AUSTRALIAN COMMISSION
ON SAFETY AND QUALITY IN HEALTH CARE

9 Role of the clinical microbiology service in antimicrobial stewardship

Antimicrobial Stewardship in Australian Health Care

2018

This chapter is part of *Antimicrobial Stewardship in Australian Health Care 2018*, Australian Commission on Safety and Quality in Health Care, 2018.

The publication summarises current evidence about AMS strategies and interventions, and their implementation. Chapters 1–7 provide strategies for implementing and sustaining AMS, and Chapters 8–12 examine the roles of the different clinicians in AMS.

The publication will continue to evolve with additional chapters over time that address AMS in specific settings, such as primary care.

As new resources become available, they will be added as hyperlinks to the resources section in each chapter or to the appendices.

Chapter contents

Acronyms and abbreviations

Abbreviation	Definition
AMR	antimicrobial resistance
AMS	antimicrobial stewardship
AURA	Antimicrobial Use and Resistance in Australia
CAR	critical antimicrobial resistance
CLSI	Clinical and Laboratory Standards Institute
CMS	clinical microbiology service
CPE	carbapenemase-producing Enterobacteriaceae
EUCAST	European Committee on Antimicrobial Susceptibility Testing
ID	infectious diseases

Key points

- The clinical microbiology service (CMS) provides a vital function in laboratory diagnosis of infections, which supports effective patient management.
- The laboratory diagnostic process involves test ordering, specimen collection, laboratory testing, and interpretation and communication of the result. The systematic application of best practice is needed at each of these stages to optimise patient care and antimicrobial use.
- Formalised processes should be in place to ensure appropriate clinical specimen collection and testing, to ensure the accuracy and quality of diagnostic testing, and timely reporting with comments that assist in interpretation.
- The CMS also plays system-wide roles in antimicrobial stewardship, including in the surveillance of antimicrobial resistance (AMR), advice on infection control issues, therapeutic drug monitoring and workforce education.
- The CMS provides input to the reporting of AMR through surveillance programs such as Antimicrobial Use and Resistance in Australia and the National Alert System for Critical Antimicrobial Resistances.

9.1 Introduction

Microbiology testing is a key component of antimicrobial stewardship (AMS).[1] The clinical microbiology service (CMS) performs the combined role of patient-specific diagnostic testing to guide direct patient care, and system-wide diagnostic stewardship, surveillance of resistant organisms and outbreak investigation.

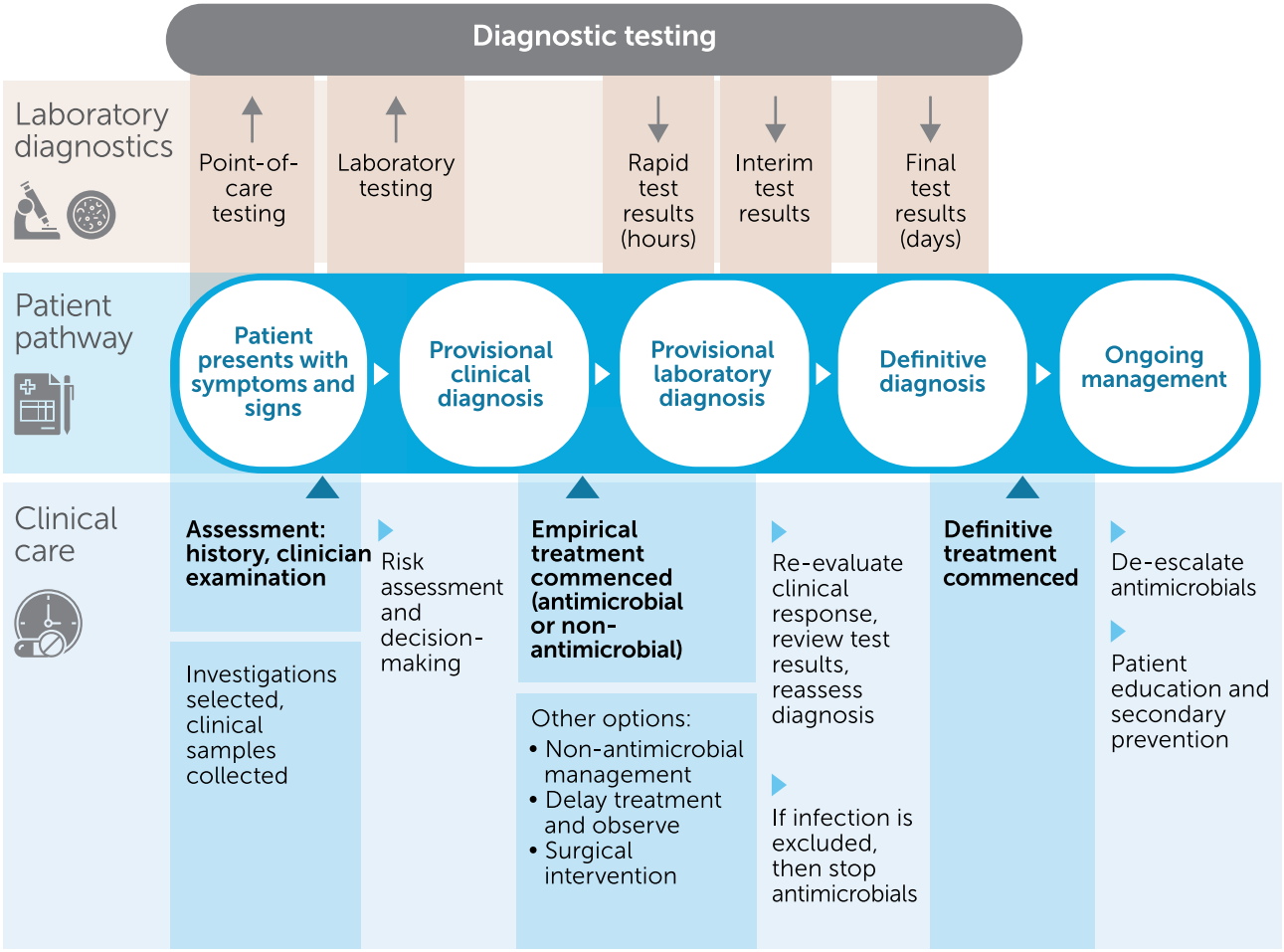
9.2 Overview of the diagnostic testing process

The CMS provides laboratory testing to support a provisional clinical diagnosis of infection, and to guide empirical and directed antimicrobial therapy. Diagnostic error is a contributor to suboptimal antimicrobial prescribing[2], and improved use of microbiology laboratory tests has been associated with better prescribing.[3] The 2015 Australian National Antimicrobial Prescribing Survey found that 12.4% of all antimicrobials were prescribed based on laboratory evidence of infection.[4] The CMS is able to contribute to AMS as part of the multidisciplinary team working to improve the use of testing to better inform treatment.

Figure 9.1 shows the process of laboratory testing as part of an episode of care. Microbiology testing involves different elements that are available sequentially as they are completed. Results from direct examination of a specimen are typically available within hours, the preliminary culture result within 24–48 hours, and the final result that includes the antimicrobial susceptibility information afterwards.[5] The timing of the result release is not always predictable, which may complicate diagnosis and antimicrobial treatment decisions.[3,6]

Figure 9.1 shows that diagnosis and management are dynamic processes that are complemented by an understanding of the time course of the disease and testing.[7] When there is a strong clinical indication to start treatment early, empirical treatment is started based on a provisional diagnosis and immediately after collecting appropriate specimens. Treatment is later modified depending on the patient's progress and the results of investigations. This can occur, for example, in patients with suspected sepsis who may not necessarily present as being acutely unwell but need urgent management.[6] If the clinical problem is subacute or chronic, treatment can be deferred until after a microbiological diagnosis has been established, although it is usually not. This is especially important for conditions that may require prolonged therapy, such as chronic osteomyelitis, septic arthritis or infected prosthetic material. AMS best practice for hospitalised patients requires that there is at least a daily review of clinical progress,

Figure 9.1: Role of diagnostic testing across the diagnostic continuum



new results of investigations and antimicrobial treatment plans.

The laboratory diagnostic process has three phases[8]:

- Pre-analytical phase – comprising test selection and ordering, and specimen collection and transport
- Analytical phase – comprising specimen processing and analysis
- Post-analytical phase – ensuring that results are delivered and read, and that the appropriate action is taken based on correct interpretation of the results; the post-analytical components of diagnostic testing are often overlooked, but their neglect can contribute to suboptimal clinical care[9] and antimicrobial misuse.

9.3 Pre-analytical phase: microbiology process

In the pre-analytical phase of diagnosis, the CMS supports practices that ensure that the right tests are performed on appropriately collected clinical samples. The CMS also helps to ensure that communication with, and delivery to, the laboratory is optimised to influence clinical care. This role also includes efforts to avoid testing when it is not clinically appropriate.

9.3.1 Selecting diagnostic tests

Culture-based tests are the principal investigations used to diagnose and guide treatment for most bacterial infections that are treated with antimicrobials. Midstream urine culture is the most frequently used microbiology test in Australia (see Box 9.1); Medicare data from 2017 indicated that more than 4.7 million tests were undertaken.[10]

Box 9.1: Urine examination and antimicrobial stewardship

Midstream urine (MSU) microscopy, culture and susceptibility (m/c/s) tests enable effective targeting of antimicrobial treatment for urinary tract infections, or may provide negative diagnostic evidence that prompts consideration of alternative diagnoses. Urine is not intrinsically sterile – the prevalence of asymptomatic bacteriuria in the healthy population ranges from 1% to 15%.[11] Requesting MSU m/c/s testing without a clear clinical indication is strongly discouraged, as it may lead to overdiagnosis and misuse of antibiotics. Failure to correctly interpret the result and correlate it to the clinical situation contributes significantly to antimicrobial misuse.[12-14]

In the absence of urinary tract symptoms, the MSU m/c/s result should not be used to diagnose urinary tract infection. MSU m/c/s testing is recommended in all cases of upper or complicated urinary tract infections.[15]

MSU m/c/s testing should consider pre-analytical factors that can affect urine culture results, including collection methods, time from collection to processing, and methods to reduce overgrowth associated with delays in transport and processing (such as boric acid or refrigeration).[16] The clinical microbiology service, in collaboration with the clinical workforce, can play a key role in ensuring that urine cultures are ordered only when appropriate, collection is optimised, and results are reported clearly to aid interpretation.

All elements of the test report, especially the white cell and epithelial cell counts, and the patient's clinical signs are used when making patient management decisions. The final result is a combination of results from biochemical tests, cell counts, quantitative culture and antimicrobial susceptibility testing. Antimicrobial susceptibilities should be reported in keeping with prescribing guidelines.[12,15,17]

Potential antimicrobial stewardship strategies relating to urinary tract infections include:

- Not performing urine cultures unless there are signs or symptoms of infection[18]
- Recommending non-antibiotic management of urinary tract infection in women with mild to moderate symptoms, or when testing is performed on patients with urinary catheters[16,19-23]
- Withholding antimicrobial susceptibility results for culture-positive urine samples from non-catheterised patients as a default, with an explanation that most of these results represent asymptomatic bacteriuria.[24]

The other commonly ordered tests are cultures of blood, wound, genital and sputum samples. Additional information about blood cultures and AMS is in Box 9.2.

Non-culture-based tests using molecular and immunology methods make up the remaining suite of microbiology tests used in clinical care. Such tests are commonplace for detecting sexually transmissible infection.

Irrespective of the test method, a positive microbiology diagnostic test is used to confirm a provisional clinical diagnosis, and the antimicrobial susceptibility results guide targeted antimicrobial management. Negative tests, from optimally collected clinical samples, may suggest that a diagnosis can be excluded and provide evidence that antimicrobial therapy is not indicated.

Tests for acute-phase reactants (for example, C-reactive protein and procalcitonin) may be used in a complementary role. They can indicate the possibility of an infectious aetiology in acute clinical syndromes before microbiological results are available or when culture-based tests are not feasible. It should be appreciated that these tests are non-specific, and their value is limited in guiding decision-making. Despite widespread use, the published evidence for their effectiveness has been limited to a range of specific scenarios. For example, these tests have been demonstrated to be useful in suggesting a bacterial aetiology in adults with acute respiratory disease presenting to emergency departments.[25,26] Serial procalcitonin measurements

Box 9.2: Sepsis and detection of bacteraemia or fungaemia, and antimicrobacterial stewardship

The detection of pathogens involved in bloodstream infection is one of the most important diagnostic tests performed by the clinical microbiology service.[5,27] Microbiological diagnosis of bloodstream infection may confirm or alter the provisional clinical diagnosis and guide definitive antimicrobial treatment, with potential impacts on mortality, morbidity, antimicrobial use, length of stay in hospital and healthcare expenses. With regard to antimicrobial stewardship (AMS), blood culture results may determine whether empirical therapy is appropriate by detecting unsuspected antimicrobial resistance, or enable switching from broad-spectrum agents to targeted choices. Negative results for optimally collected specimens can guide cessation of empirical therapy.[3,28] In the case of positive blood cultures, the organism identified may indicate the source of infection, and that information can guide non-antimicrobial treatment and overall management.

Indications for the collection of blood cultures require careful consideration.[29-31] Poorly collected blood cultures can lead to false positive or false negative results that may compound diagnostic uncertainty. This may prompt unnecessary empirical therapy and prolonged hospitalisation.[32] The collection process should ensure appropriate asepsis to reduce contamination, adequate sample volumes, and multiple sets to provide adequate sensitivity.[33-35]

Rapid blood culture analytical methods, both phenotypic and molecular, have been demonstrated to reduce the time to targeted antimicrobial therapy and to reduce mortality. This is especially true if the results are directly communicated to the clinician or via the AMS team.[36,37]

in intensive care patients treated with antimicrobials may also provide a useful guide to the timing of de-escalation or cessation of antimicrobial therapy. In essence, tests for acute-phase reactants should be used sparingly and interpreted with caution when managing infectious diseases.[38-40]

Optimal selection of diagnostic microbiology tests is critical to providing reliable guidance to clinicians who are managing patients with possible infection.[41] The type of test selected depends on the timing of presentation and the type of organisms suspected to be causing the infection. The decision to order a diagnostic test should be based on the pre-test probability of suspected infection, taking into consideration that potential pathogens may be present as part of the normal flora. Syndrome-specific diagnostic algorithms – for example, the United Kingdom Standards for Microbiology Investigations[42] – and integrated clinical pathways[6] may be useful for guiding test selection. Computerised pathology ordering systems that require better specimen description, structured clinical notes or nominated indications for testing are recommended.[43] Applications for mobile devices to guide test selection are also available[1,44] (see Chapter 4: 'Information technology to support antimicrobial stewardship').

The following general principles apply to selecting diagnostic tests:

- Avoid diagnostic testing of patients who are asymptomatic or where the likelihood of infection is low (for example, cultures of wounds without signs of infection[45])
- Provide guidelines and specifications of minimum requirements for microbiological investigations for common syndromes that require hospital admission (for example, complicated urinary tract infection, severe skin and soft tissue infection, pneumonia, acute osteomyelitis, septic arthritis and endocarditis).[46]

9.3.2 Collecting and transporting samples

Optimal specimen collection and transport are critical elements of the testing process.[5,47,48] Most samples submitted for testing are collected by the frontline clinical workforce, but the patient may self-collect urine, sputum and faeces samples. Packaged collection kits and training collection staff to optimise blood culture collection have been shown to reduce contamination and provide better samples.[44,45,49]

Samples from non-sterile sites such as urine, wounds and sputum are easily contaminated during collection. It is important that efforts are made during the collection process to increase the chance that test results reflect the organisms that are present at the site of infection. Collection of the sample after antimicrobial therapy has started may lead to false negative culture results.[50,51] Test results may also be adversely affected by suboptimal specimen labelling, an inadequate volume of material provided, incorrect specimen containers, and delays between specimen collection and performing the test.[47]

The following general principles apply to optimal sample collection and transport:

- Set up best-practice systems for sample collection to avoid contamination and maximise diagnostic accuracy
- Follow clinical guidelines on microbiology specimen collection that incorporate laboratory requirements, and are current and readily accessible
- Collect clinical samples for culture before antibiotics are commenced, whenever possible
- Provide consumer guides for self-collected samples
- Label clinical samples correctly and include relevant clinical information in the request order
- Minimise transport time to the laboratory; this is especially important when laboratory testing is performed at a distant location.

9.3.3 Commenting on specimen quality

The CMS should have in place systems to manage poor-quality specimens submitted for testing. Macroscopic and microscopic analyses are used to determine whether the sample submitted is unlikely to yield useful clinical information. Poor samples should be rejected or re-collected, or, at a minimum, a comment should be added to the laboratory report. A suggested approach for commenting on specimen quality is in Table 9.1.

9.4 Analytical phase: microbiological analytical practice

The analytical phase of diagnostic testing, from specimen processing to final result, is often complex. It can involve a range of methods, from traditional Gram-stain microscopy to whole-genome sequencing. Some elements of testing are predominantly manual, whereas others are automated. Diagnostic testing technology is rapidly evolving, with the goal of optimising negative and positive predictive values, and reducing the time to produce results.[52,53] The menu of laboratory diagnostic tests is likely to change markedly over the next decade as culture-based and traditional phenotypic methods are replaced by molecular and other methods.[1] An example is the introduction of mass spectrometry for faster species identification of colonies of bacterial and fungal organisms in culture-based testing. Similarly, testing methods for the detection of emerging antimicrobial resistances (AMRs) demand that the CMS have in place processes to ensure the timely adoption of newer laboratory processes.

9.4.1 Rapid diagnostics and testing

Early availability of diagnostic test results is critically important for the management of patients with infection. Rapid diagnostics and the enhancement of laboratory processes can have a significant effect on

Table 9.1: Examples of comments on specimen quality

Criterion for adding comment	Comment text
Sputum with profuse squamous epithelial cells	The presence of abundant squamous cells indicates probable contamination of this specimen by oropharyngeal flora.
Urine with squamous epithelial cells >50 × 10^6/L	The presence of squamous cells indicates probable contamination of this specimen by perineal flora.
Formed or soft stool submitted for viral detection, bacterial culture or *C. difficile* detection	Formed or soft stool is unsuitable for detection of enteric pathogens.

patient outcomes and optimise the use of antibiotics, by reducing the time required to confirm or exclude a diagnosis and guiding the switch from empirical to directed antimicrobial treatment.[53,54] Point-of-care testing is an example of rapid diagnostic testing. Point-of-care tests include the detection of influenza antigens from respiratory samples[55], the use of immunochromographic or latex agglutination tests for meningitis[56], and rapid tests for pneunomoccal urinary antigen to predict pneumococcal infection.[57]

Increasingly, results of molecular and advanced phenotypic methods (for example, MALDI-TOF MS[58] for the detection of pathogens and specific antimicrobial-resistant organisms direct from clinical samples) can be provided within hours, which significantly improves early treatment decisions. Direct susceptibility testing may be performed on urine and positive blood culture samples, providing preliminary information to guide management 24–48 hours earlier than the final result.[59-63]

All of the laboratory processes, from specimen transport and analytical workflow to result reporting, should be optimised to reduce the time taken for the information to be available to influence clinical care. This may require moving away from traditional laboratory practice towards a full 24-hour-a-day service with flexible processes to enable multiple runs of plate rounds, assays and on-demand result reporting.[64,65]

9.4.2 Antimicrobial susceptibility testing

Traditionally, the antimicrobial susceptibility of organisms detected in clinical samples is determined using culture-based phenotypic testing. All laboratories should test in line with requirements and interpretations specified by one or more standards organisations (see Resources).

Genotypic testing for AMR genes is now widely used for different organisms harbouring certain resistance genes. An example of this is direct detection of *Staphylococcus aureus* genes and methicillin resistance from a positive blood culture broth.

9.5 Post-analytical phase: microbiology reporting

The CMS should provide timely and accurate results and advice to support clinical management decisions and optimal antimicrobial prescribing. Results should be readily available and easy to interpret.

9.5.1 Timeliness of test reporting and integration with antimicrobial stewardship programs

Susceptibility and culture results should be reported to clinicians as soon as possible to allow them to streamline or stop antimicrobial therapy, as appropriate. AMS interventions that are prompted by susceptibility testing results have a greater impact on timely therapy change than those that are not.[37,66,67]

9.5.2 Reporting and interpreting results

Microbiology results may be qualitative or quantitative, and often include a combination of result elements. These factors can contribute to the risk of incorrect interpretation of the information. Microscopy or cell count results may be overlooked, even when they are important as indicators of colonisation, contamination or an inflammatory response to infection. Single or multiple organisms can grow in cultures, each with different susceptibility and potentially different clinical relevance. Report design is paramount in supporting the safe interpretation of the results.[68,69] Summarising or grouping results to improve visual display can improve data interpretation.[70,71] Another challenge in the comprehension of results is dealing with unfamiliar terminology related to newer diagnostic technology and changes in organism nomenclature.[1]

The addition of laboratory comments in result reports has been proven to assist clinicians with the interpretation of the information.[72,73] Report comments can prompt clinicians to consider the possibility of false negative or false positive results, or other features that suggest that the result reflects contamination or colonisation (see Table 9.2).[47]

Table 9.2: Examples of comments that interpret results, and provide clinical and infection control advice

Specimen type	Indication	Suggested reporting comment
Blood	*Staphylococcus aureus* isolated	*Staphylococcus aureus* isolated from blood is rarely a contaminant. 30-day all-cause mortality of *S. aureus* bacteraemia is approx. 21%.[78] Formal consultation with infectious diseases physician or clinical microbiologist is strongly recommended. The Staphylococcus Bacteraemia Management Guideline can be found at [location/URL]. Relapse of *S. aureus* bacteraemia occurs in up to 5% and may present up to 3 months after the event. Patients should receive a written note to this effect [reference information sheet].
Blood	Isolate of coagulase-negative *Staphylococcus* (CoNS) from an intensive care patient – mixed or isolated after prolonged incubation (>1 day), only one set taken	For optimal sensitivity and specificity, at least two separate blood culture sets (adult, 20 mL each) should be collected from separate venepuncture sites before starting antimicrobial treatment. This patient had one set collected, which has isolated CoNS. This result could indicate either infection or contamination – clinical correlation is required.
Blood	Isolate of potential contaminant organism(s) from non–intensive care unit patient – mixed or isolated after prolonged incubation (>1 day), not present in multiple sets	This isolate most likely represents contamination. To avoid contamination during blood culture collection: • Do not collect sample through pre-existing or new intravascular lines • Perform hand hygiene before the procedure • Disinfect the skin site and blood culture bottle caps with [alcohol/other preferred agent] (applied for at least 1 minute) • Use sterile gloves and no-touch technique for venepuncture • Avoid needle exchange before inoculation of bottle(s).
Faeces	Isolate of *Campylobacter*	*Campylobacter* gastroenteritis does not normally require antimicrobial treatment. However, in severe or prolonged cases, and during pregnancy, treatment is indicated – refer to *Therapeutic Guidelines: Antibiotic*.
Isolate from non-sterile site	Antimicrobial susceptibility reported for information rather than to recommend treatment	The reporting of antimicrobial susceptibility does not imply that treatment with antimicrobials is necessary. Colonisation (as opposed to infection) does not require antimicrobial treatment.
Any specimen	Isolate of carbapenemase-producing Enterobacteriaceae (CPE)	CPE detected. Treatment options are limited – consult [insert preferred reference here]. Manage CPE-colonised inpatients with standard and contact precautions. [An alert is placed on the patient record.] (For further information, see Resources.)

Antimicrobial susceptibility results should be withheld for isolates that reflect colonisation rather than infection, to avoid prompting unnecessary antimicrobial treatment.[68] Examples of circumstances in which results could be withheld include:

- Selected urine culture results[24] (see Box 9.1)
- Screening specimens, other than those for multidrug-resistant organisms
- *Candida* isolation from sputum.[74]

If results are reported in these circumstances, their significance should be discounted by providing a comment (see Table 9.2). Comments can also be used to provide treatment advice for both antimicrobial and non-antimicrobial measures.[47,75] Reports can refer to management guidelines, such as *Therapeutic Guidelines: Antibiotic*[76], or infection control recommendations.[77] Comments that assist in the interpretation of antimicrobial susceptibility results should also be included to ensure that the most appropriate treatment is selected. Examples of this type of comment are shown in Table 9.3.

9.5.3 Cascade reporting

Cascade (selective) reporting of antimicrobial susceptibilities has been shown to markedly improve the appropriateness of prescribing of antibiotics in a randomised case-vignette study.[79] A recent quasi-experimental retrospective study demonstrated a significant and sustained reduction in the use of, and resistance to, ciprofloxacin after the implementation of routine suppression of ciprofloxacin susceptibility results.[80]

The process involves withholding antimicrobial susceptibility test results for second-line agents (that is, generally those that are more broad spectrum) unless an organism is resistant to first-line agents within a particular antimicrobial class (see Table 9.4 for examples).[79] Routine reporting of susceptibility to non-formulary or restricted antimicrobial agents should be avoided.

Table 9.3: Examples of comments that interpret antimicrobial susceptibility results

Specimen type and indication	Reporting comment
Pus or skin swab with methicillin-susceptible *Staphylococcus aureus*	*S. aureus* susceptible to flucloxacillin/dicloxacillin is also susceptible to cefazolin, cefalexin and amoxicillin–clavulanate. (Flucloxacillin/dicloxacillin result reported as susceptible based on cefoxitin test.)
Any site where *Pasteurella* species is isolated	*Pasteurella* species are always resistant to dicloxacillin/flucloxacillin.
Respiratory tract or blood isolate (meningitis absent) where *Streptococcus pneumoniae* is isolated	In pneumonia, benzylpenicillin 1.2 g IV every 6 hours is enough treatment for isolates with MIC ≤0.5 mg/L. Use 1.2 g every 4 hours for isolates with MIC ≤1 mg/L. Use 2.4 g every 4 hours for isolates with MIC ≤2 mg/L. Alternative therapy should be selected for isolates with MIC ≥4 mg/L – please discuss with the on-call clinical microbiologist. (Comment derived from EUCAST.)
Pus or sterile-site aspirate, or tissue culture, where anaerobic (gram-negative) species is isolated	Agents that are generally active against gram-negative anaerobes (such as *Bacteroides* and *Prevotella* spp.) include metronidazole (use 12-hourly dosage), clindamycin and piperacillin–tazobactam. (Modify as per local formulary.)
Pus/skin swab with methicillin-resistant *S. aureus* (MRSA)	MRSA is NOT susceptible to any β-lactam antibiotic except ceftaroline. For severe infection, collect blood culture sets from different sites, use vancomycin IV (loading dose required) and consider infectious diseases or clinical microbiologist consultation. For simple cutaneous abscess, surgical drainage is usually curative. For oral therapy, use one antibiotic that has tested susceptible (NOT oral vancomycin). For advice on recurrent skin infection, refer to [url of reference site].

EUCAST = European Committee on Antimicrobial Susceptibility Testing; IV = intravenous; MIC = minimum inhibitory concentration

Table 9.4: Examples of cascade reporting of antimicrobial susceptibility results

Situation	Reporting approach
Staphylococcus aureus from blood culture	• First-line report (methicillin-susceptible *S. aureus*): flucloxacillin and cefazolin • Second-line report (methicillin-resistant *S. aureus*): vancomycin
Escherichia coli from urine culture	• First-line report: ampicillin, cefazolin/cefalexin, trimethoprim, gentamicin, nitrofurantoin • Second-line report – add amoxicillin–clavulanate if resistant to ampicillin or cefazolin – add ceftriaxone if resistant to cefazolin – add ciprofloxacin if resistant to all of ampicillin, cefazolin and amoxicillin–clavulanate • Third-line report – add tobramycin/amikacin if resistant to gentamicin – add piperacillin–tazobactam if resistant to ceftriaxone – add meropenem if resistant to piperacillin–tazobactam and ceftriaxone – test and add fosfomycin if resistant to norfloxacin

9.5.4 Communicating critical results

Critical microbiology results such as positive blood cultures should be urgently discussed with the clinician so that appropriate treatment is not delayed. For sterile-site (including blood) specimen results, contacting the clinician at the time of a positive Gram stain often leads to treatment change. For example, in a study of 123 patients with clinically important positive blood cultures, 36% of patients had their treatment changed after a Gram stain.[81] Further liaison between the CMS and the clinician after culture and susceptibility results were available led to treatment change in another 50% of patients, usually a change to a narrower-spectrum antimicrobial. Barenfanger et al. demonstrated that patient mortality was halved if Gram stains from blood cultures were performed and results communicated within one hour of the culture becoming positive.[82]

A structured approach to discussing sentinel results is useful to ensure clear communication and documentation of the discussion and recommendations. An approach adopted from the ISBAR (identify, situation, background, assessment, recommendation) clinical handover process is recommended.[83] It can also be helpful to request a read-back of the result to confirm accurate understanding. Barenfanger et al. detected a 3.5% error rate in outgoing laboratory phone calls, which was corrected by introducing a read-back policy.[84]

Automated communication of critical results to clinicians is another valuable method that improves the timeliness of notification and avoids the potential errors that can occur in verbal communication.[85] AMS ward rounds provide another opportunity for the discussion of sentinel results with clinicians.

9.6 Specific situations that need clinical microbiology service expertise

As well as influencing individual patient care, the CMS can support different specific AMS initiatives at the local and national levels.

9.6.1 Support for high-risk units

Intensive care, transplantation, haematology and oncology units have high rates of antimicrobial use and warrant particular attention from the CMS. High antimicrobial use exerts selection pressure for AMR, and this may have a spillover effect on patients managed by other services because of cross-infection.

Clinicians and managers in high-risk units should regularly consult with the CMS to review antimicrobial use, changes in cumulative antibiograms and reports on multidrug-resistant organisms for the unit. This can provide the impetus to change local antimicrobial recommendations, with reference to *Therapeutic Guidelines: Antibiotic*[76], and promotes adherence to relevant infection prevention and control measures.

A CMS representative should attend AMS team rounds, which may be on a daily, twice-weekly or weekly basis, depending on the size and case load of the particular unit. These rounds are often conducted with the infectious diseases (ID) service. AMS liaison rounds generally involve:

- Appraising the clinical presentation, previous treatment and current status of each patient
- Considering the function of antimicrobial treatment (prophylaxis, empirical or directed treatment)
- Interpreting existing microbiological results and, if required, recommending other relevant investigations
- Recommending changes (in the light of patient situation, microbiology and guidelines) to the documented diagnosis; the choice of medicine(s) and the route of administration or dosage; and the defined or agreed duration of treatment, or a date for further review.

9.6.2 Cumulative antibiogram analysis

The CMS should provide annual analyses of cumulative AMR to groups with responsibility for local antimicrobial therapy guidelines to inform recommendations for local empirical therapy and formulary management.[86]

Caution should be exercised if clinicians are provided with cumulative antibiograms. Interpretation by a clinical microbiologist or ID physician is needed, so that clinicians recognise at which point an antimicrobial is no longer a reliable empirical agent against an organism or group of organisms. Commentary should accompany the cumulative antibiogram to indicate whether the local resistance patterns show that a variation from *Therapeutic Guidelines: Antibiotic*[76] is needed locally. Examples of such commentaries are available from the AIMED website.[87]

The Clinical and Laboratory Standards Institute (CLSI) guideline M39-A2 is the accepted international standard for the analysis and presentation of antibiograms. It is recommended to use the Australian standard approach to analysing and reporting cumulative antibiograms, based on the CLSI standard.[86] The Australian standard specifies a number of 'sentinel organisms' for which local epidemiology should be examined and recommends a format for presenting the cumulative antibiogram (Figure 9.2).

Currently available software for antibiogram analyses includes OrgTRx (part of the national Antimicrobial Use and Resistance in Australia [AURA] Surveillance System), WHONET software, and various in-house and commercial options.

Locally generated antibiograms may be compared with national AMR data published by the AURA program. The AURA 2017 report provides a selected array of information about rates of resistance by specimen type and by state and territory.[89]

9.6.3 Signal and critical antimicrobial resistances (CARs)

The Australian standard antibiogram format recommends separate consideration of six important 'signal resistances' (S), which have been supplemented by a variety of other isolates with resistances that need to be reported to the National Alert System for Critical Antimicrobial Resistances (CARAlert):

- Vancomycin-resistant enterococci (S), linezolid-non-susceptible *Enterococcus* species (CAR)
- Methicillin-resistant *S. aureus* (S), and vancomycin-, linezolid- or daptomycin-resistant *S. aureus* (CAR)
- Vancomycin-intermediate and vancomycin-resistant *S. aureus* (S)
- Carbapenemase-producing Enterobacteriaceae (CPE) and other carbapenemase-producing gram-negative organisms (S), carbapenemase-producing or ribosomal methylase–producing Enterobacteriaceae (CAR)
- *Streptococcus pneumoniae* with a penicillin minimum inhibitory concentration ≥0.06 mg/L (S)
- Enterobacteriaceae that are resistant to third- or later-generation cephalosporins (S)
- Multidrug-resistant *Mycobacterium tuberculosis* (CAR)
- Ceftriaxone- or azithromycin-non-susceptible *Neisseria gonorrhoeae* (CAR)

Figure 9.2: Example of a hospital urinary isolate antibiogram, taken from John Hunter Hospital

	Organism type	Isolates	Percentage of total	Unrestricted antibiotics: Ampicillin	Amoxicillin–clavulanate	Cefazolin/cefalexin	Nitrofurantoin	Trimethoprim	Gentamicin (aminoglycoside)	Restricted antibiotics: Ceftriaxone	Norfloxacin
All isolates		5,645	Some miscellaneous/contaminant species excluded								
Gram-negative isolates	*Escherichia coli*	3,197	57%	58%	86%	86%	99%	78%	96%	96%	93%
	Klebsiella species	522	9%	R	92%	82%	n/a	87%	99%	97%	96%
	Enterobacter-like species*	316	6%	R	R	R	n/a	76%	95%	†	94%
	Proteus mirabilis	195	3%	88%	98%	92%	R	79%	96%	99%	97%
	Pseudomonas aeruginosa	290	5%	R	R	R	R	R	98%	R	95%
Gram-positive isolates	*Staphylococcus saprophyticus*	150	3%	95%	S	S	100%	94%	n/a	S	n/a
	Streptococcus agalactiae (group B strep)	300	5%	S	S	S	S	n/a	R	S	n/a
	Enterococcus faecalis	675	12%	S	S	R	S	R	R	R	R

R — Intrinsically resistant

45% — <70% of isolates susceptible

75% — 70–89% of isolates susceptible

93% — >90% of isolates susceptible

S — Susceptible by extrapolation or intrinsically susceptible

n/a — Not available – not routinely tested in this laboratory or no testing standard available

* — *Enterobacter, Serratia, Citrobacter, Providencia, Morganella* species (excludes *C. diversus*)

† — Resistance may emerge during therapy, and agent NOT recommended for these species

Refer to www.aimed.net.au for the Hunter New England Local Health District restricted anti-infective indications

Source: Pathology North[88]

- Ceftriaxone-non-susceptible *Salmonella* species (CAR)
- Multidrug-resistant *Shigella* species (CAR)
- *Streptococcus pyogenes* with reduced susceptibility to (benzyl)penicillin (CAR).

The CMS should actively monitor and report on these exceptional phenotypes. For a broader discussion of exceptional resistance phenotypes across all major pathogenic bacterial species, see the EUCAST expert rules, updated in 2016.[90]

Extra information about the epidemiology of important endemic or emerging resistant pathogens can be obtained by analysis and reporting of:

- Relevant molecular resistance mechanisms (for example, the presence of specific carbapenemase or extended-spectrum β-lactamase genes in gram-negative organisms)
- Epidemiological markers (for example, by using one of many typing methods that imply clonality).

These data can further inform AMS, and infection prevention and control strategies by identifying outbreaks and the epidemiology of pathogen transmission.

CMSs are encouraged to participate in the AURA Surveillance System[91] and its component programs, such as the Australian Group on Antimicrobial Resistance[92] and the Australian Passive AMR Surveillance system.[93]

9.6.4 Therapeutic drug monitoring and review

The CMS should collaborate with clinical chemistry and pharmacy departments to:

- Monitor blood antimicrobial levels for results that are either above or below targets (for example, for aminoglycosides, vancomycin, antifungal agents)
- Provide appropriate interpretive comments consistent with *Therapeutic Guidelines: Antibiotic*.[76]

The CMS should enable access to therapeutic drug-monitoring data by pharmacy and other auditors to enable assessments of indicators of the quality of antimicrobial use (see Chapter 6: 'Measuring performance and evaluating antimicrobial stewardship programs').

9.6.5 Linking microbiology results with electronic prescribing

Linkage of patient microbiology and antimicrobial susceptibility results with electronic prescribing system data can help to improve antimicrobial prescribing (see Chapter 4: 'Information technology to support antimicrobial stewardship').[94] In-house and proprietary systems are effective in targeting patient-level AMS interventions.[95-97] These systems may prompt review when organisms are resistant to the antimicrobial being prescribed, when prescriptions are ordered where no organisms have been isolated, and when broad-spectrum agents could be switched to narrower-spectrum[98] or less expensive antimicrobials.

9.6.6 Measuring performance of the clinical microbiology service as part of the antimicrobial stewardship program

Performance measures for CMS activities with potential impacts on AMS may include the following.

Pre-analytical phase:

- Compliance with test recommendations for the specific clinical presentation
- Proportion of patients for whom a microbiological diagnosis is obtained for the specific clinical syndrome
- Analyses of repeat specimen submission and compliance with rejection criteria
- Specimen quality measures
  - urine contamination[99]
  - blood cultures – collection of more than one set, sample volume and contamination rates[33,100-103]
  - rates of suboptimal sputum and wound samples, based on evaluation of microscopic findings (relative presence of polymorphonuclear cells and squamous cells)[104]
- Time from sample collection to arrival in the laboratory for processing.

Analytical phase:

- Laboratory external quality assurance performance
- Monitoring of turnaround times for negative and positive results of major tests.

Post-analytical phase:

- Accuracy and completeness of documentation, and actioning of critical results
- Monitoring of time to reporting urgent tests
- Compliance with cascade reporting requirements
- Clinician satisfaction surveys.

9.7 Role in education

The CMS should educate the nursing, midwifery, medical and pharmacy workforce, and pathology specimen collection personnel about clinical indications for testing, correct specimen collection, available laboratory testing procedures and optimal use of these procedures.[1,105,106] The workforce should be updated when collection or testing methods change.

The CMS can also contribute to local AMS education efforts by educating about the interpretation of, clinical significance of, and appropriate responses to, significant microbiology test results. This approach has been shown to be effective in changing clinicians' prescribing behaviour[68,81], especially if it is combined with selective reporting of antimicrobial susceptibility results that also contains interpretive comments.

Resources

International testing standards

- Public Health England: UK Standards for Microbiology Investigations
- EUCAST: Clinical breakpoints
- EUCAST: Guidance documents in susceptibility testing
- CLSI: testing standards

Reporting standards

- Australian Commission on Safety and Quality in Health Care: Structured microbiology requests and reports for healthcare-associated infections

Antibiogram specifications and tools

- Australian Commission on Safety and Quality in Health Care: specification for hospital-level cumulative antibiogram
- AIMED: antibiogram commentaries and other microbiology resources
- Software for antibiogram analyses: OrgTRx and WHONET software

Signal and critical antimicrobials resistances

- Australian Commission on Safety and Quality in Health Care: Information specific to carbapenemase-producing Enterobacteriaceae
  - *Recommendations for the Control of Carbapenemase-Producing Enterobacteriaceae (CPE): A guide for acute care health facilities*
  - information for patients
  - information for ward staff and after-hours managers
  - information for clinicians and health service managers
  - information for clinicians
- Exceptional resistance phenotypes: EUCAST expert rules
- National surveillance programs
  - AURA
  - Australian Group on Antimicrobial Resistance
  - CARAlert
- AURA 2017: national AMR data

Education

- For a detailed discussion of CMS education topics and resources, see Morgan DJ, Croft LD, Deloney V, Popovich KJ, Crnich C, Srinivasan A, et al. Choosing wisely in healthcare epidemiology and antimicrobial stewardship. Infect Control Hosp Epidemiol 2016;37(3):755–60.

References

1. Messacar K, Parker SK, Todd JK, Dominguez SR. Implementation of rapid molecular infectious disease diagnostics: the role of diagnostic and antimicrobial stewardship. J Clin Micro 2017;55(3):715–23.
2. Filice GA, Drekonja DM, Thurn JR, Hamann GM, Masoud BT, Johnson JR. Diagnostic errors that lead to inappropriate antimicrobial use. Infect Control Hosp Epidemiol 2015;36(8):949–56.
3. Braykov NP, Morgan DJ, Schweizer ML, Uslan DZ, Kelesidis T, Weisenberg SA, et al. Assessment of empirical antibiotic therapy optimisation in six hospitals: an observational cohort study. Lancet Infect Dis 2014;14(12):1220–7.
4. Australian Commission on Safety and Quality in Health Care, National Centre for Antimicrobial Stewardship. Antimicrobial prescribing practice in Australian hospitals: results of the 2015 National Antimicrobial Prescribing Survey. Sydney: ACSQHC; 2016.
5. Baron EJ, Miller JM, Weinstein MP, Richter SS, Gilligan PH, Thomson RBJ, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2013 recommendations by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM)(a). Clin Infect Dis 2013;57(4):e22–e121.
6. Roger P-M, Courjon J, Léotard S, Déchamp C, Négrin N, Vassallo M. Antimicrobial stewardship policy: time to revisit the strategy? Eur J Clin Microbiol Infect Dis 2015;34(11):2167–70.
7. Balogh EP, Miller BT, Ball JR, editors. Improving diagnosis in health care. Washington, DC: National Academies Press; 2015.
8. Lundberg GE. Acting on significant laboratory results. JAMA 1981;245(17):1762–3.
9. Epner PL, Gans JE, Graber ML. When diagnostic testing leads to harm: a new outcomes-based approach for laboratory medicine. BMJ Qual Saf 2013;22(Suppl 2):6–10.
10. Australian Government Department of Human Services, Medicare Australia Statistics. Medicare item reports. Canberra: Australian Government Department of Human Services; 2016 [cited 2016 Dec 23].
11. Trautner BW, Grigoryan L. Approach to a positive urine culture in a patient without urinary symptoms. Infect Dis Clin North Am 2014;28(1):15–31.
12. Humphries RM, Dien Bard J. Point-counterpoint: reflex cultures reduce laboratory workload and improve antimicrobial stewardship in patients suspected of having urinary tract infections. J Clin Microbiol 2016;54(2):254–8.
13. Kelley D, Aaronson P, Poon E, McCarter YS, Bato B, Jankowski CA. Evaluation of an antimicrobial stewardship approach to minimize overuse of antibiotics in patients with asymptomatic bacteriuria. Infect Control Hosp Epidemiol 2014;35(2):193–5.
14. Leis JA, Gold WL, Daneman N, Shojania KG, McGeer A. Downstream impact of urine cultures ordered without indication at two acute care teaching hospitals. Infect Control Hosp Epidemiol 2013;34(10):1113–14.
15. Burd EM, Kehl KS. A critical appraisal of the role of the clinical microbiology laboratory in the diagnosis of urinary tract infections. J Clin Microbiol 2011;49(9 Suppl):S34–8.
16. LaRocco MT, Franek J, Leibach EK, Weissfeld AS, Kraft CS, Sautter RL, et al. Effectiveness of preanalytic practices on contamination and diagnostic accuracy of urine cultures: a laboratory medicine best practices systematic review and meta-analysis. Clin Microbiol Rev 2016;29(1):105–47.
17. Pezzlo M. Laboratory diagnosis of urinary tract infections: guidelines, challenges, and innovations. Clin Microbiol Newsl 2014;36(12):87–93.
18. Morgan DJ, Croft LD, Deloney V, Popovich KJ, Crnich C, Srinivasan A, et al. Choosing wisely in healthcare epidemiology and antimicrobial stewardship. Infect Control Hosp Epidemiol 2016;37(3):755–60.
19. Gágyor I, Bleidorn J, Kochen MM, Schmiemann G, Wegscheider K, Hummers-Pradier E. Ibuprofen versus fosfomycin for uncomplicated urinary tract infection in women: randomised controlled trial. BMJ 2015;351:h6544.
20. Finucane TE. 'Urinary tract infection': a requiem for a heavyweight. J Am Geriatr Soc 2017;65(8):1650–5.
21. Falagas ME, Kotsantis IK, Vouloumanou EK, Rafailidis PI. Antibiotics versus placebo in the treatment of women with uncomplicated cystitis: a meta-analysis of randomized controlled trials. J Infect 2009;58(2):91–102.

22. Cai T, Nesi G, Mazzoli S, Meacci F, Lanzafame P, Caciagli P, et al. Asymptomatic bacteriuria treatment is associated with a higher prevalence of antibiotic resistant strains in women with urinary tract infections. Clin Infect Dis 2015;61(11):1655–61.

23. Abbo L, Hooton T. Antimicrobial stewardship and urinary tract infections. Antibiotics 2014;3(2):174–92.

24. Leis JA, Rebick GW, Daneman N, Gold WL, Poutanen SM, Lo P, et al. Reducing antimicrobial therapy for asymptomatic bacteriuria among noncatheterized inpatients: a proof-of-concept study. Clin Infect Dis 2014;58(7):980–3.

25. Falk G, Fahey T. C-reactive protein and community-acquired pneumonia in ambulatory care: systematic review of diagnostic accuracy studies. Fam Pract 2009;26(1):10–21.

26. van der Does Y, Rood PPM, Haagsma JA, Patka P, van Gorp ECM, Limper M. Procalcitonin-guided therapy for the initiation of antibiotics in the ED: a systematic review. Am J Emerg Med 2016;34(7):1286–93.

27. Berild D, Mohseni A, Diep LM, Jensenius M, Ringertz SH. Adjustment of antibiotic treatment according to the results of blood cultures leads to decreased antibiotic use and costs. J Antimicrob Chemother 2006;57(2):326–30.

28. Wang H-Y, Chiu C-H, Huang C-T, Cheng C-W, Lin Y Jr, Hsu Y-J, et al. Blood culture-guided de-escalation of empirical antimicrobial regimen for critical patients in an online antimicrobial stewardship programme. Int J Antimicrob Agents 2014;44(6):520–7.

29. Baron EJ, Weinstein MP, Dunne WM, Yagupsky P, Welch DF, Wilson DM. Cumitech 1C, blood cultures IV. Baron EJ, editor. Washington, DC: ASM Press; 2005.

30. Coburn B, Morris AM, Tomlinson G, Detsky AS. Does this adult patient with suspected bacteremia require blood cultures? JAMA 2012;308(5):502–11.

31. Willems E, Smismans A, Cartuyvels R, Coppens G, Van Vaerenbergh K, Van den Abeele A-M, et al. The preanalytical optimization of blood cultures: a review and the clinical importance of benchmarking in 5 Belgian hospitals. Diagn Microbiol Infect Dis 2012;73(1):1–8.

32. Gilligan PH. Blood culture contamination: a clinical and financial burden. Infect Control Hosp Epidemiol 2013;34(1):22–3.

33. Cockerill FR, Wilson JW, Vetter EA, Goodman KM, Torgerson CA, Harmsen WS, et al. Optimal testing parameters for blood cultures. Clin Infect Dis 2004;38(12):1724–30.

34. Garcia RA, Spitzer ED, Beaudry J, Beck C, Diblasi R, Gilleeny-Blabac M, et al. Multidisciplinary team review of best practices for collection and handling of blood cultures to determine effective interventions for increasing the yield of true-positive bacteremias, reducing contamination, and eliminating false-positive central line–associated bloodstream infections. Am J Infect Control 2015;43(11):1222–37.

35. Snyder JW. Blood cultures: the importance of meeting pre-analytical requirements in reducing contamination, optimizing sensitivity of detection, and clinical relevance. Clin Microbiol Newsl 2015;37(7):53–7.

36. Culbreath K, Petti CA. Balancing enthusiasm for innovative technologies with optimizing value: an approach to adopt new laboratory tests for infectious diseases using bloodstream infections as exemplar. Open Forum Infect Dis 2015;2(2):ofv075.

37. Buehler SS, Madison B, Snyder SR, Derzon JH, Cornish NE, Saubolle MA, et al. Effectiveness of practices to increase timeliness of providing targeted therapy for inpatients with bloodstream infections: a laboratory medicine best practices systematic review and meta-analysis. Clin Microbiol Rev 2016;29(1):59–103.

38. Aabenhus R, Jensen J-US, Jørgensen KJ, Hróbjartsson A, Bjerrum L. Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. Cochrane Database Syst Rev 2014;11:CD010130.

39. Chu DC, Mehta AB, Walkey AJ. Practice patterns and outcomes associated with procalcitonin use in critically ill patients with sepsis. Clin Infect Dis 2017;64(11):1509–15.

40. Lam SW, Bauer SR, Duggal A. Procalcitonin-based algorithms to initiate or stop antibiotic therapy in critically ill patients: is it time to rethink our strategy? Int J Antimicrob Agents 2016;47(1):20–7.

41. Morgan DJ, Malani P, Diekema DJ. Diagnostic stewardship: leveraging the laboratory to improve antimicrobial use. JAMA 2017;318(7):607–8.

42. Public Health England. Standards for microbiology investigations (SMI). London: PHE; 2014 [updated 2014 Sep 23; cited 2017 Sep 26].

43. Baron J, Dighe A. Computerized provider order entry in the clinical laboratory. J Pathol Inform, 2011;2(1):35.

44. Antimicrobial Therapy Inc. Sanford guide. Sperryville (VA): Antimicrobial Therapy, Inc.; 2016 [cited 2017 Sep 26].

45. Lipsky BA, Dryden M, Gottrup F, Nathwani D, Seaton RA, Stryja J. Antimicrobial stewardship in wound care: a position paper from the British Society for Antimicrobial Chemotherapy and European Wound Management Association. J Antimicro Chemo 2016;71(11):3026–35.

46. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Clin Infect Dis 2016;62(10):1197–202.

47. Barenfanger J. Quality assurances: decreasing clinically irrelevant testing from clinical microbiology laboratories, part II. Clin Microbiol Newsl 2006;28(4):25–9.

48. Miller JM. The impact of specimen management in microbiology. Med Lab Obs 1998;30(5):28–30.

49. Self WH, Speroff T, Grijalva CG, McNaughton CD, Ashburn J, Liu D, et al. Reducing blood culture contamination in the emergency department: an interrupted time series quality improvement study. Acad Emerg Med 2013;20(1):89–97.

50. Farrell JJ, Hujer AM, Sampath R, Bonomo RA. Salvage microbiology: opportunities and challenges in the detection of bacterial pathogens following initiation of antimicrobial treatment. Expert Rev Mol Diagn 2015;15(3):349–60.

51. Grace CJ, Lieberman J, Pierce K, Littenberg B. Usefulness of blood culture for hospitalized patients who are receiving antibiotic therapy. Clin Infect Dis 2001;32(11):1651–5.

52. Caliendo AM, Gilbert DN, Ginocchio CC, Hanson KE, May LS, Quinn TC, et al. Better tests, better care: improved diagnostics for infectious diseases. Clin Infect Dis 2013;57(Suppl 3):S139–70.

53. O'Neill J. Rapid diagnostics: stopping unnecessary use of antibiotics. London: HM Government (UK); 2015.

54. Avdic E, Carroll KC. The role of the microbiology laboratory in antimicrobial stewardship programs. Infect Dis Clin North Am 2014;28(2):215–35.

55. Abraham MK, Perkins J, Vilke GM, Coyne CJ. Influenza in the emergency department: vaccination, diagnosis, and treatment – clinical practice paper approved by American Academy of Emergency Medicine Clinical Guidelines Committee. J Emerg Med 2016;50(3):536–42.

56. Waite TD, Telisinghe L, Gobin M, Ronveaux O, Fernandez AK, Stuart JM, et al. Rapid diagnostic tests for bacterial meningitis applicable in sub-Saharan Africa. Cochrane Database Syst Rev 2015;(4):CD011634.

57. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(Suppl 2):S27–72.

58. Beganovic M, Costello M, Wieczorkiewicz SM. Effect of matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) alone versus MALDI-TOF MS combined with real-time antimicrobial stewardship interventions on time to optimal antimicrobial therapy in patients with positive blood cultures. J Clin Microbiol 2017;55(5):1437–45.

59. Brönnestam R. Direct antimicrobial susceptibility testing in bacteriuria. Acta Pathol Microbiol Immunol Scand 1999;107(1–6):437–44.

60. Burillo A, Bouza E. Use of rapid diagnostic techniques in ICU patients with infections. BMC Infect Dis 2014;14:593.

61. Coorevits L, Boelens J, Claeys G. Direct susceptibility testing by disk diffusion on clinical samples: a rapid and accurate tool for antibiotic stewardship. Eur J Clin Microbiol Infect Dis 2015;34(6):1207–12.

62. March GA, García-Loygorri MC, Simarro M, Gutiérrez MP, Orduña A, Bratos MA. A new approach to determine the susceptibility of bacteria to antibiotics directly from positive blood culture bottles in two hours. J Microbiol Methods 2015;109:49–55.

63. Stokkou S, Geginat G, Schlüter D, Tammer I. Direct disk diffusion test using European Clinical Antimicrobial Susceptibility Testing breakpoints provides reliable results compared with the standard method. Eur J Microbiol Immunol 2015;5(1):103–11.

64. Eveillard M, Lemarié C, Cottin J, Hitoto H, Mahaza C, Kempf M, et al. Assessment of the usefulness of performing bacterial identification and antimicrobial susceptibility testing 24 h a day in a clinical microbiology laboratory. Clin Microbiol Infect 2010;16(8):1084–9.

65. Hansen WLJ, Beuving J, Verbon A, Wolffs PFG. One-day workflow scheme for bacterial pathogen detection and antimicrobial resistance testing from blood cultures. J Vis Exp 2012;65:3254.

66. Beuving J, Wolffs PFG, Hansen WLJ, Stobberingh EE, Bruggeman CA, Kessels A, et al. Impact of same-day antibiotic susceptibility testing on time to appropriate antibiotic treatment of patients with bacteraemia: a randomised controlled trial. Eur J Clin Microbiol Infect Dis 2015;34(4):831–8.

67. Lockwood AM, Perez KK, Musick WL, Ikwuagwu JO, Attia E, Fasoranti OO, et al. Integrating rapid diagnostics and antimicrobial stewardship in two community hospitals improved process measures and antibiotic adjustment time. Infect Control Hosp Epidemiol 2016;37(4):425–32.

68. Cunney RJ, Smyth EG. The impact of laboratory reporting practice on antibiotic utilisation. Int J Antimicrob Agents 2000;14(1):13–19.

69. Lee A, McLean S. The laboratory report: a problem in communication between clinician and microbiologist? Med J Aust 1977;2(26–27):858–60.

70. Thursky KA, Mahemoff M. User-centered design techniques for a computerised antibiotic decision support system in an intensive care unit. Int J Med Inf 2007;76(10):760–8.

71. Willard KE, Johnson JR, Connelly DP. Radical improvements in the display of clinical microbiology results: a web-based clinical information system. Am J Med 1996;101(5):541–9.

72. Ackerman VP, Pritchard RC, Obbink DJ, Bradbury R, Lee A. Consumer survey on microbiology reports. Lancet 1979;1(8109):199–202.

73. Hickner J, Thompson PJ, Wilkinson T, Epner P, Shaheen M, Pollock AM, et al. Primary care physicians' challenges in ordering clinical laboratory tests and interpreting results. J Am Board Fam Med 2014;27(2):268–74.

74. Barenfanger J, Arakere P, Cruz RD, Imran A, Drake C, Lawhorn J, et al. Improved outcomes associated with limiting identification of *Candida* spp. in respiratory secretions. J Clin Microbiol 2003;41(12):5645–9.

75. Jogenfors A, Stark L, Svefors J, Löfgren S, Malmvall BE, Matussek A. A recommendation to perform a blood culture before the administration of intravenous antibiotics increased the detection of *Staphylococcus aureus* bacteremia. Eur J Clin Microbiol Infect Dis 2014;33(5):789–95.

76. Writing group for Therapeutic Guidelines: Antibiotic. Therapeutic guidelines: antibiotic. Version 15. Melbourne: Therapeutic Guidelines; 2014.

77. Shirts BH, Gundlapalli AV, Jackson B. Pilot study of linking web-based supplemental interpretive information to laboratory test reports. Am J Clin Pathol 2009;132(6):818–23.

78. Turnidge JD, Kotsanas D, Munckhof W, Roberts S, Bennett CM, Nimmo GR, et al. *Staphylococcus aureus* bacteraemia: a major cause of mortality in Australia and New Zealand. Med J Aust 2009;191(7):368–73.

79. Coupat C, Pradier C, Degand N, Hofliger P, Pulcini C. Selective reporting of antibiotic susceptibility data improves the appropriateness of intended antibiotic prescriptions in urinary tract infections: a case-vignette randomised study. Eur J Clin Microbiol Infect Dis 2013;32(5):627–36.

80. Langford BJ, Seah J, Chan A, Downing M, Johnstone J, Matukas LM. Antimicrobial stewardship in the microbiology laboratory: impact of selective susceptibility reporting on ciprofloxacin utilization and susceptibility of gram-negative isolates to ciprofloxacin in a hospital setting. J Clin Microbiol 2016;54(9):2343–7.

81. Cunney RJ, McNamara EB, Alansari N, Loo B, Smyth EG. The impact of blood culture reporting and clinical liaison on the empiric treatment of bacteraemia. J Clin Pathol 1997;50(12):1010–2.

82. Barenfanger J, Graham DR, Kolluri L, Sangwan G, Lawhorn J, Drake CA, et al. Decreased mortality associated with prompt Gram staining of blood cultures. Am J Clin Pathol 2008;130(6):870–6.

83. NSW Clinical Excellence Commission. Clinical handover. Sydney: CEC; 2016 [cited 2017 Sep 26].

84. Barenfanger J, Sautter RL, Lang DL, Collins SM, Hacek DM, Peterson LR. Improving patient safety by repeating (read-back) telephone reports of critical information. Am J Clin Pathol 2004;121(6):801–3.

85. Piva E, Plebani M. Interpretative reports and critical values. Clin Chim Acta 2009;404(1):52–8.

86. Australian Commission on Safety and Quality in Health Care. Specification for hospital cumulative antibiograms. Sydney: ACSQHC; 2013.

87. AIMED. Antibiograms. Newcastle (NSW): AIMED; 2016 [cited 2017 Sep 26].

88. Pathology North. Cumulative antibiograms: Maitland Hospital and Hunter sectors. Newcastle: AIMED; 2017.

89. Australian Commission on Safety and Quality in Health Care. AURA 2017: second Australian report on antimicrobial use and resistance in human health. Sydney: ACSQHC; 2017.

90. European Committee on Antimicrobial Susceptibility Testing. Expert rules and intrinsic resistance. Växjö: European Society of Clinical Microbiology and Infectious Diseases; 2016 [updated 2016 Sep 27; cited 2017 Sep 26].

91. Australian Commission on Safety and Quality in Health Care. About AURA. Sydney: ACSQHC; 2017 [cited 2018 Jan 13].

92. Australian Group on Antimicrobial Resistance. AGAR website. Murdoch: AGAR; 2017 [updated 2017 Aug 7; cited 2017 Sep 26].

93. Australian Commission on Safety and Quality in Health Care. Australian Passive AMR Surveillance (APAS). Sydney: ACSQHC; 2018 [cited 2018 Feb 8].

94. Evans RS, Olson JA, Stenehjem E, Buckel WR, Thorell EA, Howe S, et al. Use of computer decision support in an antimicrobial stewardship program (ASP). Appl Clin Inform 2015;6(1):120–35.

95. Forrest GN, Van Schooneveld TC, Kullar R, Schulz LT, Duong P, Postelnick M. Use of electronic health records and clinical decision support systems for antimicrobial stewardship. Clin Infect Dis 2014;59(Suppl):122–33.

96. Kullar R, Goff DA. Transformation of antimicrobial stewardship programs through technology and informatics. Infect Dis Clin North Am 2014;28(2):291–300.

97. Kullar R, Goff DA, Schulz LT, Fox BC, Rose WE. The 'epic' challenge of optimizing antimicrobial stewardship: the role of electronic medical records and technology. Clin Infect Dis 2013;57(7):1005–13.

98. Thursky K. Use of computerized decision support systems to improve antibiotic prescribing. Expert Rev Anti Infect Ther 2006;4(3):491–507.

99. Bekeris LG, Jones BA, Walsh MK, Wagar EA. Urine culture contamination: a College of American Pathologists Q-Probes study of 127 laboratories. Arch Pathol Lab Med 2008;132(6):913–17.

100. Bekeris LG, Tworek JA, Walsh MK, Valenstein PN. Trends in blood culture contamination: a College of American Pathologists Q-Tracks study of 356 institutions. Arch Pathol Lab Med 2005;129(10):1222–5.

101. Novis DA, Dale JC, Schifman RB, Ruby SG, Walsh MK. Solitary blood cultures. Arch Pathol Lab Med 2001;125(10):1290–4.

102. Schifman RB, Bachner P, Howanitz PJ. Blood culture quality improvement: a College of American Pathologists Q-Probes study involving 909 institutions and 289 572 blood culture sets. Arch Pathol Lab Med 1996;120(11):999–1002.

103. Schmitz RPH, Keller PM, Baier M, Hagel S, Pletz MW, Brunkhorst FM. Quality of blood culture testing – a survey in intensive care units and microbiological laboratories across four European countries. Crit Care 2013;17(5):R248.

104. Matkoski C, Sharp SE, Kiska DL. Evaluation of the Q Score and Q234 systems for cost-effective and clinically relevant interpretation of wound cultures. J Clin Microbiol 2006;44(5):1869–72.

105. Dolan VJ, Cornish NE. Urine specimen collection: how a multidisciplinary team improved patient outcomes using best practices. Urol Nurs 2013;33(5):249–56.

106. van Ingen J, Hilt N, Bosboom R. Education of phlebotomy teams improves blood volume in blood culture bottles. J Clin Microbiol 2013;51(3):1020–1.