# Microbiology as applied to surgical practice

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**Abstract**

Microbiology is integrated throughout surgical practice, and a working knowledge of its basic principles is essential in caring for surgical patients. In particular, it is important to have an understanding of the basic science behind micro-organisms and infection, as well as a knowledge of surgically important micro-organisms and methods of preventing infection in surgical patients. In this article we cover these topics with reference to the MRCS syllabus and include information about relevant micro-organisms and antibiotics.

**Keywords** Antibiotics; Antisepsis; Asepsis; Disinfection; Infection; Infection control; Infection prevention; Infectious disease; Microbiology; Sterilization; Surgically important micro-organisms

## Introduction

Principles of microbiology appear in all aspects of surgical practice, from the preparation of theatres and theatre staff preoperatively to the recognition and treatment of infectious disease in patients on the ward. The scope of this topic is vast, and a general understanding of microbiology is not something that can be appropriately conveyed in one article. The MRCS syllabus provides guidance regarding the topics relevant to the examination, and we have brought these into consideration when creating this article. We do not include soft tissue infections, perioperative fever, sepsis and septic shock. We cover microbiology as applied to surgical practice via basic science and principles of infection, including useful information about surgically important micro-organisms and antibiotics; and preventing infection in surgical patients.

## Biology of micro-organisms

### Bacteria

Bacteria are prokaryotic cells — that is, they lack membrane-bound organelles. This means all cell constituents, including DNA and enzymes, have access to all parts of the cell. They have a range of potential cellular components that varies between species, conferring certain advantages to some in specific conditions. Bacteria can be grouped in a number of ways:

- Oxygen demand:
  - Aerobic bacteria require oxygen.
  - Anaerobic bacteria require conditions without gaseous oxygen.
  - Facultative anaerobes prefer conditions with oxygen, but can tolerate anaerobic conditions.
- Energy production:
  - Heterotrophs consume organic compounds for breakdown into energy.
  - Autotrophs produce their own energy (e.g. via photosynthesis).
- Shape:
  - Cocci are round cells. Examples include staphylococci (form clumps) and streptococci (form chains).
  - Bacilli are rod-shaped. Examples include *E. coli*.
  - Vibrio bacteria are shaped like a curved rod. Examples include *Vibrio cholerae*.
  - Spirilla are longer, rigid, corkscrew spiral-shaped bacteria. Examples include *Campylobacter jejuni*.
  - Spirochetes are long, thin and more flexible corkscrew-shaped bacteria. Examples include *Treponema pallidum* and *Borrelia burgdorferi*.
- Staining properties:
  - All bacteria have some cell wall, but there is considerable variation in its composition. This has been useful in staining for bacteria, and has led to a further categorization of bacteria.
  - Hans Christian Gram in 1884 used a technique of staining bacteria purple with crystal violet and decolourizing them with acetone. Those with thick peptidoglycan cell walls resist decolourizing, whereas those without this get decolourized and are counter-stained with Safranin, giving a pink appearance.
  - From this we have categorized bacteria into Gram positive (those that retain the purple stain) and Gram negative (those that do not) (Figure 1).

Other possible cell components seen in the diagram above such as pili and flagella also contribute to a bacteria's pathogenicity (see section below).

### Viruses

All viruses have the same basic structure of a nucleic acid core (RNA or DNA), surrounded by protein (capsid). Some also have an envelope around the capsid containing proteins, glycoproteins and lipids. These structures are not cells, and each virus contains just a single type of nucleic acid (RNA or DNA). Viruses can be categorized by the nature of their genomes:

- RNA viruses, for example Influenza viruses.
- DNA viruses, for example Herpes viruses.
- Retroviruses (RNA-containing viruses that use their own reverse transcriptase enzymes to create DNA that gets implanted into the host cell genome), for example HIV.

### Fungi

Fungi are eukaryotic microbes — that is, they have a nucleus within a membrane. Fungi range from microscopic unicellular organisms to multicellular organisms covering hectares of space. They are all heterotrophs that absorb nutrients for energy production, but there is wide variation between species:

- Monokaryotic or dikaryotic.
- Asexual or sexual reproduction.

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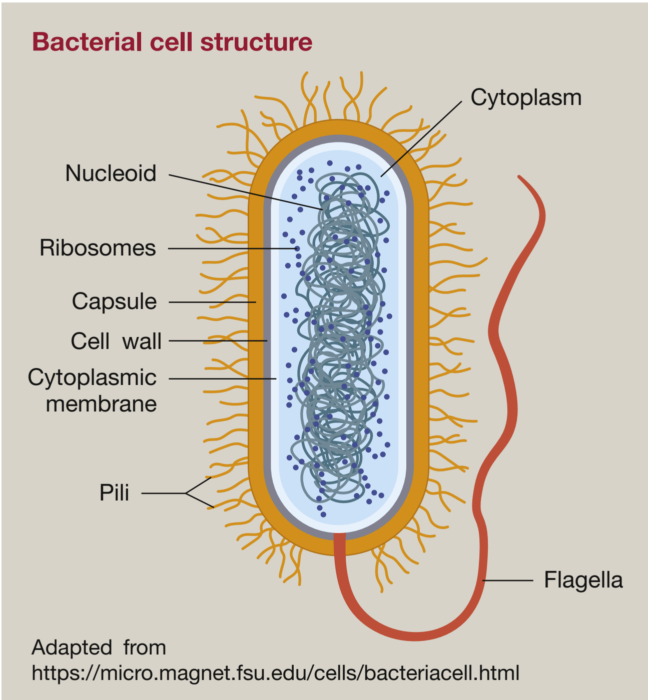


**Figure 1**

- Unicellular or filamentous. This describes one of the differences between molds and yeasts.
  - Molds, such as *Aspergillus* species, grow via multiple multicellular filaments called hyphae. Filaments grow from their ends and molds are able to reproduce by spore formation (sexual or asexual reproduction). Spores can cause allergic reactions and respiratory problems such as chronic cough. Molds can also produce toxins (mycotoxins – see section below)
  - Yeasts such as *Candida* species are single-celled organisms that generally reproduce by asexual 'budding', in which two asymmetric cells are produced. There are, however, species that also produce via sexual reproduction. Yeasts commonly cause infection as opportunistic pathogens in immunocompromised hosts.

Examples of surgically important micro-organisms are included in Table 1.

## Principles of infection and pathogenicity

Infectious disease can be defined as the establishment of a microbe on or within a host, whereby it is able to cause damage resulting in clinical symptoms and signs of disease. Some other useful definitions regarding infectious diseases include:

- Colonization – the presence of microbes in the body without disease.
- Flora – the entire microbial life in a particular region, for example the intestinal flora.
- Commensal – colonization benefits the microbe but not the host.
- Mutual – both the microbe and host benefit from colonization.
- Parasitic – parasite benefits but the host is harmed.

Infectious disease occurs when there is establishment of a microbe that is unrecognized in a tissue. This may occur when a microbe that does not normally colonize the human body enters, or when a microbe that is part of a system's normal flora enters an area of the body that it does not normally colonize, including sterile sites. Table 2 outlines some sterile sites and examples of microbes constituting the normal flora.

The extent of disease caused by infection depends on the microbial load, the virulence of the organism and the reaction of the host. Host factors dictate ease of microbe entry into tissues and also responses to eradicate infection when established. In surgery, the microbial load and host barriers are of particular relevance, with wounds made routinely during operations, and microbial load kept to a minimum at all times (see section below on 'Preventing infection in surgical patients').

The normal process of infection involves the inoculation of a tissue with an organism, adhesion of the organism to cell surfaces, infiltration and invasion through them and establishment within a tissue. This infection will then spark off a host immune response resulting in the cardinal inflammatory signs – calor (raised temperature), tumor (swelling), rubor (redness) and dolor (pain).

Virulence is the ability with which a microbe can cause infection. Factors affecting a microbe's virulence (with common examples) include:

- Motility:
  - Motility enables a microbe to reach a target tissue for infection, move towards nutrients and move away from toxic substances.
  - *E. coli* bacteria have flagella enabling their motility. These hair-like structures move to propel the bacteria forward. *E. coli* bacteria utilize this to enter the urinary tract.
  - Note that for urinary tract infections (UTIs) *Candida* species do not have the virulence factors (i.e. motility) to get into the urinary tract, but are a common cause of catheter-associated UTI.
- Adhesion:
  - Pili (or fimbriae) contain a multitude of adhesion molecules that enable cells to adhere to target tissues. There may be further interactions between adhesins and immune cells to stimulate the inflammatory response, and interaction between pathogen and host to impair function. *E. coli*'s pili reduce ureteric contractility.
  - Lipoteichoic acid is a major constituent of the bacterial cell wall Gram-positive bacteria. This adhesion molecule enables non-specific adhesion to membrane phospholipids, and similarly stimulates host immune cells.
- Invasion:
  - Invasion of pathogens is enhanced by the ability to cause local tissue damage. An example of this is *Clostridium perfringens*, which, amongst others, secretes hyaluronidase enzymes to break down local tissues.
- Immunoevasion:
  - There are a number of mechanisms that pathogens employ to avoid host immune defenses.
  - Certain species of bacteria have protective layer outside the cell membrane and cell wall, called the capsule. This

 

## Surgically important micro-organisms

| | | |
|---|---|---|
| Gram-positive cocci | *Staphylococcus aureus* | Colonizes the skin. Implicated in many infections ranging from mild folliculitis to surgical site infections (SSI), prosthetic device infection, bacteraemia and endocarditis. Certain diseases (such as toxic shock syndrome) are mediated by the release of enterotoxin, which is preformed and thus will typically result in rapid onset of symptoms. Production of coagulase enzyme converts fibrinogen to fibrin, which may protect microbe from phagocytosis — increasing virulent potential |
| | Meticillin-resistant *S. aureus* (MRSA) | Intrinsically resistant to flucloxacillin and almost all beta-lactam antibiotics. Those with colonization require MRSA suppression therapy prior to surgery, in line with local guidelines |
| | Coagulase-negative staphylococci, e.g. *S. epidermidis, S. haemolyticus* | Skin commensals, usually implicated in nosocomial infections involving prosthetic catheters and implants. Form biofilms on prostheses, which often render antibiotic therapy ineffective. This may result in the requirement for prosthesis removal |
| | *Streptococcus pyogenes* (Group A β-haemolytic streptococcus) | Infections vary from mild pharyngitis to severe necrotizing fasciitis. Important cause of SSI and outbreaks on surgical wards have been described. High virulence based on properties enabling strong adherence and invasion of epithelial cells. Left untreated, streptococcal pharyngitis is a cause of rheumatic fever (now rare). Scarlet fever and invasive disease (iGAS) require statutory notification to the local public health body |
| | *Streptococcus pneumoniae* | Normally found in the upper respiratory tract but also a cause of primary peritonitis. Commonly implicated in respiratory tract infections and middle ear infections and can be a causative organism in meningitis |
| | Alpha-haemolytic streptococci, e.g. *S. bovis,* Anginosus (milleri)-group streptococci | May be commensals of the respiratory or gastrointestinal tracts. *S. bovis* can be a causative organism for infective endocarditis and is associated with colonic cancers. *S. anginosus, S. intermedius, S. constellatus* (formerly known as the 'milleri-group') implicated in abscess formation and often co-exist alongside anaerobes |
| | Enterococci, e.g. *E. faecalis, E. faecium* | Normal colonizers of the bowel. Causes urinary tract and wound infection. *E. faecium* intrinsically resistant to amoxicillin and most beta-lactam antibiotics. Glycopeptide or vancomycin-resistant enterococci (GRE/VRE) is a cause of nosocomial infections |
| Gram-positive bacilli | *Clostridium* sp. | Mostly anaerobic, spore-forming bacteria; colonize the GI tract, found in the soil and environment. *C. perfringens* important cause of gas-gangrene, *C. novyi* associated with soft-tissue infections in injecting drug-users. *C. difficile* important cause of nosocomial diarrhoea and pseudomembranous colitis |
| Gram-negative bacilli | Enterobacteriaceae, e.g. *E. coli, Klebsiella* spp. | Normal colonizers of the bowel. Motile rods with flagellae, sometimes encapsulated. Commonly implicated in disease when introduced into other tissues or in immunocompromised hosts. Commonly cause urinary tract and intra-abdominal infections. Rare cause of respiratory tract infections |
| | *Pseudomonas aeruginosa* | Found in the environment (e.g. water and soil), but can colonize the GI tract and ulcers/wounds. Opportunistic pathogen that commonly causes disease in immunocompromised hosts. Resistant to many antibiotics and associated with hospital-acquired infections, ventilators, drainage tubes and catheters. Can cause serious infection in patients with burns or skin grafts |
| | *Acinetobacter* | May be normal skin commensal but *A. baumanii* associated with outbreaks of multi-drug resistant infections |
| | *Helicobacter pylori* | Present in half of the human population, and able to withstand the acidic environment of the stomach due to producing alkali substances. Many do not experience the well-known associated gastritis and ulcers due to slow growth of the bacteria. Can lead to gastric cancer and gastric mucosa-associated lymphoid tissue (MALT) lymphoma |

(*continued on next page*)

**Table 1** (*continued*)

| | | |
|---|---|---|
| | *Bacteroides fragilis* | Only grows in anaerobic conditions. Commonly found in GI tract where they assist in food breakdown. Introduction to other tissues, however, can cause serious infection. *Bacteroides fragilis* is the most common organism causing serious anaerobic infection, particularly after abdominal or gynaecological procedures. Infections can occur in many tissues including the central nervous system, head and neck, chest, abdomen, pelvis, skin and soft tissues |
| | *Fusobacterium* spp. | Only grows in anaerobic conditions. Found on mucous membranes and commonly associated with periodontal disease including tonsillar abscesses and other head and neck infections |
| Fungi | *Aspergillus* spp. | Genus of fungi containing pathogens known to be harmful to humans. *Aspergillus flavus* produces aflatoxin, both a toxin and carcinogen implicated in hepatocellular carcinoma. *Aspergillus fumigatus* is the most commonly implicated pathogen in aspergillosis (disseminated fungal infection, which may cause fungal balls in the lungs). *Aspergillus niger* tends to be less dangerous but can cause lung and ear infections |
| | *Candida* spp. | Many types can cause infection, most commonly *C. albicans*. A very common inhabitant of the intestinal tract, and mouth, but infection may be seen in the extremes of age or in immunocompromised patients. Infections tend to involve the skin or mucosa but can invade organs and prostheses |
| Mycobacteria | *Mycobacterium tuberculosis* (TB) | Acid-fast bacteria abundant in soil and water, and spread between hosts by respiratory droplets. Presence is confirmed with Mantoux tuberculin skin test. Children are immunized with BCG (Bacille Calmette Guerin) vaccination. Ghon focus = area of granulation in the lung which can calcify Ghon complex = a Ghon focus with associated lymph nodes |
| Parasites | *Schistosoma haematobium* | Causes schistosomiasis, the most common parasitic infection in humans. Infects the urinary tract and is associated with carcinoma of the bladder |
| Viruses | Epstein—Barr virus | Causes infectious mononucleosis (glandular fever), and is linked with several cancers including Hodgkin's lymphoma and Burkitt's lymphoma |
| | Human immunodeficiency virus (HIV) | Reduced CD4 cells and reduced effective adaptive immune response leads to acquired immunodeficiency syndrome (AIDS), resulting in dangerous susceptibility to opportunistic infection and life-threatening consequences of these |

**Table 1**

capsule is made of polysaccharides and inhibits phagocytosis — as seen with *Neisseria meningitidis.*
- ◦ *Staphylococcus aureus* secretes coagulase enzyme, which causes plasma to clot and coat the cell, which may inhibit phagocytosis.
- ◦ Other pathogens gain advantage from phagocytosis, and as they reproduce within immune cells. These include bacteria including *Legionella* species and viruses including Human Immunodeficiency Virus (HIV).
- ◦ HIV targets leukocytes — CD4 T-helper cells as an intracellular host. Virus envelope has glycoproteins and interacts with CD4 molecules on T cells.

- Immunosuppression:
  - ◦ *Streptococcus pyogenes* is an example of a bacterial species that suppresses the immune response by secreting Immunoglobulin proteases. This reduces the recognition of the pathogen by circulating immunoglobulins.
- Toxins
  - ◦ In addition to direct recognition of pathogens by immune cells and resultant release of pro-inflammatory mediators, the inflammatory response is further stimulated by toxins released by pathogens.
  - ◦ Endotoxins are bacterial cell components that can stimulate the inflammatory response.
    - Lipopolysaccharide (LPS) is the prototypical endotoxin, and is a cell membrane component of Gram-negative bacteria. LPS activates the pro-inflammatory response through binding to a wide variety of cell types, and is an exogenous pyrogen. It is thought to be part of the reason that Gram-negative bacteria such as *N. meningitidis* bring about such a profound clinical response.
  - ◦ Exotoxins are secreted by pathogens to damage the host.
    - *S. aureus* is an example of a bacterial species well known for producing a variety of exotoxins

 

**Surgically important organisms for the MRCS**

| Sterile sites | Sites colonised with commensal flora | |
|---|---|---|
| Blood/bone marrow | Mouth/nose/upper respiratory tract | *S. aureus, Strep pneumonia, Haemophilus influenza, Neisseria meningitides,* viridans group *Streptococci* |
| CSF | | |
| Sinuses/middle ear | | |
| Lower respiratory tract | Skin | Coagulase negative *Staphylococci, Corynebacterium* species (diphtheroids), *Propionibacterium* |
| Muscle/bone/joint | | |
| Liver/gallbladder | | |
| Pleura/peritoneum | GI tract | *Enterobacteriaceae (E. coli, Klebsiella), Enterococci,* anaerobes |
| Bladder and kidneys | | |
| | Female GU tract | Anaerobes and *Lactobacillus* species |
| | Urethra | Coagulase negative *Staphylococci, E. coli,* lactobacilli and anaerobes |

**Table 2**

including those that result in toxic shock syndrome (TSST-1 and enterotoxin type B), and exfoliative skin disease (i.e. staphylococcal scalded skin syndrome).
  - Fungi can also produce toxins (mycotoxins), such as *Aspergillus nigricans*, which produces aflatoxins that can be carcinogenic to the liver.
- Biofilm formation:
  - A biofilm is a coordinated functional aggregate of micro-organisms that are embedded within a self-produced matrix of extracellular polymeric substances. This can form on living or non-living surfaces including prosthetic material. These aggregate cell colonies tend to be difficult to penetrate with antibiotics and thus removal, washout and replacement of prosthetics is sometimes the best method of eradication.
  - Biofilms commonly form on the external surface of urinary catheters, between the catheter material and the urethra, and resultant infections are best managed with antibiotics and catheter removal.

## Preventing infection in surgical patients

Significant efforts are taken in the surgical care of patients to minimize the risk of iatrogenic infection before, during, and after surgical procedures. Techniques have developed over decades of experience to become embedded into surgical practice, and are outlined in Table 3. Many practices are closely based on the World Health Organization's (WHO) Global Guidelines for the Prevention of Surgical Site Infection[1] (SSI), and NICE has produced surgical site infection quality statements[2] in keeping with WHO guidance.

Decontamination of surgical equipment is also vital to prevent infection in surgical patients. Decontamination describes the processes employed to remove disease-causing organisms, spores and proteins from reusable surgical instruments. Methods include the use of heat, chemicals, and radiation to decontaminate equipment.

### Cleaning

Cleaning involves the removal of physical and visible debris from objects and equipment. This is useful in maintaining the appearance, structure and function of equipment, but will not remove some micro-organisms and their spores.

### Disinfection

Disinfection is the cleansing of equipment with the aim of destroying micro-organisms capable of causing infection, reducing their number to a level below the infective dose. This tends to be effective for the destruction of many micro-organisms but is not effective against spores. The number of micro-organisms left present depends on the technique of disinfection used. A specialized example of disinfection is the ultrasonic washer-disinfector. Here ultrasonic waves are applied to instruments fully immersed in water for decontamination, used particularly for Da Vinci robot instruments.

### High-level disinfection

This refers to a process that employs an agent that is normally used for disinfection processes, but under specific circumstances certain agents, when used in sufficient concentrations and with suitable extended exposure times, can destroy bacterial spores appropriately. For example, this is the reason why gastrointestinal endoscopes require a specific cleaning protocol in the sterilization services department, but flexible nasendoscopes used by ear, nose and throat surgeons can be disinfected chemically without the absolute need to be sent elsewhere.

### Sterilization

Sterilization is the process by which all forms of pathogen are destroyed, including all forms of microbial life (bacteria, viruses and fungi), as well as their spores. While this is the principle of sterilization, there still remain challenges in dealing with prions and endotoxin, which are still problematic.

### Prions

Human prion diseases are rare, fatal neurological disorders. The most common form is the sporadic form of Creutzfeldt-Jakob disease (sCJD). Prion diseases result in rapid-onset severe dementia, amongst other neurological symptoms, causing death within months of onset. The diseases occur by conversion of a normal protein in the body (the prion protein) to a disease-causing form. The transmission of the disease-causing form is

## Reduction of infection in surgery

**Patient care**

| | | |
|---|---|---|
| *Preoperative patient preparation* | Risk factor management | Respiratory disease, smoking<br>Cardiac disease<br>Gastro-oesophageal reflux disease<br>Hypertension<br>Anaemia<br>Diabetes<br>Obesity<br>Physical fitness<br>Anaesthetic assessment, consideration of local/regional anaesthetic procedures |
| | Nutrition | Carbohydrate loading with high energy drinks<br>Optimize hydration |
| | Antibiotics | The use of prophylactic antibiotics in surgery should be minimized to reduce the risk of contributing to the emergence of multidrug resistant infections, but for non-clean and implant surgery there is clear benefit for reducing surgical site infections, as outlined by Scottish Intercollegiate Guidelines Network (SIGN) guidelines on surgical antibiotic prophylaxis.[3] Choice of antibiotics should be made based upon recognized guidelines. According to the WHO guidance,[1] preoperative antibiotic prophylaxis should be given within 120 minutes prior to incision to maximize benefit. The half-life of the particular drug used must be taken into account, and in some cases, preoperative administration of the antimicrobial should be brought closer to the incision time. This also brings to attention those antimicrobials that will require re-dosing during long operations |
| *Postoperative patient care* | Early return to normal diet<br>Goal-directed fluid therapy to maintain normovolaemia<br>Early mobilization<br>Consideration of chest physiotherapy<br>Consideration of critical care admission for high risk patients | |

**Antisepsis = destruction of bacteria pre-existing in the surgical field**

| | | |
|---|---|---|
| *Skin preparation* | Hair removal | When hair removal is necessary it is performed in theatre. Hair clippers have a significant benefit in reducing the risk of surgical site infection when compared to shaving with razors |
| | Disinfection | Available antiseptics include those containing iodine, chlorhexidine and alcohol, and these are used to clean the skin preoperatively in theatre<br>Should be applied in a motion that does not result in the re-introduction of bacteria into a previously cleaned area<br>Alcohol-based antiseptic solutions are widely recommended as the preferred antiseptic choice, but note that pools of solution can ignite if sparks are generated (e.g. diathermy) |
| | Drapes | Cover non-prepared surfaces to prevent contact and aim maintain sterility of the surgical site and equipment<br>Act as a physical barrier to limit migration of micro-organisms to the operative site.<br>NB: plastic adhesive drapes (films placed over the skin — the surgeon cuts through the film and the skin) are not routinely recommended, and when required those impregnated with an iodophor should be used (as recommended by NICE). |
| *Bowel preparation* | Mechanical bowel preparation involves regimens of laxatives and enemas with the aim of clearing the bowel of faeces preoperatively. In theory, this was thought to reduce bacterial load, intraluminal pressures and improve handling and visualization. However, recently there has been a drive towards eliminating routine bowel preparation from colorectal surgical practice, and this is reflected in the World Health Organization's Global Guidelines for the Prevention of Surgical Site Infection, in which mechanical bowel preparation should not be used for the purpose of reducing surgical site infections in adult patients undergoing elective colorectal surgery. | |

 

| **Asepsis = preventing the introduction of bacteria into the surgical field** | | |
|---|---|---|
| *Theatre* | Design | Minimize unnecessary equipment<br>Easily cleaned<br>Easily manoeuvred without contacting walls and objects |
| | Air quality control | Positive pressure filtered ventilation may reduce entry of bacteria into operating theatres<br>Laminar airflow is a way of controlling ventilation such that air flows without turbulence in a predictable manner. This was incorporated into many operating theatres due to the theory that it would reduce the entry and settling of micro-organisms in operating theatres. Over time evidence has gathered that there is no significant difference in the rates surgical site infections when comparing laminar flow with conventional ventilation systems[4] |
| | Temperature control | Temperatures of the theatre itself and the patient should be monitored and normalized |
| | Access control | Movement through doors should be kept to a minimum |
| *Team* | Scrubbing and gloves | Surgical hand preparation aims to eliminate transient flora and reduce resident flora of the hands in order to prevent SSI. Use of sterile gloves does not negate the need for surgical hand preparation as tiny punctures in sterile gloves frequently go unnoticed<br>NICE recommends using an antiseptic surgical solution with a single-use brush or pick for the nails. Prior to this all hand jewelry, artificial nails and nail polish should be removed<br>Subsequent to this first wash, between cases hands should be washed using either an alcohol-based handrub or an antiseptic surgical solution. Visible soiling of the hands should prompt use of an antiseptic surgical solution<br>There is no quality evidence to suggest double gloving is necessary in surgical procedures, though some centres recommend this, particularly for implant surgery or high-risk patients |
| | Clothing | Gowns reduce migration of bacteria from clothing and skin into the air<br>There is no clear evidence of a significant difference between re-use and single-use gowns, and decisions are based around cost efficiency |
| | Caps | Prevent hair falling<br>Reduce migration of bacteria from the scalp to the air |
| | Masks | Deflect forceful expirations<br>No clear evidence of effect on infection rates |
| | Shoes | Plastic shoes have not been proven to reduce wound infection but are widely recommended and help to ensure bacteria from outside the hospital do not enter theatres |
| **Aseptic non-touch technique** | | |
| This technique is based on the principle that the ‘key parts’ of equipment (i.e. those parts that if colonized by micro-organisms could transmit infection to the patient) remain sterile if kept untouched. Hands should be cleaned and non-key parts of equipment used to manoeuvre equipment | | |
| **Handwashing vs alcohol gelling** | | |
| Alcohol gel is effective against many micro-organisms including MRSA, and is excellent for frequent and repeated use<br>Hand washing with soap and water should be used for hand hygiene in environments containing *Clostridium difficile* and Norovirus, as alcohol gel is not effective for these | | |

**Table 3**

thought to be the basis of transmissible forms of prion disease. Abnormal prion proteins avidly adhere to steel surgical instruments and are extremely difficult to remove, thus there is a risk of transmission during surgical procedures.

Sterilization techniques aim to reduce prion protein levels and there is guidance available regarding optimal techniques. Technologies in development aim to improve detection of prion proteins *in situ* on instruments to be applied before instrument use, and removal of proteins with sterilization techniques.

Examples of current methods for sterilization are outlined in Table 4.

Antibiotic use should be kept to a minimum and therapy regularly reviewed to ensure the shortest effective courses are used. Antibiotic types, mechanisms and examples are shown in Table 5.

## Example methods of sterilization

| | | |
|---|---|---|
| Heat | Autoclaving | Process involves pressurised steam cleaning. Temperature and length of time depend on equipment cleaned and autoclaving machine ability. Suitable for most re-useable surgical equipment, but should be physically cleaned before autoclaving. Not suitable for fragile items. Standard operating cycle is 134°C for 3–3.5 minutes, but lower temperatures can be used for longer periods |
| | Dry heat | Dry heat can be used on moisture-sensitive, heat-resistant items. Can use static air (slower) and forced air techniques. Length of time is generally hours but depends on temperature and technique. Dry heat sterilization is possible at 160°C for 60 minutes |
| Chemicals | Glutaraldehyde 2% | A widely used liquid disinfectant for endoscopes. Takes 20 minutes of soaking at 20°C, as long as proper cleaning has occurred prior to this. Can be dangerous for staff and there have been reports of allergy to the substance, so alternate chemical disinfectants should be sought |
| | Ethylene oxide | Used for items that are moisture and heat sensitive, for example equipment with plastic or electrical parts. Takes many hours, but can be used at much lower temperatures than autoclaving and dry heat. This gas is highly flammable and toxic. Mainly used in industrial processes |
| Radiation | Gamma irradiation | Suitable for batch treatment of items stable to gamma irradiation in industrial processes |

**Table 4**

## Antibiotics

**Inhibitors of cell wall synthesis**

***Beta-lactams***

Bind and competitively inhibit penicillin-binding proteins (PBPs). PBPs vary in different microbes so penicillins have differing effects. They act to inhibit peptidoglycan cross-linkage in cell walls and thus don't affect bacteria without cell walls, e.g. Chlamydia

***Resistance***

Many bacteria possess beta-lactamase enzymes that break down beta lactam ring, so we often combine a beta lactamase inhibitor to preserve activity

***Penicillins***

- **Penicillin G** (benzylpenicillin) and **penicillin V** (oral equivalent)
  - Increasing resistance of many organisms has left these compounds ineffective, including *Staphylococcus* aureus and *N. gonorrhoeae*
  - Good antibiotics for streptococci, *N. meningitidis*, and spirochaetes
  - Little useful activity against other Gram-negative/anaerobic bacteria
- *Extended spectrum penicillins*: **ampicillin** and **amoxicillin** (better bioavailability due to more resistance to stomach acid – amoxicillin has better bioavailability orally than ampicillin)
  - Better activity against some Gram-negative bacteria e.g. *H. influenzae, E. coli*
  - Combination of amoxicillin + clavulanic acid = Co-amoxiclav – broader spectrum to cover organisms including enterobacteriaceae and anaerobes
- *Antistaphylococcal penicillins*: **flucloxacillin** (and Meticillin)
  - Stable to staphylococcal beta-lactamase – active against penicillin-resistant *S. aureus*
  - Mainstay of treatment for *S. aureus* infections
  - Also active against some other Gram-positive bacteria such as streptococci, and thus beneficial in skin infections
- Antipseudomonal penicillins: **piperacillin**
  - Modification of penicillin or ampicillin, and active against *Pseudomonas aeruginosa*
  - *Tazocin*™ = piperacillin + tazobactam

***Cephalosporins***

The beta-lactam ring is fused to a dihydrothiazine ring. Divided into groups (1–6) depending on spectrum of activity and route of administration (oral/parenteral) and 'generations' (related to introduction into clinical practice). These tend to have broader spectrum of activity than penicillins:

- Most are active against *S. aureus* and streptococci (stable to staphylococcal beta-lactamase)
- NOT active against enterococci or *Listeria* (unlike penicillins – ampicillin/amoxicillin is used, for example, if there is a risk of *Listeria* meningitis)
- Variable spectrum of activity against Gram-negative bacteria
- Inactive against gastrointestinal anaerobes (need to add, for example, metronidazole)

| | |
|---|---|
| **Cefalexin** *(group 2, 1st generation cephalosporin, oral)* | - Good activity against many common Gram-positive bacteria including *S. aureus* and Streptococci<br>- Limited activity against Gram-negative bacteria (e.g. *H. influenza*)<br>- Uses = outpatient upper resp, urinary and soft tissue infections |

 

**Cefuroxime** *(group 3, 2nd generation cephalosporin, parenteral)*
- Active against wide range of Gram-positive and Gram-negative bacteria (not *Pseudomonas*)
- Uses = severe sepsis, including urinary, respiratory (used in severe community acquired pneumonia combined with macrolide e.g. clarithromycin for atypicals like Legionella) and soft tissue infections

**Ceftriaxone** *(group 4, 3rd generation cephalosporin, parenteral)*
- Active against most Gram-negative bacteria and a wider range of Gram-positive bacteria (not *Pseudomonas*)
- Long half-life with once daily administration
- When used at high doses gives high CSF levels
- Uses = wide range of severe infections including acute bacterial meningitis

**Ceftazidime** *(group 6, 3rd generation cephalosporin, parenteral)*
- Active against *Pseudomonas*
- Compared with other cephalosporins, Ceftazidime has a high minimum inhibitory concentration to staphylococci and streptococci, and as such cannot be reliably used to treat these infections.
- Uses = wide range of severe infections including necrotizing otitis externa.

***Resistance***
Extended spectrum beta-lactamases (ESBL) and AmpC beta lactamases
The above two beta-lactamases are common causes of cephalosporin resistance

***Carbapenems:*** broadest spectrum beta-lactams, such as **meropenem**
- Stable to most beta-lactamases
- Also stable to 'extended spectrum beta-lactamases' (ESBL)-producing Gram-negative bacteria
- Active against most Gram-positive and Gram-negative bacteria

***Resistance***
Carbapenems are in general stable to ESBL and AmpC producing organisms, but unfortunately carbapenemases have also been discovered
Carbapenemase- producing organisms (CPE/CRE — carbapenemase-producing/resistant enterobacteriaceae): Class A — *Klebsiella pneumoniae* carbapenemase (KPC), Class B — Metallo-beta-lactamases (MBL), Class D — OXA beta-lactamases. A class C has also been described (CMY)

***Glycopeptides*** Such as **vancomycin** and **teicoplanin**
Bind to components of peptidoglycan, preventing addition of new blocks to the cell wall. Active against most Gram-positive bacteria — including enterococci and MRSA, but not active against Gram-negative bacteria (large molecules cannot penetrate the outer membrane of Gram-negative bacteria). Poor oral availability and thus given intravenously. Also nephrotoxic and thus require therapeutic drug monitoring

**Inhibitors of protein synthesis**

Inhibition of protein synthesis is useful in preventing toxin release, e.g. in toxic shock syndrome
Some effects on mitochondria — related to bacteria — explain some of the side effects of these drugs

***Aminoglycosides*** Such as **gentamicin**, **amikacin**, **streptomycin** (used in tuberculosis)
- Potently bactericidal against staphylococci (initially developed to target staphylococci), and most Gram-negative bacteria including *Pseudomonas*
- Enter bacteria via active transport, and streptococci lack this transporter so are not usually susceptible — however, if e.g. penicillin is used to disrupt the cell wall, aminoglycosides can enter and act synergistically
- Poor oral availability, thus given intravenously
- Risk of ototoxicity and nephrotoxicity, and thus require therapeutic drug monitoring

***Tetracyclines*** Such as **doxycycline**
- Used for milder infections and some specific diseases.
- Broad spectrum (although resistance is increasing) but bacteriostatic. Good oral bioavailability.
- Uses include treatment for Rickettsia and Lyme disease (*Borrelia burgdorferi*)
- Also used in malaria prophylaxis
- Avoid in young children (taken up by bones and teeth and causes discolouration)

***Macrolides*** Such as **erythromycin**, **clarythromycin**, **azithromycin**
- Often used in patients allergic to beta-lactams
- Active against most Gram-positive bacteria and some Gram-negative bacteria (*Haemophilus, Neisseria, Moraxella*)
- Important activity against intracellular bacteria including *Chlamydia, Legionella, Mycoplasma* species (therefore used, for example, in the treatment of severe/'atypical' pneumonia)
- Increasing resistance among staphylococci and streptococci

(*continued on next page*)

**Table 5** (*continued*)

| | |
|---|---|
| ***Lincosamides*** | Such as **clindamycin** |
| | ○ Mechanism similar to erythromycin |
| | ○ Good activity against staphylococci, streptococci, and anaerobes (uses include soft tissue and bone/joint infections) |
| | ○ Active against some protozoa, e.g. *P. falciparum* malaria, and *Pneumocystis jiroveci* pneumonia (PCP) |
| | ○ Clindamycin should not be used in conjunction with macrolides or chloramphenicol, as these drugs target the same ribosomal site in some organisms and may compete |
| ***Oxazolidinones*** | Such as **linezolid** |
| | ○ Active against most Gram-positive bacteria including MRSA and vancomycin-resistance enterococci (VRE) |
| | ○ Bacteriostatic |
| | ○ Main side effect is bone marrow suppression |
| **Inhibitors of nucleic acid synthesis** | |
| ***Fluoroquinolones*** | Such as **ciprofloxacin, levofloxacin, moxifloxacin** |
| | ○ Disrupt transcription and cause DNA damage |
| | ○ Bactericidal |
| | ○ **Ciprofloxacin** is active against many Gram positive and Gram-negative bacteria including *Pseudomonas* |
| | ○ **Moxifloxacin** has better activity against staphylococci and streptococci but is NOT active against *Pseudomonas*. It is also used for tuberculosis |
| ***Folate antagonists*** | Such as **sulphonamides** and **trimethoprim** |
| | ○ Act on different enzymes of the folic acid pathway |
| | ○ **Trimethoprim** is used for treatment of uncomplicated UTIs (but resistance is increasing) |
| | ○ **Sulphonamides** – resistance easily develops, so they are only used in combination: |
| | - Co-trimoxazole (septrin) = sulfamethoxazole + trimethoprim |
| | • Synergistic effect active against a range of Gram positive and Gram-negative bacteria and some protozoa (e.g. PCP) |
| ***Nitroimidazoles*** | Such as **metronidazole** |
| | ○ Active against most anaerobes |
| | ○ Also used to treat some protozoa, e.g. *Entamoeba histolytica* (amoebic dysentery), *Giardia* |
| | ○ Excellent oral bioavailability |
| | ○ Alcohol is avoided due to disulfiram-like reaction |

**Table 5**

## Conclusion

A knowledge of basic microbiology is essential for appropriate and safe surgical practice, hence its assessment in membership examinations. The field of microbiology is extremely wide and not exhaustively covered here, with topics including sepsis, soft tissue infections and peri-operative fever required for the MRCS but not included in this article. ◆

## REFERENCES


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