Cultural and Economic Factors That (Mis)Shape Antibiotic Use: The Nonpharmacologic Basis of Therapeutics

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The use of antibiotics in both ambulatory and inpatient settings is heavily shaped by cultural and economic factors as well as by microbiological considerations. These nonpharmacologic factors are relevant to clinicians and policymakers because of the clinical and fiscal toll of inappropriate antibiotic prescribing, including excessive use, preventable adverse effects, and the increasing prevalence of resistant organisms. An understanding of the determinants of antibiotic consumption is critical to explain current patterns of use and to devise programs to reduce inappropriate use. Patient motivations include the desire for a tangible product of the clinical encounter coupled with incorrect perceptions of the effectiveness of antibiotics, particularly in viral infections. Physician behavior can be explained by such factors as lack of information, a desire to satisfy patient demand, and pressure from managed care organizations to speed throughput. Marketing campaigns directed at both physicians and patients further serve to increase demand, especially for newer, costlier products. Studies of antibiotic use patterns in inpatient and outpatient care consistently demonstrate considerable inappropriate prescribing, which is likely to exacerbate the emergence of resistant organisms.

Several approaches have been shown to improve the rationality of antibiotic use. Computer-based algorithms or reminders can prompt physicians to improve antibiotic choices at the time of prescribing; paper-based order entry forms can achieve the same goal. Interactive educational outreach ("academic detailing") is a practical implementation of social marketing principles to improve antibiotic use. Public education programs directed at consumers can help to reduce the inappropriate patient demand that helps to drive much improper antibiotic prescribing.

Ann Intern Med. 2000;133:128-135.
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Since the dawn of therapeutics, the prescribing of medications and their use by patients has been marked by substantial variability in both rationality and effectiveness. Drug use historically has reflected the highest principles of science as well as strikingly irrational behavior. This heterogeneity has been particularly vivid in the case of antibiotics. Antibiotics are among the most commonly used therapeutic agents, accounting for 12% of ambulatory care prescriptions (1). Their use ranges from treatment of minor self-limited outpatient symptoms to potentially fatal conditions in critically ill patients. Antibiotics loom large economically as well, accounting for approximately 15% of the nearly $100 billion in annual medication expenditures in the United States (2).

Because of their role in treating infections, antibiotics tap into some of our most deeply held beliefs about bodily integrity and invasion. Furthermore, other than certain vaccines, antibiotics are the only drug class whose use influences not just the patient being treated but the entire ecosystem in which he or she lives, with potentially profound consequences. The determinants of antibiotic use and misuse are thus of particular importance. They include factors as diverse as the physician–patient relationship, clinical microbiology, health economics, and the most basic definitions of illness and therapy (3).

Factors Leading to Antibiotic Misuse

In their psychosocial dimension, medications can have properties that transcend pharmacology and may take center stage in some clinical situations. Social scientists and wise clinicians have long been aware that providing a patient with a drug is an interpersonal as well as a biochemical intervention (4); this is particularly true of antibiotics. The writing of a prescription signifies that the physician has made a diagnosis and that treatment is possible. A prescription officially (and tangibly) assigns the patient to the sick role, with all of its benefits and responsibilities (5). It can also act as a termination strategy for an office visit, a sign that the visit has been consummated, the encounter is complete, and it is time for the patient to move on. This strategy creates a paradoxical outcome in the current environment, which is so preoccupied with throughput. A prescription for an antibiotic is often seen as the quickest way to end the visit of a patient with possible infectious symptoms. The number of patients seen per hour is increasing, and such "increased productivity" is frequently commended in the same management memorandum that criticizes out-of-control drug expenditures. Ironically, managers' desire to reduce the use of diagnostic tests (cultures) and prevent return visits also creates pressures that favor heavy antibiotic use.

Through the alchemy of the pharmacy, the paper pre-

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scription and its inscrutable ritualistic writings are transformed into a container of tablets or capsules. In a real sense, the drug prescription prolongs the physician–patient encounter by enabling the patient to ingest a "dose of the doctor" several times a day. As Sir William Osler noted, "The desire to ingest medicines is one of the principal features which distinguish man from the animals" (6).

This perspective helps to explain the "drug hunger" that many symptomatic patients bring to the physician visit, in which they feel satisfied only by receiving a prescription (7). Such demands are not based on clinical data as we know it (8–10). Patient expectations have been further intensified by the advent of direct-to-consumer advertising of antibiotics by pharmaceutical manufacturers. Unlike the situation of depression, incontinence, or impotence, for which undertreatment is common, no logic exists for increasing the public's demand for antibiotics. These advertisements serve primarily to persuade patients to demand newer, more costly antibiotics in clinical situations in which older, generic products, or no drug at all, would often work just as well. They are skillfully constructed to promote the ease or effectiveness of the target product and, of course, do not mention cost or note the similar effects of older therapies (11).

Two trends have intensified the effect of direct-to-consumer promotion of antibiotics. First, the credibility of many once-respected sources of authority is waning, taking a toll on physicians' professional sovereignty (12, 13). Related to this trend is the parallel rise of consumer activism; worried that their health maintenance organization will deny them needed therapy to reduce expenditures, patients demand treatments that they fear might otherwise be withheld. Taken together, these trends turn therapeutic decision making into more of a dialogue (at best) or a tug-of-war (at worst) between patient and physician, a phenomenon that would have been unthinkable a generation ago. Add to this a growing if belated concern over patient satisfaction, the drive to shorten outpatient encounters as much as possible, and aggressive marketing directed at physicians, and the stage is set for the demand and receipt of astoundingly large quantities of unnecessary antibiotics. Viewed in this context, it is not surprising that the small voice of therapeutic restraint and concern about microbial resistance is so difficult to hear above the din.

The movement favoring adoption of clinical guidelines for rational antibiotic use often runs headlong into the pressures on the primary care physician as the proprietor of a small business, just trying to get through the day and satisfy his or her customers. For example, in focus groups designed to reveal physicians' knowledge about, attitudes toward, and motivations for prescribing, some clinicians presented with clinical vignettes that were constructed to sound compellingly viral in cause still favored use of antibiotics to improve symptoms and reduce the likelihood of superinfection (14). However, a larger group argued that even if antibiotics were not indicated, they often felt obliged to prescribe them because of patient demand. This problem is still more acute in the developing world, although a full discussion is beyond the scope of this paper.

In the inpatient setting, a different set of forces conspires to encourage excessive antibiotic use. In teaching hospitals, prescribing decisions frequently are made by those with the least clinical experience (interns and residents); at the same time, each year hospitalized patients become more acutely ill and their cases increasingly complex. These factors, combined with the ubiquitous pressure to keep length of stays short (the inpatient equivalent of the shrinking office visit), make it difficult to pursue a course of watchful waiting in managing a fever of unknown origin. Such temperance is particularly difficult if the prescribing physician has been in practice for only a few months. The first priority becomes the prevention of disaster within the next 24 hours, a goal often thought to be met best by broad-spectrum antibiotics or a cacophony of narrower-spectrum agents used in combination.

Evidence for Antibiotic Misuse

The perspective outlined above helps explain why analyses of antibiotic use patterns have consistently documented that prescribing is suboptimal (15). Many randomized, placebo-controlled trials of acute bronchitis, cough, and upper respiratory illnesses have found that outcomes are no better in typical patients taking antibiotics than in those given placebo (8–10). However, of the 51 million visits for "colds," upper respiratory tract infections, and bronchitis in the United States in one recent year, 50% to 66% culminated in an antibiotic prescription (16, 17). Clinical factors often seem to play a minor role in antibiotic decision making in these illnesses. Diagnostic uncertainty also plays a role; a recent study of patients with sore throats found that two thirds of antibiotic prescriptions were written for patients whose cultures came back negative (18). A large current survey of antibiotic use in treating infectious symptoms in children revealed widespread disregard of commonly recommended diagnostic strategies and therapeutic guidelines and frequent overuse of antibiotics in upper respiratory tract infections (65%) (19). Several patient demographic factors have been found to increase the likelihood that antibiotics will be prescribed. These include being female, young, and white and living in a rural area (15). In the developing world, social and economic factors as well as suboptimal drug use have driven the emergence and spread of multidrug-resistant tuberculosis (20).

In hospitalized patients, incorrect dosing or poor choice of drug occurs often. In a study performed at one teaching hospital (21), we found that physicians usually ordered inappropriate doses or intervals for clindamycin, metronidazole, and cefazolin. At another large hospital, antibiotic prophylaxis before surgery was found to be correctly timed in only 40% of cases (22). At the same institution, physicians did not respond correctly to 25% of instances in which culture and sensitivity data were available (23).

Overuse of such antibiotics as vancomycin raises concern about the emergence of resistant organisms as well as cost. One recent study found that only 40% of orders at several hospitals were compatible with Centers for Disease Control and Prevention (CDC) guidelines (24). Overuse of vancomycin is probably an important factor in the spread of resistance (25); during a period when vancomycin use was rapidly increasing, resistance rates increased from 0.8% to 4.0% (26).

Antibiotic Resistance and Costs

The total costs associated with antibiotics come from multiple sources: medication, adverse events, and the often hidden cost of antimicrobial resistance (2). Adverse events occur in a small proportion of antibiotic courses, but because of the frequency of antibiotic use, they accounted for 23% of all adverse events recorded at one hospital (27). Many of these adverse effects are minor, such as rashes, diarrhea, or candidiasis, although serious skin eruptions and renal insufficiency also occur. The cost of such adverse events is considerable. In contrast, the true cost of antimicrobial resistance is very difficult to estimate. A recent Office of Technology Assessment report suggested that the extra hospital costs associated with drug-resistant hospital-acquired bacterial infections in the United States is at least $1.3 billion annually (28).

Antimicrobial resistance has emerged in many different human pathogens, and the rates of resistance have increased (26). At least 6 studies have suggested that rates of invasive infections with drug-resistant *Streptococcus pneumoniae* are related to recent antibiotic exposure (29–34); as a result, a working group of the CDC is focusing attention on the judicious use of antibiotics to help combat such resistance (35). Much evidence suggests that reduced use of antibiotics can decrease the prevalence of resistant organisms; one review cited at least 16 studies that demonstrated a temporal relation between decreased use of antibiotics and reduced rates of emergence of resistant organisms (36). More recent data also support the principle that curbing antibiotic use can reduce rates of infection with resistant organisms (37).

Improving Antibiotic Use

Several methods for improving the precision of antibiotic prescribing have been tested. One intervention, which did not prove effective, targeted residents' use of antibiotics in the ambulatory setting by simply placing a chart with antibiotic use guidelines on every physician's desk (38). This passive educational method was also found to have little impact on improving practice in other situations (39). However, when antibiotic guidelines are made interactive through computer technology, the effects can be more substantial. One computer-based system assesses whether specific courses of antibiotic therapy are potentially inappropriate on the basis of microbiological sensitivity data for a given patient (23). The system generates an alert and an individual consultation if the organism isolated is resistant to the antibiotic, if sensitivity tests are not performed properly, or if antibiotics are not being administered and an organism had been isolated. Sixty percent of the alerts proved to be clinically appropriate, and one third of these prompted a therapeutic change.

The same investigators also tested a computer-based "antibiotic consultant" (40) that allowed a physician to enter information about the patient and the potential site of infection. An algorithm predicted the most likely pathogens and displayed five antibiotic regimens likely to be effective. These regimens were appropriate choices for cultured organisms in 94% of isolates, and physician acceptance of the program was high. Another computer-based program at the same institution presented local consensus guidelines for antibiotic use in a decision-support system for surgical prophylaxis, empiric antibiotic treatment, and specific organisms (22). Orders were continuously surveyed by the computer system, and alerts were generated for orders that did not fall within guidelines. The timing and number of antibiotic doses for surgical prophylaxis improved, and the rate of adverse events attributed to antibiotics decreased. Over 7 years, antibiotic use decreased by 23% and antibiotic costs by 50%.

Similarly, Shojania and colleagues (24) developed a system in which the CDC recommendations for vancomycin use were presented each time this drug was ordered on a hospital's computer-based order entry system. Physicians could not proceed with the order unless they provided the reason for vancomycin use (however, they could enter "other" and override the guidelines). Compared with controls, physcians who were randomly assigned to receive the intervention wrote 32% fewer orders for vancomycin. Appropriateness of the orders was not formally investigated. In a setting without such a computerized system, administrative changes succeeded in reducing inappropriate vancomycin use from 70% of courses to 40% (41).

Several paper-based programs have likewise improved antibiotic prescribing. Our group developed a structured educational order form for antibiotics that addressed appropriate dosing of clindamycin, cefazolin, and metronidazole (21). The order forms contained targeted educational messages and suggested pharmacokinetically correct dosing regimens. Before the intervention, pharmacokinetically incorrect dosing was common; several drugs with long half-lives were given unnecessarily frequently. Immediately after the intervention, incorrect dosing accounted for less than 6% of all orders for these three antibiotics. Another group used a structured order form and found an overall reduction in broad-spectrum antibiotic use (42).

"Academic detailing," a person-to-person approach to educational outreach developed in our group in the early 1980s, has also proven to be useful in improving behavior in various prescribing situations, including antibiotic use (14). Academic detailing is a program of one-on-one education provided by a pharmacist or physician who is trained to provide evidence-based prescribing information to clinicians in a user-friendly, interactive educational encounter. It was modeled in part on pharmaceutical manufacturer marketing programs, which are effective in changing practice but exist solely to increase sales of a given company's product. The concept of academic detailing was born of the belief that evidence-based prescribing could be enhanced if the sophisticated techniques of communication and behavior change used by the pharmaceutical industry could be used to promote rational drug use (14). This has proven to be the case and has been particularly useful in improving antibiotic use.

The academic detailing presentation, which lasts 5 to 20 minutes, makes use of several behavior change strategies that reinforce and complement one another. First, utilization data are reviewed to identify areas of problematic prescribing. Next, focus groups identify prescribers' baseline attitudes and knowledge. The clinical literature is then reviewed to distill the essential evidence. In the physician's office, the educator makes a concise, practice-relevant, one-on-one interactive presentation rooted in clinical data; it is accompanied by brief, well-designed print materials with engaging graphical support that present the preferred alternative prescribing strategy. Detailers are selected for their personal communication skills and their knowledge of a given clinical area.

We studied the effectiveness of academic detailing initially in a randomized, controlled trial of 435 physicians in four states. The study was designed to reduce excessive use of several medications, including cephalexin (14). Clinicians assigned to the intervention arm reduced use of the targeted medications by 14%, with comparable reductions in medication expenses; a formal benefit–cost analysis found that the program saved twice as much as it cost (43).

In a similar study, Ray and colleagues (44) used one-on-one education to target two inappropriate antibiotic prescribing practices: antibiotics contraindicated in young children and excessive use of oral cephalosporins. Physicians visited by the physician counselor had a 30% reduction in problematic antibiotic prescribing that persisted for 2 years. This approach has been shown to be both feasible and cost-effective in settings ranging from typical office practices in rural and urban areas to tertiary care centers. Several examples of approaches that have successfully improved antibiotic use are presented in **Table 1** (3, 45).

Prospects for the Future

In the coming years, economic pressures to contain expenditures for pharmaceuticals may act to contain use of some costly new antibiotics (such as the quinolones) but will have a negligible effect on the pervasive overuse of

Table 1. **Examples of Previous Antibiotic Improvement Interventions**

Intervention	Author, Year (Reference)	Description*	Result
Traditional education	Faryna et al., 1987 (38)	Printed antibiotic use guidelines placed in the offices of physicians in training	No significant improvement
Structured antibiotic order forms	Echols and Kowalsky, 1984 (42)	Antibiotic order forms requiring a specific indication and with automatic discontinuation after 48 hours	Significant reduction in the number and duration of antibiotic courses
	Avorn et al., 1988 (21)	Antibiotic order forms with educational messages and dosing guidelines	Marked improvement in dosing
Computer-based system	Pestotnik et al., 1990 (23)	Computerized monitoring of susceptibility patterns and antibiotic orders prompting one-on-one consultation	20% of alerts resulted in an alteration in antibiotic orders
	Evans et al., 1994 (40)	Computerized "antibiotic consultant" suggests antibiotic regimens on the basis of clinical information supplied by the physician	Proposed regimens covered isolates in a high percentage of patients
	Pestotnik et al., 1996 (22)	Computer-based local antibiotic guidelines embedded in a decision-support system	Antibiotic use and costs were reduced
	Shojania et al., 1998 (24)	Embedded the Centers for Disease Control and Prevention guidelines on use of vancomycin in a computer-based order entry system	Significantly reduced vancomycin orders
Academic detailing	Avorn and Soumerai, 1983 (14)	Trained pharmacists educated physicians who were intensive cephalexin prescribers	Significantly reduced targeted prescriptions and costs
	Ray et al., 1985 (44)	Trained physicians, detailers, and pharmacists visited physicians with a history of inappropriate antibiotic prescribing	Inappropriate antibiotic use was significantly reduced
Combined	Gonzales et al., 1999 (47)	Combined patient and physician education using prescribing profiles and academic detailing	Significantly reduced antibiotic use for acute bronchitis

* See text for further description of intervention types.

older, inexpensive products. However, the preceding analysis suggests that there may be cause for guarded optimism. Growing professional and public awareness of the threat posed by multidrug-resistant organisms, punctuated by predictable episodes of "superbug" crises that will continue to appear, may increase the likelihood of the acceptance by prescribers and patients of a set of more rational attitudes toward antibiotic use. This in turn may result in a reduction in the rate of increase in bacterial resistance.

Public Awareness

The past few years have seen a gratifying proliferation of noncommercial materials prepared to educate physicians and lay persons about the importance of rational antibiotic use. The CDC has developed a series of materials for patients as part of its "Judicious Use of Antibiotics" program. Several projects are under way to test the best means of disseminating such information to the public. In addition, the Alliance for Prudent Use of Antibiotics has been active in producing informational materials on this topic for both patients and physicians. Internet addresses for several sources of such information are presented in **Table 2**.

Because patient pressure for antibiotic overuse is a product of contemporary culture, improvement will require a sea change in cultural views. Dramatic though this may sound, evidence indicates that such a change may be occurring. Preoccupation with ridding the body of infectious invaders may be replaced by a concern about the harm that excessive use of antibiotics can cause oneself as well as the ecosystem as a whole. Such attitude shifts have occurred before, for example, in the public's beliefs about tobacco use and saturated fat consumption.

The case to be made about antibiotics is more complex, because they can be life-saving as well as hazardous. Nonetheless, given enough time and attention to public education, messages about proper antibiotic use can transform expectations. If it is successful, such an educational program could shift patient attitudes from "I can't believe my doctor wouldn't give me an antibiotic!" to "Can you believe how sloppy that doctor was? He tried to prescribe an antibiotic for my cold even though I had no signs of a bacterial infection!"

It is less clear how much impact will result from arguments about the need to defend the community's flora against the emergence of resistance. Fortunately, enough motivations relate to the patient's own well-being, including the desire to avoid such common side effects as rash and diarrhea; the recognition that any cost and risk are unacceptable if the expected benefit is zero (as in treating viral infections); and the acknowledgment that unwanted organisms may infect not only one's neighbor, but also oneself (for example, candidal vaginitis or *Clostridium* *difficile* colitis). With more health care delivered each year through larger organizational structures, there will be ample opportunity for health maintenance organizations, other insurers, state Medicaid programs, the federal Medicare program, and the Veterans Administration to communicate actively with their patient populations about these issues.

Alterations in Physician Practice

Most current efforts of managed care organizations or hospitals to change physician prescribing behavior focus on reducing pharmaceutical expenditures rather than promoting appropriate prescribing. Given the availability of information systems that track every detail of a physician's prescribing behavior and can increasingly be linked to clinical data, more can be done to improve prescribing. In the coming decade, it will become possible to assess physician prescribing in terms not merely of dollars spent but of clinical intelligence. Overuse of costly antibiotics attracts notice and perhaps reprimand, whereas massive overuse of amoxicillin or trimethoprim–sulfamethoxazole often attracts no notice at all. Health care systems will need to establish surveillance systems and quality standards that consider the biological as well as the economical dimension of antibiotic misuse. Detailed data management systems will make it possible to target which physicians might need further education about rational antibiotic use. Some of that education will also be delivered through such information systems themselves, by means of computer-based feedback at the time of prescribing.

Even in the absence of sophisticated databases, physicians can immediately put into practice some simple, inexpensive, and quick approaches to improving use of antibiotics. It is increasingly easy to gain access through electronic or print media to evidence-based recommendations on antibiotic use (**Table 2**). Good patient education material is also easy to access from many Web sites; it can be downloaded, printed, and given to the patient as a kind of "un-prescription." In this case, the "dose of the doctor" is a dose of knowledge rather than a drug. Simultaneously, a preprinted prescription recommending simple, safe over-the-counter remedies for symptomatic relief of fever or congestion (for example, acetaminophen or decongestants) can help the patient feel comfortable that some pharmacologic therapy is being recommended by the physician to treat their symptoms. Finally, it takes only minutes to explain to a patient that this approach will result in equally rapid symptom relief, less risk for side effects, much lower cost, and avoidance of the creation of "superbugs" in one's own body. Such a program will not satisfy every patient, but as part of a concerted approach throughout the health care system, it will work in many cases. It is also a practical way to raise the standard of discourse between physician and patient about this important topic (46).

The ongoing battle between host and microbe has continued for millennia, and neither side is likely to score a definitive victory in the coming decade. One of the most important arenas for this struggle is the medical culture in which we and our patients live, and one of the most important battlegrounds, is the clinician–patient encounter; in many respects, these are the front lines of the fight. As in most wars, this is also where victory is most likely to be achieved or allowed to slip away.

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Table 2. **Physician and Patient Resources Promoting Rational Antibiotic Prescribing***

Focus	Organization (Web Site)	Content
Physician/patient	Centers for Disease Control and Prevention, Atlanta, GA (www.cdc.org)	"Judicious Use of Antibiotics" program contains information on appropriate antibiotic use
Physician/patient	National Institute of Allergy and Infectious Diseases, Bethesda, MD (www.niaid.nih.gov/factsheets/antimicro.htm)	Antimicrobial Resistance Fact Sheet
Physician/patient	Alliance for the Prudent Use of Antibiotics, Boston, MA (www.healthsci.tufts.edu/apua)	Educational materials with links to a network of antibiotic resistance researchers
Physician	Infectious Diseases Society of America, Alexandria, VA (www.journals.uchicago.edu/IDSA/guide/SE39_584.pdf)	References to the Society's guidelines on prevention of antimicrobial resistance in hospitals
Patient	American Medical Association, Chicago, IL (www.ama-assn.org/insight/gen_hlth/Antibiot/antibi01.htm)	Practical information on antibiotics and infectious diseases

* This table provides a selected list of Web sites and organizations whose materials we have reviewed; it is not intended to be a complete listing of all sources of information.

Requests To Purchase Bulk Reprints (minimum, 100 copies): Barbara Hudson, Reprints Coordinator; phone, 215-351-2657; e-mail, bhudson@mail.acponline.org.

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"Send for some leeches; bleed her," said Doctor Gimp.

"She has no blood left!" cried Mrs. Wilkes. "Oh, Doctor, what ails our Camillia?"

"She's not right."

"Yes, yes?"

"She's poorly." The good doctor scowled.

"Go on, go on!"

"She's a fluttering candle flame, no doubt."

"Ah, Doctor Gimp," protested Mr. Wilkes. "You but tell us as you go out what we told you when you came in!"

"No, more! Give here these pills at dawn, high noon, and sunset. A sovereign remedy!"

"Tut-tut! That's a shilling as I pass downstairs, sir."

"Go down and send the Devil up!" Mr. Wilkes shoved a coin in the good doctor's hand.

Whereupon the physician, wheezing, taking snuff, sneezing, stamped down into the swarming streets of London on a sloppy morn in the spring of 1762.

Ray Bradbury
A Medicine for Melancholy
New York: Bantam; 1960:11

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Please include a complete citation (along with page number on which the quotation was found), as done for any reference.–*The Editor*