Chapter 6
The Role of the Microbiology Laboratory

Smilja Kalenic

Key points

- Diagnosis of infection by the microbiology laboratory has two important functions: clinical and epidemiological.
- The microbiology laboratory should be able to determine the most frequent microbes causing infections, especially healthcare-associated infections.
- The microbiology laboratory should produce routine reports for infection prevention and control personnel to make incidence graphs for specific pathogens, wards, and groups of patients.
- Microbiologists, knowing the role of normal colonizing flora of humans, the pathogenesis of infections, and the characteristics of specific pathogens can interpret microbiological findings for infection prevention and control personnel.

Introduction

The diagnosis of infections performed by the microbiology laboratory has two important functions. The first is clinical - everyday management of infections. The second is epidemiological - knowledge of an infective microbe in a patient can lead to finding its source and route of transmission. This allows staff to stop infections from spreading.

The microbiology laboratory has many roles in the control of healthcare-associated infections (HAI): outbreak management, performing additional tests for epidemiology, infection surveillance, knowledge about new alert microbes or unusual resistance, design of an antibiotic formulary, interpretation of microbiological results, and education of health care staff. Daily communication of laboratory staff with the Infection Control Team (ICT) is vital, allowing for timely and rapid information transmission about HAIs. The clinical microbiologist should be a member of the Infection Control and Antibiotic Committees and a member of the ICT.

Microbiology is becoming more important in the prevention of HAIs, especially as new or antibiotic-resistant pathogens emerge, and more diagnostic technologies are developed. An important new technology is molecular diagnostics. Diagnosis can be rapid as it is not dependent on waiting for bacterial growth in cultures; it is sensitive, as it is based on detection of only a few microorganisms; it is specific, as it detects microbe-specific genes.

Clinical practice

Some infections must be diagnosed clinically and treated empirically, without isolation of causative microorganisms or determination of antibiotic susceptibility. However if there is a clinical suspicion of infection, laboratory tests may confirm the diagnosis. The microbiology laboratory should be able to isolate the commonest infectious agents, especially those causing HAIs. It should produce periodic reports on infections for each ward, broken down by pathogen species, infection site and antibiotic resistance. These reports are very important for the design of empirical therapy.

Most HAIs are caused by bacteria and fungi that are more antibiotic resistant than community acquired pathogens and their susceptibility to antibiotics is less predictable. Etiological diagnosis in hospitals is exceptionally important. Targeted antimicrobial therapy will lead to better outcomes, and as eradication of a pathogen is achieved earlier, the danger of transmission to other patients will be decreased.

The right specimens from appropriate sites must be taken using proper techniques. Microbiology laboratory staff can assist in ensuring good specimens by educating other staff. Identification of the microorganism and its antibiotic susceptibility should be as precise as possible (identification to the species level).

Infection control

Outbreaks

To determine the cause of a single-source outbreak the causative microorganism must be defined. A microbial species may contain subspecies and variants that differ in particular characteristics. Individual bacteria can differ as much as 30% in their genomes. Genetic differences are often phenotypically expressed, however this is not a rule.

Bacterial typing

Bacterial typing has to determine whether two epidemiologically connected strains are really related and differ from strains that are not epidemiologically connected. If strains are unrelated, the patients do not belong to the same outbreak. If strains are related it is impossible to say that the patients are involved in an outbreak without epidemiological analysis. So, epidemiology and typing are complementary.

Typing methods differ in several important points:

- Typability, i.e., the method can type most or even all strains of the same species;
- Discriminatory power, i.e., the method can differentiate well between different types;
- Interlaboratory and intra-laboratory reproducibility, i.e., the method can provide the same typing results in repeated testing on different sites;
- The method should be simple, unambiguous to interpret, and inexpensive.

There are two groups of typing methods: phenotyping and genotyping.

Phenotyping

Using phenotyping methods we can determine characteristics that can differ between different strains of the same bacterial species. These methods may be based on antigenic structure (serotyping), physiologic properties/metabolic reactions (biotyping), susceptibility to antimicrobial agents (resistotyping) and to colicines (colicinotyping), or bacteriophages (phage typing).

Phenotyping methods are well standardized with high reproducibility. Discriminatory power is not always high (if only a few types exist), but can be very high (if many types exist). They are simple and unambiguous to interpret. Many are cheap enough to be performed in every microbiology laboratory.

The main objection to phenotyping is that bacterial genes are not always expressed. Two phenotypically different strains can actually have the same genetic background or two phenotypically identical strains can actually differ genetically. Sometimes the emergence of a particular phenotype is specific enough to explain an outbreak. However, if a phenotype is widespread and frequent, genotyping will be required for outbreak management.

Genotyping

Molecular techniques have revolutionized the potential of the microbiology laboratory because they have very high typability and discriminatory power. Genotyping can demonstrate definitely the relatedness or difference between two isolates of the same species. However, genotyping methods require use of sophisticated and expensive equipment and materials by trained staff. Furthermore, some have a low reproducibility, especially in interlaboratory comparisons. Result interpretation is neither always simple nor unambiguous.

Additional tests

Sometimes the ICT requires data to clarify endemic or epidemic situations. Microbiological tests of blood products, environmental surfaces, disinfectants and antiseptics, air, water, hands of personnel, anterior nares of personnel, etc., may be required. During an outbreak or in endemic situations when the causative agent is known, the microbiology laboratory can use selective culture media for the agent in question to minimise expense.

Surveillance of HAIs

The microbiology laboratory should produce routine periodic reports to allow the ICT to make incidence graphs for specific pathogens, wards, and groups of patients. These data can be made available immediately if the laboratory is computerized. A 'baseline incidence' can be established and any new isolates can then be compared with this incidence. Graphs enable the ICT to discover the beginning of an outbreak earlier than it can be discovered clinically. Periodic reports are also important because they demonstrate trends of specific pathogens, and can be very useful in planning preventive measures.

Alert organism reports

The early isolation of a new or unusual microorganism, without any further typing, enables the ICT to take appropriate measures to stop it from spreading. The ICT should identify, together with laboratory personnel, possible 'alert' microorganisms, such as multiresistant or highly pathogenic microorganisms (methicillin-resistant *S. aureus*, vancomycin-intermediate *S. aureus*, vancomycin-resistant enterococci, multi-drug resistant (MDR) *Ps. aeruginosa*, MDR *A. baumannii*, MDR *M. tuberculosis*, *C. difficile*, etc.). Any new isolates should be reported immediately to the wards and the ICT. Alert organism surveillance may be all that can be performed if the facility is understaffed. In addition, laboratory staff may report clustering of infections (two related isolates in different patients in the same time frame).

Role in antibiotic policy

Determining antibiotic susceptibility patterns for microorganisms causing HAIs is vital for individual patient care. It can also help in planning antibiotic policy and designing the antibiotic formulary. The microbiology laboratory should produce periodic resistance reports for specific wards and for the whole hospital. These reports should be available for every physician who prescribes antibiotics.

Interpretation of microbiology data

Microbiologists are required to interpret microbiological data (results of isolation, identification, susceptibility tests, typing). Ideally he/she should be a medical doctor specialising in clinical microbiology. If this is not possible, then a properly educated scientist is required. Well educated microbiologists, knowing the role of normal colonizing flora of humans, the pathogenesis of infections (incubation period, inoculum size, kind of vehicle), and the characteristics of specific pathogens (natural habitat, resistance to drying, to disinfectants and to antibiotics) – can interpret laboratory data for the ICT.

Minimal Requirements for Microbiology Laboratories in the Control of HAIs

1. Should be within the hospital; if this is not possible, then negotiate a contract for diagnostic microbiology with the nearest laboratory.
2. Should be available every day, including Sundays and holidays, ideally on a 24-hour basis.
3. Should be able to examine blood, cerebrospinal fluid, urine, stool, wound exudates or swab, respiratory secretions, and perform basic serological tests (HIV, HBV, HCV).
4. Should be able to identify common bacteria and fungi to species level (*Staphylococcus aureus, Escherichia coli, Salmonella, Shigella, Pseudomonas aeruginosa, Klebsiella pneumoniae,* Group A streptococci, Group B streptococci, enterococci, *Streptococcus pneumoniae, Campylobacter jejuni/coli,* other enterobacteria, *Haemophilus influenzae, Neisseria meningitidis* and *N. gonorrhoeae, Stenotrophomonas maltophilia, Candida albicans,* aspergilli, etc.).
5. Should be able to perform susceptibility testing to relevant antibiotics using disc-diffusion methodology.
6. Should be able to perform basic typing - serotyping (for salmonellae, shigellae, *P. aeruginosa, N. meningitidis*) and biotyping (e.g., for *S. typhi*).
7. Should have quality assurance procedures (both internal quality control and external quality control [national or international]).
8. Should have a clinical microbiologist (if possible a medical doctor) who has good skills of communication with clinical and ICT staff.

9. May have the ability to perform simpler genotyping methods or access to genotyping methods centrally at state or regional laboratories. The central laboratory can then assist with epidemiological investigations of HAIs.

References and Further Reading

1. Diekema DJ, Pfaller MA. Infection Control Epidemiology and Microbiology Laboratory. In: Murray PR, Editor in Chief. Manual of Clinical Microbiology, 8th ed. Washington, DC: ASM Press; 2003. p. 129-38.
2. Stratton CW IV, Greene JN. Role of the Microbiology Laboratory in Hospital Epidemiology and Infection Control. In: Mayhall CG, editor. Hospital Epidemiology and Infection Control, 3rd ed. Philadelphia: Lippincott, Williams & Wilkins; 2004. p. 1809-25.
3. Poutanen SM, Tompkins LS. Molecular Methods in Nosocomial Epidemiology. In: Wenzel RP, editor. Prevention and Control of Nosocomial Infections, 4th ed. Philadelphia: Lippincott, Williams & Wilkins; 2003. p. 481-99.
4. Gill VJ, Fedorko DP, Witebsky FG. The clinician and the Microbiology Laboratory. In: Mandell GL, Bennett JE, Dolin R, Editors. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases, 6th ed. Philadelphia: Elsevier; 2005. p. 203-41.
5. Peterson LR, Hamilton JD, Baron EJ, **et al.** Role of clinical microbiology laboratory in the management and control of infectious diseases and the delivery of health care. Clin Infect Dis 2001;32:605-11.