Chapter 8

Pathogens Important to Infection Prevention and Control

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Key Points
• Infection prevention and control practitioners routinely address issues related to tuberculosis and multi-drug resistant microorganisms. • Tuberculosis control involves engineering controls, administrative controls, and personal protective equipment. • Many microorganisms have developed resistance to antimicrobials, making them less effective. Control measures vary by microbe. • Infection prevention and control management of these various pathogens differs depending on the institutional setting and the resources available.

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Introduction

Many microorganisms are of interest to infection prevention and control (IPC) practitioners; however there are specific microbes that are of greater concern in the healthcare setting. Several are of importance to practitioners on a daily basis including antibiotic resistant organisms (ARO) (e.g., methicillin-resistant *Staphylococcus aureus* [MRSA], vancomycin-resistant *Enterococci* [VRE], *Clostridium difficile*, multi-drug resistant Gram-negative bacteria, and tuberculosis [TB]. We have focused this chapter on these microorganisms. Section A focuses on TB and Section B focuses on the AROs. It is important that IPC programmes use information regarding local epidemiology to guide their surveillance activities.

SECTION A: Mycobacterium tuberculosis

Background[1-2]

TB is an infectious disease that affects all areas of the world. In 2014 there were 9.6 million new cases of TB and 1.5 million deaths, the majority occurring in developing countries. 80% of reported cases occur in just 22 countries with 58% of new cases in 2014 occurring in South-East Asia and Western Pacific Regions. All six World Health Organization regions show decreasing incidence rates of TB; TB mortality has decreased globally by 47% since 1990 with most of those gains occurring after 2000.

Multidrug resistant TB (MDR-TB) is resistant to both isoniazid and rifampin. Extensively drug resistant TB (XDR-TB) is resistant to isoniazid, rifampin, any fluoro-quinolone, and any second line injectable drug. There were almost 480, 000 cases of MDR-TB in 2014. As of 2015, 105 countries and all regions of the world reported at least one case of XDR-TB. It is estimated that almost 10% of people with MDR-TB have XDR-TB.

Pathogenesis and Transmission[3]

TB is spread by droplet nuclei traveling through the air when someone with active disease coughs, talks, sneezes, or spits. The bacteria are inhaled into the lungs and multiply in the alveoli. Only a small number of bacilli need to be inhaled to become infected. Once in the body the bacteria can travel to any location. People infected with TB bacilli will not necessarily become sick with the disease; latent TB occurs when the bacilli are contained by the body's host defences. Approximately 10% of people with latent TB will go on to develop active TB during their lifetime. Active TB occurs when the bacteria continue to grow in an organ and causes symptoms; lungs are the most commonly infected organ. Other common sites of infection include the pleura, central nervous system, lymphatic system, genitourinary systems, bones, and joints. TB outside the lungs is referred to as extrapulmonary TB and is generally not contagious.

Pulmonary TB symptoms include a cough that brings up thick, cloudy, and, sometimes, bloody sputum for more than 2 weeks, tiredness, appetite loss/unexplained weight loss, night sweats, fever/chills, and shortness of breath. In people with extrapulmonary TB other signs and symptoms that are specific to the site of disease may be involved. Risk factors for TB include:

- illnesses that weaken the immune system, such as cancer and HIV,
- close contact with someone with active TB,
- caring for a patient with active TB,
- living or working in crowded places like prisons, nursing homes and homeless shelters where there are other people with active TB,
- poor access to healthcare,
- alcohol or drug abuse,
- travel to places where TB is endemic,
- being born in country where TB is endemic, or

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- some treatment medications for rheumatoid arthritis.

Evaluation for TB[3]

The tuberculin skin test (TST) can be used to determine infection with TB. It can take up to three months for a newly exposed individual to develop a reaction to the TST. The management of a positive TST should occur in two steps. First, confirmation of a positive TST should be followed by a referral for a medical evaluation. Methods that can be used to determine if someone has active disease include checking their medical history for potential exposures, demographic risk factors, and identifying medical conditions that increase the risk of TB. Completing a physical examination for current and past signs and symptoms of TB can be helpful. A chest radiograph can be assistive, however it is not confirmatory. The standard method to diagnose TB is microscopic examination of stained direct smears (e.g., sputum, cerebrospinal fluid, pus), particularly in areas with a lack of ability to culture. TB may be cultured in the laboratory; however results can take up to six weeks for final confirmation. Bacteria grown on culture can be used to determine susceptibilities.

Treatment

Treatment for latent TB is generally nine (9) months with Isoniazid. Treatment for active TB should be consistent with the WHO DOTS protocol.[4] Missing doses or incomplete treatment can lead to bacterial resistance. Ensuring adherence to therapy is important to prevent resistance and treatment failures. Patients being treated must be monitored for adverse reactions.[1]

Infection Prevention and Control (IPAC) Measures[5]

IPC measures can be divided into 3 areas; engineering controls, administrative controls, and personal protective equipment.

- Engineering controls include the use of negative pressure isolation rooms, enhanced air exchanges, the use of ultraviolet lights, and high-efficiency particulate air (HEPA) filtration systems.
- Administrative controls include the use of policies and practices to identify patients with signs and symptoms of TB, the early isolation of suspected case,s and prompt treatment of active cases.
- Personal protective equipment that can be used to limit transmission includes the use of surgical masks for symptomatic patients and the use of filtering face-piece respirators (e.g., N95, P100) for healthcare workers.

Conclusion

Despite the global impact of TB, it remains a treatable and preventable disease. The impact of TB on a healthcare facility is a factor of the epidemiology of TB in the geographic area. Occupational exposure remains a significant risk in any institution. Use of IPC measures will help to mitigate potential exposures of staff or patients.

SECTION B: Antibiotic Resistant Organisms (AROs)

Introduction

Antimicrobial agents have been used since the 1940s, greatly reducing illness and death from infectious diseases when prescribed and taken correctly. However, with time, microorganisms have adapted making these drugs less effective. People infected with AROs have longer and more expensive hospital stays and are more likely to die as a result of infection. These microorganisms are prevalent all over the world and are pathogens of major concern.

Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Background[6-7]

Staphylococcus aureus is a Gram-positive coccus bacterium and one of the leading causes of human bacterial infections worldwide. Up to 30% of people are colonised in areas like the nares, pharynx, or perineum. Many people become transiently colonised, especially on hands, which is not harmful if the skin is intact. Colonisation can increase the risk of infection depending on patient-related factors.

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Mechanisms of Resistance[7]

S. aureus can become resistant to antibiotics used for treatment. Methicillin resistance in *S. aureus* is mediated by the presence of a genetic element called Staphylococcal Cassette Chromosome mec (SCC_{mec}) containing the mecA gene, which encodes the production of an altered penicillin-binding protein, called PBP2a. PBP2a does not effectively bind ß-lactam antibiotics and as a result MRSA is resistant to almost all currently available penicillins, cephalosporins, and carbapenems.

Epidemiology[8]

MRSA first became a problem in the 1960s; however its resurgence in the late 1980s into present day has reached epidemic proportions. Globally the burden of disease caused by healthcare-associated, and, more recently, community-associated MRSA is rising, resulting in considerable healthcare pressures due to increased lengths of stay, costs, morbidity, and mortality. Although there is considerable variation in MRSA rates from country to country, and even from hospital to hospital within a country, MRSA remains a significant antibiotic-resistant pathogen in hospitalised patients.

Community Associated MRSA[9]

MRSA was previously considered to be primarily a healthcare-associated issue (HA-MRSA), affecting older adults with co-morbidities. In the past decade, community-associated MRSA (CA-MRSA) has emerged in many parts of the world. In contrast to HA-MRSA, CA-MRSA occurs in healthy individuals without traditional risk factors.

First reported in remote populations in Australia, strains have now been reported in Asia, Canada, USA, South America, and throughout Europe. CA- and HA-MRSA strains have been found to be genotypically and phenotypically different.

CA-MRSA may be able to colonise more easily and be more virulent than HA-MRSA strains given its ability to become endemic in so many countries so quickly. The acquisition of CA-MRSA is associated with crowding, compromised skin integrity, contaminated items or surfaces, and lack of cleanliness. Populations with high numbers of CA-MRSA infections include military personnel, sports players, and children in day care centres. The range of diseases caused by CA-MRSA is the same as *S. aureus*, with the most common manifestation being skin and soft tissue infection. CA-MRSA can be especially virulent causing overwhelming tissue destructive infections, such as necrotising fasciitis and fulminant necrotising pneumonia.[6]

Decolonisation

There is a lack of evidence supporting the routine use of decolonisation. Many patients have issues that make the likely success of decolonisation poor, such as open wounds or prosthetic devices. Patients only colonised at skin sites may have a more successful decolonisation, however they may not remain MRSA free permanently.

Control Measures

See Table 8.1- Major Pathogens of Concern in Healthcare Facilities.

Vancomycin Resistant *Staphylococcus aureus* (VRSA)

Vancomycin is often the drug of choice in the treatment of MRSA infections. Of concern is the subsequent appearance of *S. aureus* with a reduced susceptibility to vancomycin. VRSA is MRSA that contains the resistance genes Van-A or Van-B which confer vancomycin resistance. Transmission of these strains between patients has the potential for major public health consequences.

S. aureus with a reduced susceptibility to vancomycin was first identified in Japan in 1996, subsequently being identified in many other countries. VRSA was identified in 2002 in the USA. The lack of epidemiological data for VRSA has some areas recommending strict adherence to Contact Precautions and potentially higher levels of additional precautions for patients carrying these bacteria.

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Vancomycin Resistant Enterococcus (VRE)

Background

Enterococci are facultative anaerobic Gram-positive cocci that are part of the normal gut flora, however they may also be present in the oropharynx, vagina, or skin.[10] Enterococci can also be found on environmental surfaces. These bacteria can cause serious infections, such as septicaemia, endocarditis, urinary tract infections, and wound infections, especially in immunocompromised patients.[11]

Infections with enterococci are treated with a group of antibiotics called glycopeptides, for example vancomycin. Glycopeptides inhibit the synthesis of the microbial cell wall in susceptible bacteria. VRE is an *Enterococcus* that is resistant to vancomycin. There are two types of resistance. Intrinsic resistance, demonstrated by *E. gallinarum* and *E. casselflavis*, is naturally occurring, low-level vancomycin resistance. These bacteria are less commonly associated with serious infections and are not associated with outbreaks.

Acquired resistance is demonstrated by *E. faecium* and *E. faecalis*. These are the most common species of clinically relevant VRE. There are several genes encoding for vancomycin resistance, with Van-A and Van-B being the most clinically relevant. Van-A strains have high level vancomycin resistance and moderate level teicoplanin resistance. Van-B strains are vancomycin resistant, however they are consistently susceptible to teicoplanin.[12]

Epidemiology[13-14]

VRE was first isolated in Europe in the 1980s. After its initial discovery, VRE spread rapidly throughout hospitals in the United States in the 1990s. Since then, reports of VRE colonisation and infection have rapidly increased and VRE outbreaks have occurred in hospitals globally. According to European Antimicrobial Resistance Surveillance System (EARSS) data from 2014, high-level aminoglycoside resistance in *E. faecalis* occurs frequently, with the majority of countries reporting resistance isolates between 20 – 50%. In the USA, VRE was responsible for 33% of all enterococcal infections in 2006-2007.

Clinical Significance[10,15]

There is a lack of available antibiotics to treat VRE infections since it is resistant to multiple antibiotics. Recent reports have documented the transfer of the Van-A gene from vancomycin-resistant *E. faecalis* to MRSA raising concern that the healthcare-associated spread of VRE is creating a reservoir for mobile resistance genes. There is a threat of large scale emergence of VRSA to add to the global crisis of antimicrobial resistance.

In high-risk populations, acquisition of VRE is associated with higher mortality rates, prolonged hospital stay, and increased cost of healthcare. Despite these concerns, some jurisdictions have started to decrease active surveillance activities related to VRE. However, best practice guidelines still recommend the continued use of IPC measures to decrease VRE transmission.

Acquisition and Transmission

Patients who are colonised carry VRE as part of their gut flora, show no symptoms of carriage, but may act as a reservoir for spread in institutional settings. The length of time a patient may remain colonised is variable. VRE is transmitted by direct contact via the hands of healthcare workers or indirectly through contaminated materials or equipment. The environment plays a large role in the spread of VRE. VRE can survive on inanimate objects for weeks. Proper cleaning and disinfection of environmental surfaces and shared equipment is extremely important in preventing transmission. Equipment that may normally be shared between patients such as thermometers and blood pressure cuffs should be dedicated to individual VRE positive patients if possible.[10]

Treatment

Treatment of VRE infections is a challenge. Most experts recommend linezolid as a drug of choice to treat serious infections. Other treatment options include quinupristin/dalfopristin, daptomycin and tigecycline. However, these drugs are only approved for certain indications and resistance has already been reported. Treatment for colonisation is not recommended.[15]

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Laboratory Testing Methods

Accurate and early detection of colonisation and infection is important to prevent the spread of VRE. Diagnosis is usually made by microbial culture or by molecular methods such as polymerase chain reaction (PCR) assays. Pulsed-field gel electrophoresis (PFGE) is widely used to type VRE as part of an outbreak investigation.[12]

Control Measures

See Table 8.1 Management of Major Pathogens of Concern in Healthcare Facilities.

Clostridium difficile Infection (CDI)

Background

The prevalence of CDI has been steadily increasing globally for many years. Recently, in the USA CDI has surpassed MRSA as the leading microorganism of concern for many IPC programs.[16] CDI primarily occurs in patients who are exposed to antibiotics and healthcare facilities contaminated with spores.[17] The estimated financial impact of CDI ranges from €7000 per case in the United Kingdom, $1.1 billion a year in the USA, and $46.1 million in Canada.[18] The spectrum of disease caused by *C. difficile* includes uncomplicated diarrhoea to pseudomembraneous colitis to, on rare occasions, ileus or toxic megacolon and death.[16]

Pathology[16]

Clostridium difficile is an anaerobic Gram-positive spore-forming toxin-producing bacillus that is transmitted among humans through the faecal oral route. It is widely distributed in the environment. The vegetative form (active state) can produce toxins and be killed by antibiotics. The spore form (dormant state) does not produce toxins, however it is resistant to many types of disinfectants, heat, acid, drying, and antibiotics. With less than optimal cleaning, spores may persist in the environment for months on bed rails, commodes, electronic thermometers, stethoscopes, or skin folds.

There are toxigenic and non-toxigenic strains. The toxigenic strain produces 2 cytotoxins (Toxin A and Toxin B) which bind to receptors on intestinal epithelial cells leading to inflammation and diarrhoea. Both toxins appear to be cytotoxic and enteropathic.

Infection is facilitated by the disruption of normal intestinal flora as a result of antimicrobial therapy permitting colonisation with *C difficile* spores. Exposure to antibiotics which disrupt the colonic microbial flora seems to be a more important risk factor for infection. Commonly implicated antibiotics include clindamycin, penicillins, cephalosporins, and fluoroquinolones.

Additional risk factors for infection include increasing age, chemotherapy, inflammatory bowel disease, organ transplantation, chronic kidney disease, immunodeficiency, severe underlying disease, and exposure to an infant carrier or infected adult. Mild disease is characterised by non-bloody diarrhoea that is often mucoid and foul smelling, cramping, nausea, dehydration, low grade fever, and leukocytosis. Severe disease can include colitis, watery diarrhoea, abdominal pain, fever, nausea, abdominal distension, and pseudomembranes.

North American Pulse Field Type 1 Ribotype 027 (NAP1) Strain[19]

Since 2000 there has been an increase in the incidence of the toxin type III, restriction endonuclease analysis group B1, North American pulse field gel electrophoresis type (NAP1) and polymerase chain reaction (PCR) type 027 strain, subsequently known as the BI/NAP1/027. This strain is more severe, more refractory to standard therapy, more likely to relapse, and is associated with higher mortality. The strain produces approximately 16 times the amount of toxin A and 23 times the amount of toxin B because of a partial deletion of the gene that is responsible for down regulation of toxin production.

Colonisation[20]

Approximately 3 to 5% of healthy adults and 20 to 40% of hospitalised patients may be colonised with inactive spores of *C. difficile*. Colonised patients or carriers are generally not symptomatic; however they may be a potential reservoir for transmission. Evidence suggests that spores on the skin of asymptomatic

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patients can contaminate the hands of healthcare workers. There are no recommendations to treat carriers, especially in the face of potential vancomycin resistance.

Diagnosis

Generally, cases of diarrhoea associated with *C. difficile* will occur within 8 weeks of discontinuing antibiotics. *C. difficile* infection can be diagnosed by either DNA-based tests, such as PCR, that identify toxin genes in unformed stool, or enzyme immunoassay for toxins in stool. Stool culture requires anaerobic culture and is not widely available.[16] Until recently, enzyme immunoassay has been the usual testing method for *C. difficile* due to its ease of use and rapid turnaround time. Many hospitals have begun using DNA-based tests because of their higher sensitivity and specificity. Endoscopy can be useful in cases with negative laboratory results or for atypical presentations or overlapping conditions like inflammatory bowel disease. If there are negative results upon initial testing, depending on the testing method, repeat testing may be helpful. However, the negative predictive value of PCR in average risk groups is over 95%, therefore a negative result should prompt investigation into other causes. Asymptomatic patients should not be tested or treated.[20]

Treatment

Usual treatment for CDI is to stop all current antibiotics and to start metronidazole or vancomycin. Both antibiotics have similar effects with mild cases of infection.[20] Given the potential for increased vancomycin resistance, metronidazole is the first line of treatment, however initial treatment with vancomycin may be considered for complicated patients. Patients treated with vancomycin appear to have undetectable levels of *C. difficile* faster, have faster resolution of diarrhoea, and higher cure rates. Evidence for the use of probiotics is insufficient to recommend for routine treatment.[16]

Donor faecal transplant, the administration of fecal flora from a healthy donor, shows promising results, especially for patients with severe or recurrent disease who fail standard treatment. Given the efficacy of faecal transplantation there is interest in using it for primary severe disease however more work is needed to understand the role of transplantation in primary infection. More work is also needed in finding a suitable mixture of faecal bacteria as a substitute for stool. The risk of *C.diifficile* recurrence can range from 20% after the first episode to 60% in patients with multiple recurrences. Recurrence may be due to a second exposure or to reactivation of spores in patients with decreased normal flora.[21]

Control Measures

Many control measure have been used to stop transmission and prevent further spread of *C. difficile*. See Table 8.1 for strategies for managing CDI. Increasing evidence indicates that along with IPC measures to prevent the spread of *C. difficile* within an institution, healthcare facilities should also have strategies for antibiotic stewardship, e.g., limiting inappropriate use of antibiotics. Prompt notification of patients with diarrhoea to IPC personnel can assist in focusing interventions. Adherence to proper hand hygiene for all 5 moments is imperative. Alcohol-based hand sanitizer, although effective against the vegetative bacteria, may be less effective against the spore than soap and water.

Environmental audits can assist in identifying environmental sources, such as multiuse patient care equipment, that can be targeted for cleaning. Strict adherence to cleaning of the patient care environment is also important. For areas with high rates of *C. difficile*, consideration should be given to using a sporicidal agent for cleaning, especially during outbreaks. Current agents include various formulations of hydrogen peroxide and chlorine-based products like bleach. If sporicidal agents are not used, consideration should be given to environment and equipment cleaning using proper mechanical friction to physically remove bacteria and spores. Repeat cleaning may be needed to ensure effective removal of *C. difficile* from the environment. Patient and visitor education should be a part of any control programme. Approaches that are not recommended include routine identification of asymptomatic carriers and repeat laboratory testing at the conclusion of treatment.[20]

Multidrug Resistant Gram-Negative Organisms (MDRGN)

Background

Treatment of serious bacterial infections is increasingly complicated by antibiotic resistance including

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rising resistance rates among Gram-negative pathogens. Many different definitions have been used in the medical literature to characterise varying patterns of antimicrobial resistance. In general, multi-drug resistance is defined as resistance to three (3) or more classes of antimicrobials whereas extensively drug resistant microorganisms are resistant to all but one or two classes of antibiotics. Pan-drug resistant microorganisms are resistant to all classes of antimicrobials.[22]

Extended- Spectrum β-Lactamase (ESBL) Producing Bacteria

Beta-lactamase is an enzyme produced by some bacteria that inactivates the beta-lactam class of antibiotics (penicillins and cephalosporins- including 3rd generation cephalosporins). Most ESBLs are *Escherichia coli* and *Klebsiella pneumoniae* which are part of the Enterobacteriaceae family. These bacteria cause a range of infections including urinary tract infection and bacteraemia.[10] *E. coli* and *K. pneumoniae* have ESBL enzymes that are plasmid-mediated, therefore the genes encoding these enzymes are easily transferable among different bacteria.[23-24]

Over the last 20 years, ESBL-producing bacteria have spread worldwide, both in hospital and community settings. Infections with these microorganisms often require treatment using carbapenem antibiotics.[23-24]

Carbapenem- Producing Enterobacteriaceae (CPE)

Carbapenem-producing Enterobacteriaceae are resistant to carbapenem antibiotics (e.g., imipenem, meropenem, ertapenem). To date, carbapenemases are most commonly found in *E. coli* and *Klebsiella spp*., however they have also been found in other Gram-negative bacteria.[10]

There has been a significant increase in carbapenemases reported over the last decade. Carbapenemases are often located on a mobile genetic element, such as a plasmid or transposon. They can easily move between bacterial strains and often carry resistance to other classes of antibiotics.[10] Carbapenem antibiotics are relied upon for the treatment of serious bacterial infections, such as those associated with transplantation or hospitalisation in the intensive care unit.[24] Infections with carbapenemases are often treated with polymyxin antibiotics which are a last resort and used only if all other antibiotics are determined to be ineffective or contraindicated.

There are several different classes of carbapenemase, each associated with a 3-letter acronym and often associated with the geographic area in which they first occurred. KPC is endemic in the USA and Greece and has been reported worldwide. VIM and IMP have also been reported worldwide, however there is a higher prevalence in Europe and Asia. OXA-48 has been identified mostly in Mediterranean and European countries and in India. More recently, NDM-1 has been found to be most prevalent in India and Pakistan, however it has already spread worldwide.[24]

Other Notable Multidrug Resistant Gram-Negative Bacteria

Acinetobacter species are commonly found in soil and water. The most common species to cause human infection is *Acinetobacter baumanni*. Pseudomonas is also found widely in the environment with the most common human pathogen being *Pseudomonas aeruginosa*. Both Acinetobacter and Pseudomonas species are opportunistic pathogens that often cause infections in the healthcare setting, mainly in immunocompromised patients or those admitted to intensive care. At-risk patients include those on a ventilator, those with a prolonged hospital stay, or those with open wounds or invasive devices. Both Pseudomonas and Acinetobacter are often resistant to commonly prescribed antibiotics and antimicrobial resistance in these microorganisms is on the rise.[25-26]

Of note is the discovery of the MCR-1 gene by Chinese researchers. The MCR-1 gene confers plasmid-mediated resistance to polymyxin antibiotics. Further investigation has led to the discovery of MCR-1 in several additional countries in Asia and Europe. Polymyxin antibiotics had been heralded as the last resort for treatment of certain multidrug-resistant infections.

Control Measures

See Table 8.1 Major Pathogens of Concern in Healthcare Facilities.

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Treatment

Infections with ESBL-producing bacteria are often treated with carbapenem antibiotics such as meropenem. Infections with carbapenemases are often treated with polymixin antibiotics such as colistin.[23-24] The discovery of the MCR-1 gene may mean that polymyxin antibiotics could then prove to be ineffective.[27] Other options include tigecycline (a parenteral glycylcline) and doripenem (a parenteral carbapenem). It is important to conserve the efficacy of existing antimicrobials, as there is a shortage of novel drugs being produced.[24]

Significance of Multidrug-Resistant Gram-Negative Bacteria

Gram-negative bacteria naturally reside in the gastrointestinal tract of humans. Asymptomatic carriage of MDRGNs can be a source of spread, especially in the healthcare environment. Patients with MDRGN infections are more likely to have received antimicrobials in the past. They experience increased lengths of hospital stay and increased infection-related hospital costs. Initial antimicrobial therapy in these patients is often less successful, leading to greater morbidity and mortality.[10]

Opportunities for spread also exist in the community setting as MDRGNs become more widespread through the environment. MDRGNs have been found in water sources, such as rivers and treated sewage, and in farm animals. The use of antibiotics in animal husbandry is significant in many parts of the world. This means that there is both agricultural and medicinal exposure of humans to antibiotics. Global trade and worldwide travel has contributed to the evolution and movement of antibiotic resistance genes.[23]

Considerations for Management of Pathogens of Concern

Appropriate IPC management of the various pathogens differs depending on the institutional setting and the resources available. At a minimum, adherence to diligent hand hygiene practices should be a focus in all healthcare institutions. Healthcare workers should clean their hands before and after contact with patients or the patients' environment. This is the single most important measure for controlling pathogens of major concern.

Transmission- based precautions may apply depending on the setting. The use of transmission- based precautions may be considered depending on the particular pathogen, especially in an acute care setting or during an outbreak. Patient accommodation should also be a consideration. Patients colonised or infected with a particular pathogen may be placed in a private room or cohorted with another positive patient as a control measure.

Many healthcare facilities perform active surveillance testing, particularly for MRSA, VRE, and MDRGN, to manage the prevalence, incidence, and transmission of these AROs. Active surveillance can assist in reviewing the status of patients with a known history of colonisation or infection, identifying transmission to new patients, evaluating treatment, and identifying patients that are not know to harbour these bacteria.[10]

Prompt and appropriate antimicrobial therapy for an infected patient can make the difference between successful treatment and death. Low resource countries are particularly challenged in this regard because the true extent of antimicrobial resistance is unknown in many developing countries. Issue include lack of regulation of antibiotic use, sparse diagnostic testing, and a lack of surveillance for prevalent types of pathogens and sensitivity patterns. Other issues include patient perception that they must be treated with an antibiotic leading to pressure to prescribe, fear of bad clinical outcomes contributing to overuse, lack of availability of drugs, and a lack of regulation and enforcement of the drugs that are available. Unfortunately, the misuse of antimicrobials has caused an increase in the number of resistant microbes leading to a loss of antimicrobial efficacy.[23-24]

Information on local disease patterns, trends in antimicrobial resistance, and antimicrobial usage is needed to support clinical decisions and to guide the development of treatment guidelines so that they reflect infection and resistance patterns.

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Conclusion

Antimicrobial resistance is a world-wide public-health problem whose solution is multifaceted. According to the World Health Organization, low income countries play an important role in the emergence of resistance.[23] Therefore, improving the behaviours of prescribers, dispensers and consumers should be a major focus of intervention efforts. Global awareness of the issue of resistance and surveillance for significant pathogens in the parts of the world where these pathogens are prevalent are primary considerations. Integration of antimicrobial stewardship processes may be beneficial. In addition, ongoing antimicrobial research is needed to increase future therapeutic options. Implementation of appropriate IPC practices will help to mitigate the spread of these microorganisms.

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	MRSA	VRE	MDRGN	CDI
Patients at Risk	• Previous antibiotic use • Severe underlying illness • Prolonged hospital stay • Previous contact with medical facility • Presence of invasive procedures • Close proximity to a patient that is colonised or infected	• Previous antibiotic use • Severe underlying illness • Prolonged hospital stay • Previous contact with medical facility • Presence of invasive devices • Close proximity to a patient that is colonised or infected	• Previous antibiotic use • Severe underlying illness • Prolonged hospital stay • Previous contact with medical facility • Contact with a facility with known outbreaks	• Previous antibiotic use • Severe underlying illness • Prolonged hospital stay • Advanced age • Gastrointestinal surgery/ manipulation • History of irritable bowel disease • Patients on proton pump inhibitors
Admission Screening **Body Sites**	Based on local regulations and epidemiology and patient risk factors Nares, rectal, wounds, exit sites swabs	Based on local regulations and epidemiology and patient risk factors Rectal swab	Based on local regulations and epidemiology and patient risk factors Rectal swab	N/A
Route of Transmission	Contact (add droplet for symptomatic patients with pneumonia)	Contact	Contact (add droplet for symptomatic patients with pneumonia)	Contact
Isolation Precautions	Yes	Yes	Yes	Yes
Accommodation	Single room preferred	Single room preferred Separate toileting facilities	Single room preferred Separate toileting facilities	Single room preferred Separate toileting facilities
Documentation (flagging of patients)	It may be of benefit to implement a system to designate patients known to be colonised or infected with antibiotic resistant organisms for early notification on readmission			
Environmental Cleaning	Routine cleaning with attention to high-touch surfaces	Routine cleaning with attention to high-touch surfaces Consider double cleaning in outbreak situations	Routine cleaning with attention to cleaning of high touch surfaces	Routine cleaning with attention to high-touch surfaces and the use of a sporicidal agent Consider double cleaning for outbreak situations
Discontinuation of Precautions	This is an unresolved issue. Some institutions use the following criteria: Negative results from all colonised/infected body sites- 3 consecutive negative cultures taken at least one week apart in the absence of antibiotic therapy **Note:** *Recolonisation is known to occur, ongoing monitoring is recommended *Consider maintaining isolation precautions in an outbreak setting			No diarrhoea for at least 48 hours
Follow-up of Contacts	2 sets of specimens taken on different days, with one taken a minimum 7 days after last exposure, especially in an outbreak setting		Based on local regulations and epidemiology and patient risk factors	No
Point Prevalence	**In an outbreak setting:** • Conduct serial (e.g., weekly) unit-specific point prevalence culture surveys of the target antibiotic resistant organism to determine if transmission has decreased or ceased • Consider discharge and/or transfer screening of patients until transmission has decreased or ceased			No
Additional Outbreak Measures	• Strict cleaning of multi-use patient equipment in between patients • Dedicated patient equipment to positive cases • Education of staff, patients and visitors • Auditing of outbreak unit/area including hand hygiene, isolation practices, and environmental cleaning			