Infection Prevention and Control.

Module 7. Antibiotics and Antiseptics

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- Each drug, to verify the recommended dose, method of administration, and precautions for use
- Each device, instrument, or piece of equipment to verify recommendations for use and/or operating instructions

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Chapter 1: Rational Use of Antibiotics

Key Topics

- Definition of antibiotic resistance
- Consequences and magnitude of antibiotic resistance
- Causes of antibiotic resistance
- Antibiotic stewardship programs
- Components of an antibiotic stewardship program
- Rational use of antibiotics
- Promotion of rational use of antibiotics

Key Terms

- **Antibiograms** are periodic summaries of antimicrobial susceptibilities of bacterial isolates submitted to a hospital’s clinical microbiology laboratory. Clinicians and other health care workers (HCWs) use antibiograms to assess local susceptibility rates, aid in the selection of empiric antibiotic therapy, and monitor resistance trends within a facility over time.

- **Antibiotic** is a drug that fights infections caused by bacteria in both humans and animals. Antibiotics fight these infections either by killing the bacteria or making it difficult for the bacteria to grow and multiply. Antibiotics do not have any effect on viruses or fungi.

- **Antibiotic consumption** is the rate of antibiotic use, which is used for measurement purposes and can be measured in various ways, such as defined daily dose or antibiotic days.

- **Antibiotic resistance** is the ability of bacteria to resist the effects of an antibiotic. Antibiotic resistance occurs when bacteria change in a way that reduces the effectiveness of antibiotics to treat or prevent infections. The bacteria survive and continue to multiply, creating more bacteria that are resistant.

- **Antimicrobial** is a broad category of drugs that fight infections caused by microorganisms such as bacteria, viruses, parasites, and fungi. Antibiotics are a type of antimicrobial.

- **Antimicrobial resistance** is the ability of a microorganism to resist the effects of an antimicrobial agent using various resistance mechanisms. Antimicrobial resistance occurs when microorganisms such as bacteria, viruses, fungi, and parasites develop ways to avoid the effects of medications used to treat infections (such as antibiotics, antivirals, and antifungals) and pass these changes on to their offspring, or in some cases to other bacteria via plasmids.

- **Antimicrobial resistance surveillance** consists of programs designed to identify trends and provide information regarding pathogen incidence and antimicrobial resistance.

- **Antimicrobial stewardship** is the coordination of interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration. Antimicrobial stewards seek to achieve optimal clinical outcomes related to antimicrobial use, minimize toxicity and other adverse events, reduce the costs of health care for infections, and limit the selection for antimicrobial-resistant strains.
Rational Use of Antibiotics

- **Days of therapy**, or antibiotic days, is the aggregate number of days for which any amount of a specific medication was documented as administered to an individual patient by route of administration.

- **Defined daily dose** is the assumed average maintenance dose per day for a drug used for its main indication in adults, which allows for meaningful comparisons of drug use. An alternative is days of therapy.

- **Empiric treatment** is initiated based on knowledge or experience with the expected pathogens causing an infection and/or disease based on signs and symptoms, epidemiology, and preliminary laboratory results (such as Gram staining), in the absence of complete clinical, radiological, and/or laboratory information.

- **Minimal inhibitory concentration** is the least amount of an antibiotic necessary to inhibit growth of the organism.

- **Rational use of antimicrobials** ensures that patients receive antimicrobial agent(s) that are appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.

**Background**

For the past 70 years, antimicrobial drugs, such as antibiotics, antifungals, antivirals, and antiparasitics, have been successfully used to treat patients with infectious diseases and have been one of the most useful discoveries in medical history.

The first antibiotic, penicillin, was discovered in 1928; the most recent class of antibiotics was introduced in 1987. In the 2000s, several new antibiotics, including daptomycin, tigecycline, linezolid, and fidaxomicin, were approved for use. Since 2000, few new antibiotics have been introduced to treat infections. Several of these new agents are still not available for wide use in low- and middle-income countries (LMIC) and when available, they are very expensive.

A critical aspect of the broader global response to antimicrobial resistance are efforts to minimize the emergence and transmission of resistance to drugs used to treat tuberculosis (TB), HIV, and malaria.

Antimicrobials have saved millions of lives and their use has contributed significantly to the control of infectious diseases, some of which were once the leading causes of morbidity and mortality worldwide (e.g., staphylococcal infections, gonorrhea, syphilis, tuberculosis, HIV, and malaria). In some cases, early antimicrobial therapy for an infected patient can make the difference between cure and long-term disability or death. However, the use and misuse of antimicrobials have led to persistent expansion of antimicrobial resistance, thereby lowering the effectiveness of some of these drugs (e.g., chloroquine and penicillin). Resistance to the most commonly available antimicrobials requires the use of more expensive alternative regimens. Unfortunately, while resistance has created a demand for new treatment options, there has been a significant drop in the development of new antimicrobial agents in recent decades. This has compromised the ability of HCWs to treat infectious diseases and has increased health care costs. Therefore, improvements in the thoughtful use of antimicrobials must be a global priority. It is critical that necessary measures to respond to the resistance crisis be taken at all levels (by institutions as well as local and national governments). Measures should include rational use of antimicrobials through the incorporation of careful antimicrobial stewardship activities and programs. Ultimately, improving antimicrobial use involves actions at the national level to guide treatment decisions made by informed HCWs as well as the awareness and cooperation from patients. While this
chapter focuses on antibiotics, its recommendations can be applied to all antimicrobials. (WHO 2015; WHO 2016)

**Antibiotic Resistance**

Antibiotic resistance makes it harder to eliminate infections from the body as existing drugs become less effective. The microbes that were effectively treated a few decades ago are now more difficult to treat. Antibiotic resistance is present in all parts of the world and threatens the effective prevention and treatment of a long list of infections, including multidrug-resistant *Mycobacterium tuberculosis*, methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE), and multidrug-resistant *Neisseria gonorrhoeae*. Mortality among patients infected with resistant microbes can be about twice that of patients with infections caused by the same species of bacteria that is sensitive to antibiotics. (NIAID 2011)

**Consequences of Antibiotic Resistance**

Antibiotic resistance leads to increased medical costs, extended hospital stays, increased toxicity, adverse effects, and mortality. The increased use and misuse of antibiotic drugs accelerate the emergence of drug-resistant strains of microorganisms, which threatens our ability to treat common infectious diseases (WHO 2016). Infections such as pneumonia, tuberculosis, bloodstream infections (sepsis), and sexually transmitted infections are becoming more difficult, and at times impossible, to treat due to antibiotic resistance.

**Magnitude of Antibiotic Resistance**

WHO has classified priority pathogens into three categories for which new antibiotics should be developed (see Table 1-1).

<table>
<thead>
<tr>
<th>Priority 1: Critical</th>
<th>Priority 2: High</th>
<th>Priority 3: Medium</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acinetobacter baumannii, carbapenem-resistant</td>
<td>• <em>Enterococcus faecium</em>, vancomycin-resistant</td>
<td>• <em>Streptococcus pneumoniae</em>, penicillin-non-susceptible</td>
</tr>
<tr>
<td>• <em>Pseudomonas aeruginosa</em>, carbapenem-resistant</td>
<td>• <em>Staphylococcus aureus</em>, methicillin-resistant, vancomycin-intermediate and resistant</td>
<td>• <em>Haemophilus influenzae</em>, ampicillin-resistant</td>
</tr>
<tr>
<td>• <em>Enterobacteriaceae</em>, carbapenem-resistant, Extended Spectrum Beta Lactamase-producing</td>
<td>• <em>Helicobacter pylori</em>, clarithromycin-resistant</td>
<td>• <em>Shigella</em> spp., fluoroquinolone-resistant</td>
</tr>
<tr>
<td>• <em>Campylobacter</em> spp., fluoroquinolone-resistant</td>
<td>• <em>Salmonellae</em>, fluoroquinolone-resistant</td>
<td></td>
</tr>
<tr>
<td>• <em>Neisseria gonorrhoeae</em>, cephalosporin-resistant, fluoroquinolone-resistant</td>
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</tbody>
</table>

Adapted from: WHO 2017c.
Causes of Antibiotic Resistance

Natural causes

Selective Pressure: Bacteria will die or stop multiplying in the presence of an antibiotic to which they are susceptible, but if they are resistant to the antibiotic, the bacteria will survive and continue to grow. Thus in the presence of an antibiotic, only the resistance microbes will continue to survive and grow and become the dominant population. This phenomenon is called “selective pressure” and results in growth of resistant bacteria that will replace the susceptible bacteria (see Figure 1-1).

Figure 1-1. Development of Antibiotic-Resistant Bacteria

Societal Contributions

Some antibiotic use practices by HCWs and communities create pressure that allows resistant organisms to survive and grow. These “societal pressures” can accelerate the development of microbial resistance. Societal pressures include:

- Inappropriate selection, dosage, and duration of antibiotics prescribed by clinicians, including issuing prescriptions for viral diseases such as diarrhea and seasonal influenza.
- Prescribers not complying with prescribing the right drug (only when indicated), in the right dose, for the right duration, and with the right route of administration.
- Prescription of broad-spectrum antibiotics rather than a specific antibiotic in situations where laboratory support is not available to identify specific causative organisms and their susceptibility to antibiotics.
- Admission to hospitals of critically ill patients who are more susceptible to infections and therefore are more likely to be on antibiotics. The heavier use of antibiotics in these patients can worsen the problem by promoting the selection of antibiotic-resistant microorganisms. The extensive use of antibiotics and close contacts among sick patients promote the spread of antibiotic-resistant microorganisms.
- Poor compliance with recommended infection prevention and control (IPC) practices, such as Standard Precautions and Transmission-Based Precautions, including respiratory infection prevention and control, contributes to transmission of resistant microorganisms from one patient to another.
- Antibiotic use in agriculture and the poultry industry exposes humans to unnecessary and inadequate doses of antibiotics that may lead to antibiotic resistance in humans.
In some countries, policies and regulatory frameworks to control misuse of antibiotics are not available. This results in antibiotics being available without a prescription from a clinician authorized to prescribe, which increases inappropriate use of antibiotics. (NIAID 2011; WHO 2015; WHO 2016)

**Commonly Available Antibiotics**

Table 1-2 provides examples of the classes and the individual antibiotics within each class that are commonly available. When bacteria develop resistance to an antibiotic, resistance to other members within the same class is possible.

<table>
<thead>
<tr>
<th>Class</th>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-lactams</strong></td>
<td>Penicillins: <strong>penicillin G</strong>*</td>
</tr>
<tr>
<td></td>
<td>Penicillin V, propicillin</td>
</tr>
<tr>
<td></td>
<td>Aminopenicillins: <strong>amoxicillin</strong>, amoxicillin-clavulanate, <strong>amipicillin</strong>, ampicillin-sulbactam</td>
</tr>
<tr>
<td></td>
<td>Anti-staphylococcal penicillins: methicillin, oxacillin, dicloxacillin, flucloxacillin</td>
</tr>
<tr>
<td></td>
<td>Extended-spectrum penicillins: ticarcillin, ticarcillin-calvulanate, <strong>piperacillin</strong>, <strong>piperacillin-tazobactam</strong></td>
</tr>
<tr>
<td></td>
<td>Cephalosporins:</td>
</tr>
<tr>
<td></td>
<td>First generation: <strong>cefazolin</strong>, cefadroxil, <strong>cephalexin</strong>, cephalothin</td>
</tr>
<tr>
<td></td>
<td>Second generation: <strong>cefoxitin</strong>, cefotetan, <strong>cefuroxime</strong></td>
</tr>
<tr>
<td></td>
<td>Third and fourth generation: <strong>cefdinir</strong>, <strong>cefpodoxime</strong>, <strong>ceftaxime</strong>, <strong>ceftazidime</strong>, <strong>ceftriaxone</strong>, <strong>cefepeim</strong></td>
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<tr>
<td></td>
<td>Fifth generation: <strong>ceftaroline</strong></td>
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<tr>
<td></td>
<td>Carbapenem: <strong>imipenem-cilastatin</strong>, ertapenem, doripenem, <strong>meropenem</strong></td>
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<tr>
<td></td>
<td>Monobactams: aztreonam</td>
</tr>
<tr>
<td><strong>Glycopeptides</strong></td>
<td><strong>Vancomycin</strong>, teicoplanin, dalbavancin, telavancin, oritavancin</td>
</tr>
<tr>
<td><strong>Aminoglycosides</strong></td>
<td>Gentamicin, tobramycin, amikacin, streptomycin, neomycin, kanamycin, paromomycin</td>
</tr>
<tr>
<td><strong>Chloramphenicol</strong></td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td><strong>Ansamycins</strong></td>
<td>Rifampicin, geldanamycin</td>
</tr>
<tr>
<td><strong>Sulphonamides</strong></td>
<td>Sulfadiazine, sulfamethoxazole, sulfasalazine, sulfamethizole</td>
</tr>
<tr>
<td><strong>Tetracyclines</strong></td>
<td>Tetracycline, oxytetracycline, doxycycline, minocycline</td>
</tr>
<tr>
<td><strong>Macrolides</strong></td>
<td>Erythromycin, azithromycin, clarithromycin</td>
</tr>
<tr>
<td><strong>Oxazolidinones</strong></td>
<td>Linezolid, tedizolid</td>
</tr>
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### Antibiotic Stewardship Programs

Antibiotic stewardship programs are coordinated interventions at the health care facility level intended to improve and monitor the appropriate use of antibiotics by encouraging the selection of the optimal drug regimen, dose, duration of therapy, and route of administration. Antibiotic stewardship programs are designed to:

- Achieve optimal clinical outcomes associated with antibiotic use
- Minimize adverse events
- Reduce infection-related health care costs
- Reduce antibiotic resistance
- Prevent the creation of antibiotic-resistant strains

(Barlam et al. 2016; CDC 2015a)

The goals of an antibiotic stewardship program should include:

- Optimization of clinical outcomes while minimizing unintended consequences of antibiotic use, such as toxicity and selection of pathogenic organisms (e.g., *Clostridium difficile*)
- Reduction of health care costs without an adverse impact on quality of care

### Core Elements of an Antibiotic Stewardship Program

The core elements of an antibiotic stewardship program described below should be implemented throughout the health care system, including in all hospitals and health care facilities, to achieve the above goals. Core elements include:

1. Leadership commitment
2. Accountability and drug expertise
3. Implementation of policies and interventions
4. Tracking and reporting antibiotic use and outcomes

5. Education

1. Leadership commitment

Leadership support is an important component of successful stewardship programs. It can take different forms, including creating formal statements supporting antibiotic monitoring efforts, incorporating antibiotic stewardship-related components into job descriptions, supporting antibiotic stewardship-related training and education endeavors, and ensuring contributions from all groups that can support stewardship activities. Financial support can enhance the capacity and impact of stewardship programs. Stewardship programs often can end up being self-supporting through the direct and indirect health care savings for the facilities where they are implemented. Most of the time, facility administrative and management team members, clinicians, and pharmacy staff can play a leadership role at facility level.

2. Accountability and drug expertise

Designated leadership of the program helps to ensure accountability and provide drug expertise. The following are example of leaders and other staff members beneficial to a stewardship program:

- An antibiotic stewardship program leader who will be responsible for program outcomes. Clinicians with infectious disease expertise are ideally suited, but in settings where this specialty is not available, a clinician with an interest and willingness to seek out information on the topic and implement program activities can perform this role.

- A pharmacy leader who will co-lead the program. Pharmacists with infectious disease training are ideally suited, but in settings where this expertise is not available, pharmacy staff with an interest and willingness to work with the clinician leader can fulfill this role.

- Other individuals in the hospital or health care facility who can assist with and support the program activities. At large hospitals these may include clinical microbiologists, laboratory staff, information system staff, quality improvement staff, IPC staff, hospital epidemiologists, department heads, clinicians, and nursing staff (see Table 1-3). At small clinics with staff shortages, the clinic nurse could be the only person who may prescribe/dispense antibiotics and at the same time ensure the rational use of antibiotics. (CDC 2015a)

<table>
<thead>
<tr>
<th>Staff Member</th>
<th>Contribution to Antibiotic Stewardship Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinicians with authority to prescribe antibiotics</td>
<td>• Make day-to-day decisions about prescribing antibiotics.</td>
</tr>
<tr>
<td>IPC staff</td>
<td>• Coordinate facility-wide monitoring and prevention of health care-associated infections.</td>
</tr>
<tr>
<td></td>
<td>• Provide skills such as auditing, analyzing, and reporting data.</td>
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<td></td>
<td>• Assist with resistance-trend monitoring and reporting.</td>
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<tr>
<td></td>
<td>• Include the importance of appropriate antibiotic use in staff education.</td>
</tr>
</tbody>
</table>
### Contribution to Antibiotic Stewardship Program

<table>
<thead>
<tr>
<th>Staff Member</th>
<th>Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality improvement staff</td>
<td>- Align goals of both the antibiotic stewardship and quality of care programs with patient safety programs. Improving antibiotic use is a medical quality and patient safety issue.</td>
</tr>
<tr>
<td>Laboratory staff</td>
<td>- Guide the proper use of tests and the flow of results.</td>
</tr>
<tr>
<td></td>
<td>- Create the hospital’s antibiogram.</td>
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<td></td>
<td>- Work with stewardship staff to ensure that lab reports present data in a way that supports optimal antibiotic use.</td>
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<td></td>
<td>- (See Module 1, Chapter 3, Basic Microbiology for Infection Prevention and Control, for more information on the role of the clinical microbiology laboratory.)</td>
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<tr>
<td>Nurses (The role of nurses will vary based on the size of the facility as well as the country’s policy and regulatory framework for prescribing antibiotics.)</td>
<td>- Provide support by helping with integration of stewardship protocols into existing workflow.</td>
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<tr>
<td></td>
<td>- Operationalize prompts that trigger a review of antibiotic use in key situations, such as on the day culture results arrive (only applicable where facilities are available) or the number of days of empiric treatment, etc.</td>
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<tr>
<td></td>
<td>- In facilities where laboratory capacity is available, ensure that samples are collected for cultures prior to the start of antibiotics.</td>
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<tr>
<td>Pharmacy staff</td>
<td>- Change from parenteral (i.e., IV) to oral antibiotic therapy.</td>
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<td></td>
<td>- Adjust dosage and optimize dosage.</td>
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<td></td>
<td>- Avoid therapeutic duplication.</td>
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<td></td>
<td>- Issue time-sensitive automatic stop orders.</td>
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<tr>
<td></td>
<td>- Detect and prevent antibiotic-related drug interactions.</td>
</tr>
<tr>
<td>Information technology staff</td>
<td>- Facilitate the management and reporting of antibiotic use data.</td>
</tr>
</tbody>
</table>

Source: CDC 2015a.

### 3. Implementation of policies and interventions

Key activities would fall under implementing policies that support optimal antibiotic use and identifying interventions under three categories:

- Broad interventions
- Pharmacy-driven interventions
- Infection- and syndrome-specific interventions

Examples of policies that apply in all situations to support optimal antibiotic prescribing include:
Rational Use of Antibiotics

- Document dose, duration, and indication for all courses of antibiotics in the patient’s medical record. This helps to ensure the timely discontinuation and/or modification of antibiotics by clear communication and thoughtful prescribing.
- Implement national standard treatment guidelines, which can optimize antibiotic selection and duration, especially for common indications for antibiotic use such as community-acquired pneumonia, urinary tract infections, and surgical prophylaxis. Adapt national guidelines to local conditions if indicated.
- Implement broad, pharmacy-driven, infection- and syndrome-specific interventions (see details in this chapter in the Facility-Level Recommendations and Strategies section).

**Broad interventions**

- **Antibiotic time-outs**: Antibiotics are frequently started empirically in hospitalized patients before diagnostic information is available. In places where laboratory tests including culture results are not available, the only option that the clinicians will have is to reassess each patient’s situation more frequently and make decision on continuing, stopping, and choosing an alternative antibiotic if the patient’s conditions does not improve. An antibiotic “time-out” prompts a reassessment of the continuing need for and choice of antibiotics when the clinical picture is clearer and more diagnostic information is available. Some important questions that should be asked by clinicians when performing a review of antibiotics 48–72 hours after they are initiated include the following:
  - Does this patient have an infection that will respond to antibiotics?
  - If so, is the patient on the right antibiotic, dose, frequency, and route of administration?
  - Can a more targeted antibiotic be used to treat the infection?
  - For how long should the patient receive the antibiotic?
- **Prior authorization**: Though not common practice in a majority of health care facilities in LMIC, hospitals can restrict the use of particular antibiotics based on their effectiveness, cost, and associated toxicities, or to ensure that they are used only when indicated. While effective, this intervention requires individuals (such as pharmacists or physicians) with expertise in infectious diseases and antibiotics to be readily available, as authorization will likely need to be provided quickly.
- **Prospective audits and feedback**: A prospective audit and feedback program allows the antibiotic stewardship staff to interact directly with the treating clinician to tailor antibiotic therapy for each patient. These strategies are employed after antibiotics have been initially prescribed and dispensed. Target patient populations, such as those receiving vancomycin for suspected MRSA infections, are audited for de-escalation (de-escalation includes starting a broad-spectrum antibiotic and then modifying the therapy—antibiotic agent, route, and duration—based on the identification of specific microorganisms and improvement in the patient’s condition) or cessation of unnecessary antibiotic therapy. Unlike antibiotic “time-outs,” antibiotic stewardship program staff conduct prospective audits of patients and provide feedback to the treating clinician; the clinician initiates therapy and the antibiotic stewardship staff intervene only in selected cases. These programs address both over- and under-treatment. (Griffith et al. 2012)

**Pharmacy-driven interventions**

Availability of qualified pharmacists in LMIC settings is limited to large tertiary care teaching hospitals and some regional hospitals. Some district-level hospitals and health centers have pharmacy technicians
and pharmacy assistants or other clinical staff assigned to ordering, receiving, dispensing, and reporting the drug use.

Involving pharmacists, when available, in ensuring rational use of antibiotics at the health care facilities in LMIC can be challenging, as it requires a change in culture. However, efforts should be made to engage any staff performing the tasks of pharmacy technician and pharmacy assistant in active involvement in antibiotic stewardship programs to ensure rational use of antibiotics. The interventions that can be performed by the pharmacist or trained pharmacy staff include:

- Changing from parenteral (i.e., IV) to oral antibiotic therapy: A pharmacist can change antibiotic therapy from parenteral to oral in consultation with the clinician, based on a patient’s ability to take an appropriate oral alternative. This change should improve patient safety and may decrease the length of hospital stay.

- Adjusting dosage: A pharmacist, when available, can review the prescription before dispensing the antibiotic to ensure that the medication is prescribed at the right dose for the indication. The pharmacist can alert the clinician about dose adjustments for admitted patients in cases of organ dysfunction (e.g., renal or hepatic adjustment).

- Optimizing dosage: A pharmacy staff member, when available, can suggest an optimal dose of an antibiotic based on the causative microorganism, site of infection (for example, higher doses may be needed to penetrate the central nervous system), frequency of administration, and drug interactions.

- Avoiding therapeutic duplication: A pharmacy staff member can perform a daily assessment of antibiotic therapy, looking for duplication of same-spectrum antibiotics, including use of multiple agents active against anaerobes or dual therapy with broad-spectrum antibiotics effective against gram-negative bacteria.

- Issuing time-sensitive automatic stop orders: The facility antibiotic stewardship team can work with the prescribing clinicians so that pharmacy staff can be authorized to stop antibiotics after a certain duration or doses. A member of the pharmacy staff can stop antibiotic use when prolonged therapy has not been effective. For example, antibiotic therapy used for the prevention of infections after surgical procedures should be limited to a single dose given preoperatively or for a maximum of up to 24 hours.

- Detecting and preventing antibiotic-related drug interactions: Pharmacy staff should be trained to review the prescription of antibiotics and other drugs to identify any drug-drug interactions. For example, simultaneous use of rifampicin and oral contraceptives reduces the effect of the oral contraceptive. Consuming alcohol while taking metronidazole or tinidazole can cause some unpleasant side effects. In settings where online resources are not available, textbooks, guidelines, and other job aids can be used. (CDC 2015a)

**Infection- and syndrome-specific interventions**

Antibiotic stewardship interventions are intended to improve prescriptions for specific syndromes but should not interfere with timely and effective treatment for severe infection or sepsis.

Standard treatment guidelines for prescribing antibiotics for a given infection help avoid the use of multiple antibiotics for managing an infection that can be treated with a single, specific antibiotic. Use of standard treatment guidelines can guide day-to-day prescription and use of antibiotics at the facility. Standard treatment guidelines include those for:

- Sexually transmitted infections
Rational Use of Antibiotics

- Community-acquired pneumonia
- Urinary tract infections
- Skin and soft tissue infections
- Empiric treatment of MRSA infections
- *C. difficile* infections
- Maternal sepsis

Guidelines should include individual condition, diagnosis, treatment (first-line and second-line antibiotic agent, dose, route of administration, and duration), drug toxicity monitoring, and drug interactions. Conducting regular periodic review of the implementation of standard treatment guidelines and continuously improving the quality of implementation will allow the most appropriate use of antibiotics and help avoid unnecessary continuation and prescribing of inappropriate antibiotic therapy.

4. Tracking and reporting antibiotic use and outcomes

Data on antibiotic use can be collected to monitor antibiotic prescription, distribution, and resistance patterns and to evaluate the process and outcome of antibiotic stewardship programs. This system is designed to serve as a tool for tracking drug utilization in order to improve the quality of drug use. For example, antibiotic use for a ward can be compared with use in different units within a facility and with other facilities. (WHOCC 2009)

Monitoring antibiotic use and outcomes includes both process and outcome measures. Evaluation of the process may include monitoring the implementation of policies and guidelines about antibiotic use and the number of prescriptions issued, whereas outcome measures include monitoring patient outcomes.

- **Antibiotic use process measure:** Process measures include qualitative assessment of antibiotic prescribing patterns in the health care facility. Examples of process measures include but are not limited to:
  - Using accurately applied diagnostic criteria as per the standard treatment guidelines, if available
  - Prescribing the appropriate antibiotic, in the right dose, right duration, and right route of administration for the specific indication
  - Collecting samples for laboratory investigations before administration of antibiotics
  - Modifying treatment based on laboratory test results if indicated
  - Conducting periodic assessments to review the effectiveness of treatment and potential change

  Though the process reviews can be carried out retrospectively by doing chart reviews, given the quality of documentation on antibiotic use, conducting prospective process monitoring could be a better option.

- **Antibiotic use measure:** Health care facilities implementing antibiotic stewardship programs measure antibiotic use either as days of therapy or defined daily dose. (See Appendix 1-A for more information on antibiotic use measures.)

Management of information on drug utilization requires dedicated training of pharmacy staff. Health care facilities embarking upon such activities should ensure that the pharmacy staff are appropriately trained.
5. Education

Stewardship programs should provide regular updates on antibiotic prescribing, antibiotic resistance, IPC measures, and infectious disease management to ensure behavior change to improve antibiotic prescribing among HCWs. To be effective in changing prescribing practices, this education should be incorporated with corresponding interventions. (The information in this chapter and resources listed as references in this chapter can be used for educational programs.)

Rational Use of Antibiotics

Medications are used rationally when they are:

- Clinically appropriate for the patient
- Prescribed in doses that meet the patient’s requirements
- Taken for the recommended time period
- Taken at the recommended frequency
- The lowest cost option for the patient and the community

Medications are not used rationally in the following circumstances:

- Excessive use of multiple medicines for the same purpose in the same patient, also known as polypharmacy
- Use of injections when oral formulations would be an equally appropriate or more preferred route of administration
- Inappropriate use of antibiotics, such as failure to narrow the therapy when culture results are known, or use of antibiotics to treat viral infections
- Antibiotic selection that differs from what is recommended in standard treatment guidelines
- Self-medication with antibiotics, such as buying them without a prescription written by a health care provider
  
  (Holloway 2011)

Determinants of Irrational Use of Antibiotics

There are several determinants of irrational use of antibiotics:

- Lack of provider knowledge, particularly with regard to prescribers who are insufficiently qualified, supervised, or supported
- Prescriber habits (prescribing without following the guidelines)
- Non-availability of standard treatment guidelines for prescribing antibiotics
- Non-availability of a specific drug to treat a clinical condition, resulting in prescribing a less effective or inappropriate alternative
- Lack of unbiased, independent, government-funded continuing medical education and supervision that include prescribing
- Excessive promotion and incentives for prescribing offered by the pharmaceutical industry
Rational Use of Antibiotics

- Short consultations that do not provide time to explain to the patients that there is no need for antibiotics and that the condition will improve in a few days without antibiotics
- Following practices of senior practitioners
- Perceived patient demand
- Lack of diagnostic and laboratory support
- Inappropriate procurement of antibiotics by hospitals and the public sector supply chain

(Radyowijati and Haak 2003; Rowe et al. 2005; Sketris et al. 2009; WHO 2002)

Promoting Rational Use of Antibiotics

Promoting rational use of antibiotics and other medicines requires concerted efforts at all levels, starting from the Ministry of Health at the national level and extending out to the community.

WHO recommends the following core interventions to promote rational use of medicines, including antibiotics, at the national level:

- A mandated multidisciplinary national body to coordinate the development of medicine use policies
- Up-to-date standard treatment guidelines for prescribing antibiotics
- An essential medicines list based on treatments of choice, consistent with standard treatment guidelines
- Drugs and therapeutics committees to oversee antibiotic use in districts and health care facilities
- Strengthening of pre-service curricula to include problem based pharmacotherapy
- Continuing in-service medical education as a regulatory requirement
- Supervision, audits, and feedback on antibiotic use
- Independent information on medicines
- Avoidance of any financial incentives in order to prevent over-prescribing
- Public education about rational use of medicines
- Appropriate and enforced regulation
- Sufficient government expenditure to ensure availability of medicines and trained staff

(WHO 2002)

Facility-level recommendations and strategies

Ideally, facility-level activities to promote rational use of antibiotics in large hospitals are organized by a stewardship technical working group in collaboration with the IPC technical working group. While IPC staff can contribute significantly to reducing antimicrobial resistance, other interventions to ensure rational use of antibiotics should have support of the management team of the health care facility as well as the quality improvement technical working group or other clinical staff members interested in promoting rational use of antibiotics. Small successes can be built upon over time to reach the goal of having an antibiotic stewardship program. (For details, see the Antibiotic Stewardship Programs section of this chapter. The recommendations and strategies mentioned in this section should be appropriately adjusted for smaller health care facilities.)
• **Provide continuing education:** Education is a fundamental element of any program designed to improve prescribing behavior. Education can also provide a foundation of knowledge that will enhance and increase the acceptance of stewardship strategies. However, education alone, without the inclusion of active interventions, is not very effective in changing antibiotic prescribing practices and will not produce a prolonged impact. (Barlam et al. 2016)

• **Improve use of standard treatment guidelines:** Clinical practice guidelines are being produced with increasing frequency to improve the quality of care (see Box 1-1). Antibiotic stewardship programs should improve clinicians’ access to and use of national, evidence-based practice guidelines that integrate local microbiology and resistance patterns. Guidelines implementation can be facilitated through provider education and feedback on antibiotic use and patient outcomes. (Barlam et al. 2016; Ministry of Health, Republic of Ghana 2010)

• **Streamline or de-escalate therapy:** Antibiotic streamlining or de-escalation should be based on culture results and elimination of redundant combination therapies to effectively target the causative microorganisms. This will ultimately help to decrease antibiotic exposure and result in cost savings. (Barlam et al. 2016; Masterton 2011)

• **Convert parenteral therapy to oral therapy:** See details in the Pharmacy-Driven Interventions section in this chapter.

• **Practice good IPC:** Good IPC will reduce health care-associated infections and the resulting use of antibiotics.

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**Box 1-1. Reputable, Evidence-Based Clinical Practice Guidelines on Antimicrobial Use**

- The European Society of Clinical Microbiology and Infectious Diseases: [https://www.escmid.org/escmid_publications/medical_guidelines/](https://www.escmid.org/escmid_publications/medical_guidelines/)

All guidelines are updated on a yearly basis. Always ensure that you are referring to the most up-to-date version.

---

**General public/community-level recommendations and strategies**

Steps should be taken at all levels of society to reduce antibiotic resistance. Patients and the community can be educated in the following actions to increase rational antibiotic use:

- Prevent the spread of infections through regular handwashing, good food preparation practices, respiratory etiquette, avoiding close contact with sick people, and keeping individual vaccinations up to date.
- Use antibiotics only when prescribed by a licensed health care professional.
- Take all antibiotics according to the clinician’s advice—right dose, right duration (e.g., number of days), and at the right time of day.
- Do not use antibiotics left over from previous illnesses or from other people.
Rational Use of Antibiotics

- Refrain from sharing antibiotics with others.
- Refrain from pressuring the doctor to prescribe antibiotics when it is determined that antibiotics are not indicated for the condition (such as for viral upper-respiratory illness).

There are a variety of ways to inform patients and the community within the facility (such as patient education and information material, posters in the clinics, direct reinforcement from HCWs) and through community outreach (TV/radio messages, involvement of informal leaders).

Summary

Antibiotics have been able to save many lives and their use has significantly contributed to the control of infectious diseases, which were once the leading causes of morbidity and mortality. However, the use and misuse of antibiotics have led to significant antibiotic resistance, thereby limiting their effectiveness. Therefore, the adoption of rational antibiotic use must be a global priority addressed at all levels: nations, facilities, individual clinicians, and the public. Measures at the facility level include activities to promote the rational use of antibiotics using broad interventions, pharmacy-driven interventions, and interventions targeted at effective treatment of specific infections or syndromes. Clinicians can increase the rational use of antibiotics in their practices by streamlining or de-escalating therapy, changing from parenteral to oral therapy, following standard treatment guidelines, and using good IPC practices.

Antibiotic stewardship programs are coordinated interventions at the facility level intended to improve and monitor the appropriate use of antibiotics. They are designed to achieve desirable outcomes, including optimizing clinical outcomes, minimizing adverse events, reducing infection-related health care costs, and reducing antibiotic resistance. Everyone (countries, hospitals, physicians, and individuals) plays a part in the prevention of antibiotic resistance but rational use cannot be achieved without knowledge of the problem. IPC staff can help prevent the irrational use of antibiotics and encourage the implementation of strategies that reduce the development of antibiotic resistance.
Appendix 1-A. Antibiotic Use Measures

Health care facilities implementing antibiotic stewardship programs measure antibiotic use either as days of therapy or defined daily dose.

Days of Therapy

Days of therapy (DOT), or antibiotic days, are aggregate days for which any amount of a specific antibiotic is administered or dispensed to a particular patient, divided by a standardized denominator (e.g., patient-days, days present, or days admitted in facility) (see Table A-1). If a patient received two antibiotics for 10 days, the DOT will be 20 days. DOT are reported monthly for inpatient locations, all inpatients, or selected outpatient settings (e.g., outpatient emergency department, pediatric emergency department, 24-hour observation area) for selected antibiotics stratified by route of administration (e.g., intravenous [IV], intramuscular, digestive, and respiratory) (Registers 1, 2, and 3).

DOT does not take into account the dose of antibiotic administered on any day. Given in any dose it will be counted as 1 day of therapy. Data from various departments and wards where antibiotics are used should be aggregated to calculate drug-specific DOT for the whole facility. These data should be reviewed and individual antibiotic use should be monitored to track antibiotic use. (CDC 2016)

Table A-1. Example of Calculation of DOT

During the month of December, the Female Medical Ward admitted one patient, Patient A. Register 1 shows that Patient A in the Female Medical Ward was administered 1 gram of meropenem intravenously once on Monday, three times on Tuesday, and once on Wednesday. Patient A also received amikacin intravenously once on Monday and once on Tuesday.

Register 1. Patient A Housed in the Female Medical Ward

<table>
<thead>
<tr>
<th>Medical Ward</th>
<th>Monday December 28</th>
<th>Tuesday December 29</th>
<th>Wednesday December 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meropenem 1 g intravenously every 8 hours</td>
<td>Given: 2300</td>
<td>Given: 0700, 1500, 2300</td>
<td>Given: 0700</td>
</tr>
<tr>
<td>Amikacin 1,000 mg intravenously every 24 hours</td>
<td>Given: 2300</td>
<td>Given: 2300</td>
<td></td>
</tr>
</tbody>
</table>
Register 2 shows that administration of 1 dose of meropenem on Monday counts as 1 meropenem day, as do the 3 doses on Tuesday, and the 1 dose on Wednesday. Administration of 1 dose of amikacin on Monday counts as 1 amikacin-day as does the 1 dose on Tuesday.

Register 2. Calculation of DOT for the Female Medical Ward

<table>
<thead>
<tr>
<th>Calculation</th>
<th>Monday December 28</th>
<th>Tuesday December 29</th>
<th>Wednesday December 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug-specific DOT (total)</td>
<td>Meropenem days = 1 Amikacin days = 1</td>
<td>Meropenem days = 1 Amikacin days = 1</td>
<td>Meropenem days = 1 Amikacin days = 0</td>
</tr>
<tr>
<td>Drug-specific DOT by route of administration</td>
<td>Meropenem days (IV) = 1 Amikacin days (IV) = 1</td>
<td>Meropenem days (IV) = 1 Amikacin days (IV) = 1</td>
<td>Meropenem days (IV) = 1 Amikacin days (IV) = 0</td>
</tr>
</tbody>
</table>

Register 3 reflects the monthly totals. If other patients were admitted to the ward and also received an antibiotic, their totals would also be added.

Register 3. DOT for December for the Female Medical Ward

<table>
<thead>
<tr>
<th>Month/Year – Location</th>
<th>Antibiotic Agent</th>
<th>Total</th>
<th>IV</th>
<th>IM</th>
<th>Digestive</th>
<th>Respiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>December – Female Medical Ward</td>
<td>Meropenem</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>December – Female Medical Ward</td>
<td>Amikacin</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Adapted from: CDC 2016.

**Defined Daily Dose**

Defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication in adults. This measure is generally used for purposes of monitoring drug use. As compared to the DOT, the DDD for antibiotics allows for estimated total antibiotic use in the hospital by aggregating the total number of grams of each antibiotic procured, dispensed, or administered during a period of interest, divided by the WHO-assigned DDD. (WHO has assigned DDDs to all medications including antibiotics; see Table A-2.) DDDs are not appropriate for use for children and patients with reduced drug excretion, such as in renal impairment, and are less accurate for between-facility benchmarking. DDD does allow for calculation of antibiotic use in a specific unit of the health care facility. While DDD does not necessarily reflect the recommended or prescribed dose, it does provide a fixed unit of measurement independent of price.
Table A-2. WHO-Assigned DDD for Ciprofloxacin

<table>
<thead>
<tr>
<th>Drug</th>
<th>DDD</th>
<th>Unit</th>
<th>Route of Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>1 g</td>
<td>Oral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5 g</td>
<td>Parenteral</td>
<td></td>
</tr>
</tbody>
</table>

For products that contain a combination of active ingredients, the DDDs are based on the principle of counting the combination as one daily dose, regardless of the number of active ingredients included in the combination.

Defined daily dose can be calculated both at community level and in a health care facility using number of DDDs per 1,000 population and per 100 bed-days per day respectively. For example, 10 DDDs/1,000 inhabitants/day indicates that 1% of the population on average receives a certain treatment daily.

The examples given below explain the DDD of single and combination products:

- **Example 1**: Treatment with two separate products, each containing one active ingredient:
  
  Product A: Tablets containing 20 mg of drug X (DDD = 20 mg)
  Product B: Tablets containing 25 mg of drug Y (DDD = 25 mg)

  The dosing schedule 1 tablet of A and 1 tablet of B daily will be calculated as consumption of 2 DDDs; if both tablets were taken two times a day it will make 4 DDDs, and if both tablets were taken three times a day it will make 6 (remember, DDD considers the amount of medication used).

- **Example 2**: Treatment with a combination product containing two active ingredients:
  
  Product C: Tablet containing 20 mg of drug X and 12.5 mg of drug Y.

  The DDD of the combination products is assigned as 1 Unit Dose (UD) = 1 tablet. The dosing schedule 1 tablet of C daily or 1 tablet twice a day will be calculated as 1 DDD and 2 DDDs respectively (even though it will be equivalent to 1.5 DDD of the single active ingredients).

  While calculating DDD, the total amount of drug used is the key measure. If the DDD for product A above is 20 mg, and if a patient receives 20 mg three times a day, it is 3 DDDs. If the dose used was 40 mg twice a day, it will make 4 DDDs a day, if 1 DDD is 20 mg.
References


Society for Healthcare Epidemiology of America; Infectious Diseases Society of America; Pediatric Infectious Diseases Society. 2012. Policy statement on antimicrobial stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS). Infect Control Hosp Epidemiol. 33(4):322–327.


Rational Use of Antibiotics


Chapter 2. Use of Antiseptics in Health Care Facilities

Key Topics
- The use and selection of antiseptics
- Storing and dispensing antiseptics
- Surgical hand preparation
- Preparing the patient’s skin for surgery
- Preparing the cervix or vagina for a procedure
- Advantages and disadvantages of different surgical antiseptics

Key Terms
- **Antisepsis** is the process of reducing the number of microorganisms on skin, mucous membranes, or other body tissue by applying an antimicrobial (antiseptic) agent.
- **Asepsis and aseptic techniques** are the combination of efforts made to prevent entry of microorganisms into any area of the body where they are likely to cause infection. The goal of asepsis is to **reduce to a safe level, or eliminate**, the number of microorganisms on both animate (living) surfaces (skin and mucous membranes) and inanimate objects (surgical instruments and other items).
- **Antiseptic agents** are chemicals applied to the skin or other living tissue to inhibit or kill microorganisms (both transient and resident). These agents, which include alcohol (ethyl or isopropyl), dilute iodine solutions, iodophors, and chlorhexidine, are used to reduce the total bacterial count. For the purpose of surgical site preparation, alcohol-based chlorhexidine and povidone-iodine solutions are recommended to reduce the total bacterial count on the skin.
- **Microorganisms** are causative agents of infection, and include bacteria, viruses, fungi, and parasites. Some bacteria can exist in a vegetative state (during which the organism is active and infective) and as endospores (in which a tough, dormant, non-reproductive structure protects the cell). Endospores are more difficult to kill due to their protective coating.
- **Resident flora** are microorganisms that live in the deeper layers of the skin and within hair follicles and cannot be completely removed, even by vigorous washing and rinsing with plain soap and clean water. In most cases, resident flora are not likely to be associated with infections; however, the hands or fingernails of some health care workers (HCWs) can become colonized by microorganisms that do cause infection (e.g., *Staphylococcus aureus*, gram-negative bacilli, or yeast), which can be transmitted to patients.
- **Surgical hand preparation** refers to an antiseptic handwash or antiseptic handrub performed preoperatively by the surgical team using a product containing antiseptic, time and specific techniques to eliminate transient flora and reduce resident skin flora. Antiseptics use for surgical hand preparation often have persistent antimicrobial activity.
  - **Surgical handrub** refers to surgical hand preparation with a waterless, alcohol-based handrub.
  - **Surgical hand scrub** refers to surgical hand preparation with antimicrobial soap and water.
Use of Antiseptics

- **Surgical site infection (SSI)** is an incisional or organ/space infection occurring at the site of the surgery, either within 30 days of surgery if there was no implant or within 90 days if there was an implant.

- **Transient flora** are microorganisms acquired through contact with individuals or contaminated surfaces during the course of normal, daily activities. They live in the upper layers of the skin and are more amenable to removal by hand hygiene. They are the microorganisms most likely to cause health care-associated infections.

**Background**

The concept of antisepsis to prevent surgical infection began in 1867 when British surgeon Joseph Lister developed the principles of aseptic surgery, including using skin antiseptics. Since then, the use of antiseptic agents has become standard practice, drastically reducing the occurrence of infections after surgery (in Lister’s time, up to 60% of cases became infected), thus enabling the development and expansion of surgery as a specialty.

Surgical antisepsis plays an important role in preventing postoperative wound infections by limiting the type and number of microorganisms transferred into the wound during surgery. Preoperative surgical antisepsis includes preoperative bathing of the patient prior to entering the operating theater (OT), the use of antiseptics in surgical hand scrubs performed by the scrub team, and the use of antiseptics on the patient’s skin surrounding the surgical site. See Module 10, Chapter 1, Preventing Surgical Site Infections, for details on perioperative asepsis.

**Selection of Antiseptics**

Plain soap and clean water physically remove dirt, other materials, and some transient flora from the skin. Antiseptic solutions, however, kill or inhibit almost all transient and many resident microorganisms, including most bacteria (except spores) and many viruses. Antiseptics are designed to remove as many microorganisms as possible without damaging or irritating the skin or mucous membranes. In addition, some antiseptic solutions have a residual effect (i.e., continue to kill microorganisms for a while after they have been applied).

Many chemicals qualify as suitable antiseptics for use on skin or mucous membranes. Appendix 2-A and Table A-1 list recommended antiseptic solutions, their microbiologic activity, and potential uses. Recommended antiseptics are chlorhexidine gluconates (CHG) (Hibitane and Hibiclens) and iodophors (e.g., Betadine and Wescodyne). Preparations of these antiseptics that also contain alcohol (e.g., Chloraprep and Duraprep), for fast killing of microorganisms, are recommended for skin antisepsis.

Some antiseptics are not recommended for skin preparation prior to clinical procedures, including Savlon (containing 0.3% w/v CHG and 3.0% w/v centrime). Some chemicals qualify as suitable antiseptics for use on skin or mucous membranes. Appendix 2-A and Table A-1 list recommended antiseptic solutions, their microbiologic activity, and potential uses. Recommended antiseptics are chlorhexidine gluconates (CHG) (Hibitane and Hibiclens) and iodophors (e.g., Betadine and Wescodyne). Preparations of these antiseptics that also contain alcohol (e.g., Chloraprep and Duraprep), for fast killing of microorganisms, are recommended for skin antisepsis.

When deciding which antiseptic agents to use, consider several factors:

- Appropriateness for desired use
- Recommendations (e.g., the World Health Organization’s [WHO’s] 2016 *Global Guidelines on the Prevention of Surgical Site Infection*)
Use of Antiseptics

- Cost of the antiseptic agent
- Effectiveness in killing microorganisms
- Fast-acting properties
- Persistent activity against regrowth of microorganisms

Other factors to consider include environmental impact, fire risks, risk of influencing antimicrobial resistance, adverse effects and patient outcomes.

The different types of antiseptic agents used to reduce the risk of SSI have been extensively reviewed. The results of these studies have shown the following:

- Preoperative skin preparation using an antiseptic agent, when done correctly, effectively reduces skin flora, both transient and resident, and subsequently infection rates.
- Alcohol-based antiseptic solutions for surgical site skin preparation are more effective compared to aqueous solutions. (WHO 2016)
- Alcohol-based CHG is beneficial in reducing SSI rates compared to alcohol-based povidone-iodine (i.e., tincture of iodine). (WHO 2016)
- The use of surgical hand preparation with either an alcohol-based handrub (ABHR) or an antiseptic soap solution in reducing the number of bacteria and fungi on hands has also been well-studied and has been found to be effective. (WHO 2009a)

Use of Antiseptics

In surgery, for preoperative preparation of the patient, antiseptics used include those for surgical hand scrub, preoperative bathing, and skin and mucous membrane preparations (e.g., surgical site and vaginal preparations).

Surgical Hand Scrub

The purpose of surgical hand scrub is to mechanically remove soil, debris, and transient organisms prior to surgery and to reduce resident flora for the duration of surgery (residual effect). It is performed to prevent wound contamination by microorganisms from the hands and arms of the surgical team. This is especially important because sterile gloves alone do not prevent wound contamination due to micro-tears or potential punctures in the gloves.

Before performing surgical hand scrub, members of an operating team will change into a hospital-laundered scrub suit and put on appropriate OT attire: protective, closed-toe shoes; shoe covers (if used); a surgical head cover, and a surgical mask and eye protection (see Module 3, Chapter 1, Personal Protective Equipment). And after the surgical procedure, team members should remove their gloves and inspect their hands for blood or body fluids, wash with soap and water if any residual or biological fluids are present, or apply ABHR if their hands are not visibly soiled.

Various protocols are available for preoperative hand scrubbing. Alcohol-based surgical handrub is thought to be at least as effective as traditional water-based surgical scrubs. Use of alcohol-based surgical hand scrub, however, does require that team members have thoroughly washed their hands prior to using it for the first time each day (see Table 2-1). (Widmer et al. 2010)
Skin damage caused by allergic reactions to certain antiseptics provides an ideal place for microorganisms to multiply and should be avoided. One strategy for reducing exposure of HCWs to irritating soaps and detergents is to promote the use of ABHRs, including for surgical hand preparation. Several studies have demonstrated that such products are tolerated better by HCWs and are associated with a better skin condition when compared with either plain or antimicrobial soap. (WHO 2009a)

**Table 2-1. Surgical Hand Preparation Using Medicated Soap and ABHR**

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Performed surgical hand preparation before putting on sterile gloves.</td>
</tr>
<tr>
<td>• Use either an antimicrobial soap or ABHR, preferably with a product ensuring sustained activity e.g., chlorhexidine).</td>
</tr>
<tr>
<td>• Perform surgical hand preparation using an ABHR if the quality of water is not assured in the OT area.</td>
</tr>
<tr>
<td>• Keep nails short and pay attention to them when washing your hands. Most microbes on hands come from beneath the fingernails (subungual).</td>
</tr>
<tr>
<td>• Do not wear artificial nails or chipped or cracked nail polish.</td>
</tr>
<tr>
<td>• Remove all jewelry (rings, watches, bracelets) before entering the OT area.</td>
</tr>
<tr>
<td>• Wash hands and arms with a non-medicated soap before entering the OT area.</td>
</tr>
</tbody>
</table>

**Surgical Hand Scrub Using Antimicrobial Soap** (see Table 2-2):
• Do not use a brush for surgical hand scrub.
• Surgical scrub of 2–5 minutes is adequate; long scrub times are not necessary.

**Surgical Hand Scrub Using ABHR:**
• When using an ABHR product, follow the manufacturer’s instructions for application times. Apply the product only to dry hands.
• When using an ABHR, use a sufficient amount to keep hands and forearms wet with the handrub throughout the surgical hand-preparation procedure.
• Do not use a combination of surgical hand scrub and surgical handrub with alcohol-based products at the same time.

**Table 2-2. Surgical Hand Scrub Using Medicated Soap**

Clean subungual areas (under the fingernails) with a nail cleaner to remove any deposits before the first scrub of the day.

**STEP 1:** Start timing. For 2 minutes, scrub each side of each finger, between the fingers, and the back and front of the hands.

**STEP 2:** Proceed to scrub the arms, keeping the hands higher than the arm at all times. This helps to avoid recontamination of the hands by water from the elbows. It also prevents bacteria-laden soap and water from contaminating the hands.

**STEP 3:** For 1 minute, wash each side of the arms from the wrist to the elbow.
**STEP 4:** Repeat the process on the other hand and arm. Keep hands above elbows at all times. If the hand touches anything at any time, the scrub time must be lengthened by another 1 minute for the same area that has been contaminated.

**STEP 5:** Rinse hands and arms by passing them through the water flow in one direction only, from fingertips to elbow. Do not move the arm back and forth through the water.

**STEP 6:** Proceed to the OT without contaminating hands or arms and holding hands above elbows.

**STEP 7:** At all times during the scrub procedure, care should be taken not to splash water onto surgical attire.

**STEP 8:** Once in the OT, hands and arms should be dried using a sterile towel and aseptic technique before putting on gown and gloves.

*Sources:* Widmer et al. 2010; WHO 2009a; WHO 2009b.
Use of Antiseptics

Figure 2-1. Steps for Performing Surgical Hand Preparation Using ABHR

Surgical Handrubbing Technique

- Handwash with soap and water on arrival to OR, after having donned theatre clothing (cap/hat/bonnet and mask).
- Use an alcohol-based handrub (ABHR) product for surgical hand preparation, by carefully following the technique illustrated in Images 1 to 17, before every surgical procedure.
- If any residual talc or biological fluids are present when gloves are removed following the operation, handwash with soap and water.

1. Put approximately 5ml (3 doses) of ABHR in the palm of your left hand, using the elbow of your other arm to operate the dispenser.
2. Dip the fingertips of your right hand in the handrub to decontaminate under the nails (5 seconds).

3-7. Smear the handrub on the right forearm up to the elbow. Ensure that the whole skin area is covered by using circular movements around the forearm until the handrub has fully evaporated (10-15 seconds).

8. Images 8-10: Now repeat steps 1-7 for the left hand and forearm.
9. Put approximately 5ml (3 doses) of ABHR in the palm of your left hand as illustrated, to rub both hands at the same time up to the wrists, following all steps in Images 12-17 (20-30 seconds).
10. Cover the whole surface of the hands up to the wrist with ABHR, rubbing palm against palm with a rotating movement.
11. Rub the back of the left hand, including the wrist, moving the right palm back and forth, and vice-versa.
12. Rub palm against palm back and forth with fingers interlinked.
13. Rub the back of the fingers by holding them in the palm of the other hand with a sideways back and forth movement.
14. Rub the thumb of the left hand by rotating it in the clasped palm of the right hand and vice versa.
15. When the hands are dry, sterile surgical clothing and gloves can be donned.

Use of Antiseptics

Preoperative Bathing
Patients should bathe or shower before surgery to ensure that their skin is as clean as possible and to remove as much bacteria as possible at the site of incision. Either a plain or antimicrobial soap may be used for this purpose. (WHO 2016) In many settings, chlorhexidine gluconate (CHG) bathing the night before and morning of surgery is practiced. Though evidence for preventing SSI is not conclusive, preoperative patient bathing does not do any harm and reduces transient and resident flora on the patient’s skin. (Kamel et al. 2011; WHO 2016)

Preparation of the Patient’s Skin Prior to Surgical Procedures
Although skin cannot be sterilized, applying an antiseptic solution minimizes the number of microorganisms around the surgical incision that may contaminate and cause infection. Alcohol-based antiseptic solutions containing on chlorhexidine (e.g., 2–4% with 60–90% alcohol) for surgical site skin preparation in patients undergoing surgical procedures are recommended (WHO 2016).

Contraindications (i.e., potential adverse side effects), environment risks (e.g., potential fire hazards from the use of alcohol-based antiseptics and electrosurgery), patient allergies, skin conditions (wounds, premature infants), the surgical site (mucous membranes, neurological tissue), and the manufacturer’s recommendations for the agent (limitations on use in infants) are all factors to consider when choosing a skin prep agent (Zinn et al. 2010). For example, chlorhexidine is not approved for use on neonates or in mucosa, although, many facilities do. Chlorhexidine solutions must not be allowed to come into contact with the brain, meninges, eye, or middle ear (WHO 2016). Alternatives include alcohol-based iodine solutions such as tincture of iodine (iodine [3%] with alcohol [60–90%]) and aqueous chlorhexidine and iodine solutions (for mucous membranes).

Always refer to the antiseptic package instructions prior to use.

Equipment and supplies
- Scissors or clippers
- New or cleaned clipper blade
- Appropriate skin antiseptic
- Sterile forceps (if manufacturer-supplied application device not available)
  - High-level disinfected forceps are acceptable if sterile items not available
- Sterile gauze (if manufacturer-supplied application device not available)
- Sterile gloves

Instructions for skin preparation

STEP 1: Do not shave hair around the operative site. If hair interferes with the surgical procedure and must be cut, trim the hair close to the skin surface with scissors, clip the hair using clippers immediately before surgery, or use a depilatory (hair removal) cream as an alternative to clipping. (Alexander et al. 2011; Jose and Dignon 2013)

STEP 2: Determine if the patient has any allergies to antiseptic solutions during the preoperative assessment. Choose iodine preparations if the patient has an allergy to chlorhexidine.

STEP 3: Prepare Equipment: use a skin preparation kit containing the above listed items
STEP 4: Perform hand hygiene.

STEP 5: Place absorbent linens on either side of the surgical site before the antiseptic skin preparation to catch any pooling of the antiseptic solution.

STEP 6: Open the preparation kit, and put on sterile gloves (or non-sterile gloves, if the length of the handle of the antiseptic applicator prevents contamination of the patient’s skin).

STEP 7: Apply the antiseptic agent to the patient’s skin:
- Work from the planned incision site outward, extending skin preparation to an area large enough to accommodate drape shifting, incision extension, and the potential for drains.
- Use a back-and-forth motion (chlorhexidine) or a circular motion from the center out to prevent recontamination of the operative site (tincture of iodine). Always move from areas of least contamination to most contamination (e.g., do the groin area last).
- Allow the antiseptic enough time to be effective. Both chlorhexidine and iodophors require 2 minutes of contact time to become effective once applied to the skin.

STEP 8: Allow the antiseptic agent to dry per the manufacturer’s instructions before draping the skin. Draping before the area is dry traps vapors beneath the drape, which can cause burns and creates a fire hazard. Do not wipe the incision area with gauze but allow the antiseptic to dry completely.

STEP 9: Remove any antiseptic-soaked material from the patient and room to prevent a fire hazard.

STEP 10: Discard supplies, remove gloves, and perform hand hygiene.

Preparing the Cervix and Vagina for Surgical and Other Procedures

For cervical and vaginal procedures, select an aqueous (water-based) antiseptic, such as an iodophor (e.g., povidone-iodine) or 2–4% CHG (e.g., Hibiclens), prior to inserting a uterine elevator for minilaparotomy or after completing an endometrial biopsy. Do not use alcohols or alcohol-containing preparations for cervical or vaginal procedures. Alcohol burns, dries, and irritates mucous membranes, which promotes the growth of microorganisms. In addition, hexachlorophene (pHisOHex) is neurotoxic and should not be used on mucous membranes (e.g., vaginal mucosa) because it is readily absorbed (see Module 10, Chapter 5, Preventing Maternal and Newborn Infections in Health Care Settings, for more information on cesarean sections and SSI prevention). (Larson 1988; Larson 1995).

Equipment and supplies:
- Water based antiseptic solution (e.g., CHG or iodophore)
- Sterile stainless steel bowl to pour antiseptic solution
- Sterile or high-level disinfected sponge-holding forceps
- Gauze or cotton squares
- Alcohol-based hand rub for hand hygiene
- Gloves (sterile)
- Speculum
- Tenaculum for preparing cervix

Note: Do not allow the antiseptic to pool underneath the patient’s body; this can irritate the skin.
Use of Antiseptics

Instructions for preparing the cervix and vagina for a procedure

**STEP 1:** Ask if the patient has any allergies to antiseptic solutions (e.g., chlorhexidine) before selecting an antiseptic solution. **Do not** use antiseptic solution containing alcohol for prepping the cervix and vagina.

**STEP 2:** Gently wash the external genital area with soap and clean water and dry the area before applying the antiseptic. It is not necessary to wash the external genital area with antiseptic solution if it appears clean.

**STEP 3:** After inserting the speculum, apply antiseptic solution liberally to the cervix and vagina (two times). Chlorhexidine aqueous solutions (2–4%) is ideal for prepping the cervix and vagina.

**STEP 4:** If an iodophor is used, allow time (2 minutes) before proceeding with the surgical procedure.

Storing and Dispensing Antiseptics

Health care-associated infection outbreaks have been linked to contaminated antiseptics and disinfectants (Weber et al. 2007). Contamination can occur from introducing bacteria into the product during use (e.g., using in a patient care area or double dipping contaminated instruments into the solution) or over-dilution of antiseptics (e.g., adding too much water to the solution, thus diluting the antiseptic properties of the solution). Microorganisms that can contaminate antiseptic solutions include *Staphylococcus epidermidis*, *S. aureus*, *Serratia marcescens*, *Pseudomonas aeruginosa*, other gram-negative bacilli, and some endospores. Contaminated antiseptics can cause subsequent infection when used for surgical hand preparation or prepping a patient’s skin prior to surgery. The following can prevent contamination of antiseptic solutions:

- Pour the antiseptic into a small, reusable container for single use, unless supplied commercially in small quantities. This prevents evaporation and contamination. Each time, make sure the container is labelled with the name of the solution that it contains.

- Do not store antiseptic solutions in patient care areas.

- Do not store antiseptic solutions in open containers.

- Do not store gauze or cotton swabs in antiseptics.

- Establish a routine schedule for preparing new solution. (Solutions are at an increased risk of becoming contaminated after 1 week of storage.)

- Empty and clean reusable containers before refilling. Do not “top off” antiseptic dispensers (i.e., do not add new solution to existing solution in the container, but instead, empty and clean first). Wash reusable containers thoroughly with soap and clean water, rinse with clean water, if available, and air-dry completely before refilling.

- Label reusable containers with the date they are refilled.

- Store concentrated antiseptic solutions in a cool, dark area. Never store them in direct sunlight or in excessive heat (e.g., upper shelves in a tin-roofed building) because this can reduce the antimicrobial effectiveness of the solution.
Summary

Surgical antisepsis plays an important role in preventing postoperative wound infections by limiting the type and number of microorganisms transferred into the wound during surgery. Surgical hand preparation with either an ABHR or an antiseptic solution can reduce the number of bacteria on hands before putting on sterile gloves. Preoperative bathing of the patient before entering the OT is good clinical practice. Alcohol-based chlorhexidine is recommended for preoperative skin preparation in most situations. Follow manufacturers’ instructions and consider patient and surgical site factors when applying antiseptics. If not stored following recommended procedures, antiseptics may become contaminated with microbes, which can result in infection outbreaks.
# Appendix 2-A. Antiseptic Agents

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Gram-Positive</th>
<th>Most Gram-Negative</th>
<th>TB</th>
<th>Viruses</th>
<th>Fungi</th>
<th>Endospores</th>
<th>Relative Speed of Action</th>
<th>Affected by Organic Matter</th>
<th>Surgical Scrub</th>
<th>Skin Prep</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcohols</strong>&lt;br&gt;(60–90% ethyl or isopropyl)</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Excellent</td>
<td>None</td>
<td>Fast</td>
<td>Moderate</td>
<td>Yes</td>
<td>Yes</td>
<td>Not for use on mucous membranes; not good for physical cleaning of skin; no persistent activity</td>
</tr>
<tr>
<td><strong>Chlorhexidine</strong>&lt;br&gt;(2–4%) (Hibitane, Hibiscrub)</td>
<td>Excellent</td>
<td>Good</td>
<td>Fair</td>
<td>Excellent</td>
<td>Fair</td>
<td>None</td>
<td>Intermediate</td>
<td>Slight</td>
<td>Yes</td>
<td>Yes</td>
<td>Has good persistent effect; toxic to ears and eyes</td>
</tr>
<tr>
<td><strong>Iodine preparations</strong>&lt;br&gt;(3%)</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Good</td>
<td>Fair</td>
<td>Intermediate</td>
<td>Marked</td>
<td>No</td>
<td>Yes</td>
<td>Not for use on mucous membranes; can burn skin; remove after several minutes</td>
</tr>
<tr>
<td><strong>Iodophors</strong>&lt;br&gt;(7.5–10%) (Betadine)</td>
<td>Excellent</td>
<td>Excellent</td>
<td>Fair</td>
<td>Good</td>
<td>Good</td>
<td>None</td>
<td>Intermediate</td>
<td>Moderate</td>
<td>Yes</td>
<td>Yes</td>
<td>Can be used on mucous membranes</td>
</tr>
<tr>
<td><strong>Chloroxylenol</strong>&lt;br&gt;(PCMX) (0.5–4%) (Dettol)</td>
<td>Good</td>
<td>Excellent</td>
<td>Fair</td>
<td>Good</td>
<td>Fair</td>
<td>Unknown</td>
<td>Slow</td>
<td>Minimal</td>
<td>No</td>
<td>No</td>
<td>Penetrates the skin and should not be used on newborns; Not recommended for skin prepartion</td>
</tr>
<tr>
<td><strong>Savlon</strong>&lt;br&gt;0.3% w/v CHG and 3.0% w/v centrimide</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

Adapted from: Boyce et al. 2002; Olmsted 1996.
**Alcohol Solutions (Ethyl and Isopropyl Alcohol)**

Ethyl and isopropyl alcohols (60–90%) are safe and excellent antiseptics that are commonly available and inexpensive. Their rapid-killing action makes them very effective in reducing numbers of microorganisms on the skin. A 60–70% solution of ethyl or isopropyl alcohol is effective, less drying to the skin, and less expensive than higher concentrations. Methyl alcohol is the least effective of the alcohols and should not be used alone as an antiseptic. (WHO 2009a; WHO 2009c)

Alcohol solutions should **not** be used on mucous membranes (e.g., for vaginal preparation, procedures involving the cornea or ears). Alcohol solutions dry and irritate mucous membranes, which, in turn, promotes the growth of microorganisms. (Anderson et al. 2014)

**Advantages of alcohol solutions**

- Rapidly kill all fungi and bacteria, including mycobacteria:
  - Isopropyl alcohol kills most viruses, including hepatitis B, hepatitis C, and HIV.
  - Ethyl alcohol kills all viruses.
  - Ethyl alcohol solutions kill bacteria such as *S. aureus*, *Streptococcus pyogenes*, *Enterobacteriaceae*, and *P. aeruginosa* within 10–90 seconds in tests.
- Although alcohols have no persistent killing effect, the rapid reduction of microorganisms on skin protects against regrowth of organisms, even under gloves, for several hours.
- Alcohol solutions do not stain and are not allergenic.
- The solutions are relatively inexpensive and widely available throughout the world.

**Disadvantages of alcohol solutions**

- Need emollient (e.g., glycerin or propylene glycol) to prevent drying of skin (ethyl alcohol may be less drying than isopropyl) when used repeatedly for the purpose of hand hygiene with ABHR
- Not suitable for use during surgery that is on or close to mucous membranes or the eyes
- Easily inactivated by organic materials, such as blood or sputum
- Flammable (require storage in cool, well-ventilated areas)\(^1\)
- Will damage rubber (latex) over time
- Not a good environmental cleaning agent, except for small surfaces (e.g., rubbers top of medication vial.

**Chlorhexidine Gluconate**

Chlorhexidine gluconate (CHG) is an excellent antiseptic. It remains active against microorganisms on skin many hours after use (residual effect) and is safe for use on children older than 2 months old. CHG is inactivated by soap, its residual antimicrobial activity is dependent upon the concentration of CHG in the commercial product. The recommended concentration is 2–4% chlorhexidine. (WHO 2009c) To be most effective, CHG must be used according to the manufacturers’ instructions, including application with a scrubbing motion for the recommended time and abiding by the dry time.

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\(^1\) Residual alcohol on hands or skin may be ignited by static electricity. Allow hands to dry thoroughly after using antiseptic handrub.
Use of Antiseptics

**Advantages of chlorhexidine gluconate**
- Broad spectrum of antimicrobial action
- Persistent microbial action on skin (chemically active for at least 6 hours)
- Chemical protection (the number of microorganisms inhibited) increases with repeated use
- Effective against certain viruses (e.g., HIV, influenza, herpes simplex type 1 and 2)
- Minimally affected by organic material
- Several products available commercially for preoperative skin preparations, surgical hand preparation, and preoperative bathing

**Disadvantages of chlorhexidine gluconate**
- Expensive and not always available
- Little activity against bacterial and fungal spores (except at high temperatures), poliovirus, coxsackie virus, and rotavirus
- Action reduced or neutralized by natural soaps, substances present in hard tap water, and some hand creams
- Not effective against tubercle bacillus, only fairly active against fungi
- Cannot be used above pH of 8, because it decomposes
- Must not come in contact with eyes (e.g., can cause conjunctivitis) and ears (e.g., can cause ototoxicity)
- Can cause severe allergic reactions (e.g., anaphylaxis) in some individuals
- Use not approved in infants under 2 months

**Iodine and Iodophor Solutions**

Three percent (3%) iodine solutions are very effective antiseptics and are available as both aqueous (Lugol) and tincture (iodine in 70% alcohol) solutions. Seven and a half (7.5) percent to 10% iodophors are solutions of iodine mixed with a carrier, which is a complexing agent—such as polyvinyl pyrrolidone (povidone)—that releases small amounts of iodine. Povidone-iodine is the most common iodophor and is available globally. The amount of “free” iodine present determines the level of antimicrobial activity of iodophors (e.g., 10% povidone-iodine contains 1% available iodine, yielding a “free” iodine concentration of 1 part per million [0.0001%]). Iodophors have a broad spectrum of activity; they kill vegetative bacteria, mycobacteria, viruses, and fungi. However, they require up to 2 minutes of contact time to release free iodine, which is the active chemical. To be effective, iodophors must be used according to the manufacturers’ instructions. Once released, the free iodine has rapid-killing action. Iodophors generally are nontoxic and nonirritating to skin and mucous membranes, unless the person is allergic to iodine. (Larson 1995; WHO 2009c).

**Advantages of iodine and iodophor solutions**
- They have a broad spectrum of antimicrobial action.
- Aqueous iodine preparations are inexpensive, effective, and widely available.
• Iodophors are non-irritating to skin or mucous membranes (unless the person is allergic to iodine), making them ideal for vaginal use (e.g., before IUD insertion).
• They can be used as a prophylaxis against neonatal conjunctivitis; a 2.5% ophthalmic solution of povidone-iodine is recommended.
• Up to 3% aqueous solutions does not stain skin.

Disadvantages of iodine and iodophor solutions
• Iodine and iodophors have slow to intermediate antimicrobial action.
• Iodophors have little residual effect.
• Like alcohols, iodine and iodophors are rapidly inactivated by organic materials, such as blood or sputum.
• Iodophor skin solutions are not recommended for disinfecting hard surfaces.
• Tincture or aqueous iodine may cause skin irritation and staining and must be removed from skin after drying (alcohol can be used to remove skin stains).
• Absorption of free iodine through skin and mucous membranes may cause hypothyroidism in premature and newborn infants so use should be limited.
• Allergic reactions to iodine and iodophors can occur; check the patient for history of allergy (e.g., iodine and shellfish).
Use of Antiseptics

References


http://www.who.int/gpsc/5may/tools/9789241597906/en/.


