Microbe of the month

Breaking The Chain of Infection

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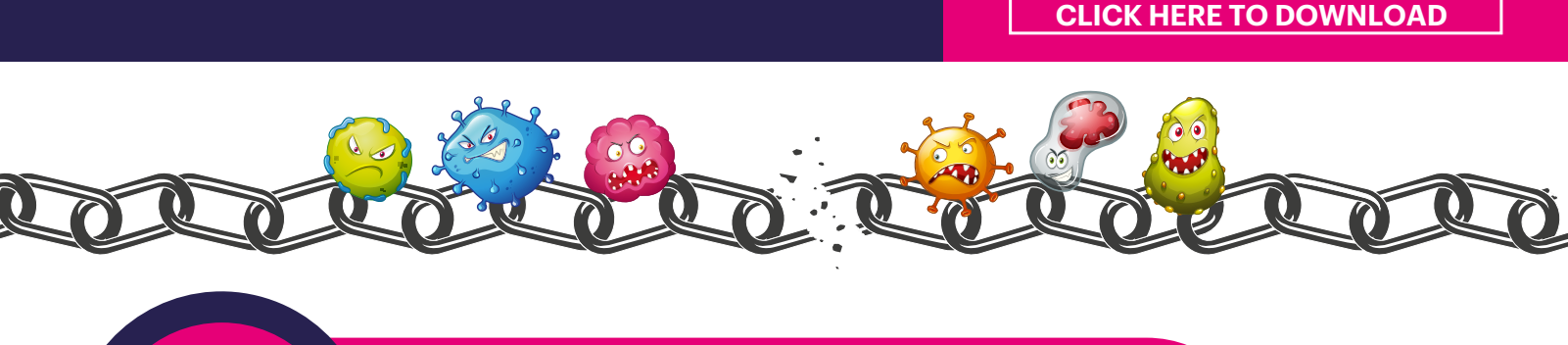


Featured this month:

Acinetobacter baumannii

An update on the 'wolf in sheep's clothing'

Hello readers!

The aim of the Microbe of the Month newsletter is to help create awareness about microorganisms of clinical importance, in an easy to read and understand format. Each newsletter provides insights into prevalent healthcare-related pathogens and those aspects which are relevant to Infection Prevention and Control (IPC), and Antimicrobial Stewardship (AMS) practice.

Please use this newsletter as a teaching tool in your workplace, share it widely and start an 'infectious dialogue' about topical issues in infection control!

Background – the 'ESKAPE' pathogens

The '**A**' in 'ESK**A**PE' (a medical microbiology acronym coined in 2008) denotes the Gram-negative coccobacillus ***Acinetobacter baumannii,*** which remains at the top of both the **World Health Organisation's** as well as **The Centers for Disease Control and Prevention's** (CDC) list of 'priority pathogens' (i.e., those antibiotic-resistant bacteria that currently pose the greatest threat to human health, and for which new antibiotics are urgently needed).[1,2,3]

The other five **antibiotic resistant bacteria in the 'ESKAPE' group** comprise ***E**nterococcus faecium, **S**taphylococcus aureus, **K**lebsiella pneumoniae, **P**seudomonas aeruginosa,* and ***E**nterobacter* species. These pathogens comprise both Gram-positive and Gram-negative bacteria, able to evade or 'escape' commonly-used antibiotics due to the increasing multi-drug resistance (MDR) mechanisms they employ.

*Readers are referred to Microbe of the Month **January 2020 'Global Action on AMR'** for more information on this topic.*

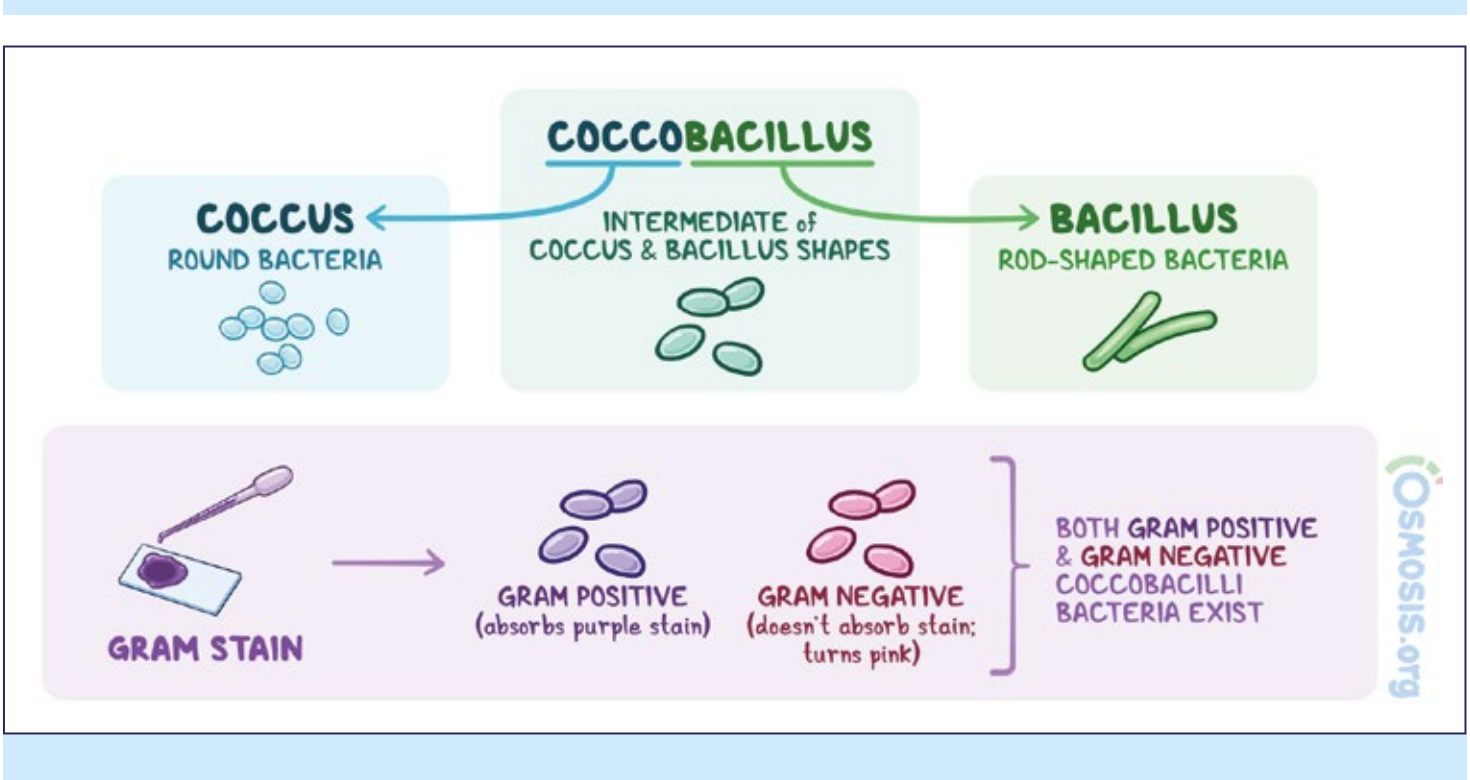
Acinetobacter baumannii (formerly known as *Acinetobacter calcoaceticus*) is an opportunistic pathogen found in soil and water, and is associated with life-threatening healthcare-associated infections in immunocompromised, intensive care unit and burns injury patients due to its ability to live on a variety of surfaces and environments.

Key words: *priority pathogen, intrinsic antibiotic resistance, healthcare-associated infection (HAI) outbreaks, carbapenem resistance, pan-resistance.*

THE MICROBIOLOGY OF ACINETOBACTER BAUMANNII [4,5,6,11]

A. *baumannii* is an encapsulated Gram-negative coccobacillus that is generally non-motile.

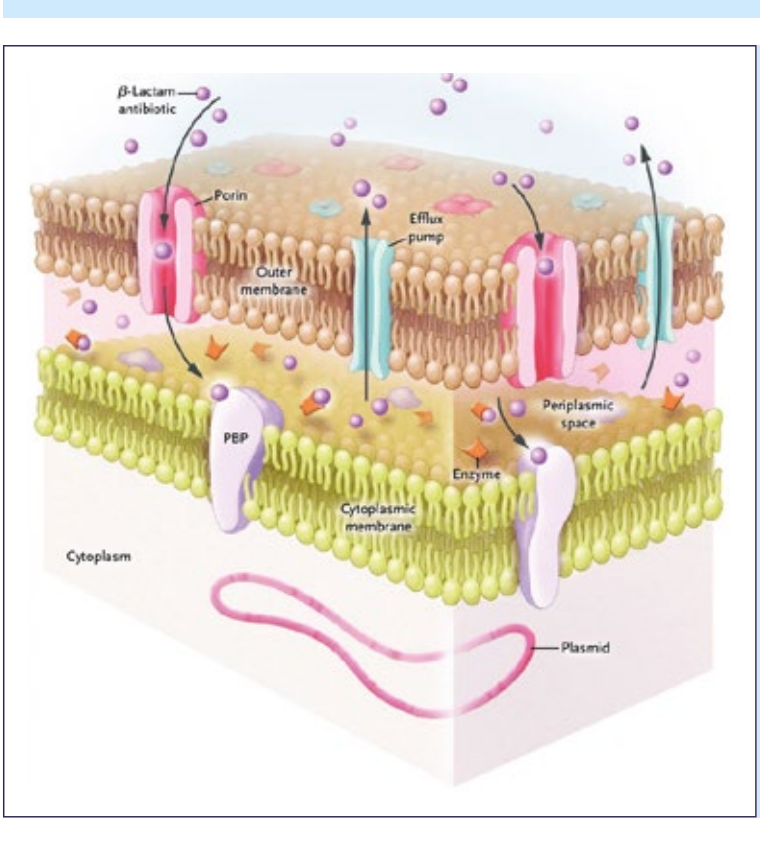
A ***coccobacillus*** (plural *'coccobacilli'*) is a type of bacterium with a shape in between cocci (spherical bacteria) and bacilli (rod-shaped bacteria).



Acinetobacter has specific features on its outer cell membrane which include **porins** and **efflux channels,** which contribute to its inherent **antibiotic resistance**.

Porins are protein channels that allow the transport of molecules across the cell membrane and are also sites of attachment for antibiotics. However, A. *baumannii* has fewer and smaller porins than other Gram-negative bacteria, thereby decreasing cellular permeability and increasing its antibiotic resistance.

Efflux pumps located in the cell membrane are used to pump chemicals and antibiotics out of the cell, modifications which recent advances in molecular technology have shown to have been acquired via horizontal gene transfer from other Gram-negative bacteria such as *E. coli* and *Pseudomonas aeruginosa*.



The cell wall on A. *baumannii* is not static, **but changes** (i.e., it becomes 'thicker') **in response to dry or adverse environmental conditions**.

This is believed to be caused by a change in the distance between the outer and plasma membranes, while decreased cell division changes the shape of A. *baumannii* from rod shaped to cocci.

Figure 1. Potential mechanisms of antibiotic resistance in *Acinetobacter*.[5]

Clinical significance?
Its appearance may occasionally cause errors of judgement in preliminary laboratory identification (e.g., it may resemble Gram-positive cocci such as *Staphylococcus aureus* on microscopy). Therefore, in critically ill patients at risk of septicaemia or ventilator-associated pneumonia, the possibility of colonisation or secondary infection with multi-drug resistant A. *baumannii* should always be considered, and specimen results discussed with the medical microbiologist if necessary.

The term 'pan-resistance' has been used to describe strains of Acinetobacter which are resistant to all standard antimicrobial agents tested (except colistin).[5]

EPIDEMIOLOGY AND MODE OF TRANSMISSION [1,2,3,4,5,8]

Acinetobacter species pose very little risk to healthy people. Outbreaks of *Acinetobacter* infection typically occur in intensive care and burns units, causing ventilator-associated pneumonia, and blood stream, wound and urinary infections. Very ill patients (e.g., those with chronic lung diseases, diabetes, large wounds, ventilated and/or with invasive catheters, prolonged hospital stay, etc.) are at greater risk for Acinetobacter infection.

A. baumannii can live for long periods of time on a variety of environmental surfaces (including dry items such as sheets and furniture) and shared patient equipment if they are not properly cleaned. The bacterium secretes *exopolysaccharides* **(EPS)** - biological polymers which are one of the main components of an extracellular **biofilm matrix** - to help protect the pathogen from unfriendly environmental conditions, including variations in temperature, pH, antibiotics, disinfectants, and host immune defences.

The bacteria are spread from one person to another through contact with these contaminated surfaces, shared equipment, or person-to-person spread, often via contaminated hands. (Figure 2)

Outbreaks of *A. baumannii* have been traced to common-source contamination, particularly contaminated respiratory therapy and ventilator equipment, as well as cross-infection by the hands of healthcare workers who have cared for colonised or infected patients (or touched contaminated fomites), and the occasional healthcare worker who carries an epidemic strain.

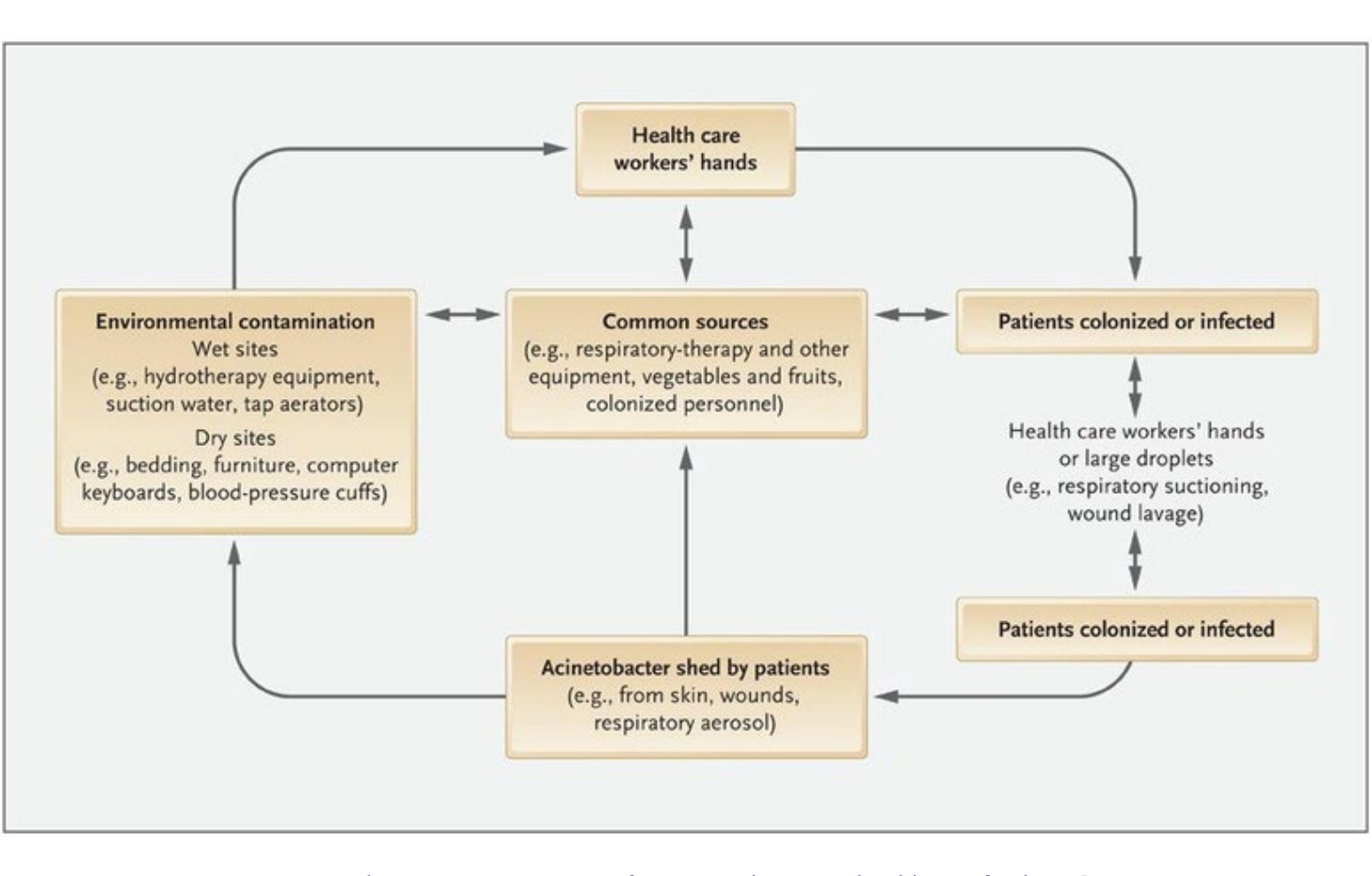
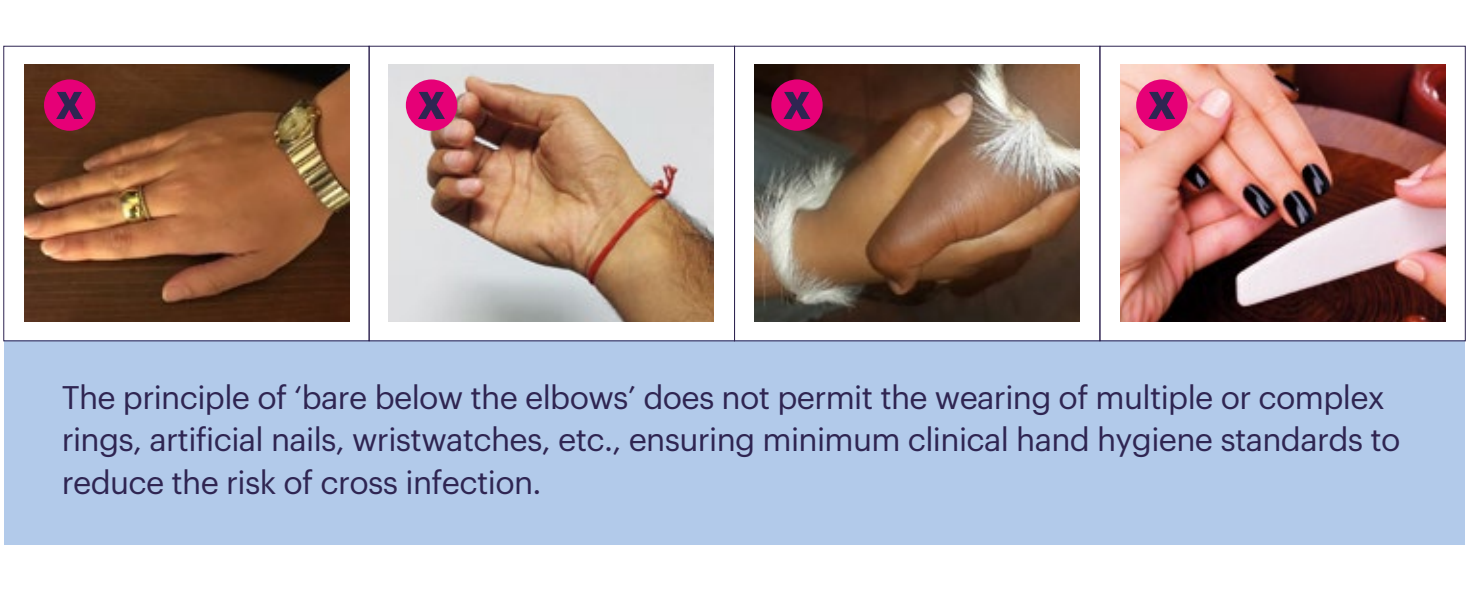


Figure 2. Reservoirs, sources and transmission patterns for Acinetobacter in healthcare facilities.[5]

Clinical significance?
Once introduced into a hospital, Acinetobacter species often have an epidemiologic pattern of serial or overlapping outbreaks caused by various multidrug-resistant strains, with a single endemic strain usually predominating at any one time. Prolonged colonisation (months to years) may result in *A. baumannii* becoming endemic in a ward after an outbreak.[5]

Note: Multi-drug resistant *Acinetobacter* is commonly susceptible to approved hospital-grade disinfectants. Reports of failure to contain the bacteria are likely ***due to personnel not following correct cleaning procedures than disinfectant resistance***. An outbreak will be more successfully controlled if the source is identified and eliminated.[8]



The principle of 'bare below the elbows' does not permit the wearing of multiple or complex rings, artificial nails, wristwatches, etc., ensuring minimum clinical hand hygiene standards to reduce the risk of cross infection.

ANTIMICROBIAL MANAGEMENT OF ACINETOBACTER INFECTION

The management of carbapenem-resistant *A. baumannii* ('CRAB') infections is difficult for several reasons. Firstly, CRAB is commonly recovered from respiratory specimens or wounds. Therefore, it is not always clear if an isolate is merely a colonising organism in patients who are ill for underlying reasons (e.g., corticosteroid therapy, mechanical ventilation, or patients with extensive burns), or if CRAB represents a true infection, which leads to uncertainty about the need for antibiotic therapy.[7]

Unfortunately, there is no clear "standard of care" antibiotic regimen for CRAB infections, so consultation with a medical microbiologist or infectious diseases specialist is recommended because of differences in regional resistance data.
Antibiotic therapy usually includes meropenem, tigecycline, minocycline, colistin, amikacin, rifampicin, and polymyxin B. **Combination therapy may be required for the growing number of carbapenem-resistant cases.**[7,8,9,10,11]

In South Africa, carbapenem resistance in *A. baumannii* is 80%, with consistent findings across the country, and with increasing levels of resistance over time. (Figure 3.) **One in five isolates now shows non-susceptibility to tigecycline.**

This limits treatment options, especially with respect to the 'last-resort antimicrobial' colistin, which is not registered locally. The use of colistin to treat pan-resistant Gram-negative infections requires a Section 21 approval through the South African Health Products Regulatory Authority (SAHPRA) in order to procure it.[9,10]

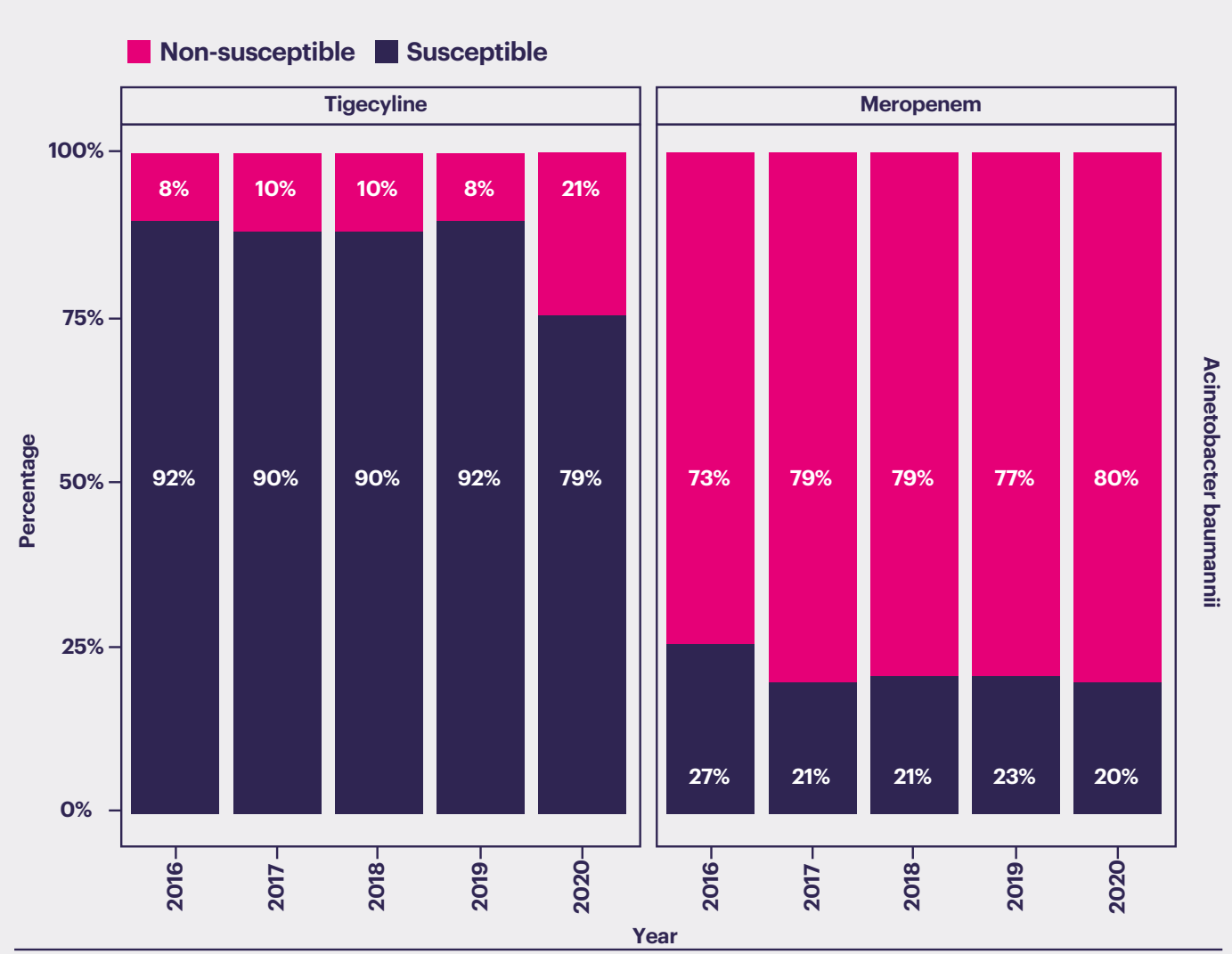


Figure 3. Percentage of non-susceptible *Acinetobacter baumannii* isolates to aminoglycosides and meropenem, 2016-2020.[10]

To optimise the effect of available agents, alternative therapeutic approaches have been used, such as the extended or continuous administration of intravenous (IV) antibiotics. It appears that continuous IV infusion of antibiotics with time-dependent bacterial killing is superior to normal intermittent IV administration. For example, extended infusion of beta-lactams such as carbapenems or cefepime can achieve drug concentrations above the minimum inhibitory concentration (MIC) for a longer time against less susceptible organisms, and may even reduce the incidence of antibiotic resistance.[11]

THE BOTTOM LINE... [1,2,3,5,7,8]

- The Infection Control Practitioner (IPC) should undertake active laboratory surveillance for *Acinetobacter* species.
- Strict hand hygiene protocols and 'bare below the elbows' are non-negotiable – a rule against the wearing of jewellery, wrist watches, long sleeves and artificial nails should be an enforceable institutional policy.
- Physicians should liaise with the Medical Microbiologist to determine whether results indicate *Acinetobacter* colonisation versus infection, and prescribe appropriate antibiotic regimens in line with current clinical guidelines and AMS principles.
- Monitor AMS practices and limit the use of broad-spectrum antibiotics, such as fluoroquinolones or carbapenems, where possible.
- Contact isolation precautions (hand hygiene, and the use of gloves and aprons for contact with wounds and secretions) must be implemented and closely supervised for colonised and infected patients.
- Supportive care includes removing or replacing lines, catheters or drains timeously, and the use of strict protocols and documentation for their insertion and aftercare.
- Patient decolonisation (BD skin cleansing with chlorhexidine gluconate 4% liquid soap) in ICUs and burns units should be standard procedure.
- Avoid fresh flowers and potted plants in high-risk clinical areas.
- Audit environmental cleaning and disinfection practices and review IPC antiseptic and disinfectant guidelines for appropriate product selection, use and storage.
- Hydrogen peroxide vapor is an effective mode of decontamination for isolation rooms following thorough environmental cleaning, if available.
- Conduct multidisciplinary in-depth investigations for all *Acinetobacter*-related HAIs and outbreaks; determine the source/s where possible, and update risk assessments and IPC protocols.

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