---|
| PO Doxycycline 200mg stat **THEN** 100mg OD **OR** PO Levofloxacin 500mg BD (If Nil By Mouth use IV) | As for 1st and 2nd line | 5-7 days |
| IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) **PLUS** PO Levofloxacin 500mg BD (If Nil By Mouth use IV) | PO Co-amoxiclav 625mg TDS **PLUS** PO Clarithromycin 500mg BD **OR** PO Levofloxacin 500mg BD | 7 days |
| IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) **PLUS** IV Ciprofloxacin 400mg BD-TDS **AND** IV Metronidazole 500mg TDS | PO Co-amoxiclav 625mg TDS | 5-7 days |
| IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) **PLUS** PO Levofloxacin 500mg BD | PO Co-amoxiclav 625mg TDS | 5-7 days |
| IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) **PLUS** IV Ciprofloxacin 400mg BD-TDS | PO Co-amoxiclav 625mg TDS depending on culture results | 5-7 days |
| IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) **PLUS** IV Ciprofloxacin 400mg BD-TDS **AND** IV Metronidazole 500mg TDS | PO Co-amoxiclav 625mg TDS depending on culture results | 5-7 days |
| IV Teicoplanin 400mg BD for 3 doses **THEN** OD (or 6mg/kg if >70kg) **PLUS** IV Ciprofloxacin 400mg BD-TDS | No oral treatment | 5-7 days |

## Sepsis

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Septic shock is sepsis with circulatory, cellular or metabolic dysfunction, and has a high mortality.

Sepsis and septic shock are clinical diagnoses not laboratory diagnoses:

- **Sepsis** - infection with evidence of a systemic response to that infection e.g. hypoxia, oliguria, confusion
- **Septic shock** - sepsis associated with organ dysfunction, hypoperfusion or hypotension

**Sepsis and septic shock are medical emergencies and early recognition and treatment improve survival.**

### Risk Factors for Sepsis

- Age <1 year or >75 years
- Frailty or comorbidities e.g. diabetes, renal failure, liver failure
- Trauma, surgery or other invasive procedure within 6 weeks
- Immunosuppression
- Intravascular device
- Breaches to skin integrity e.g. cuts, burns, blisters
- Current or recent pregnancy (within 6 weeks)

### Clinical Features

**Potential source of infection OR NEWS ≥4?**

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

**New signs or symptoms of infection? TWO or more of the following:**

- Temperature >38.3°C
- Heart Rate >90bpm
- WBC <4x$10^9$/L
- Altered mental state
- Temperature <36°C
- Respiratory Rate >20 bpm
- WBC >12x$10^9$/L
- Blood glucose >7.7mmol/L

**Evidence of organ dysfunction remote to the site of infection? ONE of the following or SOFA ≥2 (see opposite):**

- Lactate >2mmol/L
- Systolic blood pressure <90mmHg **OR** Mean arterial pressure <65mmHg
- Systolic blood pressure >40mmHg below baseline
- Creatinine >175mmol/L **OR** urine output 0.5ml/kg/hour for more than 2 hours
- Bilateral pulmonary infiltrates **PLUS** $O_2$ required to keep $O_2$ saturations >92%
- Bilateral pulmonary infiltrates **PLUS** $PaO_2/FiO_2$ ratio <300*
- Bilirubin >34 mmol/L
- Coagulopathy INR >1.5 **OR** APTT >60 seconds
- Platelet count <100x$10^9$/L

**If YES to questions 1 +2 + 3 = criteria for SEPSIS**

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

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

**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<br>**PLUS**<br>IV Gentamicin |
| 2nd line (if 1st line contraindicated) | IV Teicoplanin **OR** IV Vancomycin<br>**PLUS**<br>IV Gentamicin<br>**PLUS**<br>IV Metronidazole |
| If previous ESBL or AmpC positive bacteria | IV Meropenem<br>**PLUS**<br>IV Gentamicin |
| If MRSA positive | **ADD** IV Teicoplanin **OR** IV Vancomycin |

In addition to antibiotics a source of sepsis should be identified and managed as soon as possible e.g. removal of infected CVC, drainage of abscess, repair of perforated abdominal viscus.

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

| **Children** | |
|---|---|
| 1st line | IV Cefotaxime<br>**PLUS**<br>IV Gentamicin |
| 2nd line (if 1st line contraindicated) | IV Chloramphenicol<br>**PLUS**<br>IV Gentamicin |

**Total Duration**

7-10 days

Unless a causative microorganism or focus of infection requires longer treatment e.g. *Staphylococcus aureus* bacteraemia, listeriosis or meningitis (see section – Antibiotics, Adult Empirical Antibiotic Guidelines)

**Dosing**

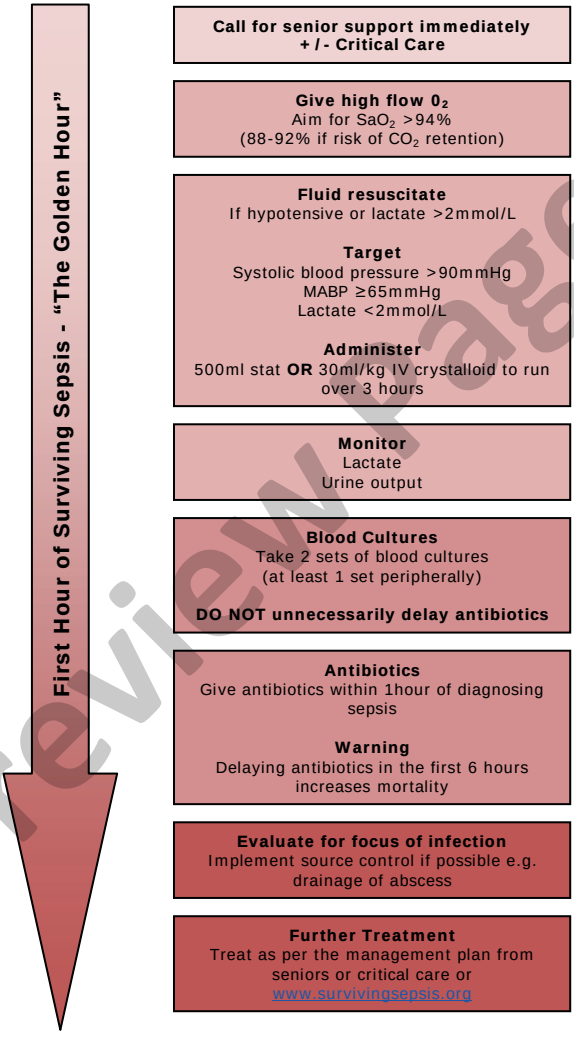
See section - Antibiotics, Empirical Antibiotic Guidelines Emergencies.

**Warning - Prognosis and Complications**

Mortality in sepsis increases if adequate antibiotic treatment is delayed:

- Septic shock - mortality increases by 7% per hour for the first 6 hours that treatment is not adequate
- Sepsis without shock – mortality increases 1-1.5% per hour for the first 6 hours that treatment is not adequate

## Adult Sepsis "Golden-Hour" Management Flowchart



**Sequential Organ Failure Assessment Score (SOFA)**

| | Score | | | | |
|---|---|---|---|---|---|
| **Parameter** | **0** | **1** | **2** | **3** | **4** |
| **$PaO_2/FiO_2$ mmHg** | ≥400 | <400 | <300 | <200 with respiratory support | <100 with respiratory support |
| **Platelets X $10^9$/L** | ≥150 | <150 | <100 | <50 | <20 |
| **Bilirubin µmol/L** | <20 | 20-32 | 33-101 | 102-204 | >204 |
| **Cardiovascular status*** | MABP ≥70 mmHg | MABP <70 mmHg | Dopamine <5 **OR** Dobutamine any dose | Dopamine 5.1-15 **OR** Epinephrine **OR** Norepinephrine ≤0.1 | Dopamine <5 **OR** Epinephrine **OR** Norepinephrine >0.1 |
| **Glasgow Coma Scale** | 15 | 13-14 | 10-12 | 6-9 | <6 |
| **Creatinine µmol/L or Urine output ml/day** | 110 | 110-170 | 171-299 | 300-440 <br> <500 | >440 <br> <200 |

**Note:** *Inotrope doses are in µg/kg/min

**Warning**
If vasopressors (e.g. Norepinephrine) are required to keep MABP ≥65mmHg **AND** Lactate >2mmol/L despite fluid resuscitation then the patient has **SEPTIC SHOCK**

**Hints and Tips**
Use the abbreviated qSOFA (quick Sepsis-Related Organ Failure Assessment) to quickly assess sepsis severity, if ≥2 there is an increased risk of death or prolonged ICU stay. Take action!
- Respiratory rate ≥22/min
- Altered mental status
- Systolic blood pressure ≤100mmHg

**Causes**

| | |
|---|---|
| Common | • *Staphylococcus aureus*<br>• Group A Beta-haemolytic *Streptococcus*<br>• Enterobacteriaceae e.g. *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp.,<br>• *Pseudomonas* spp.<br>• *Neisseria meningitidis* |

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

# Microbiology Nuts & Bolts

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.

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The author is a Consultant Microbiologist with over 21 years of clinical experience within the NHS. He has worked in various areas of adult and paediatric medicine and surgery. He has a keen interest in teaching all healthcare staff about microbiology and infections, from consultants and junior doctors, to medical students and nurses.

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