

Rational Use of Antibiotics in Hospitals

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Overuse and misuse of antibiotics can unnecessarily increase bacterial resistance, adverse reactions, and expense. Briefly discussed in this article are problems in the use of antibiotics and policies that can help improve their use in hospitals. Some facts that can help in safer prescribing of antibiotics are also given.

1. INTRODUCTION

1.1 Over the last half century or so, antibiotics have probably saved more lives than any other group of drugs.¹ Many infectious diseases that were potentially fatal in the past can now be treated effectively with appropriate use of these agents.

1.2 Undoubtedly, antibiotics are one of the most important groups of drugs available today. However, they are also one of the most widely misused groups of drugs.²

2. USE, MISUSE, AND PROBLEMS

2.1 Many studies from different countries show that antibiotics are **extensively used**.^{3,4} As a therapeutic group, they are the most frequently prescribed drugs in many health care settings.

2.2 **Expenditure** on antibiotics is often more than on any other group of drugs. They usually make up 15 to 30% of the total drug bill;⁵ sometimes they account for up to 50% of the total expenditure.^{4,6}

2.3 A number of reports show that antibiotics are often **inappropriately used**.⁷⁻¹⁰

Problems in relation to treatment with antibiotics are use:
for conditions in which they are ineffective;
of inappropriate doses;
for inappropriate duration;
of unnecessary combinations;
without bacteriological support even where this is possible and should be done;
of broad spectrum agents without necessity;
of parenteral preparations where oral preparations could be used effectively;
of expensive agents where cheaper alternatives could work equally well.

2.4 One-third to half of all the antibiotics used in hospitals are for **prophylaxis in surgery**.¹¹ Use of antibiotics for this purpose has often been found to be inappropriate.^{11,12}

2.5 Many doctors overprescribe antibiotics because of (i) the **fear** of possible bacterial infection which might have been undetected or overlooked, and (ii) **pressure** from patients who often expect medicines when ill.³

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As with the use of all drugs in general, the use of antibiotics is governed not only by the 'real need' of patients but also by several other factors that influence prescribing behaviour of physicians. Such factors are training standard, experience and attitude of the physician, time constraint, investigative facility, patient demand, drug regulation, and promotional activities of drug companies.^{5,11,13}

2.6 Promotional activities of pharmaceutical companies and encouragement of antibiotic use by prescribers may create wrong expectations for consumers.^{14,15} Many people today have what can be called **antibiotic mentality**. They think antibiotics are sort of **wonder drugs** that can cure a wide variety of diseases.⁶

2.7 In most of the developing countries antibiotics can be obtained **without prescription**.^{6,16} Many times these agents are sold and purchased in **incomplete courses**.^{16,17} The practice of self administration of antibiotics in insufficient quantities can unnecessarily increase the problem of bacterial resistance.

2.8 Antibiotics are used in large quantities not only in human beings but also in **livestock farming**.¹⁸ Careless use of antibiotics in food production and animal husbandry may also increase the problem of bacterial resistance.

2.9 There is a big problem of **bacterial resistance**, especially in developing countries.^{1,16} A number of bacteria that were earlier susceptible to many useful and cheap antibacterial agents have now acquired resistance to these agents. The problem is exemplified by sulphonamide-resistant meningococci, penicillin-resistant pneumococci, multiresistant gonococci, streptococci, staphylococci and *Shigella*, trimethoprim-resistant enterobacteria, ampicillin-resistant *H. influenzae*, chloramphenicol-resistant *Salmonella typhi*, ampicillin- and sulphonamide-resistant *E. coli*, tetracycline-resistant *V. cholerae*, and isoniazid- or streptomycin-resistant *M. tuberculosis*.^{1,6,16,18,19}

The use of antibiotics inevitably leads to increase in resistance development because of

selection pressure. But the problem has been intensified by their excessive and indiscriminate use.^{18,20}

2.10 Antibiotics are one of the common causes of **adverse reactions**.^{11,21} In five different studies antibiotics were found to be the cause of 9.3%, 10.0%, 16.1%, 21.2%, and 41.5% of all adverse drug reactions in hospitalized patients.²²

3. STRATEGIES FOR IMPROVING ANTIBIOTIC USE IN HOSPITALS

3.1 An **antimicrobial agents team** having representatives from multiple disciplines such as general medicine, microbiology, clinical pharmacy, etc, can be of great help in improving antibiotic use in hospitals.⁷ If such a team cannot be formed, the 'drug and therapeutics committee' or some other pertinent committee can take up the task of making and implementing antibiotic policies.

3.2 Existence of a **formulary** or an **antibiotic guidelines booklet** can be of help in making antibiotic selection, carrying out educational activities, and reducing pharmacy expenditure.⁷ The formulary or booklet should be periodically updated. A good example of antibiotic guidelines booklet is the one prepared by Victorian Drug Usage Advisory Committee, Australia.¹¹

3.3 A system that helps in rational use of antibiotics is their categorization into three groups: unrestricted, restricted, and controlled.²³ **Unrestricted** antibiotics can be made freely available for use by all doctors in the hospital. **Restricted** antibiotics can be made available for use only for specific conditions or by selected doctors or after consultation with and approval of an infectious disease specialist / medical microbiologist. (There should, however, be a mechanism by which all doctors can use such restricted antibiotics in emergency situations without prior formalities.) **Controlled** or **excluded** antibiotics would not normally be available in the hospital pharmacy. Such controlled antibiotics would be the ones which are usually ineffective, very toxic, or normally unnecessary

because they offer no advantage over the ones already held in the hospital pharmacy. Provision should, however, be made for making such items available under special circumstances.¹¹

A WHO Expert Committee (1989) has proposed that some antibiotics such as the quinolones, third generation cephalosporins, and vancomycin be kept as **reserve antibiotics** for restricted use.¹⁸ Keeping some of the antibiotics as 'reserve agents' can help in lessening the risk of resistance development and in reducing cost.¹⁶

3.4 A system can be developed whereby doctors are required to fill up **antimicrobial order form** for prescribing antibiotics.⁷ In such an order form, the treating physician would be required to mention the aim of use (prophylactic or therapeutic), dose, route, frequency and duration of use, age of the patient, history of allergy, and any impairment in hepatic or renal function. A study in America showed that use of an antibiotic order sheet led to a significant decrease in antibiotic prescribing.²⁴

3.5 The supply of an antibiotic by the hospital pharmacy can be made to **stop automatically** after certain period of time (for example, after 48 hours if used for prophylaxis and after 7 days if used for therapy) unless the treating physician places a second order for continued use of the antibiotic.⁷

3.6 Microbiology laboratory of the hospital can periodically supply the clinicians with a **list of locally prevalent organisms** responsible for different infections and their current sensitivity to relevant antimicrobials.^{7,25} This can be of much assistance in empirical treatment with antimicrobials before the results of bacteriological tests (if done) are available.

To influence antimicrobial prescribing by clinicians, the microbiology laboratory can also do:

- a) **selective susceptibility testing** with only a limited number of relevant antibiotics and/or
- b) **selective reporting** of only a limited

number of antibiotics to which the cultured microorganism is sensitive.²³

3.7 **Periodic audit of antibiotic usage** in hospitals can be done and the reports presented before the prescribing doctors. It can help the doctors get feedback on their prescribing habits and compare their practices with those of other colleagues. It can also help in getting ideas as to which are the problem areas in prescribing that need educational campaigns.^{7,11}

Specific prescription audits can be done to identify specific problems. Examples of areas that might need specific audit are: continuous use of an antibiotic for more than 21 days; use of more than 5 antibiotics in a patient during a single hospitalization; use of more than 2 antibiotics together; surgical prophylaxis with antibiotics for more than 48 hours or for procedures in which it is not an accepted practice; and unjustified use of parenteral preparation of an antibiotic when its oral form could be effectively used.⁷

3.8 Different **educational activities** on proper use of antibiotics can be carried out in hospitals.

An activity that has been demonstrated to be effective in improving prescribing habits of physicians is face-to-face education.²⁶

Journal clubs, group discussions, seminars, symposia, conferences, etc, can be held on the proper use of antibiotics.

Clinical pharmacologists and/or medical microbiologists can accompany treating physicians during ward rounds.^{23,27} This can help in sharing of ideas and working as a team.

'Aide-memoire' giving antibiotics of choice and their dose for treating common infections can be displayed at appropriate places in both in-patient and out-patient departments.

3.9 There should be some **control over advertising** done by medical representatives.

of pharmaceutical companies. A policy can be developed whereby the representatives have to register themselves with the hospital pharmacy for advertising their products and also have to make appointments for visiting the physicians. The time and place for drug detailing can be specified.⁷

4. SOME USEFUL FACTS ABOUT THE USE OF ANTIBACTERIALS

4.1 In Table I is given the **suggested empirical treatment** with antibacterial agent(s) based on the site of infection.^{11,28} The empirical therapy can be continued, modified, or changed depending on the results of bacteriological investigations and clinical response of the patient.

4.2 In Table II are given situations (both surgical and non-surgical) in which **antibacterial prophylaxis** is of value.^{11,28,30}

4.3 In Table III are given clinically more important **interactions** between antibacterial agents and other drugs.^{28,30,32}

4.4 Antibacterials that need to be avoided in **new-born babies** are sulphonamides, trimethoprim, and co-trimoxazole.^{2,8} Chloramphenicol should be used with great caution in neonates.

Antibacterials that need to be avoided in small **children** are tetracyclines and 4-quinolones.¹¹

4.5 Antibacterials that need to be avoided or

cautiously used in **pregnancy** are aminoglycosides, tetracyclines, chloramphenicol, sulphonamides, trimethoprim, co-trimoxazole, 4-quinolones, nitrofurantoin, metronidazole, rifampicin, and dapsone.^{28,31}

4.6 Antibacterials that need to be cautiously used in **elderly patients** are aminoglycosides, tetracyclines, co-trimoxazole, and nitrofurantoin.³¹

4.7 Antibacterials that need to be avoided or used cautiously in patients with **liver disease** are tetracyclines, chloramphenicol, rifampicin, pyrazinamide, isoniazid, erythromycin, clindamycin, and fusidic acid.^{28,31}

4.8 Antibacterials that need to be avoided or used cautiously in patients with **renal impairment** are aminoglycosides, cephaloridine, cephalothin, cephazolin, ceftazidime, cefuroxime, tetracyclines (except doxycycline and minocycline), colistin, vancomycin, lincomycin, nitrofurantoin, ethambutol, cycloserine, capreomycin, sulphonamides, cephalexin, and 4-quinolones.^{28,31}

4.9 Gastrointestinal absorption of phenoxymethylpenicillin (penicillin V), ampicillin, cloxacillin, isoniazid, and rifampicin is reduced by food; so they are best taken at least 30 minutes **before food**. Absorption of all tetracyclines (except doxycycline and minocycline) is reduced by milk; so they should be taken separately from dairy products.^{31,33}

Table I. Suggested empirical treatment with antibacterial agent(s) based on the site of infection.

Infection	Antibacterial(s) suggested
ENT & RESPIRATORY SYSTEM	
Acute bacterial otitis media/sinusitis	Amoxycillin or doxycycline or trimethoprim
Dental infections	Phenoxymethylpenicillin or erythromycin or metronidazole or tetracycline
Tonsillitis	Phenoxymethylpenicillin or erythromycin

Table I. (continued)

Acute epiglottitis	Chloramphenicol or ceftriaxone or cefotaxime
Acute bronchitis	Amoxycillin or erythromycin or doxycycline
Exacerbations of chronic bronchitis	Amoxycillin or trimethoprim or erythromycin or doxycycline
Pneumonia in previously healthy persons	Benzylpenicillin or amoxycillin (cloxacillin to be added if staphylococcal infection suspected, eg, in measles or influenza; erythromycin to be added if <i>Legionella</i> infection suspected)
Pneumonia in persons with previously unhealthy chest	Cloxacillin + (amoxycillin or trimethoprim or erythromycin)
Pneumonia in hospitalized or immuno-compromised patients	(Benzylpenicillin + gentamicin) or cefotaxime or ceftriaxone
CARDIOVASCULAR SYSTEM	
Endocarditis	Benzylpenicillin + cloxacillin + gentamicin (In penicillin-allergic patients, vancomycin + gentamicin)
GASTROINTESTINAL SYSTEM	
Acute cholecystitis	(Amoxycillin + gentamicin) or cephalothin or cephalazolin
Peritonitis	Amoxycillin + gentamicin + (metronidazole or clindamycin)
Typhoid / paratyphoid fever	Chloramphenicol or amoxycillin or co-trimoxazole or ciprofloxacin
Cholera	Doxycycline or co-trimoxazole
<i>Shigella</i> dysentery	Ampicillin or trimethoprim or norfloxacin
Invasive <i>Salmonella</i> enteritis	Amoxycillin or trimethoprim or ciprofloxacin
<i>Campylobacter</i> enteritis	Erythromycin
CENTRAL NERVOUS SYSTEM	
Meningitis	Benzylpenicillin + (chloramphenicol or cefotaxime or ceftriaxone)
GENITOURINARY SYSTEM	
Lower urinary tract infection	Amoxycillin or trimethoprim or nitrofurantoin or cephalixin
Acute pyelonephritis	Trimethoprim or gentamicin or cephalosporin or ciprofloxacin
Gonococcal urethritis	(Amoxycillin with probenecid) or spectinomycin or ciprofloxacin or ceftriaxone (Better to give doxycycline also because non-gonococcal urethritis frequently co-exists)
Non-gonococcal urethritis	Doxycycline
Pelvic inflammatory disease	Doxycycline + (metronidazole or tinidazole)

Table I. (continued)

Syphilis	Procaine penicillin or doxycycline or erythromycin
Acute prostatitis	Amoxycillin + gentamicin
Chronic prostatitis	Trimethoprim or norfloxacin or ciprofloxacin
BLOOD	
Septicaemia	(Amoxycillin + gentamicin) or cefotaxime or ceftriaxone (Metronidazole to be added if anaerobic infection suspected; cloxacillin or vancomycin to be added if gram positive infection suspected)
MUSCULOSKELETAL SYSTEM	
Osteomyelitis / septic arthritis in adults	Cloxacillin or clindamycin
Osteomyelitis / septic arthritis in children < 5 years of age	cloxacillin + (amoxycillin or cefotaxime or ceftriaxone)
SKIN	
Cellulitis / erysipelas	Benzylnicillin (cloxacillin if <i>Staphylococcus aureus</i> suspected)
Boil / carbuncle	Cloxacillin
Impetigo	Topical povidone-iodine or chlorhexidine or chlortetracycline (cloxacillin or erythromycin if systemic toxicity present)

Note: Wherever amoxycillin is suggested in Table I, ampicillin can be used.

Table II. Situations in which antibacterial prophylaxis is of benefit (or in common use).

SURGICAL
Cardiac valve replacement;
Abdominal surgery (involving abdominal aorta or groin incision);
Amputation (especially of an ischaemic leg);
Incision through nasal, oral, or pharyngeal mucosa;
Oesophagus, stomach, duodenum, colon, rectum, appendix, or biliary tract surgery;
Ruptured viscus;
Caesarean section;
Hysterectomy (especially vaginal);
Abortion;
Joint replacement;
Open fractures;
Severe soft tissue trauma;
Trauma with CSF leakage;
Craniotomy involving prosthetic material implantation.
NON-SURGICAL
For prevention of infection in 'contacts' of meningitis caused by <i>N. meningitidis</i> or <i>H. influenzae</i> type b;
For prevention of recurrence of rheumatic fever;
For prevention of tuberculosis in susceptible close contacts;
For prevention of endocarditis in patients (with cardiac valve disease, prosthetic valve, septal defect, or patent ductus) who are undergoing procedures that might cause bacteraemia.

Table III. Clinically more important interactions of antibacterials with other drugs.

Drug A	Drug B	Result of interaction
Aminoglycosides	Loop diuretics	↑ risk of ototoxicity
	Cisplatin Amphoterecin Vancomycin Cephalothin NSAIDs	↑ risk of nephrotoxicity
Cephaloridine Cephalothin	Aminoglycosides Loop diuretics (large doses) Vancomycin	↑ risk of nephrotoxicity, especially in old persons
Chloramphenicol	Phenytoin Sulphonylureas Alcohol	↑ plasma concentration of B
Ciprofloxacin Norfloxacin	Antacids Oral iron Sucralfate	↓ gastrointestinal absorption of A
Doxycycline	Phenytoin Carbamazepine Phenobarbitone Primidone	↓ plasma concentration of A
Erythromycin	Theophylline	↑ plasma concentration of B
Metronidazole	Alcohol	Disulfiram-like reaction
	Oral anticoagulants	↓ metabolism of B
Penicillins Cephalosporins	Probenecid	↑ plasma concentration of A
Rifampicin	Antacids	↓ gastrointestinal absorption of A
	Oral contraceptives	↑ metabolism of B (risk of pregnancy)
	Oral anticoagulants Quinidine Theophylline Propranolol Sulphonylureas Corticosteroids	↑ metabolism of B
Tetracyclines	Antacids Sucralfate Oral iron Calcium Bismuth	↓ gastrointestinal absorption of A

Note: ↑ = increased; ↓ = decreased.

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