Antimicrobial Stewardship for Nursing Practice

Edited by **Molly Courtenay** and **Enrique Castro-Sánchez**

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3 Antimicrobials and Antimicrobial Resistance

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Objective: For the student to understand the core knowledge underpinning the concept of antimicrobial resistance and apply this knowledge to nursing practice to help prevent it.

Introduction

Despite the benefits of antibiotic use in healthcare, including reduced mortality, increased life expectancy and as adjuvants to other therapies, such as chemotherapy, infections caused by multidrug-resistant bacteria are now more frequent, globally, with therapeutic options to treat them increasingly limited (Blair *et al.*, 2015). Evidence points out that resistance to antimicrobials is part of the natural evolution of bacteria, and is likely to have existed before their discovery by humans (Fair and Tor, 2014). However, the contribution of humans to this evolutionary process and selective pressure is undoubtedly significant, which will be the core approach of this chapter. Antimicrobial resistance (AMR) is the capability of a micro-organism to overcome the action of an antimicrobial. When micro-organisms are exposed to antimicrobials, the susceptible strains will be killed, leading to the survival of the resistant ones. AMR is driven by the overuse of antibiotics in medicine, livestock farming and agriculture, and poultry production. Moreover, a further contributory factor is the lack of development of new antibiotics by the pharmaceutical industry (Blair *et al.*, 2015; Pontes *et al.*, 2018).

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Nurses have a crucial role to play in the early recognition of infection and actively take part in antimicrobial therapy (Courtenay *et al.*, 2018, 2019). It is therefore essential that they understand the underlying concepts of antimicrobial therapy and the process that leads to AMR.

Signs and Symptoms of Infection

An infection results from the imbalance between the mechanisms employed by the micro-organisms causing diseases and the host response to prevent this aggression. The outcome of this episode will depend on the number of micro-organisms and their ability to find the mode of entry, overcome host defences, invade tissue and produce toxins. Micro-organisms can be installed in a susceptible host by a number of routes including inhalation, ingestion, direct contact, direct inoculation and rupture of skin barriers (Fischbach and Dunning, 2015).

During healthcare, numerous situations allow pathogens to get in contact with a host. Hence, understanding the micro-organisms' routes of transmission, the pathogenic mechanisms and the susceptibility of the host is key to guiding the prevention measures adopted during care. The presence of pathogenic micro-organisms in a patient does not necessarily characterize an infection. If signs and symptoms of infection are absent, the patient can be considered colonized by pathogens. Thus, colonization is the process by which micro-organisms are present in the host, with a certain level of multiplication, but without producing clinical disease. Infection, however, involves the invasion of micro-organisms in the host's body tissues, with the generation of an inflammatory and immunological response, leading to clinical disease and resulting in signs and symptoms such as fever, purulent exudate from a wound, high blood cell count or pneumonia (Dani, 2014).

Not all colonization, however, results in infection. Some people may become temporarily or permanently colonized with pathogenic micro-organisms but never develop symptomatic disease, whereas others can become seriously ill and may even die due to the infection. The process of colonization is complex and sometimes involves changes in the colonizing strains, only detected by molecular studies (Padoveze *et al.*, 2008). In many situations, individuals immediately progress from colonization (or after a period of colonization) to symptomatic disease. The evolution of an initial colonization is frequently difficult to predict. Immune status at the time of exposure to an infectious agent and aspects of the pathogen's own virulence would ultimately define the evolution of the case (Siegel *et al.*, 2007).

Healthcare professionals should be aware of the early signs and symptoms of an infectious process (Singer *et al.*, 2016). The clinical presentation may be restricted to a certain anatomical location and include local signs and symptoms such as pain, erythema (redness), presence of purulent exudate (pus) and abscess formation. General signs and symptoms such as fever, tachycardia, sweating and changes in biomarkers reflected in laboratory tests (such as haemogram and cerebrospinal fluid) may indicate a systemic infection. The signs and symptoms of an infection vary depending on which area of the body is infected. Table 3.1

Table 3.1. Common infection sites and main signs and symptoms.

Major infection sites	Main signs and symptoms
Bloodstream	Fever, tachycardia, tachypnoea, hypotension, mental confusion, oliguria
Digestive tract	Nausea, vomiting, diarrhoea, abdominal pain
Respiratory tract	Tachypnoea, presence or change of secretion (changes in amount, colour, appearance)
Skin	Erythema, heat, pain, pus, macules, papules, vesicles
Urinary tract	Dysuria, polyuria, low abdominal pain
Wound	Erythema, heat, pain, pus, necrosis

describes common anatomical sites of infection and their main signs and symptoms. Of note, infections in neonates and children may exhibit atypical signs and symptoms, which may result in a diagnostic delay.

Nurses have a pivotal role to play in the early identification of infection. In in-patient settings, nurses provide bedside care around the clock, and are therefore in a privileged position to detect any changes, albeit slight, in the patient's condition. In primary and community care settings, nurses are usually the first and often the only point of contact for patients and families with the healthcare system.

Several nursing care activities, other than the measurement of vital signs and physical examination, provide opportunities to facilitate early detection of infection. For example, when administering intravenous medication, signs of inflammation may be observed at the catheter insertion site. If dressing a wound, the presence of purulent secretion or necrosis may be evidenced. Erythema, heat, or macules and papules may be noted when bathing a patient. During the emptying of a catheter bag, nurses can perceive changes in the urine, including pyuria.

All healthcare professionals should recognize the importance of adequate specimen collection during relevant stages of antimicrobial use (prior, during and post-antibiotic treatment). The optimal time for specimen collection varies according to the type of infection; however, for diagnostic purposes, sample collection is more profitable in the early stages of an infection episode (O'Donnell and Guarascio, 2017). Nurses should be aware of the need to correlate the signs and symptoms of infection and the optimal time for specimen collection. Ideally, nurses should ensure that cultures are performed before starting antibiotics, although antibiotic administration should not be delayed if this would affect the clinical outcome for the patient. Please refer to Pollack and Srinivasan (2014).

The adequate conservation of samples of blood, urine, faeces and secretions, and their delivery to the laboratory in a timely manner, is essential to ensure the quality of the samples collected and the results obtained. Negligence or carelessness in sample collection can lead to misdiagnosis, wasting laboratory time and delayed effective treatment (Fischbach and Dunning, 2015). This aspect is detailed in Chapter 2.

Qualified, sensitized and attentive nursing staff, with an appropriate workload, have demonstrated adherence to good practices with a decrease in the risk of healthcare-associated infection (Siegel *et al.*, 2007).

How Antimicrobials Work

Generally speaking, antimicrobials include any agent (such as antibiotics, antivirals, antifungals and antimalarials) with biological activity against micro-organisms. Antibiotic is a type of antimicrobial substance active against bacteria. Antimicrobials may be produced biologically by micro-organisms or synthetically by chemists. During the stages of pharmaceutical development, the antimicrobial activity of the drug is usually tested against several groups of micro-organisms to determine its spectrum of activity. A broad-spectrum drug is one that has activity against Gram-positive as well as Gram-negative species. A narrow-spectrum drug has activity against only one group of micro-organisms or only one species. The antimicrobial agents may either kill micro-organisms (-cidal) or inhibit their growth (-static), e.g. bactericidal or bacteriostatic.

The biochemical activities of micro-organisms are so similar to those in mammalian cells that the drug will affect both cell types. However, most antimicrobials have selective toxicity, i.e. show greater affinity to the microbial component than to the mammalian cells. The therapeutic index refers to the level of selective toxicity of a given drug comparing the blood concentration at which a drug causes a therapeutic effect to the amount of toxicity produced in humans (Tamargo *et al.*, 2015). A low therapeutic index indicates that the concentration of the drug that is therapeutic is also harmful to host tissue.

A complete description of the morphology and physiology of the micro-organisms' cells is beyond the scope of this chapter (see Chapter 2 instead). However, it is important to point out that viruses, for instance, are primarily intracellular pathogens, while bacteria may have a free life. This means that viruses need to use the structures and metabolism of host cells in order to survive and reproduce. Bacteria, on the other hand, can survive and reproduce without being sheltered in a host cell, which ensures their ability to survive in the environment. Among the relevant differences between Gram-positive and Gram-negative bacteria, the latter have thinner cell walls that are surrounded by lipid membrane, while Gram-positive bacteria have a tough and rigid mesh cell wall that surrounds the cytoplasmic membrane (Kapoor *et al.*, 2017). In bacterial cells, protein synthesis occurs in ribosomes from a messenger Ribonucleic acid (mRNA) in a process called translation. The ribosomes are a cell structure that makes protein. Proteins are needed for several cell functions such as repairing damage or directing chemical process. Bacterial ribosome represents one of the major targets for antibiotics in the cell. This structure is composed of three Ribonucleic acid (RNA) chains (16S, 23S and 5S) and more than 50 proteins assembled in two individual subunits, the small one known as 30S and the large one as 50S (Lin *et al.*, 2018).

Classification of antimicrobials may vary according to the targeted microorganisms (i.e. antibiotics, antivirals, antifungals, antimalarials), their molecular structure or their antimicrobial mechanisms (i.e. their ability to affect various essential cellular functions) (Hoerr *et al.*, 2016). Table 3.2 provides some examples of the mechanism of action of currently available antimicrobials.

- *Inhibitors of cell wall synthesis:* Antimicrobials may target the bacterial cell wall, mainly interfering with the building of the peptidoglycan chain. The penicillin-binding protein (PBP) is a transpeptidase, which plays a role in the cell wall building process. However, the β-lactam ring, that is part of the core structure of several antibiotic families, interacts with PBP, which then is unavailable for the synthesis of new peptidoglycan. Lysis of bacteria occurs due to disruption of the peptidoglycan layer (Dowling *et al.*, 2017).
- *Inhibitors of cytoplasmic membrane function:* Antimicrobials with affinity for lipids can bind irreversibly to cytoplasmic membrane sterols, such as ergosterol; others interfere with lipid biosynthesis. These actions lead to alterations in permeability, resulting in loss of nutrients and other compounds.
- *Inhibitors of protein synthesis:* The process of inhibition of protein synthesis can occur through a variety of ways of binding to ribosomes, which causes a misreading of mRNA, resulting in an abnormal protein or impairment of protein synthesis. Once incorporated in the cytoplasmic membrane, some of the abnormal protein will produce pores that enable more antibiotic to enter the bacterial cell. As more antibiotic reaches the cytoplasm and binds to ribosomes, the process continues up to shutting down the cell. Antibiotics such as macrolides, aminoglicosides and tetracyclines bind to the 30S subunit of ribosome, whereas chloramphenicol binds to the 50S subunit. In these binds, the aminoacyl and peptidyl transfer may be blocked. The binding of antimicrobial to free ribosomes allows the formation of a small peptide but prevents further elongation of the RNA chain (Dowling *et al.*, 2017; Kapoor *et al.*, 2017).
- *Inhibitors of nucleic acid synthesis:* Some antibiotics exert their antibacterial effects by disrupting Deoxyribonucleic acid (DNA) synthesis and causing lethal double-strand DNA breaks during the replication process. Antimicrobials interfere with nucleic acid synthesis by using several mechanisms:
    - binding to a subunit of the DNA-dependent RNA polymerase and therefore interfering with the initiation of transcription of this enzyme;
    - inhibition of enzymes such as Topoisomerase II (DNA gyrase) and Topoisomerase IV, so impairing DNA replication (Kapoor *et al.*, 2017);
    - phosphorylation of 5-fluorouracil and incorporation into RNA, interfering with normal protein synthesis;
    - inhibition of the viral primary transcription process, and preventing uncoating of the virus capsid;
    - inhibition of early viral replication step and subsequent impairment of viral nucleic acid synthesis;
    - acting as analogue of thymidine to be incorporated into viral DNA;
    - inhibition of enzymes that convert viral RNA into viral DNA;
    - blocking the pathway for folic acid synthesis, which inhibits DNA synthesis (Tenover, 2006).

Table 3.2. Mechanisms of antimicrobial action according to class compound and respective antimicrobial drug.

Mechanism of antimicrobial action	Class compound	Antimicrobial drug
Inhibitors of cell wall synthesis	Beta-lactams	Penicillins, ampicillin, amoxicillin, carbenicillin, methicillin
	Beta-lactams	Cephalosporins (cephalothin, cefamandole, cefotaxime, cefoxitin, cefazolin, cefoperazone, cefixime, cefprozil, cefpodoxime, ceftaroline, ceftolozane-tazobactam, ceftazidime-avibactam)
	Beta-lactams	Carbapenems (imipenem, meropenem, ertapenem, doripenem)
	Glycopeptides	Vancomycin, teicoplanin
Inhibitors of cytoplasmic membrane function	Polyenes	Amphotericin B, nystatin, candicidin, pimaricin, trichomycin, hamycin*
	Azoles	Ketoconazole, fluconazole, itraconazole*
	Polymixins	Polymixin B, polymixin E (colistin)
Inhibitors of protein synthesis	Aminoglycosides	Streptomycin, kanamycin, gentamycin, tobramycin, sisomycin, amikacin, neomycin, fortimicin A, netilmicin, 5-episisomicin, spectinomycin
	Tetracyclines	Tetracycline, doxycycline
	Amphenicols	Chloramphenicol
	Macrolides	Erythromycin, azithromycin, spiramycin, josamycin, roxithromycin, clarithromycin
	Lincosamides	Lincomycin, clindamycin
	Oxazolidinones	Linezolid
Inhibitors of nucleic acid synthesis	Ansamycins	Rifampicin, rifamycin B
	Quinolones	Nalidixic acid, fluoroquinolones (norfloxacin, ciprofloxacin, ofloxacin)
	Pyrimidines	Flucytosine*
	Amines	Amantadine, rimantadine**
	Virazole	Ribavirin**
	Nucleoside analogues	Idoxuridine, thymidine, vidarabine, acyclovir, zidovudine (azidothymidine or AZT)**
Antimetabolites	Sulfonamides	Sulfanilamide, sulfadiazine, sulfamethoxazole, sulfathiazole, sulfasoxazole, sulfapyridine

Continued

Table 3.2. Continued.

Mechanism of antimicrobial action	Class compound	Antimicrobial drug
	Sulfones	Dapsone
	Aminopyrimidines	Trimethoprim, ormetoprim
	Nitrofurans	Nitrofurantoin
	Others	Ethambutol, isoniazid (INH)
		Para-aminosalicyclic acid

*antifungals; **antivirals.

- *Antimetabolites:* These are compounds structurally similar to normal cellular metabolites and can compete with them for attachment to enzymes (Hoerr *et al.*, 2016; Kapoor *et al.*, 2017). For example:
  - similarity with para-aminobenzoic acid (PABA), competing for the enzyme dihydrofolate synthase and therefore preventing the synthesis of folic acid (Dowling *et al.*, 2017);
  - structural analogue of pteridine, preventing the synthesis of folic acid, and interfering with amino acid, and purine and pyrimidine synthesis;
  - structural analogue of nicotinamide, impairing the synthesis of nicotinamide adenine dinucleotide;
  - binding and inhibition of β-lactamase, resulting in a restoration of the antimicrobial activity (Dowling *et al.*, 2017).

Appropriate Antimicrobial Use

As previously mentioned, antibiotic resistance is the capacity of bacteria to survive and replicate in the presence of antibiotics that normally act to inhibit or kill them (Pontes *et al.*, 2018). There are two types of antimicrobial resistance: intrinsic and acquired (Dowling *et al.*, 2017).

- *Intrinsic resistance* is related to the innate ability of all or almost all prokaryotes (unicellular organisms that lack organelles or internal membrane-bound structures) to resist specific drugs; i.e. it occurs naturally in bacterial genomes.
- *Acquired resistance* may arise from spontaneous chromosomal mutations or exchange of genetic elements among micro-organisms. The latter situation occurs through mobile genetic elements, such as plasmids, integrons, transposons or genomic islands. Both these mechanisms of resistance are important for the dissemination of resistance between different species. They also contribute to the bacterial genome evolution. Acquired resistance is also associated with a gradual increase in antibiotic concentrations (Pontes *et al.*, 2018). This gradual increase creates an environmentally selective pressure and bacteria develop reversible drug-resistance profiles. It is important to note that, in small antibiotic doses (non-lethal concentrations), bacteria

can survive and grow normally. Nevertheless, non-lethal concentrations can induce specific resistance mechanisms (Lin *et al.*, 2015; Pontes *et al.*, 2018). These mechanisms are the dependant of the type of drug used and may induce resistant mechanisms against both the drug in use and related drugs (Pontes *et al.*, 2018). This phenomenon points out an implication for nursing practice highlighting the importance of proper antibiotic administration. Missing doses can lead to suboptimal drug concentration in the target-body sites, inducing the expression of resistant mechanisms or favouring the selection of resistant strains.

The main mechanisms found in bacteria to impair the action of antimicrobials are: (i) reduction of bacterial membrane permeability; (ii) increases in both expression and activity of efflux pump systems; (iii) synthesis of enzymes that are able to destroy or modify the drug; (iv) modification, substitution or disruption of antibiotic bacterial targets; and (v) biofilm formation.

Mechanisms (i)–(iv) are associated with antimicrobial resistance to the main antibiotic groups used in clinical practice: β-lactams, glycopeptides and aminoglycosides (Lin *et al.*, 2015; Pontes *et al.*, 2018). These mechanisms are discussed below.

- *Reduction of bacterial membrane permeability:* Cellular membrane is an important compound in a micro-organism's structure. This membrane has an intrinsic permeability that allows nutrient intake and acts as a first barrier to external agents. When the permeability on the cell surface is low, antibiotic blocking occurs, so drugs cannot achieve their targets. Compared to Gram-positive species, Gram-negative bacteria are usually less permeable to many antibiotics, as their outer membrane forms a permeability barrier. For instance, the glycopeptide antibiotic vancomycin inhibits peptidoglycan cross-linking. It does not occur in Gram-negative bacteria, in which this drug cannot cross the membrane and reach these substances in the periplasm (Blair *et al.*, 2015; Pontes *et al.*, 2018).
- *Synthesis of enzymes that are able to destroy or modify the drug:* A large number of enzymes that have been identified can degrade and modify antibiotics of different classes, such as β-lactams, aminoglycosides, amphenicols and macrolides. There are also subclasses of enzymes that can destroy or degrade different antibiotics which belong to the same class. An example is the β-lactam antibiotics group, where penicillin, cephalosporins, clavams, carbapenems and monobactams are hydrolysed by a variable range of β-lactamases, which are enzymes that destroy the β-lactams (Blair *et al.*, 2015; Lin *et al.*, 2015; Pontes *et al.*, 2018).
- *Modification, substitution or disruption of antibiotic bacterial targets:* This is one of the most common mechanisms of antimicrobial resistance. Most antibiotics bind to the bacterial targets in a specific way, thus preventing their normal role. Modifications in these targets, characterized by small mutations that prevent efficient antibiotic binding, can confer resistance (Blair *et al.*, 2015; Pontes *et al.*, 2018).

- *Increases in both expression and activity of efflux pump systems:* Bacterial efflux pumps are an important mechanism of resistance in which many antibiotics are actively transported out of the cells to the environment prior to reaching their intended targets. Efflux pumps are a kind of protein that constitutes all bacterial plasma membranes. When an over-expression (abnormal increase in the expression of a certain gene) occurs, the efflux pumps can provide a high level of resistance to antibiotics that were previously useful in the clinical practice. This mechanism has been seen since 1990 among some bacteria including *Enterobacteriaceae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* (Blair *et al.*, 2015; Lin *et al.*, 2015; Pontes *et al.*, 2018).

The speed with which micro-organisms have acquired resistance by increasingly diverse mechanisms demonstrates that better practices related to antibiotic use within the multidisciplinary health team are necessary (Pontes *et al.*, 2018).

By recognizing the mechanisms that lead to resistance, and the selective pressure exerted on the environment by the excessive use of antimicrobials, nurses can adopt a proactive attitude regarding antibiotic therapy. As part of their activities, nurses should obtain an allergy history from the patient to support optimal prescribing of antimicrobials, as well as monitoring and reporting adverse events of antimicrobial therapy. Nurses should review daily the clinical condition of patients, perform a proper choice of vascular access according to the therapy, and actively take part in multidisciplinary team discussions regarding antibiotic treatment, indication and duration. Please refer to Pollack and Srinivasan (2014).

The group of micro-organisms that each antimicrobial can target is identified during the pharmaceutical development. However, there are various behaviours of susceptibility and resistance among micro-organisms. In clinical practice, the microbiological examination of specimens collected from infected or colonized patients would provide information about the species that are the probable etiologic agent, as well as the antibiogram or antibiotic susceptibility report. Due to their characteristics of intracellular reproduction, culture tests and antibiograms are not routinely requested for viruses in clinical settings, but may be performed in research centres or public health laboratories.

The antibiogram will guide the choice of drug therapy by providing specific information regarding the susceptibility of a particular pathogen to certain antibiotics, including the minimum inhibitory concentration (MIC). MICs have established breakpoints to define susceptibility or resistance according to international organizations such as the Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) (O'Donnell and Guarascio, 2017). A timely microbiological examination with antibiogram will favour informed decisions earlier in the course of the infection and positively influence treatment outcomes. In many cases, however, antibiotics are prescribed and administered empirically, as microbiologic results may not be available at the time of making the clinical decision. Once the antibiogram is available, if etiologic agents are susceptible to antibiotic therapy, it would be possible to adjust the treatment accordingly, i.e. antibiotic de-escalation.

Aiming to support the prudent use of antimicrobials in both human and veterinary medicine, the World Health Organization (WHO) has published a list of critically important antimicrobials for human medicine (WHO, 2017). Nurses should be aware of the antimicrobials that have restricted indication and the need to save them for specific purposes. For instance, isoniazid is a drug used solely to treat tuberculosis or other mycobacterial diseases. Another example is rifampicin, which is considered as limited therapy as part of the treatment of mycobacterial diseases, including tuberculosis. Both these drugs are categorized as critically important antimicrobials (WHO, 2017). One strategy to combat the increasing antimicrobial resistance is the discovery of new antimicrobials as well as finding strategies to expand the useful life of those in existence. Bacteria, however, possess a great diversity of genes that allow them, at any time, to counteract the action of newly formulated or discovered antibiotic compounds (Lin *et al.*, 2015).

Finally, there is a significant worldwide effort towards a 'One Health' approach to defeat antimicrobial resistance. This approach refers to designing and implementing programmes, policies, legislation and research in which multiple sectors (e.g. human and animal health) work together to achieve better public outcomes (Ryu *et al.*, 2017). Nurses are the biggest healthcare workforce in the world; they are in a unique position to embrace the concept of One Health and be the propellant for a more collaborative, multidisciplinary and global effort against antimicrobial resistance (Premji and Hatfield, 2016).

Conclusion

Nurses are frontline professionals engaged in the fight against antimicrobial resistance. This includes active participation in early detection of infection, and taking responsibility regarding antimicrobial treatment to optimize the use of antimicrobial agents.

Case Study 1: Antimicrobial Stewardship in Action

A three-year-old child arrived at the Primary Health Care Unit (PHCU) with clear/ transparent rhinorrhoea and fever (38°C). The mother stated that the child had been tearful and had had a poor appetite for 3 days. After a medical evaluation that revealed regular overall clinical condition and hydrated mucous membranes with no signs of bacterial infection in the ears, throat and lungs, the child was discharged from the PHCU. The medical prescription included nasal saline, antipyretic (to reduce fever discomfort) and the recommendation to reinforce oral hydration and to return within 2 days for reassessment. The mother expressed concern about the sufficiency of the treatment. She did not agree with the prescription and questioned why antibiotics were not prescribed to prevent worsening of the child's condition.

Continued

Case Study 1: Continued.

Questions and answers

What were the clinical characteristics that pointed out that there was no bacterial infection?
Answer: There was a clear/transparent rhinorrhoea. Medical evaluation revealed regular overall clinical condition and hydrated mucous membranes with no signs of bacterial infection in the ears, throat and lungs.

What arguments would you use to reassure the mother that there is no need for antibiotics?
Answer: The clinical presentation suggested a viral upper airways infection, which is usually self-limiting, with spontaneous remission within a few days. Antibiotics do not act on viruses, and therefore would not improve the child's condition, and may even worsen appetite. In addition, the inappropriate use of antibiotics could contribute to select antimicrobial resistant strains, decreasing the treatment options for eventual future bacterial infections. Emphasize the need for the child's reassessment within 2 days or earlier in the case of any worsening in the child's overall clinical condition.

Case Study 2

An obese patient with diabetes arrived at the emergency room with pulmonary thromboembolism. The patient had no other signs. Intubation and mechanical ventilation were carried out. On the fifth day of hospitalization, the patient developed a fever with a large amount of purulent secretion on tracheal aspirations. Samples of blood and tracheal secretions (semi-quantitative method) were collected for culture. The physician prescribed vancomycin and meropenem empirically. The results of the microbiological exams revealed *Klebsiella pneumoniae* sensitive to the antibiotics tested.

Questions and answers

What are the characteristics that point to an ongoing infection?
Answer: The patient presented with fever and a change in respiratory secretions and had an invasive device that would reduce the body's natural immunity. Because clinical signs and symptoms were not present on admission, and as the length of hospital stay was greater than 72 hours, this was considered a healthcare-associated infection.

What argument would you use to discuss with the physician the need to review the antimicrobial prescription?
Answer: Despite being a healthcare-associated infection, the micro-organism identified is Gram-negative and susceptible to other drugs. De-escalation of antibiotics and exclusion of vancomycin (which is mainly addressed to Gram-positive) should be considered.

Key Points

- An infection results from the imbalance between the mechanisms employed by the micro-organisms causing diseases and the host response to prevent this aggression.
- Infections may be detected by specific local or systemic signs and symptoms.
- Antimicrobials' mode of action includes inhibition of cell wall synthesis, inhibition of cytoplasmic membrane function, inhibition of protein synthesis, inhibition of nucleic acid synthesis and antimetabolite activity.
- Antimicrobial resistance may be intrinsic or acquired.
- The main mechanisms found in bacteria to impair the action of antimicrobials are: reduction of bacterial membrane permeability, increases in both expression and activity of efflux pump systems, synthesis of enzymes which are able to destroy or modify the drug; modification, substitution or disruption of antibiotic bacterial targets, and biofilm formation.

Further Reading

Casadevall, A. and Pirofski, L.A. (2000) Host-pathogen interactions: basic concepts of microbial commensalism, colonization, infection, and disease. *Infection and Immunity* 68(12), 6511–6518.

WHO (World Health Organization). One health. Available at: https://www.who.int/features/qa/one-health/en (accessed 14 September 2019).

WHO (2018) *WHO Competency Framework for Health Workers' Education and Training on Antimicrobial Resistance*. Available at: http://apps.who.int/medicinedocs/documents/s23443en/s23443en.pdf (accessed 14 September 2019).

References

Blair, J.M., Webber, M.A., Baylay, A.J., Ogbolu, D.O. and Piddock, L.J. (2015) Molecular mechanisms of antibiotic resistance. *National Review of Microbiology* 13(1), 42–51.

CDC (Centers for Disease Control and Prevention) (2014) Core elements of hospital antibiotic stewardship programs. Atlanta, Georgia: US Department of Health and Human Services, CDC [cited 02/04/2019]. Available at: http://www.cdc.gov/getsmart/healthcare/implementation/core-elements (accessed 10 September 2019).

Courtenay, M., Lim, R., Castro-Sánchez, E., Deslandes, R., Hodson, K., *et al*. (2018) Development of consensus-based national antimicrobial stewardship competencies for UK undergraduate healthcare professional education. *Journal of Hospital Infection* 100(3), 245–256.

Courtenay, M., Castro-Sánchez, E., Gallagher, R., McEwen, J., Bulabula, A.N.H., *et al*. (2019) Development of consensus based international antimicrobial stewardship competencies for undergraduate nurse education. *Journal of Hospital Infection*, 103(3): 244–250.

Dani, A. (2014) Colonization and infection. *Central European Journal of Urology* 67(1), 86–87.

Dowling, A.M., Adley, C. and O'Dwyer, J. (2017) Antibiotics: mode of action and mechanisms of resistance. In: Méndez-Filas, A. (ed.) *Antimicrobial Research: Novel Bioknowledge and Educational Programs*. Formatex Research Center, Badajoz, Spain.

Fair, R.J. and Tor, Y. (2014) Antibiotics and bacterial resistance in the 21st century. *Perspectives on Medicinal Chemistry* 28(6), 25–64.

Fischbach, F. and Dunning, M. (2015) *Nurse's Quick Reference to Common Laboratory and Diagnostic Tests*, 6th Edition. Wolters Kluwer Health/ Lippincott Williams & Wilkins, Philadelphia, Pennsylvania.

Hoerr, V., Duggan, G.E., Zbytnuik, L., Poon, K.K., Grosse, C., *et al*. (2016) Characterization and prediction of the mechanism of action of antibiotics through NMR metabolomics. *BMC Microbiology* 16, 82.

Kapoor, G., Saigal, S. and Elongavan, A. (2017) Action and resistance mechanisms of antibiotics: a guide for clinicians. *Journal of Anaesthesiology Clinical Pharmacology* 33(3), 300–305.

Lin, J., Nishino, K., Roberts, M.C., Tolmasky, M., Aminov, R.I. and Zhang, L. (2015) Mechanisms of antibiotic resistance. *Frontiers in Microbiology* 6, 34.

Lin, J., Zhou, D., Steitz A.T., Polikanov, Y.S. and Gagnon, M.G. (2018) Ribosome-targeting antibiotics: modes of action, mechanisms of resistance, and implications for drug design. *Annual Review of Biochemistry* 87(1).

O'Donnell, L.A. and Guarascio, A.J. (2017) The intersection of antimicrobial stewardship and microbiology: educating the next generation of health care professionals. *FEMS Microbiology Letters* 364(1).

Padoveze, M.C., de Jesus Pedro, R., Blum-Menezes, D., Bratfich, O.J. and Moretti, M.L. (2008) Staphylococcus aureus nasal colonization in HIV outpatients: persistent or transient? *American Journal of Infection Control* 36(3), 187–191.

Pollack, L.A. and Srinivasan, A. (2014) Core elements of hospital antibiotic stewardship programs from the Centers for Disease Prevention and Control. *Clinical Infectious Diseases* 59(3), S97–S100. Available at: https://academic.oup.com/cid/article/59/suppl_3/S97/318001 (accessed 14 September 2019).

Pontes, D.S., de Araujo, R.S.A., Dantas, N., Scotti, L., Scotti, M.T., de Moura, R.O. and Mendonca-Junior, F.J.B. (2018) Genetic mechanisms of antibiotic resistance and the role of antibiotic adjuvants. *Current Topics in Medicinal Chemistry* 18(1), 42–74.

Premji, S.S. and Hatfield, J. (2016) Call to action for nurses/nursing. *BioMed Research International* 2016, art. ID 3127543.

Ryu, S., Kim, B.I., Lim, J.S., Tan, C.S. and Chun, B.C. (2017) One health perspective on emerging public health threats. *Journal of Preventive Medicine and Public Health* 50(6), 411–414.

Siegel, J., Rhinehart, E., Jackson, M., Chiarello, L. and HICPAC (2007) *Healthcare Infection Control Practices Advisory Committee: 2007 Guidelines for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings*. Available at: https://www.cdc.gov/niosh/docket/archive/pdfs/NIOSH-219/0219-010107-siegel.pdf (accessed 15 September 2019).

Singer, M., Deutschman, C.S., Seymour, C.W., Shankar-Hari, M., Annane, D., *et al*. (2016) The third international consensus definitions for sepsis and septic shock (Sepsis-3). *Jama* 315(8), 801–810.

Tamargo, J., Le Heyzey, J.Y. and Mabo, P. (2015) Narrow therapeutic index drugs: a clinical pharmacological consideration to flecainide. *European Journal of Clinical Pharmacology* 71, 549–567.

Tenover, F. (2006) Mechanisms of antimicrobial resistance in bacteria. *American Journal of Infection Control* 34(5), S3–S10.

WHO (World Health Organization) (2017) *WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance. Critically Important Antimicrobials for Human Medicine*, 5th Edition. World Health Organization, Geneva, Switzerland.