Anesthesia in patients with infectious disease caused by multi-drug resistant bacteria

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Purpose of review
Up to 50% of specific bacterial strains in healthcare admission facilities are multi-drug resistant organisms (MDROs). Involvement of anesthesiologists in management of patients carrying/at risk of carrying MDROs may decrease transmission in the Operating Room (OR).

Recent findings
Anesthesiologists, their work area and tools have all been implicated in MDRO outbreaks. Causes include contamination of external ventilation circuits and noncontribution of filters to prevention, inappropriate decontamination procedures for nondisposable equipment (e.g. laryngoscopes, bronchoscopes and stethoscopes) and the anesthesia workplace (e.g. external surfaces of cart and anesthesia machine, telephones and computer keyboards) during OR cleaning and lack of training in sterile drug management.

Summary
Discussions regarding the management of potential MDRO carriers must include anesthesia providers to optimize infection control interventions as well as the anesthesia method, the location of surgery and recovery and the details of patient transport. Anesthesia staff must learn to identify patients at risk for MDRO infection. Antibiotic prophylaxis, although not evidence based, should adhere to known best practices. Adjuvant therapies (e.g. intranasal Mupirocin and bathing with antiseptics) should be considered. Addition of nonmanual OR cleaning methods such as ultraviolet irradiation or gaseous decontamination is encouraged. Anesthesiologists must undergo formal training in sterile drug preparation and administration.

Keywords
anesthesiologists, decontamination, drug resistance, infection control, microbial, operating rooms

INTRODUCTION

Multi-drug resistant organisms (MDROs) are microorganisms resistant to more than one class of antimicrobial agents. Data gathered from several thousands of admission facilities show that up to 50% of specific bacterial strains may be categorized as MDROs [1▪].

Coexistence of a predisposing mix of host and environmental factors leads to appearance of MDROs. These include the use of multiple and/or broad-spectrum antibiotics for lengthy periods with resultant iatrogenic disturbance of patient microbiome and proliferation of resistant organisms, disruption of intrinsic protective barriers of the body by invasive procedures/surgery/indwelling foreign bodies and extremes of age, diabetes and immune suppression. MDROs are therefore most prevalent in hospital areas where patients fulfill these characteristics (e.g. ICUs [2]). Although anesthesia drugs have been implicated in modulation of the immune response to infection [3,4], the effects found thus far have not been associated with MDRO epidemiology.

Once they have appeared, MDROs persist in environments conducive to their survival. Thus, *Clostridium difficile* and VRE may be found in toilets, *Klebsiella* spp. in sinks and on endoscopes [5], *Pseudomonas* spp. prevail in plumbing (e.g. tap water) [6] and methcillin-resistant *Staphylococcus aureus* (MRSA) and *Acinetobacter* – bacterial species that create an adhesive biofilm – are found on surfaces [7,8].

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KEY POINTS

- The perioperative period is a key occasion for infection control in patients with MDROs and anesthesiologists are optimally situated to be the agents of this opportunity.
- Preoperative patient assessment and preparation may include identification of patients at risk based on their characteristics, eradication of already colonized patients and individual consideration of appropriate antimicrobial prophylaxis and treatment.
- Intraoperatively, the location of surgery, logistics of patient transport, operating room scheduling, mode of anesthesia and matching of precautions to pathogen (e.g. ventilation for airborne pathogens) all require optimization.
- Postoperatively, appropriate cleaning and disinfection of the multiple components of the anesthesia and OR environment carries far-reaching implications for hospital-wide infection control.

CONVENTIONAL MANAGEMENT OF MULTIDRUG-RESISTANT ORGANISMS

The perioperative management of patients with MDROs is based principally on the interventions proven effective for infection control in any acute healthcare setting. These include education regarding prevention and treatment, hand hygiene, adherence to relevant precautions, meticulous environmental cleaning and constant communication regarding patient infectious status. The isolation measures required for patients with known MDROs are summarized in Table 1.

Surgery is often required before the causative pathogen has been identified. Anesthesia staff must thus also learn to identify patients at risk for MDRO infection, as these patients too require adherence to relevant precautions. The identifying features and precautions required for patients at risk but without proven MDRO infection are detailed in Table 2.

Additional issues that must be taken into consideration in the unique perioperative setting include antibiotic prophylaxis, the choice of anesthesia method, the preferred location of surgery, OR ventilation systems, precautions to be taken during patient transport to the OR and prevention of transmission to other patients in the OR.

ANTIBIOTIC PROPHYLAXIS

Patients requiring airborne transmission precautions (e.g. tuberculosis) should not undergo elective surgery until drug therapy has been administered for a sufficient amount of time to decrease the risk of transmission.

The guidelines for surgical antimicrobial prophylaxis for patients with past infection or colonization with gram-negative MDROs are not evidence based. In general, if the antibiotics the patient is already receiving for MDRO infection also adequately cover the planned surgical procedure, an additional dose should be administered 30–60 min before surgical incision. If they do not provide adequate coverage, the antimicrobial prophylaxis recommended for the planned surgical procedure should be added. MDROs cultured from indwelling tubes or drains also require appropriate antimicrobial coverage before procedures [9,10▪]. Regardless, the ability of the patient to respond adequately to infection, the procedure at hand and the proximity of the likely reservoir of the pathogen to the surgical site require case-by-case deliberation [9].

Nonselective administration of Vancomycin rather than Cefazolin confers no advantage in the prevention of surgical site infection (SSI) [11]. Vancomycin prophylaxis (single dose) should therefore be added to routine surgical prophylaxis only for patients with known MRSA colonization, those admitted from wards with recent MRSA outbreaks and those admitted from areas at high risk for MRSA colonization [9].

Adjuvant therapies that merit consideration include intranasal administration of Mupirocin and whole-body bathing with antiseptic solutions [10▪]. Intranasal Mupirocin decreases SSIs due to *Staphylococcus aureus* in colonized patients [12]; this, however, may lead to an increased risk of SSI with organisms other than *S. aureus* [12]. Some strains of MRSA are resistant to Mupirucin [13]. Whole-body bathing with Chlorhexidine significantly reduces blood culture contamination with MRSA in adult ICU patients [14] and reduces candiduria and bacteriuria in male ICU patients [15], but this strategy has yet to be evaluated in the perioperative setting.

CHOICE OF ANESTHESIA

Microorganisms causing neuraxial infection may enter sterile body areas via hematogenous spread, through direct inoculation at the time of needle/catheter insertion or by migration along the catheter tract.

Hematogenous spread during neuraxial block is a potential risk in patients with bacteraemia regardless of the infecting microorganism. Patients with overt signs of systemic infection should therefore preferably undergo general anesthesia.

Indwelling neuraxial catheters have been associated with abscesses caused by resistant bacteria in

Table 1. Special precaution measures by type of pathogen and its transmission mode

		Type of precaution required		
		Contact	**Droplet**	**Airborne**
Examples of pathogens that may require these measures				
MDR bacteria		*Clostridium difficile*[a], ESBL-producing Enterobacteriaceae Carbapenem resistant *Acinetobacter*, Carbapenem resistant Enterobacteriaceae, MRSA and VRE	Diphtheria, pertussis, meningococcus and *Streptococcus* group A	Tuberculosis
Viruses		Hepatitis A and respiratory syncytial virus	Influenza and hemorrhagic fevers (e.g. Ebola)	SARS corona virus, Varicella and measles
Ideal isolation conditions				
Room	*n* patients per room	Cohorting allowed together with other patients carrying the same pathogen	1	
	Door of room	Open	Closed	Closed and sealed
	Air cycling and filtering	–	–	15–20 cycles per hour. Preferable laminar flow and HEPA filters
	Pressure	No need	No need	Negative
Personal protective equipment	Gloves	At the time of contact with patient	On room entry	
	Gown	At the time of contact with patient	On room entry	
	Mask	No need	Surgical mask	N-95 mask or portable respirator
	Eye and mucous membrane protection	When there is the risk of splash or droplet dispersal (e.g. suctioning, intubation and extubation)		
Disposables	Packed and sterile syringes and needles, gloves, pads, tubing and so on	Once placed within 'patient zone' can no longer be transferred elsewhere		
Anesthesia	Machine	No change from standard		
	Equipment	No change from standard		

[a]*Clostridium difficile* is unique in that its eradication requires hand hygiene with water and antimicrobial soap rather than with alcohol.
ESBL, extended spectrum β lactamase; MRSA, methcillin-resistant *Staphylococcus aureus*; SARS, severe acute respiratory syndrome; VRE, vancomycin-resistant *Enterococci*.

numerous cases [16,17]. The rate of catheter colonization and bacterial migration along the catheter increases with poor aseptic technique at the time of catheter insertion [18]. Patients at risk but lacking proven MDRO infection may undergo neuraxial blockade provided that aseptic technique is meticulously adhered to. Adding octenidine dihydrochloride to the disinfectant used for skin cleaning results in lower rates of skin recolonization at the catheter insertion site and may also reduce the risk of infection [19].

About 2% of healthcare workers are MRSA carriers. Colonization is most common in the anterior nares and hands [20]. Anesthesia staff diagnosed as nasopharyngeal carriers of pathogenic bacteria have been implicated in Central Nervous System infections following the performance of neuraxial blocks [21,22]. Thus, aseptic technique requires the use of both gloves and mask [23].

LOCATION OF SURGERY, PATIENT TRANSPORT AND DESIGNATION

The OR generally remains the preferred location for most surgical procedures. However, when relevant, concerns regarding infectious spread (particularly airborne pathogens) may be added to the other factors determining the location of surgery (e.g. patient condition and OR availability). Discussions regarding intraoperative and postoperative patient

Table 2. Patients at risk for multi-drug resistant organism infection without proven cultures and their respective isolation requirements

Patient characteristic		Type of precautions required
Medical history	History of colonization/infection with MDRO	Contact
	Current hospital stay in area that is MDRO endemic	Contact
	Recent stay in other facility where MDROs are endemic	Contact
	Known or suspected HIV infection with respiratory symptoms and pulmonary infiltrates	Airborne
Signs and symptoms	Acute diarrhea post antibiotic treatment (e.g. suspected *Clostridium difficile colitis*)	Contact
	Persistant, prolonged paroxysmal cough (e.g. suspected pertussis)	Droplet
	Any fever and cough following recent travel to areas with ongoing respiratory outbreaks (e.g. influenza, SARS and MERS-CoV)	Contact
	Respiratory tract infection in children	Contact and droplet
Physical examination	Fever with vesicular rash (e.g. suspected Varicella)	Contact and airborne
	Maculopapular rash with cough and fever (e.g. suspected measles)	Airborne
	Petechial/echymotic rash with fever (e.g. suspected meningococcal meningitis)	Droplet
	Open infected wound/abscess	Contact
	Cough and fever with upper lobe infiltrate in patient from an endemic area (suspected tuberculosis)	Airborne

Updates regarding new outbreaks may require additional precautions.

placement, including the option of direct transfer from the OR to the ward, should take place before transfer. Hospital staff in all areas that will be involved in perioperative patient treatment should be notified a priori to allow sufficient time for preparation.

Efforts should be made to maintain relevant infectious control precautions during transport. For contact precautions, the transport team should remain appropriately clothed and gloved and avoid physical contact with surrounding surfaces and staff. Ideally, additional staff with no patient contact should accompany the transport team to open doors/elevators as required. Maintenance of droplet and/or airborne precautions requires that the accompanying healthcare staff remain adequately protected. If spontaneously breathing, the patient should wear a surgical mask [24]. If intubated, mechanical ventilation during transport may decrease staff exposure to unintended droplet dispersal due to inadvertent tubing disconnections and/or spraying from exhalation valves. Minimal gas flows should be used and unfiltered exhaled gases should be directed downward toward the patient bed rather than to the surrounding air. As the Center for Disease Control (CDC) recommends that a filter be added to the breathing circuit in the OR [24], it had best be connected before patient transport. Patient handover between teams should take place within the designated OR after door closure.

OR VENTILATION SYSTEMS AND AIRBORNE MULTIDRUG-RESISTANT ORGANISMS

The aspects of OR ventilation systems relevant to airborne infection control are the pressure differential, flow characteristics and filtering systems.

OR ventilation systems have positive pressures to prevent the infiltration of contaminating airborne pathogens into the OR airspace. This creates a hypothetical risk of airborne pathogen spread from the room outward. Whether this risk can actually translate into outbreaks remains unclear. There have been several reports of suspected droplet transmission of group A β-hemolytic *streptococci* from colonized OR personnel to and from patients without direct contact; however, these anecdotes include little direct evidence for airborne transmission.

Standard and critical care rooms should have at least six air exchanges per hour. ORs require 15–20 exchanges of air per hour [24,25]. Higher flows theoretically decrease environmental contamination. Laminar flow systems, which are not commonly available, both minimize turbulence and remove particles more than 0.3 μm in diameter (smaller than most bacteria) through high-efficiency particulate arrestance (HEPA) filters. Intubation and extubation – known coughing triggers – should ideally take place within the OR because of its higher air exchange rates. Open airway suction should be avoided if possible. The time elapsing between intubation/extubation and door opening

and/or initiation of surgery should also be planned to allow maximal clearance of airborne pathogens (as determined by local OR ventilation characteristics). During surgery, staff exchanges should be minimized and airborne transmission precautions should be adhered to by all OR personnel (e.g. door closed and the use of N95 masks). The infected patient should be scheduled last in the room to maximize air exchange before the next case. If the OR does not have HEPA filters, the CDC recommends using a portable HEPA filter to expedite removal of airborne contaminants [24].

POSTOPERATIVE PREVENTION-ENVIRONMENTAL CLEANING

The OR should be maintained at a maximal level of decontamination (Table 3), yet high patient turnover, staff and equipment transfers from room to room, role exchanges (e.g. environmental cleaning performed by nurses), poor oversight and training of some of the staff in infection control and surgical exposure of anatomic areas of heavy colonization [26] all contribute to OR contamination.

Most MDROs are sensitive to commonly used disinfectants, but even meticulous manual cleaning overlooks contaminated areas [27]; this has led to the promotion of adjuvant nonmanual cleaning methods. Ultraviolet germicidal irradiation (UVGI) can reduce airborne bacterial and viral infections, but does not affect fungal spores [24,28,29]. Duct and upper room air UVGI systems are considered safe for healthcare settings [24]. In duct UVGI, waste air is irradiated by Ultraviolet (UV) lamps located within the air ducts before recycling. In upper room UVGI, UV lamps hanging from the ceiling or on walls irradiate the nearby air. The effectiveness of both methods depends on air exchange patterns, thus neither is considered a substitute for air exchange or HEPA filtration. Complete room irradiation (rather than air irradiation alone) can also be performed with transportable UV equipment. Gaseous decontamination techniques most commonly use hydrogen peroxide (H_2O_2) [30]. As there are still no studies comparing manual to nonmanual room disinfection methods and no cost-effectiveness studies of nonmanual methods, there remain insufficient data to recommend the routine use of nonmanual cleaning methods in the OR, despite their promise [31▪].

ANESTHESIA EQUIPMENT

Anesthesia machines are considered an unlikely source of microorganism transmission based on two assumptions: that the alkali condensates lining the bottom of the CO_2 absorber inhibit bacterial proliferation and that the environment within the anesthesia machine (i.e. high gas flows, low temperatures and lack of humidity) is nonconducive to bacterial survival. These assumptions are founded upon a handful of very early, poor quality studies [32,33].

Soda lime has some bactericidal effects [34], but these are largely insufficient [35,36]. Internal breathing circuits may be contaminated if hygienic measures are not adhered to during/after their reprocessing [37], particularly in areas with low flow [36]. However, the assumption that the internal anesthesia machine environment is overall sufficiently hostile to bacterial growth to prevent patient cross-contamination has not been disproved.

Regarding external anesthesia circuits, some studies show that contamination does occur, and is more heavy on the patient side [34,36], whereas others maintain that cross-patient contamination does not occur when the anesthesia workplace is properly cleaned [38]. However, single-use sterile breathing circuit components have become the standard of care as studies showed that their use significantly reduces postoperative pneumonia [39].

Breathing circuit filters (0.1–0.2 μm pore size) are recommended by the CDC [24] and the American Society of Anesthesiologists [40] as adjunct infection control measures based on a single laboratory study [41]. Filters only prevent bacterial transfer when entirely dry. In conditions simulating clinical reality (including moisture), most filters will allow the free passage of bacteria and fungi with even minimal ventilation pressures [42]. Excessive levels of contamination have been documented on the machine side of filters when coughing occurs and after prolonged surgery [43]. Similar rates of postoperative respiratory infections were also found in studies randomizing to filtered sterile breathing circuits versus nonfiltered washed circuits [44] and in surveillance of cases undergoing regional versus general anesthesia without filters [45]. Thus, using filters is harmless, but probably not really protective.

Anesthesiologists' hands can become bacterial reservoirs; it has been surmised that this usually occurs through indirect transmission from anesthesia workplaces which may not have been cleaned as thoroughly as other OR surfaces [46▪]. Bacteria isolated from the anesthesia workplace have been directly linked to 30-day postoperative infections [47,48] and to contamination of anesthesia drugs and intravenous fluids administered in the OR [49▪].

Implementation of simple precautions, for example disinfection of exterior surfaces of the anesthesia machine with a detergent wipe, can significantly decrease such contamination [50]. Additional high-touch surfaces that are commonly

Table 3. Cleaning processes, the microbiological organisms they render nonviable and the methods used to implement them

Process	Microbiological organisms rendered nonviable				Methods	Required for items	Examples
	Bacteria	Viruses	Fungi	Bacterial spores			
Sterilization	Yes	Yes	Yes	Yes	Pressurized steam, dry heat, ethylene oxide and hydrogen peroxide	Intended to come into contact with a normally sterile body area/cavity	Surgical equipment and single-use disposables (e.g. needles, scalpels, ventilation tubing and filters, endotracheal tube, urinary catheter and drains)
						That may inadvertently be inserted into a normally sterile body area/cavity	Esophageal stethoscope
High-level disinfection	Yes	Yes	Yes	No	Aldehydes, peracetic acid and chlorine dioxide	Come into contact with mucous membranes but do not penetrate the membrane or come in touch with blood	Ventilation masks, components of the laryngoscope, endoscopes, oral and nasal airways, and connectors
Intermediate-level disinfection	Yes (including TB)	Most. Not small viruses without envelopes	Yes	No	Alcohol, sodium hypochlorite, phenols and iodophors	Items that come into touch with the external parts of the body (i.e. skin and hair)	Blood pressure cuffs, stethoscopes, pulse oximeter probes, head rests and straps, and electrocardiogram electrodes
Low-level disinfection	Most (not TB)	Some	Some	No	Alcohol and quaternary ammonium compounds		

All contaminated equipment/devices must first be cleaned (thus decreasing their bacterial load) in order to achieve appropriate disinfection or sterilization. When items have been within the vicinity of a patient with an MDRO (i.e. in the same room), disposable items should generally be discarded even if they have not been used and multiple use items should be assumed to have been in direct contact with the patient.

overlooked include the OR bed and its control, OR doors [51], roll boards [52] and telephones [53]. Stethoscopes may become reservoirs for multiple MDROs [54▪], and ultrasound probes and coupling gel may grow infectious pathogens when cultured [55,56▪] and have been associated with outbreaks of MDROs [57]. These devices and probes should be cleaned with chlorhexidine and/or alcohol [58].

Laryngoscopes (both blade and handle) may also be a source of cross-infection; there is still lack of consensus in current guidelines regarding their cleaning [59]. Laryngoscopes supposedly come into contact with intact mucous membranes, thus theoretically require only high-level disinfection. However, sterilization is preferable, as contact may occur with nonintact membranes [60]. The use of disposable laryngoscopes and blades, single-use sheaths and laryngoscopes with smooth surfaces (i.e. easier to disinfect) should also be considered.

Faulty cleaning of bronchoscopes has also been associated with outbreaks of MDRO infections [61–63]. Bronchoscopes require high-level disinfection [64]. Anesthesia masks, ambu bags, y-connectors and even inspiratory and expiratory valves have all been implicated in transmission of infections [65]. Even written medical charts [66] and computer keyboards [67] may be contaminated with pathological bacteria. Impregnation of computer keyboards with antimicrobial polymer may solve this issue in the future [67,68].

Anesthesia drugs should be drawn after the OR has been properly cleaned (including the anesthesia area) and after hand hygiene and gloving. Faulty anesthesia drug preparation technique has been shown to contribute to syringe contamination [69]. Thus, anesthesiologists must undergo training in sterile drug preparation.

Drugs should be used immediately after being drawn. Temporary capping with a sterile cap is allowable only if the syringe will be used again within minutes. The likelihood of syringe and content contamination increases over time [69] and in emergencies [48]. Positive cultures from syringe tips and contents often contain bacterial species similar to those found in the anesthesia environment [49▪].

Gloves should also be used during drug administration, as pathological microorganisms can be injected inadvertently during administration of intravenous anesthesia drug boluses [70▪]. A new needle and syringe are required not only per patient, but also each time a new vial is used [71,72].

CONCLUSION

MDROs are endemic in hospitals. Anesthesiologists, their work area and tools have all been implicated in MDRO outbreaks. Management of patients with MDROs requires training, organization and multidisciplinary coordination. As not all MDRO carriers are identifiable prior to OR entry, the assumption should always be that anesthesia is taking place in a potentially contaminated environment. Anesthesiologists should learn to identify patients at risk for MDRO infection/colonization, to practice the required precautions and to adhere to antibiotic protocols and aseptic techniques. Anesthesia areas and equipment should undergo meticulous high-level decontamination similar to other OR areas.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
- ▪▪ of outstanding interest

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This summary of evidence includes a subsection dedicated to the clinical effectiveness of nonmanual room disinfection methods for prevention of infections in the operating room.

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