Clinical Microbiology in the Intensive Care Unit: Time for Intensivists to Rejuvenate this Lost Art

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ABSTRACT

We live in an era of evolving microbial infections and equally evolving drug resistance among microorganisms. In any healthcare facility, intensivists play the most pivotal role with critically ill patients under their direct care. Majority of the critically ill patients already harbor a microorganism at admission or acquire one in the form of healthcare-associated infections during their course of intensive care unit stay. It is therefore rather imperative for intensivists to possess sound knowledge in clinical microbiology. On a negative note, most clinicians have very meager and remote knowledge acquired during their undergraduate years. This knowledge is rather theoretical than applied and wanes over the years becoming nonbeneficial in intensive patient care. We, therefore, intend to explore important concepts in applied microbiology and infection control that intensivists should know and implement in their clinical practice on a day-to-day basis.

Keywords: Antibiogram, Antibiotics, Critical care, Immunoprophylaxis, Intensivist, Knowledge, Microbiology, Microorganisms, Outbreaks.

INTRODUCTION

The inputs of a clinical microbiologist are useful in areas of the hospital where majority of infections are encountered. Intensive care and critical units are the best examples of this scenario where one encounters a combination of community-acquired infections, healthcare-acquired infections, highly contagious infections, and outbreaks. Clinical microbiology does not end with pathogen identification, susceptibility determination, and teaching students but has evolved from bench reporting in the laboratory to active involvement with clinicians in an antibiotic prescription for infections, infectious diseases, as well as in infection control. Active case discussions, sharing knowledge, understanding diagnostic tests, awareness of drug resistance patterns, rapidly identifying outbreaks are some of the areas where liaison between an intensivist and a clinical microbiologist would be a great boon to patient care. We are therefore discussing this and more thoughts in the following pages of this review.

Following topics and questions that are frequent gray areas in clinical practice are discussed.

Hospital Antibiogram Updates

Recommended ideal duration of generating a hospital antibiogram is at least annual; however, it is solely based on individual healthcare facilities as well as number of isolates analyzed. Customization according to every hospital need is advisable unless standard guidelines are followed in generating the cumulative antibiogram. “Enhanced” antibiogram is the one which is generated based on data from a specific patient location/site of care; one such segregated data stratified for intensive care units (ICUs) is preferable. This is more useful in targeting specific resident pathogens in the ICU environment while initiating empiric antibiotics. It also helps in analyzing trends in changing susceptibility patterns within ICUs. An exclusively enhanced antibiogram for ICUs can ideally be prepared and circulated or concisely displayed in order to inculcate awareness on antibiotic resistance patterns. It is mandatory to know as well as initiate empiric therapy based on the stratified antibiogram. ICU wise distribution of multidrug-resistant (MDR) pathogens like rate of methicillin-resistant Staphylococcus aureus (MRSA), extended-spectrum beta-lactamase (ESBL), carbapenem-resistant enterobacteriaceae (CRE), vancomycin-resistant enterococci (VRE) should be notified on a regular basis.

The major role of a microbiologist also involves interaction with intensivists to notify the change in pathogen trends, susceptibility patterns, and evolution of unusual isolates, etc. They should discuss the usefulness of newer Food and Drug Administration-approved antimicrobial agents in treating complicated infections. In vitro susceptibility testing for newer agents should be performed and susceptibility pattern informed to clinicians. Their usefulness in therapy based on susceptibility pattern and pharmacodynamics is the clinician’s call. These implementations can be made feasible through meetings conducted on a regular basis with clinicians. This practice is recommended to ensure antimicrobial stewardship within ICUs.

What Drugs for What Bugs

The major challenge in initiating empiric antimicrobial therapy is in understanding the spectrum of antibiotic action. Anticipation of particular microorganisms at specific sites is the key to judgment on the choice of appropriate antibiotics. Empiric therapy cannot be used as a blanket rule but rather targeted for site-specific action.

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Healthcare-associated infections in ICUs are of importance to be managed based on antibiotic policy. One has to choose antibiotics based on the severity of infection, previous antibiotic therapy, environmental bugs, drug interactions, etc.\textsuperscript{6,7}

National antibiotic policies, as well as institutional antibiotic policies, are framed according to specific infective conditions. This is particularly important since certain sites like the blood are simple to target, whereas sites like the bone are complex by providing niches for trapping bacteria within the matrix and collagen.\textsuperscript{8,9} The complexity of body sites plays a major role in antibiotic action warranting adequate exposure of microorganisms to the antibiotics. Considering common sites of infection in the body, the pharmacodynamics and pharmacokinetics are described as follows.

- **Blood:** Bloodstream is considered to be a simple site that allows direct interaction of antibiotics with microorganisms in the bloodstream. The only concern is alteration of pharmacokinetics of antimicrobials due to volume resuscitation and inotropes used in bacteremic patients. Appropriate dosing is very crucial in bacteremia for rapid bacterial clearing from bloodstream and prevention of mortality.\textsuperscript{7} Most encountered failure of therapy and mortality is associated with hydrophilic antibiotics such as beta-lactams, vancomycin, and aminoglycosides.\textsuperscript{8,9} There is a specific need for optimal dosing of these antibiotics in comparison with other lipophilic antibiotics (e.g., fluoroquinolones), which remain unaltered in the bloodstream. The next important consideration is antibiotic therapy in infective endocarditis, which necessitates optimal dosing and concentration enabling adequate penetration into the bacterial biofilm and vegetations in the heart.\textsuperscript{10} National and international guidelines based recommendations should be stringently followed for optimally dosing antibiotics in these individuals. Higher drug concentrations optimized for sufficient exposure of microorganisms within the vegetation are ideal in treating endocarditis.\textsuperscript{11}

- **Lungs:** Extracellular pulmonary pathogens are targeted at the level of epithelial lining fluid (ELF) where the antibiotic achieves optimal concentration. Another consideration should be based on ELF:plasma ratio which is described as the ELF penetration of antibiotics. There occur differences in this ratio measured for penetration of various antibiotics in healthy and ill patients. Lower extent of ELF penetration was observed among carbapenems compared to penicillins and cephalosporins.\textsuperscript{12-14} These studies and findings from clinical trials warrant the judicious use of carbapenems for treating patients with pneumonia. Better ELF:plasma ratio was observed with fluoroquinolones thereby justifying its superiority for use in respiratory tract infections.\textsuperscript{15,16}

- **Bone:** Bone is considered to be the most complex site for antibiotic penetration due to the skeletal and connective tissue framework within a bone. Higher dose of antibiotics is required to treat conditions like osteomyelitis for this reason. Bone:serum ratio is much lesser for most antibiotics compared to fluoroquinolones. More hydrophilic antibiotics do not readily penetrate the bone matrix when compared to hydrophobic ones (e.g. aminoglycosides).\textsuperscript{17}

- **Soft tissue:** Target site exposure to be considered in soft tissues will be the interstitial fluid concentration of antibiotics. Antibiotic permeability through the vascular endothelium is good for all antibiotics. Major consideration should be based on adipose tissue concentration in the individual since lipophilic antibiotics might not attain appropriate concentration in comparison with hydrophilic agents.\textsuperscript{18}

- **Cerebrospinal fluid:** Blood-brain barriers which are tight junctions in the capillary endothelium of the brain are impendent to most antibiotic entry into brain tissue. The only class of antibiotics which appear to cross the barrier in uninfamed meninges are lipophilic fluoroquinolones. However, in meningitis, there is marked inflammation resulting in disruption of blood-brain barrier resulting in a profound increase of antibiotic penetration including hydrophilic compounds through brain capillaries.\textsuperscript{19} This necessitates the use of higher doses of antibiotics if meningitis patients are given steroids in addition to antibiotic therapy since steroids tend to reduce inflammation of the vascular endothelium in the brain.\textsuperscript{20} These factors establish the importance of target site penetration as pharmacokinetic differences of various antibiotics exist at all sites.

Regimens for antibiotic administration are based on pharmacokinetic properties reiterating the importance of the appropriate choice of antibiotic (right drug for the right bug at right dose given at the right time for the right duration). Suboptimal dosing results in treatment failure due to recurrence of infection especially in complex sites of the body.\textsuperscript{21}

### Understanding the Normal Microbiota

Whenever an infection is encountered, a sound knowledge of normal flora/microbiota in the specific site of infection will help in choosing antibiotics to target probable microorganisms. Infections at specific sites are almost always caused by resident flora; however, rare occurrences such as melioidosis, cutaneous anthrax, tetanus, gas gangrene, sporotrichosis, zygomycosis, etc. are associated with trauma/inoculation of infectious pathogen from an environmental source.\textsuperscript{22-24} In case of healthcare-associated infections, the microbial flora in the ICU environment is usually attributed to infections. Few documented examples highlighting the association of microbial flora with infections are as follows:

- **Peritonitis** is caused as a result of the transmigration of microorganisms from the gut into the peritoneum.\textsuperscript{25}
- **Healthcare-associated infections** (e.g., meningitis, ventriculitis, bloodstream infection (BSI), surgical site infection, pneumonia) caused by pathogens in the hospital environment. For these reasons resistant hospital-acquired pathogens are the usual suspects.\textsuperscript{26}
- **Clostridioides difficile** infection arising as a result of endogenous intestinal colonization of the organism as a result of antibiotic pressure.\textsuperscript{27}
- **Surgical antibiotic prophylaxis** targeting skin commensals which can be possible sources of infection postsurgical procedures.\textsuperscript{28}
- **Empiric regimens for tackling hospital-acquired pneumonia, as well as ventilator-associated pneumonia (VAP), are based on local microbial flora and their resistance profile.**
- **Abdominal surgical procedures and cesarean sections which are complicated with infections are associated with endogenous flora (aerobic and anaerobic) to which a possible exposure during the procedure can be related.\textsuperscript{29,30}**

The above evidence-based judgment should form the foundation of antimicrobial prescription principles. Uncommon/ unusual microorganisms can be exceptions to this rule since culture-based evidence of their presence will help in choosing appropriate antibiotics.
When should I De-escalate/Stop Antibiotics?

An empiric therapy comprises of broad-spectrum antimicrobial agents. De-escalation is commonly described as switching over from broad-spectrum empiric antimicrobial therapy to a narrower spectrum within 48–72 hours after systemic assessment and microbiological data in order to reduce antimicrobial exposure.\textsuperscript{31} Empiric therapy is always based on an antibiogram of the hospital initiated at admission prior to collection of samples for culture. The major drawback of collecting culture specimens while the patient is on antibiotics is the suppression of bacterial growth under antibiotic pressure.

De-escalation encompasses two key aspects: 1. intend to give a narrow spectrum of antibiotics based on clinical response and culture reports and 2. cessation of antimicrobial therapy if organisms fail to be isolated in pure culture. Continuing antibiotics in absence of infection promotes pressure on bacteria for resistance development.\textsuperscript{32} Another major drawback of antibiotic therapy without indication is the predisposition to the colonization of resistant bacteria, \textit{Candida} species as well as \textit{C. difficile} thereby increasing length of hospital stay as well as morbidity and mortality. Previous studies suggest reassessment of patients on antibiotics on day 3 to further decide on stopping, de-escalating to narrow-spectrum or continuing antibiotics. There is evidence of improvement in the clinical outcome of patients when de-escalation is done especially in cases of sepsis and VAP.\textsuperscript{33} An often overlooked use of de-escalating antibiotics whenever advocated is reduction in the cost of patient care. De-escalation therapy is safe and effective for specific infective conditions such as sepsis, meningitis, urinary tract infection (UTI), pneumonia, intra-abdominal infections, etc. Few exceptions in intensive care units on questionable effectiveness of de-escalation therapy is when unusual pathogens are encountered. An intensivist’s judgment on implications and usefulness of de-escalation is possible with the help of microbiologists and infectious disease specialists as the benefits are well documented.

A liaison among various specialists in this regard would escalate the quality of patient care.

How do I Distinguish True Pathogens from Colonizers?

Colonization may be regarded in two aspects—one being prior colonization of individuals during admission to hospital and the next being colonization after admission which is often confused as infection and does not warrant antimicrobial therapy.\textsuperscript{34} Considering three common organisms associated with prior colonization such as MRSA, ESBL producing enterobacteriaceae, CRE, colonization rates vary in different parts of the world.

The average percentage of MRSA carriers worldwide as reported in 2008 was estimated to be as low as 2.7%; however, healthcare workers possess a higher carriage rate of 5%.\textsuperscript{35} As anticipated, an increase in MRSA colonization rate has been reported recently by authors in 2018.\textsuperscript{36} This MRSA prevalence rate varies between various countries over time thereby highlighting the importance of regular studies on the same. Gram-negatives on the other hand possess multiple MDR genes (example: ESBL, carbapenemases, and AmpC). Factors leading to their rampant spread across the globe are travel and lack of hand hygiene and poor infection control practices within hospitals.\textsuperscript{37} Table 1 illustrates prevalence rates of ESBL and CRE among individuals in various parts of the world.

With enough supporting evidence of the rise in colonization rate during admission, the choice of empiric therapy should be considered with this background information. Therapeutic failure in most individuals results due to predisposing drug-resistant pathogen colonization contributing to the development of infection. Initial days of therapeutic response and failure of empiric therapy depends solely on patient-centered factors especially prior colonization of MDR pathogens.\textsuperscript{38}

On the other hand, upon prolonged hospital stay, one is prone to acquire healthcare-associated infections which usually begin as colonization with drug-resistant pathogens present in the ICU environment. Careful distinction is imperative since colonizers should never be treated with antimicrobial agents. This forms the basis of antimicrobial stewardship in ICUs.\textsuperscript{39} Evidence to help distinguish the dilemma between colonization from true infection is discussed below under each category of healthcare-associated infection.

- **VAP:** Laboratory diagnosis of VAP should always have a clinical basis for justification. Common pointers to microbiological evidence of true infection in ventilated patients are lack of squamous epithelial cells (<1% or <10 epithelial cells/low power field), presence of mucous strands (suggests inflammatory response), presence of intraneutrophil microorganisms (denotes active infection/phagocytosis), and >10^5 colony-forming units (CFUs) of organism in quantitative or semiquantitative culture. The above along with clinical prediction using clinical pulmonary infection score is used to establish VAP.\textsuperscript{38,40}

- **BSI:** The most important factor determining a diagnosis of BSI is blood culture positivity. Improper collection does result in blood culture contamination rate which might jeopardize the decision on antimicrobial therapy and also hamper antimicrobial stewardship by failure in isolating the pathogen. Various determinants in blood culture collection which play a vital role are as follows:
  - **Blood volume:** Optimal volume of blood is required for maximum yield. A ratio of 1:5 to 1:10 blood to broth ratio is mandatory.\textsuperscript{41}
  - **Number of sets:** Inadequate volume of blood results in low organism yield from culture. One set (20 mL) results in 73.1% yield, two sets (40 mL) result in 89.7% yield, and three sets (60 mL) result in 98.3% yield of bacteria.\textsuperscript{42} In patients with suspicion of infective endocarditis, three sets of blood collected from three separate sites at intervals of minimum 1 hour apart, and all samples collected within 24 hours duration are recommended.\textsuperscript{43}
  - **Contamination rate:** At any given point of time a contamination over 2% is unacceptable. Contamination rates result in increased length of stay, prolonged antibiotic therapy, cost of antibiotics, etc.

| Authors       | Country and year | ESBL | CRE |
|---------------|------------------|------|-----|
| Azim et al.\textsuperscript{38} | India, 2010     | 59–63% | 10–16% |
| McConville et al.\textsuperscript{39} | USA, 2017     | 28% (Either ESBL or CRE) | – |
| Salomao et al.\textsuperscript{40} | Brazil, 2017 | – | 6.8% |
| Kaarme et al.\textsuperscript{41} | Sweden, 2018    | 16.8% | – |
| Pilmis et al.\textsuperscript{42} | France, 2018  | 17.7% | – |
| Ramanathan et al.\textsuperscript{43} | Chennai, 2018 | – | 7.8% |
| Goodman et al.\textsuperscript{44} | USA, 2018      | – | 3.9% |
| Mahamat et al.\textsuperscript{45} | Chad-Central Africa, 2019 | – | 44.5% |
| Hagel et al.\textsuperscript{46} | Germany, 2019  | 12.7% | – |
• Differential time to positivity: Blood culture drawn from central venous catheter flags positive 2 hours prior to sample taken from peripheral vein is suggestive of central line related bloodstream infection (CRBSI). This parameter is useful in distinguishing colonization of central catheter from true CRBSI.

• Catheter tip culture: Identifying catheter as source of BSI such as semiquantitative/quantitative cultures of catheter tip and isolation of the same organism in blood could be indicative of CRBSI. A positive catheter tip culture with negative blood culture is suggestive of colonization of the central venous catheter.

• Catheter-associated urinary tract infection (CAUTI): Apart from clinical symptoms, a microbiological diagnosis of CAUTI may be established if quantitative culture yields ≥10^3 CFUs per mL in the absence of symptoms or ≥10^4 CFU/mL with symptoms. No more than two microorganisms are associated with CAUTI, such instances being colonizers. If the criterion is not fulfilled, the isolated organism is more likely to be colonizer warranting a change of catheter.

When to Suspect Unusual Pathogens in My Patient?

Rare isolates are interesting by making clinical as well as laboratory diagnosis challenging. The first and foremost concept to remember is that most unusual/exotic pathogens are not targeted in empiric therapy. Empiric antibiotics are formulated for commonly isolated microorganisms overlooking uncommon microorganisms. Clinical suspicion followed by diagnostic results remains the mainstay of handling unusual pathogens. Few clinical syndromes and presentations which help in diagnosis are listed in Table 2.

Opportunistic pathogens should always be considered as differential diagnosis in immunosuppressed individuals. These pathogens should also be kept as differential diagnosis in bone marrow transplant recipients, stem cell transplant patients, people living with human immunodeficiency virus, neutropenic individuals, etc.

Apart from these factors, epidemiological links have to be made with current epidemics and pandemics whenever an unusual infectious clinical presentation is encountered. In such instances, a detailed travel history, infection prevention measures, surveillance reports to state/national health authorities are appropriate considerations in containing the spread of infection.

Understanding and Supporting Diagnostic Stewardship

Diagnostic stewardship gained importance after the 2015 World Health Organization’s implementation of antimicrobial resistance (AMR) surveillance famously known as GLASS (global AMR surveillance system). Diagnostic stewardship is defined in the GLASS manual as “coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions. It should promote appropriate, timely diagnostic testing, including specimen collection, and pathogen identification and accurate, timely reporting of results to guide patient treatment.” The responsibility of diagnostic stewardship, therefore, lies with the clinicians, laboratory and surveillance staff, administrators, and organizational heads.

Major implications of diagnostic stewardship are 1. choice of appropriate diagnostic tests and specimen, 2. proper collection of specimen following standard procedures mentioned in easily available “sample collection manual” of the hospital, and 3. collection of specimens for culture before initiating empiric antimicrobials. Apart from these considerations, factors such as transport delay should be carefully avoided. If delay in transport is anticipated, appropriate storage in recommended temperature is mandatory for maximum probability of organism yield from sampling.

Table 2: Clinical profile of unusual pathogens encountered in ICUs

| Condition      | Microorganism         | Key features                                                                 |
|----------------|-----------------------|------------------------------------------------------------------------------|
| Meningococcemia| Neisseria meningitides| Petechiae/purpura, shock, bilateral adrenal hemorrhage, meningitis, disseminated intravascular coagulation, multiorgan failure. |
| Melioidosis    | Burgholderia pseudomallei | Risk factors: diabetes mellitus, alcoholism. Multiple abscesses, high-grade fever, mimics tuberculosis (TB). |
| Diphtheria     | Corynebacterium diphtheriae | Fauclal diphtheria: pseudomembrane adherent to mucosal base and bleeds on removal, bull neck. |
| Anthrax        | Bacillus anthracis     | Cutaneous/pulmonary (hemorrhagic pneumonia)/gastrointestinal anthrax.          |
| Nocardiosis    | Nocardia sp.           | Pulmonary (lobar pneumonia), disseminated.                                    |
| Brucellosis    | Brucella sp.           | Triad: fever with profuse night sweats, arthralgia/arthritis, hepatosplenomegaly. |
| Leptospirosis  | Leptospira interrogans | Well's disease—hemorrhages, jaundice, and renal failure.                     |
| Scrub typhus   | Orientia tsutsugamushi | Triad: eschar, regional lymphadenopathy, maculopapular rash.                  |
| Strongyloidiasis| Strongyloides stercoralis | Hyperinfection syndrome (colitis, enteritis, and malabsorption), disseminated strongyloidiasis. |
| Amoebic encephalitis | Naegleria fowleri | Primary amoebic meningoencephalitis—acute suppurative infection of central nervous system, changes in taste and smell (olfactory nerve involvement). |
| Rabies         | Rabies virus           | Encephalitis, autonomic dysfunction (increased salivation, lacrimation, perspiration, and cardiac arrhythmia), hydrophobia, aerophobia, flaccid paralysis (quadriparesis with facial palsy) |
| Viral hemorrhagic fever | Crimean–Congo hemorrhagic fever, Nipah, etc. | Contact with wild animals/mammals, fever, headache, myalgia, vomiting, diarrhea, rash with hemorrhages (bleeding or bruise), shock. |
| Cryptococcosis | Cryptococcus neoformans | Pulmonary cryptococcosis, cryptococcal meningitis, skin lesions, osteolytic bone lesions. |
| Histoplasmosis | Histoplasma capsulatum | Pulmonary granulomas, skin and oral lesions, disseminated histoplasmosis.     |
specimens. Specimens sent for culture should mandatorily contain information on key clinical findings for meaningful interpretation and in arriving at microbiological diagnosis. A list of mandatory core patient information to be provided according to the GLASS manual for early implementation are unique identification number, name, gender, date of birth, type of specimen, and date of sample collection. As a clinician, active case discussion with the microbiologist definitely throws more light in appropriateness of diagnosis as well as in ruling out colonization wherein such isolates need not be subjected to antimicrobial susceptibility testing.

Turnaround time is crucial in infectious disease diagnosis often considered as the backbone of diagnostic stewardship. On suspicion of an infective syndrome in a patient empiric therapy is initiated. Narrowing spectrum of therapy is key to antimicrobial stewardship and avoiding selection pressure of drug-resistant bugs in the body. Overuse, as well as underuse, of diagnostic tests lead to inappropriate diagnosis and treatment emphasizing the importance of both. Real-time diagnostic platforms for identification of microorganisms with susceptibility pattern are the recent trend which has not obtained maximum development in most countries. Common examples of modalities used as rapid diagnostic platforms for infectious disease diagnosis are real-time molecular diagnostic tests, cartridge-based molecular assays, rapid sepsis screen assays, next-generation sequencing, etc. Availability of round the clock microbiology laboratory 24×7 is the most valuable practice for a major leap in diagnostic as well as antimicrobial stewardship. This will definitely shorten turnaround time as well as help in precise decision making of clinicians.

Outbreaks in ICU—Suspicion and Investigation
Outbreaks unlinked to global epidemics or pandemics are usually confined within particular ICUs. Outbreaks occurring within ICUs are usual contributors to healthcare-associated infections which are severe in form, BSI being the forerunner. Other infections resulting due to outbreaks are gastrointestinal infections and pneumonia. Most healthcare facilities report more than half of the outbreaks from ICUs thereby compelling the vigilance of healthcare professionals especially intensivists. Data extracted from one of the largest meta-analyses including 1,022 outbreak studies on source of outbreaks in hospitals record the following: patients are major source of outbreaks, followed by medical devices, environment, and staff. Either direct (hands of healthcare workers) or indirect contact transmission (fomites and environment) is known to be the most common mode of transmission of microorganisms associated with outbreaks. Many times, the patient can themselves be the source of outbreak. It is imperative for one to understand that in about 37% of outbreaks the source remains unidentified. Possible sources of outbreaks to be considered during outbreak investigations are listed in Table 3.

Outbreak investigations are mandatory to identify the source, isolate suspected cases, prevent spread of outbreak, and intervene to remove the source in order to prevent future outbreaks. A team of doctors including clinicians and microbiologists, epidemiologists, nurses, and other healthcare workers should be framed for obtaining inputs in order to solve outbreaks. Most frequent associations causing outbreaks have been made with S. aureus (MRSA), *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Serratia marcescens*, hepatitis B and C, *Legionella pneumophila*, *Acinetobacter baumannii*, *Burkholderia cepacia*, etc. Whenever an outbreak investigation is carried out, these background data may be used for source tracing as well as organism suspicion.

**Table 3:** Common source of outbreaks

| Intrinsic contamination (at production) | Extrinsic contamination (in use) |
|----------------------------------------|----------------------------------|
| Parenteral nutrition                    | Disinfectants                    |
| Disinfectants                          | Contrast media                   |
| Plasma                                 | Heparin/anesthetic agents        |
| Immunoglobulins                        | Multidose vials                  |
| Creams                                 | Milk powder                      |
| Peritoneal liquids                     | Endoscopes/bronchoscopes         |

Multidrug Resistance in ICU
There are enough supportive evidence to portray high colonization rates of ICU environment and types of equipment with a variety of drug-resistant pathogens. Risk of acquiring MDR pathogens during the course of treatment from these sources is tremendously high. Interestingly, gram-negative bacteria are the ones commonly colonizing ICU environment with very negligible colonization rate of gram-positive bacteria and fungi. Prevention of colonization is the first step to prevent biofilm formation and transmission of drug-resistant microorganisms within ICUs.

Few documented methods to implement for preventing colonization of ICU environment are as follows:

- **Standard precautions:** A group of infection control practices followed on all patients irrespective of their infectivity are termed as standard precautions. Components of standard precautions include hand hygiene, use of personal protective equipment, safe handling of sharps, biomedical waste management, linen handling, and environmental disinfection. These are Centers for Disease Control and Prevention (CDC) recommended basic level of infection control measures in any healthcare facility.
- **Transmission based precautions:** The additional precautions suggested for few transmission-specific infections are of three types—contact, droplet, and airborne isolations. These are intended to be used as supplementary to standard precautions on certain patients [Table 4].
- **Environmental cleaning and disinfection:** Survival of various microorganisms on objects in hospital environment is variable ranging from few hours (*C. difficile* vegetative form for up to 6 hours) to many days (calcivirus for 21–28 days) and some (*A. baumannii*, *P. aeruginosa*, *K. pneumoniae*, *C. difficile* spores) for weeks or months. Certain microorganisms have a very variable survival period on inanimate objects (examples: enterococci may survive from 5 days up to 30 months and *Mycobacterium tuberculosis* may survive from 1 day up to 4 months). These data reinforce the importance of frequent environmental cleaning and disinfection in order to prevent colonization, biofilm formation, and transmission of microorganisms from surfaces to patients through indirect contact. A disinfection policy should be framed by every hospital being the collaborative efforts of infection control team and housekeeping department. These guidelines and specific disinfectants should be used appropriately in patient care areas. Frequency of cleaning and disinfection in ICUs should be every 6 hours since ICUs fall under “very high risk” area in hospitals.
- **Terminal cleaning and disinfection:** Terminal cleaning refers to all measures of disinfecting of patient zone or rooms.
Table 4: Transmission based precautions in intensive care units

| Type of isolation | Application in patient care |
|-------------------|-----------------------------|
| Airborne isolation | Patients suspected with TB, varicella, measles are placed in airborne isolation. Inhalation of small droplet nuclei (≤5 μm) which are suspended in air over long periods beyond 3 ft/1 m of particle source. Negative pressure room with closed doors is mandatory. N95 should be used upon entry into room. Susceptible healthcare workers (e.g., negative for IgG antibodies to varicella) caring for these patients may be replaced with non-susceptible healthcare workers (e.g., past infection and positive for IgG antibodies to varicella). |
| Droplet isolation | Inhalation of large droplet nuclei (>5 μm) which are suspended in air within 3 ft/1 m of particle source and do not remain suspended in air over long periods. Droplet transmission requires close contact with the infected individual. It does not require special ventilation/negative pressure rooms. Conditions requiring droplet isolation: pertussis, influenza, measles, mumps, rubella, meningococci. |
| Contact isolation | Direct as well as indirect contact transmissions occur through hands of healthcare workers. Conditions requiring contact isolation: Clostridioides difficile, MRSA, Escherichia coli O157, VRE, scabies. |

Table 5: Vaccine recommendations for healthcare personnel

| Vaccine | Recommendations |
|---------|----------------|
| Hepatitis B | Three doses at 0, 1, 6 months. Protective antibody response (antiHBs) is ≥10 mIU/mL. Route of administration: intramuscular. |
| Influenza | Single-dose vaccine is recommended yearly, administered intramuscularly. Intranasal vaccine can be used as an alternative. |
| Measles, mumps, rubella | HCP born in 1957 or later: two doses of MMR vaccine given 4 weeks apart for those with no evidence of immunity or prior vaccination. HCP born prior to 1957: usually considered protected against MMR. However, two doses are administered for unvaccinated HCP and one dose for those with no laboratory evidence of disease or immunity. Route of administration: subcutaneous. |
| Varicella | Two doses given 4 weeks apart for those HCP with no evidence of immunity or past infection. Route of administration: intramuscular. |
| Diphtheria, pertussis, tetanus | Single dose of tetanus diphtheria acellular pertussis as soon as feasible without regard to the previous dose of tetanus diphtheria (Td). Pregnant HCP should be revaccinated during each pregnancy. All HCP should then receive Td boosters every 10 years thereafter. Route of administration: intramuscular. |

between occupying patients. Currently used methods for this purpose are chemical disinfectants such as bleach, quaternary ammonium compounds. No-touch cleaning methods are gaining investigational importance commonest of these being ultraviolet light, hydrogen peroxide vapors, etc. Efficacy of terminal disinfection in ICUs of developed countries has been documented to be 44, 49.5 and 72, 82% preintervention and postintervention techniques for improving cleaning methods. These interventions have proven to improve cleaning efficacy upon training personnel on strict adherence to cleaning protocols for reducing environmental bacterial load.

**Immunoprophylaxis and Me!!**

An often overlooked entity in any healthcare setting is immunoprophylaxis of healthcare personnel (HCP), especially doctors. Employee safety is as important as patient safety because healthcare workers are at high risk of acquisition of transmissible pathogens from infected individuals. Clear guidelines have been provided by the CDC in this regard to effectively convert “susceptible” healthcare workers to “non-susceptible” individuals. CDC and Healthcare Infection Control Practices Advisory Committee encourage an exclusive vaccination policy for each healthcare facility with a preferable secure computerized recording of vaccination data.

Diseases for which vaccines might be indicated in certain circumstances: meningococcal, typhoid, poliomyelitis.

Other recommended vaccines for adults: pneumococcal, tetanus and diphtheria, human papillomavirus, zoster, hepatitis A.

Apart from the above recommendations, occupational exposure, travel and catch-up vaccinations are also recommended for HCP according to the requirement as well underlying conditions and age.

**Conclusion**

This review aimed to focus on key issues and difficulties in managing infections as well as infectious diseases in an intensivist’s day-to-day practice. Although one might not find an answer to every question in the topics discussed, an overview has been provided on key issues in present practice. Intensive care units are often considered as hotbeds for transmission of antimicrobial-resistant bacteria within any hospital. The role of each clinician, intensivist, and microbiologist is immense in the prevention of infections within ICUs since teamwork conveniently outweighs individual efforts. Practical implementations of these thoughts however challenging require perseverance with the only goal being escalating patient care.

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