Part I: Policy and economic issues	Part II: Pharmaceutical management	Part III: Management support system
	Selection	
	Procurement	
	Distribution	
	Use	
	27 Managing for rational medicine use	
	28 Investigating medicine use	
	29 Promoting rational prescribing	
	30 Ensuring good dispensing practices	
	31 Community-based participation and initiatives	
	32 Drug seller initiatives	
	33 Encouraging appropriate medicine use by consumers	
	34 Medicine and therapeutics information	
	35 Pharmacovigilance	

### CHAPTER 27

Maı	naging for rational med	licine	use	
Summar	ry 27.2	ILLUSTRA	TIONS	
27.1 De	efinition of rational medicine use 27.2		The medicine-use process 27.3	
	27.2 Examples of irrational medicine use 27.3 Polypharmacy • No medicine needed • Wrong		Factors influencing prescribing 27.7 What countries are doing to promote the rational use of medicines 27.8	
medicines • Ineffective medicines and medicines with doubtful efficacy • Unsafe medicines • Underuse of		C	Framework for improving medicine use 27.10	
	ailable effective medicines • Incorrect use of medicines	BOXES Box 27-1		
	27.3 Adverse impact of irrational medicine use 27.5 Impact on quality of medicine therapy and medical care •		Antimicrobial resistance global prevalence rates: 2000–2003 data 27.6	
Impact on quanty of meaterne metapy and meater tare  Impact on antimicrobial resistance • Impact on cost • Psychosocial impact		Box 27-2	Intervention strategies to improve medicine use 27.9	
,	7.4 Factors underlying irrational use of medicines at		Core strategies to promote rational use of	
various levels of the health system 27.6 Health system • Prescriber • Dispenser • Patient and community		Box 27-4	medicines 27.12 Useful organizations and websites on rational medicine use and antimicrobial resistance 27.14	
27.5 Stı	rategies to improve medicine use 27.9			
27.6 De	eveloping a strategy 27.10	COUNTRY STUDIES		
Step 1. Identify the problem and recognize the need for action • Step 2. Identify underlying causes and motivating factors • Step 3. List possible interventions • Step 4. Assess resources available for action • Step 5. Choose an intervention or interventions to test • Step 6. Monitor the impact and restructure the intervention		CS 27-1 CS 27-2	Overuse of therapeutic injections 27.4  The practices of dispensing prescribers in  Zimbabwe 27.8	
		CS 27-3	Building a national drug policy to improve the rational use of medicines: assessing implementation in Lao P.D.R. 27.11	
1		CS 27-4	Chile's efforts to combat the overuse of	
Glossary			antimicrobials 27.11	
	ent guide 27.15			
Reference	ces and further readings 27.15			

### SUMMARY

This chapter defines rational medicine use and gives examples of irrational medicine use and the adverse effects that can result. It considers some of the factors underlying irrational medicine use and possible strategies to address the problem.

Rational use of medicines requires that "patients receive medications appropriate to their clinical needs, in doses that meet their individual requirements, for an adequate period of time, and at the lowest cost to them and their community" (WHO 1985).

Irrational medicine use occurs with polypharmacy (when more than one medicine is used unnecessarily), with the use of wrong or ineffective medicines, or with underuse or incorrect use of effective medicines. These actions negatively affect the quality of medicine therapy, raise health care costs, and may cause adverse reactions or negative psychosocial effects.

Prescriber lack of knowledge and experience is only one factor in irrational medicine use. Other underlying factors can affect the dispensing process, patient or community decisions and use, and the health system itself.

Strategies to address irrational medicine use can be characterized as educational, managerial, economic, or regulatory. Whichever method is selected, a successful intervention is likely to focus on key factors, target facilities with the poorest practices, and use credible sources

and communication channels. Personal contact (face-to-face meetings, for example) can sometimes be used to convey a limited number of key messages; these can be repeated and clarified using a variety of media.

When implementing an intervention strategy, the logical steps are to—

- Identify the problem
- Understand the underlying causes
- List possible interventions
- Assess available resources
- Choose an intervention
- Monitor and restructure the activity as necessary

Interventions should be based on an understanding of the cause of the problem and focus on active strategies to change behavior. Experience indicates that the most effective interventions are those that—

- Identify key influence factors
- Target individuals or groups with the worst practices
- Use credible information sources
- Use credible communication channels
- Use personal contact whenever possible
- Limit the number of messages
- Repeat key messages using a variety of methods
- Provide better medicine use alternatives to existing practices

### 27.1 Definition of rational medicine use

The aim of any pharmaceutical management system is to deliver the correct medicine to the patient who needs that medicine. The steps of appropriate selection, procurement, and distribution are necessary precursors to the rational use of medicines.

The Conference of Experts on the Rational Use of Drugs, convened by the World Health Organization (WHO) in Nairobi in 1985, defined rational use as follows: "The rational use of drugs requires that patients receive medications 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." Depending on the context, however, many factors influence what is considered rational. It may be rational, for example, for a drug seller to sell antibiotics without a prescription to earn enough income to survive.

This book uses the term *rational medicine use* in a biomedical context that includes the following criteria—

- Appropriate indication—that is, prescribing is based on sound medical considerations
- Appropriate medicine, considering efficacy, safety, suitability for the patient, and cost
- Appropriate dosage, administration, and duration of treatment
- Appropriate patient—that is, no contraindications exist, and the likelihood of adverse reactions is minimal
- Correct dispensing, including appropriate information for patients about the prescribed medicines
- Patient adherence to treatment

To conform to these criteria, prescribers should follow a standard process of prescribing, which starts with a diagnosis to define the problem that requires treatment. Next, the therapeutic goal should be defined. The prescriber must decide which treatment is required, based on up-to-date information on medicines and therapeutics, to achieve the desired goal for an individual patient. When the decision

is made to treat the patient with medicines, the best drug for the patient is selected based on efficacy, safety, suitability, and cost. Then dose, route of administration, and duration of treatment are determined, taking into account the condition of the patient. When prescribing a medicine, the prescriber should provide proper information to the patient about both the medicine and the patient's condition. Finally, the prescriber should decide how to monitor the treatment, after considering the probable therapeutic and adverse effects of treatment.

Next, the medicine should be dispensed to the patient in a safe and hygienic manner, making sure that the patient understands the dosage and course of therapy; then the patient takes the medicine. Adherence occurs if the patient (and the community) understands and appreciates the value of using specific medicines for specific indications (see Figure 27-1 on the medicine use process).

### 27.2 Examples of irrational medicine use

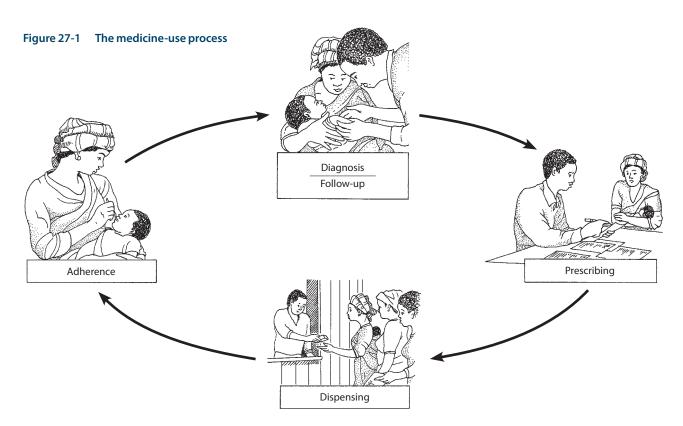
Irrational medicine use occurs in all countries and in all settings for health care—from hospitals to homes. It involves cases in which no medicine is needed but is prescribed; cases in which the wrong medicines, or ineffective or unsafe medicines, are prescribed or dispensed; cases in which effective and available medicines are not used; and those in which medicines are used incorrectly by patients.

### **Polypharmacy**

Polypharmacy occurs when patients use more medicines than are necessary; for example, a patient with an upper respiratory infection receiving prescriptions for antibiotics, cough remedies, analgesics, and multivitamins. Use of too many medicines may be a particular problem with prescribers who also dispense medicines, especially when they have a financial incentive; for example, dispensing prescribers in Zimbabwe tended to prescribe a medicine for every symptom reported by the patient, resulting in their prescribing more antibiotics, cough syrups, mixtures, and analgesics per patient than nondispensing prescribers (Trap and Hansen 2003). Polypharmacy is usually judged by measuring the average number of medicines per prescription.

### No medicine needed

Many times, medications may be used unnecessarily. Use of medicines when none is needed involves many nontherapeutic uses. For example, in many countries—both developed and developing—the majority of children suffering from minor upper respiratory infections are treated with antibiotics, which are not needed. Overuse of antibiotics is not a problem limited to developing countries. France, for example, uses over three times more antibiotics per patient in primary care than does the Netherlands (Goossens et al. 2005).



### Wrong medicines

For various reasons, the wrong medicine may be prescribed and dispensed. Data from developing and transitional countries indicate that less than 40 percent of patients are treated according to standard treatment guidelines (WHO 2010). In some countries, for example, many children with acute diarrhea are indiscriminately prescribed and dispensed unnecessary and ineffective antimicrobials or antidiarrheals, instead of the recommended oral rehydration therapy (ORT). Also, because of spreading antimicrobial resistance (AMR), a medicine that was once efficacious may now be the wrong treatment choice; for example, chloroquine was once standard first-line treatment for malaria, but it is now largely ineffective in many areas of Asia, South America, and East Africa.

### Ineffective medicines and medicines with doubtful efficacy

Medicines that are ineffective are sometimes given to patients because of common practice or because the patient thinks that the more medicines prescribed, the better. Excessive and unnecessary use of multivitamin preparations or tonics is an example of this prescribing pattern. A review of prescription quality at a pharmacy in India showed that in one week, 40 percent of prescriptions included multivitamin or tonic preparations (Patel et al. 2005).

#### **Unsafe medicines**

The likelihood of adverse reactions outweighs the therapeutic effects when unsafe medicines are prescribed. A common

### **Country Study 27-1** Overuse of therapeutic injections

Poor injection practices, especially in developing countries, include the prescription of unnecessary injections and the reuse of equipment without sterilization. Unsafe injections increase the risk of transmitting hepatitis B and C, HIV, and a number of other bloodborne pathogens. Although usage studies have shown a gradual trend toward lessened use of injections, progress still remains to be made in certain geographic areas—especially countries in the Middle East and Southeast Asia.

**Egypt.** In a household survey of 4,197 people in two regions of Egypt, more than 26 percent reported having received an injection in the previous three months. Overall, respondents reported receiving an average of 4.2 injections per year. Of those who had recently received an injection, 8 percent reported that the providers did not take the syringe from a sealed packet. Respondents reported receiving injections from public- and privatesector physicians, pharmacists, barbers, doctor's assistants, housekeepers, relatives, and friends (Talaat et al. 2003).

Mongolia. The Ministry of Health in Mongolia collected information on injection practices through interviews and observations of a sample of prescribers, injection providers, and members of the population. The sixtyfive members of the population reported receiving an average of thirteen injections per year. All twenty health care facilities surveyed used single-use injection devices, but almost 30 percent of the providers admitted reusing infusion bottles. Observations of practices showed other

breaks in infection-control procedure. Even with the high rate of injections, 90 percent of the prescribers and 49 percent of the population were aware of the potential risk of HIV transmission through unsafe injections (Logez et al. 2004).

Pakistan. A study of 198 adult patients in Karachi collected information on injection practices using a questionnaire about respondents' last interaction with a health care provider. It revealed that nearly one-half (49 percent) of respondents had been given an injection during their last visit; 91 percent of respondents reported that the doctor always recommended an injection; and 83 percent of respondents believed injections to be more powerful than alternatives. When treatments were equally effective, 83 percent of respondents preferred alternatives (pills or advice) to injections. Respondents reported that the nature of their complaint did not affect the likelihood of injection, and 30 percent had received ten or more injections in the previous year (Raglow et al. 2008).

Interventions to decrease the number of unnecessary injections and improve injection practices have shown that-

- Better communication between patients and providers can reduce injection overuse
- Increased access to single-use injection devices improves injection safety
- Managerial approaches (that is, restricting access to selected unnecessary and dangerous injectable medicines) can improve injection practices

example is the use of anabolic steroids for growth or appetite stimulation in children or athletes.

#### Underuse of available effective medicines

Several studies have shown that ORT was prescribed for only a small proportion of children with acute diarrhea. Regrettably, the underuse of effective oral rehydration therapy for acute diarrhea in children still occurs in many countries.

A large, multicountry survey conducted for WHO found that many people with serious mental disorders were not receiving any treatment, despite the availability of effective medicines. In developed countries, up to one-half of serious cases were untreated, while in less developed countries the figure was up to 85 percent (Demyttenaere et al. 2004).

### Incorrect use of medicines

A frequent incorrect use of medicines is giving a patient only one or two days' supply of antibiotics rather than the full course of therapy. Patients may also take only as much medicine as needed to feel better, then save the remainder for a future illness; in addition, patients often self-medicate, using antibiotics or other prescription-only medicines bought from untrained drug sellers in retail drug outlets. Another common example of irrational use is overusing injectable preparations when using oral preparations would be easier and safer. This often occurs because prescribers and patients believe that injections are more efficacious than pills (see Country Study 27-1).

### 27.3 Adverse impact of irrational medicine use

The inappropriate use of medicines on a wide scale can have significant adverse effects on health care costs and the quality of drug therapy and medical care, as well as being a primary contributor to the spread of antimicrobial resistance. Other negative effects are the increased likelihood of adverse drug reactions and encouraging patients' inappropriate reliance on medicines.

### Impact on quality of medicine therapy and medical care

Inappropriate prescribing practices can, directly or indirectly, jeopardize the quality of patient care and negatively influence the outcome of treatment. The underuse of ORT for acute diarrhea, for instance, can hinder the goal of treatment: namely, to prevent or treat dehydration and thus prevent death in children. Widespread ORT use has resulted in significant reductions in childhood death from diarrhea in the last twenty-five years; however, improvements could



still be made, as diarrhea remains the second-leading cause of mortality among children (WHO/UNICEF 2009).

The likelihood of adverse drug reactions increases when medicines are prescribed unnecessarily (see Chapter 35 on pharmacovigilance for a full discussion of the effects of adverse drug reactions and events). An overdosage of gentamicin, for example, can lead to permanent hearing problems. Misuse of injectable products raises the risk of transmitting HIV/AIDS, hepatitis B and C, and other bloodborne diseases.

### Impact on antimicrobial resistance

A chronic use or underdosage of antibiotics and chemotherapeutic agents can contribute to the rapid emergence of resistant strains of bacteria or the malaria parasite. Health gains stemming from the discovery of antimicrobial agents are in jeopardy because of the spread of microbes that are resistant to inexpensive first-choice, or first-line, medicines. Resistance to antimicrobials is a natural biological phenomenon that can be amplified by a variety of factors, including human practices. The use of an antimicrobial in any dose and over any time period forces microbes to either adapt or die; the microbes that adapt and survive carry genes for resistance, which can be passed on. The bacterial infections in which microbial resistance is most evident are diarrheal diseases, respiratory tract infections, meningitis, sexually transmitted infections, tuberculosis, and hospital-acquired infections. The development of drug-resistant malaria and tuberculosis is of particular concern, as is the emergence of resistance to anti-HIV drugs. Box 27-1 lists the global prevalence rates of AMR for several infections.

When infections become resistant to first-line antimicrobials, treatment must be switched to second- or third-line medicines, which are almost always more expensive and sometimes more toxic. In many countries, the

### Box 27-1 Antimicrobial resistance global prevalence rates: 2000–2003 data

Malaria: Chloroquine resistance in 81/92 countries

**Tuberculosis:** 0–17% Primary multidrug resistance

HIV/AIDS: 0–25% Primary resistance to at least one antiretroviral drug

**Gonorrhea:** 5–98% Penicillin resistance in *Neisseria gonorrhoeae* 

**Pneumonia and bacterial meningitis:** 0–70% Penicillin resistance in *Streptococcus pneumoniae* 

**Shigellosis:** 10–90% Ampicillin resistance; 5–95% co-trimoxazole resistance

**Hospital infections:** 0–70% Resistance of *Staphylococcus aureus* to all penicillins and cephalosporins Source: Holloway 2005.

high cost of these replacement medicines is prohibitive, meaning that some diseases can no longer be treated in areas where resistance to first-line medicines is widespread. The economic cost of antimicrobial resistance in the European community is estimated to be 9 billion euros per year (SCORE 2004). Most alarming of all are diseases for which resistance is developing to virtually all available medicines.

### Impact on cost

Overuse or incorrect use of medicines, even essential ones, causes both patients and the health care system to spend excessively on pharmaceuticals and waste financial resources. For example, in Nepal, up to half of total medicine costs in one study were related to inappropriate prescribing (Holloway et al. 2001). In many places, people buy medicines out-of-pocket—particularly antimalarials—and spending money on irrational treatment can dramatically affect household expenditure, especially in the poorest homes (Breman et al. 2006).

In many countries, expenditures on nonessential pharmaceutical products, such as multivitamins or cough mixtures, drain limited financial resources that could otherwise be allocated for more essential and vital products, such as vaccines or antibiotics. Inappropriate underuse of medicines at an early stage of a disease may also produce excess costs by increasing the probability of prolonged disease and eventual hospitalization.

As an example of the global impact of irrational medicine use on costs, the switch to artemisinin-based combination

therapies (ACTs) for malaria from ineffective antimalarials has had an enormous effect on the cost of malaria control. Estimates indicate that the additional annual costs of ACT range from 300 million U.S. dollars (USD) to USD 500 million globally, which does not include the resources required to strengthen health systems to effectively deliver ACTs, including the costs of improving pharmaceutical regulations, pharmacovigilance, diagnostics, and implementing different medicine policies for different population groups (Arrow et al. 2004).

### Psychosocial impact

Overprescribing encourages patients to believe that they need medications for any and all conditions, even trivial ones. The concept that there is a pill for every ill is harmful. Patients come to rely on medicines, and this reliance increases the demand for them. Patients may demand unnecessary injections because during years of exposure to modern health services, they have become accustomed to having practitioners administer injections. Studies have also shown that patient demands and expectations can lead prescribers to prescribe unnecessary antibiotics for viral infections.

# 27.4 Factors underlying irrational use of medicines at various levels of the health system

Many interrelated factors influence medicine use (see Figure 27-2). The health system, prescriber, dispenser, patient, and community are all involved in the therapeutic process, and all can contribute to irrational use in a variety of ways.

### Health system

Factors affecting the health system include unreliable supply, medicine shortages, expired medicines, and availability of inappropriate medicines, including substandard and counterfeit products. Such inefficiencies in the system lead to a lack of confidence in the system by the prescriber and the patient. The patient demands treatment, and the prescriber feels obliged to give what is available, even if the medicine is not the correct one to treat the condition. Financial incentives inherent in a health system can promote better use; for example, Kyrgyzstan implemented an outpatient drug benefit program that based prescription reimbursements on the use of standard treatment guidelines and generics (Kadyrova et al. 2004).

A government can show its commitment to rational medicine use by implementing key policies and regulations and by providing resources for rational-medicine-use programs and research (Figure 27-3). For example, less

than one-third of low- and middle-income countries have either national AMR strategies or national AMR task forces (WHO/TCM 2006). In addition, health systems that fail to implement policies on standard treatment guidelines, essential medicines lists, and medicine formularies are missing out on well-proven methods to increase the rational use of medicines.

### Prescriber

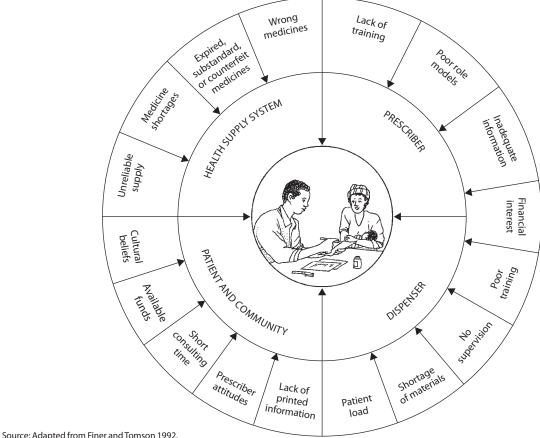
The prescriber can be affected by internal and external factors. He or she may have received inadequate training either preservice or in-service, or his or her prescribing practices may have become outdated because of a lack of continuing education and a poor supervisory system. Prescribing role models who are imitated may not prescribe rationally. Objective information on medicines may be lacking, and the information provided by supplier representatives may be unreliable. Temptation can be strong to generalize inappropriately about the effectiveness or side effects of medicines on the basis of limited personal experience. Externally, a heavy patient load and pressure to prescribe from peers, patients, and pharmaceutical company representatives all

complicate prescribing decisions. In India, doctors often prescribe ineffective tonics because many patients believe in them and will not return to a doctor who will not prescribe them, which impinges on the doctor's livelihood. Finally, profit may affect a prescriber's choice if the prescriber's income is dependent on medicine sales. Country Study 27-2 describes the prescribing practices of doctors who also dispense medicines.

### Dispenser

The dispenser plays a crucial role in the therapeutic process. Dispensing quality may be affected by the training and supervision the dispenser has received and the medicine information available to the dispenser. A shortage of dispensing materials and short dispensing time caused by a heavy patient load may also have an adverse impact on dispensing. As with prescribers, dispensers, especially private drug sellers, may have a financial incentive to dispense irrationally. In addition, in some countries, drug sellers in retail outlets are rarely trained and there is little to no structure for monitoring or supervision. Finally, the low status of dispensers affects the quality of dispensing.





Drug use audit in last 2 years National strategy to contain AMR Public education in last 2 years Independent CME for prescribers DTCs in most referral hospitals Information center for prescribers EML for insurance reimbursement STGs updated in last 5 years EML updated in last 5 years 0 10 20 30 40 50 60 70 80 90 100 Percentage of countries implementing policies to promote rational use

What countries are doing to promote the rational use of medicines

 $AMR = antimicrobial\ resistance; CME = continuing\ medical\ education; DTCs = drug\ and\ therapeutics\ committees; EML = essential\ medicines\ list;\ STGs = standard$ treatment guidelines

Source: Holloway 2005.

### Patient and community

The individual's adherence to prescribed treatment is influenced by many factors, including cultural beliefs, the communication skills and attitudes of the prescriber and dispenser, the limited time available for consulting, the shortage of printed information, the affordability of treatment, and community beliefs about the efficacy of certain medicines or routes of administration. For example, patients may believe that injections are more powerful than capsules, or that capsules are more effective than tablets. In addition, many individuals practice selfmedication, selecting and using medications on their own

for recognized illnesses. Self-medication often leads to irrational use and may include either over-the-counter or prescription medicines.

It is clear that, although the prescriber's knowledge and experience are important aspects influencing the use of medicines, they are not the only ones. As discussed above, there are many causes for irrational medicine use and many factors involved in the decision-making process.

These factors vary for each person and situation. Therefore, specific interventions to improve prescribing may work in some circumstances but not in others. Because of the complexity of factors involved, any single intervention is unlikely to work in every situation.

### **Country Study 27-2** The practices of dispensing prescribers in Zimbabwe

A study of twenty-nine randomly chosen private-sector dispensing doctors and twenty-eight private-sector nondispensing doctors in Harare investigated differences in prescribing practices. Data on prescribing for upper respiratory tract infections were collected from patient records and evaluated by a panel of experts based on standard treatment guidelines and the WHO/ International Network for the Rational Use of Drugs (INRUD) rational drug-use indicators.

Results of the study showed major differences between the prescribing habits of dispensing and nondispensing physicians. Dispensing doctors prescribed significantly more medicines (35 percent more), antibiotics (33 percent more), and mixtures (72 percent more) per patient. The more symptoms reported by the patient, the more medicines he or she received. In addition, dispensing doctors prescribed three times more injections, and they prescribed subcurative doses of antibiotics almost 20 percent of the time.

Source: Trap and Hansen 2003.

### 27.5 Strategies to improve medicine use

Before attempting to change medicine use, the scale of the problem should be assessed and quantified. The underlying reasons for the problem behavior then need to be investigated. Quantitative and qualitative methods for assessing medicine use are described in Chapter 28. It is a mistake to intervene before understanding the reasons for a problem behavior.

Several choices exist for interventions to change medicine-use practices. These approaches can be characterized as educational, managerial, economic, or regulatory (see Box 27-2). Whichever approach is used, interventions should focus on specific problem behaviors and should target prescribers, dispensers, facilities, or the public, depending on where the assessment shows the problems lie. A single intervention rarely results in sustainable changes, so a combined strategy is preferred. Figure 27-4 shows a framework for improving uses.

Possible interventions for prescribers, such as training, accessing unbiased information, and using opinion leaders, are described in Chapter 29. After prescribing has been addressed, the next stage of medicine use is dispensing. This crucial aspect of the provider-patient relationship is often

neglected or delegated to an untrained person. Chapter 30 describes ways to ensure good dispensing. The final stage of medicine use is when the patient takes the medicine. The patient is more likely to take medicines as advised if he or she understands how to take the medicine and if there is general community awareness of rational medicine use. Developing informational materials for patients and planning public education campaigns requires an understanding of cultural norms, values, and practices. These issues as well as those surrounding patient adherence are covered in Chapter 33.

Whatever problem is being addressed, health care providers and consumers need impartial drug and therapeutics information. Such information can serve as the basis for standard treatment guidelines or therapeutic standards. Information can be made available actively through drug bulletins or in a largely passive manner through drug information centers. However, in a 2003 survey, less than half of all countries—no matter what income level—had independent national drug information services for prescribers, dispensers, or consumers (WHO/TCM 2006). Medicine information is covered in Chapter 34.

No matter which point in the medicine-use process becomes the focus of an intervention strategy, there are

## Box 27-2 Intervention strategies to improve medicine use

### **Educational strategies**

Training of prescribers

- Formal education (preservice)
- Continuing education (in-service)
- · Supervisory visits
- · Group lectures, seminars, and workshops

#### Printed materials

- Clinical literature and newsletters
- Treatment guidelines and medicine formularies
- Illustrated materials (flyers, leaflets)

### Approaches based on face-to-face contact

- · Educational outreach
- Patient education
- · Influencing opinion leaders

### Managerial strategies

Monitoring, supervising, and feedback

- Hospital drug and therapeutics committees
- District health teams
- Government inspectorate
- Professional organizations
- · Self-assessment

Selection, procurement, and distribution

- Limited procurement lists
- Drug use review and feedback
- Hospital and regional drug committees
- Cost information

### Prescribing and dispensing approaches

- Structured medicine order forms
- Standard diagnostic and treatment guidelines
- Course-of-therapy packaging

### **Economic strategies**

- Price setting
- Capitation-based budgeting
- Reimbursement and user fees
- Insurance

### Regulatory strategies

- Medicines registration
- Limited medicine lists
- Prescribing restrictions
- Dispensing restrictions

 $Source: Adapted from \ Quick, Laing, and \ Ross-Degnan\ 1991.$ 

Health Facilities | Laboratories | Pharmacies | Drug Shops | Communities | Households **Providers** Systems **End users** Public Prescribers **Patients** Private Dispensers Caregivers Technicians Strategies to improve use Education | formal and informal training Management | guided decision making Regulation | standards enforcement and accreditation Economic | cost sharing and incentives/disincentives (selected examples)

Figure 27-4 Framework for improving medicine use

Source: CPM/MSH 2011.

common characteristics of effective interventions. These interventions—

*Identify key influence factors.* Use qualitative methods to understand why a person behaves in a certain way, and identify influences that can promote and prevent change. *Target individuals or groups with the worst practices.* For the greatest impact, focus on these individuals or facilities.

*Use credible information sources.* Involve influential, respected authorities and ensure that resource materials are well referenced and authoritative.

*Use credible communication channels.* Enhance the message and acceptability of its content by communicating through existing, credible channels.

*Use personal contact whenever possible.* Communicate key messages most effectively with face-to-face individual or small-group meetings.

*Limit the number of messages.* Improve understanding by confining the intervention to a few key messages.

Repeat key messages using a variety of media. People learn in different ways—some learn visually from text or graphics, some learn through spoken messages, and some learn through a combination of media. Help reinforce key messages by repeating them using a variety of approaches.

Provide better alternatives. Whenever possible, give a positive message that encourages people to do something. Negative messages tend to alienate people. With an emphasis on the positive, the negative behavior can be excluded. For example, a positive message: DO treat diarrhea with ORT. Antidiarrheals are not necessary.

### 27.6 Developing a strategy

Six steps to follow in developing a strategy to promote rational medicine use are described below.

### Step 1. Identify the problem and recognize the need for action

Within the facility, district, or country, a consensus must exist about the most important problems in medicine use. Recognition of the primary problems may come as a result of an indicator survey or drug use review, a disaster in which patients have been adversely affected, or an economic analysis of medicine expenditures. An effective response can be planned only after all the involved parties, including prescribers, patients, and health service managers, recognize that a problem exists. If an influential prescriber or politician refuses to accept that a specific problem exists, it will be very difficult to intervene effectively. Thus, compiling the evidence that clearly details the scope of the problem, establishing a consensus that action is needed, and securing support from all interested parties are important tasks. Country Study 27-3 shows how the Lao People's Democratic Republic approached the implementation of a national medicine policy to improve rational use.

### Step 2. Identify underlying causes and motivating factors

As described in Section 27.4, many factors contribute to the irrational use of medicines. These factors must be investigated and understood before intervening. If this step has not been taken, the intervention is likely to fail. For example, a campaign to promote the use of generic medicines by hanging up posters in a health clinic will fail if the underlying reason for the lack of use is that the doctors do not know the generic names of the medicines. Also, a prescriber who is allowed to dispense and earn money from medication sales is going to be motivated to prescribe (and sell) more medicines and more expensive medicines, including brand-name products.

### **Country Study 27-3**

### Building a national drug policy to improve the rational use of medicines: Assessing implementation in Lao P.D.R.

The National Drug Policy (NDP) of Laos was created in 1993 to improve the quality and use of medicines through developing drug legislation, quality control, guidelines, training, inspections, and health systems research. Since 1995, Lao P.D.R.'s National Drug Policy program has implemented the NDP through a pilot intervention program in five provinces. In each province in the assessment (pilot and control), four pharmacies at public hospitals and twenty private pharmacies were randomly selected.

The intervention comprised a number of activities in both the public and private sectors, including training private drug sellers and inspectors, developing standard treatment guidelines and indicators for rational medicine use, establishing drug and therapeutics committees, and implementing outreach to the general public on rational medicine-use concepts.

To measure the intervention outcome, researchers analyzed 110 prescriptions for children under five with simple diarrhea and 240 adult outpatient prescriptions based on twenty-nine indicators; in addition, twelve health care managers were interviewed on knowledge and attitudes. The results of the analysis showed that—

- Health care managers in the pilot province had better knowledge of NDP concepts.
- Significantly more essential medicines were available in the private pharmacies in the pilot province.
- The proportion of prescriptions of essential medicines in hospitals was higher in the pilot province (95 percent compared with 86 percent; p < 0.001).
- The management of simple diarrhea in children in the pilot province was significantly more likely to follow standard treatment guidelines.
- Fewer drugs were prescribed per patient in the pilot province (2.7 compared with 3.3; p < 0.001).

In conclusion, the pilot province performed significantly better in several aspects of rational medicine use. This operational research provided evidence to help the Lao Ministry of Health tailor the development and implementation of a national drug policy to its own context.

Source: Paphassarang et al. 2004.

### **Country Study 27-4** Chile's efforts to combat the overuse of antimicrobials

In 1998, a study showing an alarming trend of increased sales and use of antibiotics in Chile was submitted to the Ministry of Health. The findings showed that in the previous ten years, sales of amoxicilline and oral fluoroquinolones had increased almost 500 percent, and sales of oral cephalosporins had increased more than 300 percent. Ministry of Health officials met with a number of stakeholders, including representatives from scientific and professional associations, the pharmaceutical regulatory agency, and consumer groups, to jointly develop a strategy to address the issue.

In September 1999, with stakeholder support, the Ministry of Health instituted measures to control the use of antibiotics by making them available only through pharmacists and only by prescription. The new policy was backed up with the distribution of

informational leaflets, posters, and widespread media coverage.

Three months later, an evaluation of sales and use pre- and postintervention showed that consumption of amoxicilline had decreased by 36 percent, consumption of ampicillin had decreased by 56 percent, and consumption of erythromycin had decreased by 30 percent between the last quarter of 1998 and the last quarter of 1999. In addition, expenditures on antimicrobials in private pharmacies dropped by USD 6.5 million.

Chile's experience has shown that political commitment, stakeholder cooperation, and public education can be combined to save money and reduce the irrational use of antibiotics.

Source: Bavestrello and Cabello 2000.

### Box 27-3 Core strategies to promote rational use of medicines

Evidence suggests that the following core policies, strategies, and interventions promote more rational use of medicines.

**Establishing a mandated multidisciplinary national body to coordinate medicine-use policies.** Ensuring rational medicine use requires many activities that need coordination among many stakeholders. Therefore, a national body is necessary to coordinate strategies and policy at the national level, in both the public and private sectors. This body should involve government, health professions, academia, the pharmaceutical industry, consumer groups, and the national regulatory authority.

Implementing procedures for developing, using, and revising standard treatment guidelines. Standard treatment guidelines (STGs) (or clinical guidelines or prescribing policies) are systematically developed statements to help prescribers make decisions about appropriate treatments for specific clinical conditions. STGs are made more credible through the use of evidence-based recommendations. They vary in complexity from simple algorithms to detailed protocols on diagnostic criteria, patient advice, and costs.

Implementing procedures for developing and revising an essential medicines list (or hospital formulary) based on treatments of choice. An essential medicines list makes pharmaceutical management easier at all levels: procurement, storage, and distribution are easier with fewer items, and prescribing and dispensing are easier for professionals. A national essential medicines list should be based on national STGs, and both should be revised regularly.

Establishing a drug and therapeutics committee in districts and hospitals, with defined responsibilities for monitoring and promoting rational use of medicines.

This committee, also called a pharmacy and therapeutics committee, is responsible for ensuring the safe and effective use of medicines in the facility or area under its jurisdiction. The committee should operate independently, and members should represent all the major medical specialties and the administration. The primary tasks of the committee are to develop and revise institutional STGs (based on national guidelines) and to maintain an institutional essential medicines list or formulary.

Using problem-based training in pharmacotherapy based on national STGs in undergraduate curricula.

The quality of basic pharmacotherapy training for undergraduate medical and paramedical students can

significantly influence future prescribing habits. Training is most successful when it is problem based, concentrates on common conditions, takes into account students' level of knowledge, and is targeted to their future prescribing requirements. In most settings, rather than focusing on basic science, problem-solving skills should be promoted and interdisciplinary problem-based learning encouraged. If the existing focus is not on problem-based training in pharmacotherapeutics, national consultative workshops may help build awareness of the value of the approach.

Continuing in-service medical education as a licensure requirement and targeted educational programs by professional societies, universities, and the government. Unlike in developed countries, opportunities for continuing medical education in less developed countries are limited because continuing education is not required for licensure. Governments should support efforts by university departments and national professional associations to offer independent, unbiased continuing medical education courses to health professionals, including medicine dispensers. The most effective in-service training is likely to be problem based, repeated on multiple occasions, focused on practical skills, and linked to STGs.

Developing a strategic approach to improve prescribing in the private sector through regulation and collaborations with professional associations. Most efforts in improving use of medicines have focused on the public sector, but the private sector often provides greater access to pharmaceuticals. Changing practices in the private sector requires an understanding of the motivations of private prescribers. A range of strategies should be considered to improve rational medicine use, including licensing regulations with appropriate enforcement, accreditation and continuing education through professional associations, and financial incentives.

Monitoring, supervision, and using group processes to promote rational medicine use. Supervision that is supportive, educational, and face-to-face will be more effective with prescribers than inspection and punishment. Effective forms of supervision include prescription audit and feedback, peer review, and group processes of self-identifying medicine-use problems and solutions in a group of prescribing professionals. Group process interventions with practitioners and patients to improve prescribing practices have been effectively used to change prescribing behavior.

Training pharmacists and drug sellers to offer useful advice to consumers, and supplying independent medicine information. In many countries with shortages of trained health professionals, pharmacies and medicine shops are a major source of information for consumers. Interventions have shown that the skills of untrained prescribers and dispensers can be upgraded. In addition, sometimes the only information about medicines that prescribers receive is from the pharmaceutical industry, which may be biased. Pharmaceutical information centers and drug bulletins are two useful ways to disseminate independent, unbiased information. They may be administered by the government, a university teaching hospital, or a nongovernmental organization, under the supervision of a health professional.

Encouraging involvement of consumer organizations, and devoting government resources to public education about medicines. Governments have a responsibility to ensure the quality of information about medicines available to consumers. Without sufficient knowledge about the risks and benefits of medicine use, people will often fail to achieve their expected clinical outcomes and may even suffer adverse effects. Regulation of consumer advertising and promotion by pharmaceutical

companies, as well as public education activities led by consumer organizations, may influence medicine use by the public.

Avoiding perverse financial incentives. Financial incentives may strongly promote rational or irrational use of medicines. Examples include the ability of prescribers to earn money from medicine sales; flat prescription fees that lead to overprescription; and dispensing fees that are calculated as a percentage of the cost of medicines, which encourages the sale of expensive medicines.

Ensuring sufficient government expenditure and enforced regulation. Appropriate regulation of the activities of all those involved in the use of medicines is critical to ensure rational medicine use. For regulations to be effective, they must be enforced, and the regulatory authority must be sufficiently funded and backed by the government's judiciary. Without sufficient competent personnel and finances, none of the core components of a national program to promote rational use of medicines can be carried out.

Sources: WHO 2002; Laing et al. 2001.

### Step 3. List possible interventions

Educational, managerial, economic, and regulatory interventions can be used to address the problem of irrational use (see Chapter 29 for details). Whenever possible, a combination or sequence of interventions should be used, and there should be evidence that the interventions are effective in similar settings. As seen in Country Study 27-4, the government of Chile changed its regulations to restrict sales of antimicrobials to prescription only in the private sector, and supported the legal measure with a public and professional education and media campaign.

### Step 4. Assess resources available for action

When deciding which intervention or combination of interventions to test, it is important to take stock of what resources are available. The most important limiting resource is usually human. Ask the following questions: Who will implement the intervention? Will that person have enough time to work on the intervention? Try to identify groups or individuals who would support the intervention. For example, manufacturers of generic medicines would support an intervention to popularize generics. Financial, transport, and material resources also need to be assessed.

### Step 5. Choose an intervention or interventions to test

Factors to consider when choosing an intervention include the effectiveness with which it addresses the underlying causes of the problem; its previous success rate in similar situations, areas, or countries; its cost; and whether it can be sustained with available resources. Whichever intervention is chosen, it must be tested before widespread implementation. Again, if feasible, a strategy that combines a mix of interventions will be more effective and sustainable.

### Step 6. Monitor the impact and restructure the intervention

During testing of the intervention, it is important to monitor related medicine use in order to evaluate the intervention's efficacy or unexpected and negative effect; for example, an intervention aimed at banning antidiarrheals may lead to an increased use of antibiotics. On completion of the intervention, evaluate the results to decide whether it should be expanded to involve a larger population. An intervention's effectiveness in a small area with a limited number of people does not guarantee widespread

Box 27-3 has a list of core strategies to promote the rational use of medicines.

The remaining chapters in this section address the task of improving medicine use. All these chapters should be reviewed before planning an intervention. In addition, Box 27-4 lists useful organizations and their websites, which provide further information on specific related topics.

### Glossary

Adherence to treatment (also compliance): The degree to which patients adhere to medical advice and take medicines as directed. Adherence depends not only on the patient's acceptance of information about the health threat but also on the practitioner's ability to persuade the patient that the treatment is worthwhile and on the patient's perception of the practitioner's credibility, empathy, interest, and concern.

**Antimicrobial resistance:** A biological phenomenon where, as part of the natural selection process, microbes mutate and develop drug-resistant genes that can be passed on. Antimicrobial resistance can be amplified or accelerated by human behaviors, including the irrational use of medicines.

**Clinical pharmacist:** An individual trained in pharmacy, usually with the minimum of a bachelor's degree, who has had special-

ized training in the uses, side effects, contraindications, and dosages of medications for human use.

Clinical pharmacologist: A physician who has had specialized training in the uses, side effects, contraindications, and dosages of medications for human use.

**Course-of-therapy prepackaging:** Prepackaging of medicines in sealed plastic bags, each bag containing a complete course of treatment, as established by standard treatment guidelines. The package usually contains a complete label with instructions for use.

**Dispense:** To prepare and distribute to a patient a course of therapy on the basis of a prescription.

**Dispenser:** A general term for anyone who dispenses medicines. Also specifically used to mean an individual who is not a graduate pharmacist but who is trained to dispense medications, maintain stock records, and assist in procurement activities.

**Generic substitution:** Dispensing of a product that is generically equivalent to the prescribed product, with the same active ingredients in the same dosage form, and identical in strength, concentration, and route of administration.

**Irrational prescribing:** Prescribing that does not conform to good standards of treatment—for example, extravagant prescribing, overprescribing, incorrect prescribing, multiple prescribing, or underprescribing of medications.

### Box 27-4 Useful organizations and websites on rational medicine use and antimicrobial resistance

APUA (Alliance for the Prudent Use of Antibiotics) http://www.tufts.edu/med/apua

BUBL Catalogue of Internet Resources—Infectious Diseases

http://bubl.ac.uk/link/i/infectiousdiseases.htm

EARSS (European Antimicrobial Resistance Surveillance System)

http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/Pages/index.aspx

Essentialdrugs.org

http://www.essentialdrugs.org

Infectious Disease News

RDUCD.htm

http://www.infectiousdiseasenews.com

International Conference on Improving Use of Medicines (ICIUM 2011, ICIUM 2004, and ICIUM 1997) http://www.icium.org

International Network for the Rational Use of Drugs http://www.inrud.org

International Society for Infectious Diseases http://www.isid.org

Promoting Rational Drug Use: A CD-ROM Training Program http://archives.who.int/PRDUC2004/RDUCD/

Réseau Médicaments et Développement (Network of Medicines and Development) http://www.remed.org

Therapeutics Initiative http://www.ti.ubc.ca

United Kingdom Health Protection Agency ("Infectious Diseases")

http://www.hpa.org.uk/Topics/InfectiousDiseases

United Nations Children's Fund-United Nations
Development Fund-World Bank-World Health
Organization Special Programme for Research and
Training in Tropical Diseases
http://www.who.int/tdr

U.S. Centers for Disease Control and Prevention ("Drug Resistance") http://www.cdc.gov/drugresistance

World Health Organization ("Drug Resistance") http://www.who.int/topics/drug\_resistance/en

World Health Organization ("Essential Medicines and Pharmaceutical Policies")
http://www.who.int/medicines/en

World Health Organization ("Infectious Diseases") http://www.who.int/topics/infectious\_diseases/en

### **ASSESSMENT GUIDE**

- Have studies been done to identify possible problems with rational medicines use? In the country? In the province? In the facility?
- If problems have been identified, what might be some of the underlying causes in the health system? With prescribers? With dispensers? With the public?
- Does the country have a national medicine policy or policies in place to promote rational medicine use, such as national standard treatment guidelines or an essential medicines list? Are there any regulations that seek to control medicine use? For example, restricting the sales of antibiotics to prescription only?
- Does the government have any campaigns to promote rational use in the public?

- Do prescribers follow a standard process of prescribing and monitoring treatment?
- What unbiased resources are available to prescribers regarding information on pharmaceuticals?
- At each level of the health care system, who is responsible for dispensing medicines? Are prescribers allowed to dispense medicines?
- Are injections a preferable way to deliver medicines with prescribers? With the public?
- Has an assessment been done to evaluate the level of antimicrobial resistance in the country?
- Have any interventions been designed and carried out to improve rational medicine use? What were the results? Were the results shared with other stakeholders?

Labeling: Placing written or symbolic instructions on the container in which medicine is dispensed to the patient.

Medicine use: The process of diagnosis, prescribing, labeling, packaging, and dispensing and of adherence to medicine treatment by patients.

**Pharmacology:** The study of medicines and their actions.

Polypharmacy: The practice of using too many medicines per patient.

**Prescribing:** The act of determining which medication the patient should have and writing the dosage, frequency, and duration of treatment on a form.

Self-medication: The selection and use of medicines by individuals to treat self-recognized symptoms.

Standard treatment guidelines: Agreed-upon treatment practices for a diagnosed illness; may include more than details of medicine treatment.

Symbolic labeling: A system of providing written instructions for patients, using sketches or other graphic representations.

Therapeutic substitution: Interchange of one drug product with another that differs in composition but is considered to have similar pharmacologic and therapeutic activities, in accordance with written protocols previously established and approved.

### References and further readings

 $\star$  = Key readings.

Arrow, K. J., C. B. Panosian, and H. Gellband, eds. 2004. Saving Lives, Buying Time: Economics of Malaria Drugs in an Age of Resistance. Washington, D.C.: National Academy Press for Institute of Medicine.

Bavestrello, L., and A. Cabello. 2000. How Chile Tackled Overuse of Antimicrobials. Essential Drugs Monitor 28/29:13-4. <a href="http://apps.">http://apps.</a> who.int/medicinedocs/pdf/s2248e/s2248e.pdf>

Breman, J. G., A. Mills, R. W. Snow, J. Mulligan, C. Lengeler, K. Mendis, B. Sharp, et al. 2006. Conquering Malaria. In Disease Control Priorities in Developing Countries, 2nd ed, D.T. Jamison, J. G. Breman, A. R. Measham, and G. Alleyne, eds. Washington, D.C.: Disease Control Priorities Project.<a href="http://files.dcp2.org/pdf/">http://files.dcp2.org/pdf/</a> DCP/DCPFM.pdf>

CPM/MSH (Center for Pharmaceutical Management/Management Sciences for Health). 2011. Center for Pharmaceutical Management: Technical Frameworks, Approaches, and Results. Arlington, Va.:

Demyttenaere, K., R. Bruffaerts, J. Posada-Villa, I. Gasquet, V. Kovess, J. P. Lepine, M. C. Angermeyer, et al. 2004. Prevalence, Severity, and Unmet Need for Treatment of Mental Disorders in the World Health Organization World Mental Health Surveys. Journal of the American Medical Association 291(21):2581-90.

Finer, D., and G. Tomson, eds. 1992. Essential Drug Information: The Story of a Workshop. Stockholm: Karolinska Institutet.

Goossens, H., M. Ferech, R. Vander Stichele, and M. Elseviers for the ESAC Project Group. 2005. Outpatient Antibiotic Use in Europe and Association with Resistance: A Cross-National Database Study. The Lancet 365:579-87.

Hogerzeil, H., V. Bimo, D. Ross-Degnan, R. O. Laing, D. Ofori-Adjei, B. Santoso, A. K. Azad Chowdhury, et al. 1993. Field Tests for Rational Drug Use in Twelve Developing Countries. Lancet 342:1408-10.

Holloway, K. A. 2005. "Rational Use of Drugs: An Overview." Paper presented at the WHO/UNICEF Technical Briefing Seminar on Essential Medicines Policies, September 18-22, Geneva. <a href="http://">http://</a> archives.who.int/tbs/tbs2005/holloway.ppt>

Holloway, K. A., B. R. Gautam, and B. C. Reeves. 2001. The Effects of Different Kinds of User Fee on Prescribing Costs in Rural Nepal. Health Policy and Planning 16:421-7.

Hutin Y. J. F., A. M. Hauri, and G. L. Armstrong. 2003. Use of Injections in Healthcare Settings Worldwide, 2000: Literature Review and Regional Estimates. BMJ 37(7423):1075-8.

INRUD (International Network for Rational Use of Drugs) Bibliography. No date. <a href="http://www.inrud.org/Bibliographies/">http://www.inrud.org/Bibliographies/</a> INRUD-Bibliography.cfm>

A searchable annotated database of published and unpublished articles, books reports, and other documents focusing on rational use of medicines, mainly in developing countries. Updated every six months.

- Institute of Medicine. 2003. The Resistance Phenomenon in Microbes and Infectious Disease Vectors: Implications for Human Health and Strategies for Containment: Workshop Summary. Washington, D.C.: National Academies Press. <a href="http://www.nap.edu/openbook.php?record\_id=10651&page=1">http://www.nap.edu/openbook.php?record\_id=10651&page=1</a>
- Kadyrova, N., B. Waning, and C. Cashin. 2004. "Kyrgyzstan Outpatient Drug (OPD) Benefit Program: Use of Automated Claims Data to Evaluate the Impact of the OPD Benefit Program on Rational Drug Prescribing by Physicians and Generic Drug Use by Patients." Paper presented at ICIUM 2004 Conference, March 30–April 2, Chiang Mai, Thailand.
- Kardas, P. 2002. Patient Compliance with Antibiotic Treatment for Respiratory Tract Infections. *Journal of Antimicrobial Chemotherapy* 49(6):897–903.
- ★ Laing, R., H. V. Hogerzeil, and D. Ross-Degnan. 2001. Ten Recommendations to Improve the Use of Medicines in Developing Countries. *Health Policy and Planning* 16(1):13–20.
- Logez, S., G. Soyolgerel, R. Fields, S. Luby, and Y. Hutin. 2004. Rapid Assessment of Injection Practices in Mongolia. *American Journal of Infection Control* 32(1):31–7.
- Paphassarang, C., R. Wahlström, B. Phoummalaysith, B. Boupha, and G. Tomson. 2004. "Building the National Drug Policy on Evidence: Assessing Implementation in Lao P.D.R." Presented at ICIUM 2004 Conference, March 30–April 2, Chiang Mai, Thailand. <a href="http://www.icium.org/icium2004/resources/ppt/AC092.ppt">http://www.icium.org/icium2004/resources/ppt/AC092.ppt</a>
- Patel, V., R. Vaidya, D. Naik, and P. Borker. 2005. Irrational Drug Use in India: A Prescription Survey from Goa. *Journal of Postgraduate Medicine* 51(1):9–12.
- Quick, J. D., R. O. Laing, and D. Ross-Degnan. 1991. Intervention Research to Promote Clinically Effective and Economically Efficient Use of Pharmaceuticals: The International Network for Rational Use of Drugs. *Journal of Clinical Epidemiology* 44(Suppl. 2):57–65.
- Radyowijati, A., and H. Haak. 2003. Improving Antibiotic Use in Low-Income Countries: An Overview of Evidence on Determinants. Social Science and Medicine 57(4):733–44.
- Raglow, G. J., S. P. Luby, and N. Nabi. 2008. Therapeutic Injections in Pakistan: From the Patients' Perspective. *Tropical Medicine and International Health* 6(1):69–75. <a href="http://www3.interscience.wiley.com/cgi-bin/fulltext/118999307/PDFSTART">http://www3.interscience.wiley.com/cgi-bin/fulltext/118999307/PDFSTART</a>
- ★ Ross-Degnan, D., R. O. Laing, J. D. Quick, H. M. Ali, D. Ofori-Adjei, L. Salako, and B. Santoso. 1992. A Strategy for Improved Pharmaceutical Use: The International Network for Rational Use of Drugs. Social Science and Medicine 35:1329–41.
- SCORE (Strategic Council on Resistance in Europe). 2004. *Resistance:* A Sensitive Issue. Utrecht: SCORE.
- Soumerai, S. B., S. Majumdar, and H. L. Lipton. 2005. "Evaluating and Improving Physician Prescribing." In *Pharmacoepidemiology*, 4th ed., B. Strom, ed. Chichester, England: John Wiley & Sons.
- Stevenson, F. A., N. Britten, C. A. Barry, C. P. Bradley, and N. Barber. 2002. Perceptions of Legitimacy: The Influence on Medicine Taking and Prescribing. *Health* 6(1):85–104.

- Talaat, M., S. el-Oun, A. Kandeel, W. Abu-Rabei, C. Bodenschatz, A. L. Lohiniva, Z. Hallaj, and F. J. Mahoney. 2003. Overview of Injection Practices in Two Governorates in Egypt. *Tropical Medicine and International Health* 8(3):234–41.
- Trap, B., and E. H. Hansen. 2003. Dispensing Prescribers—A Threat to Appropriate Medicines Use? Essential Drugs Monitor 32:9.
- ★ Whyte, S. R., S. van der Geest, and A. Hardon. 2003. Social Lives of Medicines. Cambridge: Cambridge University Press.
- ★ WHO (World Health Organization). 2010. Medicines: Rational Use of Medicines. Fact Sheet No. 338. Geneva: WHO. <a href="http://www.who.int/mediacentre/factsheets/fs338/en/">http://www.who.int/mediacentre/factsheets/fs338/en/</a>
- ★ \_\_\_\_\_\_. 2007. Progress in the Rational Use of Medicines. Geneva: WHO. <a href="http://apps.who.int/gb/ebwha/pdf\_files/WHA60/A60\_24-en.pdf">http://apps.who.int/gb/ebwha/pdf\_files/WHA60/A60\_24-en.pdf</a>
- 2005. Containing Antimicrobial Resistance. Geneva: WHO. <a href="http://www.who.int/medicines/publications/policyperspectives/">http://www.who.int/medicines/publications/policyperspectives/</a> ppm\_10\_en.pdf>
- ——. 2004. Safety of Injections: Global Facts and Figures. Geneva: WHO. <a href="http://www.who.int/injection\_safety/about/resources/en/FactAndFiguresInjectionSafety.pdf">http://www.who.int/injection\_safety/about/resources/en/FactAndFiguresInjectionSafety.pdf</a>
- ——. 2001. WHO Global Strategy for Containment of Antimicrobial Resistance. Geneva: WHO. <a href="http://apps.who.int/medicinedocs/index/assoc/s16343e/s16343e.pdf">http://apps.who.int/medicinedocs/index/assoc/s16343e/s16343e.pdf</a>
- ——. 1985. The Rational Use of Drugs: A Review of the Major Issues. Report of the Conference of Experts, November 22–29, Nairobi, Kenya. <a href="http://whqlibdoc.who.int/hq/1985-86/WHO\_CONRAD\_WP\_RI.pdf">http://whqlibdoc.who.int/hq/1985-86/WHO\_CONRAD\_WP\_RI.pdf</a>
- ★ WHO and FIP (World Health Organization and International Pharmaceutical Federation). 2006. *Developing Pharmacy Practice: A Focus on Patient Care*. Geneva: WHO and FIP. <a href="http://www.who.int/medicines/publications/WHO\_PSM\_PAR\_2006.5.pdf">http://www.who.int/medicines/publications/WHO\_PSM\_PAR\_2006.5.pdf</a>
- WHO/TCM (World Health Organization/Technical Cooperation for Essential Drugs and Traditional Medicine). 2009. Medicines Use in Primary Care in Developing and Transitional Countries: Fact Book Summarizing Results from Studies Reported Between 1990 and 2006. Geneva: WHO. <a href="http://whqlibdoc.who.int/hq/2009/WHO\_EMP\_MAR\_2009.3\_eng.pdf">http://whqlibdoc.who.int/hq/2009/WHO\_EMP\_MAR\_2009.3\_eng.pdf</a>
- . 2006. Using Indicators to Measure Country Pharmaceutical Situations: Fact Book on WHO Level I and Level II Monitoring Indicators. Geneva: WHO. <a href="http://apps.who.int/medicinedocs/documents/s14101e/s14101e.pdf">http://apps.who.int/medicinedocs/documents/s14101e/s14101e.pdf</a>
- WHO/UNICEF (World Health Organization/United Nations Children's Fund). 2009. *Diarrhoea: Why Children Are Still Dying and What Can Be Done*. Geneva: WHO/UNICEF. <a href="http://whqlibdoc.who.int/publications/2009/9789241598415\_eng.pdf">http://whqlibdoc.who.int/publications/2009/9789241598415\_eng.pdf</a>