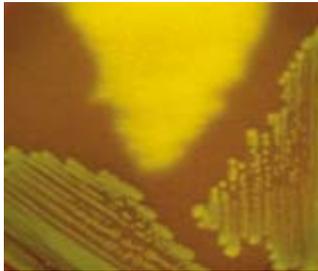


Antibiotic Resistance:

Are We Killing the Cures?

by *Alexandre Spatuzza*



Resistant strains of bacteria develop through normal Darwinian evolution. But the process is accelerated by microbes' abundant numbers, their rapid rates of division, and their unusual ability to share resistant genes. (Photo ©WHO)

The misuse of antibiotics in both developed and developing countries has begun to diminish the potency of these valuable drugs, prompting calls for an international response. In Latin America, where drug controls are lax and self-medication is rampant, countries are just starting to implement programs to fight antibiotic abuse.

Mr. Marin Carmelo owns the largest pharmacy in the Vila Nhocuné neighborhood in São Paulo's populous *zona leste*, or "east side." His store is modern and well stocked, and it towers over the smaller drugstores on the other side of the street. In his 28 years of business in the neighborhood, Carmelo has made a name for himself: "the doctor," as customers call him. People from all over the area come to him for medical advice, increasingly so, he says, in the last few years. "I know what kind of medicine a customer wants just by looking at him," boasts Carmelo. "I just try to do my best."

Doing his "best" means liberally giving out paramedical advice as well as medication, selling most kinds of drugs over the counter, even those labeled with a red band indicating they require a doctor's prescription. "People don't trust doctors," Carmelo explains matter of factly, "or else they don't have the patience to wait for hours or days to get treatment."

The lack of effective monitoring and enforcement of controls on the sale and use of antibiotics is cited by the World Health Organization (WHO) as one of the main causes of growing resistance of the world's microbes to antimicrobial drugs. The indiscriminate and improper use of antibiotics results in a survival-of-the-fittest selection process for microbes, which can both inherit and acquire resistance to drugs, through mutation or by sharing DNA. Just as in normal Darwinian evolution but accelerated umpteen times by the division of millions of microbes, an infection treated with the wrong drug or for too short a time results in most bacteria being killed while the resistant ones survive to multiply. Using antibiotics for viral

infections, against which they are impotent, promotes the growth and spread of resistant microbes in patients, their families, and the community.

Countries in Europe and North America have been tackling this issue (with mixed results) since the 1980s. In Latin America and the Caribbean, however, attention has been focused on the issue only during the last 10 years. Experts have only begun to map out the details of the problem, and information remains incomplete on which microbes are resistant and just how widely antibiotics are used. What researchers have found, however, are certain commonalities across the Region. Besides free-dealing pharmacists, these include weak or poorly enforced regulation, inequitable availability of health services, and working conditions that foster inappropriate prescribing practices by health professionals.

Losing the battle?



Pharmacies in many Latin American and Caribbean countries dispense antibiotics to their customers with or without a physician's prescription. (Photo ©Armando Waak/PAHO)

Visit a large hospital in downtown São Paulo, Mexico City, or Buenos Aires, and the problem is likely the same: a growing number of infections of the urinary, intestinal, or respiratory tract or bloodstream with microbes that are resistant to the most common antibiotics. In community settings, resistant bacteria are increasingly causing diarrhea, pneumonia, sexually transmitted diseases, and even tuberculosis.

In São Paulo's Children's Institute, one of Brazil's top pediatric hospitals, Dr. Alfio Rossi Jr., chief of the hospital infection control center, says he sometimes feels he is losing the battle against the bugs. Rossi has seen some microbes attain resistance of 60 percent to frontline antibiotics, despite his efforts to introduce special practices for keeping infections isolated.

"My impression is that resistant strains and the spread of infection are increasing," he says, citing as culprits the lack of national control policies, poor antiseptic conditions, badly trained or overworked health care workers, and a popular culture of freewheeling antibiotic use. Despite strict controls on the administration of drugs in his own wards, he frequently finds his staff treating patients who have already consumed antibiotics in other hospitals and are now serving as hosts to resistant strains.

In one of the few studies of antibiotic resistance in healthy children in a developing country, Dr. Alessandro Bartoloni found an alarmingly high level of antibiotic resistance of the common *E. coli* bacteria in healthy Bolivian children. What he discovered while looking for causes for this resistance was equally compelling. Sending out teams of consumers with fabricated symptoms to assess the practices of pharmacies in one community, he found that "over two-thirds of pharmacies dispensed antimicrobials without a medical prescription, and the quantity dispensed varied according to the patient's ability to pay." The pharmacies gave antibiotics inappropriately for 92 percent of adults and 40 percent of children with "watery diarrhea but no fever," indicating an absence of infection. Sixty percent gave antidiarrheal drugs to children, although none gave oral rehydration salts, the medically preferred treatment. All of the local pharmacies dispensed enough

antibiotics for only two days or less, even though the recommended therapy ranged from one to five days.

Such results do not surprise Dr. Liliana Clara, an infectious disease specialist at Buenos Aires' Italian Hospital and head of the Argentine chapter of the international Alliance for the Prudent Use of Antibiotics (APUA). She often sees parents medicating children with antibiotics for virally induced runny noses or diarrhea. "There's been a law to control sales since the 1960s, but nobody cares," she says, but is quick to add: "On the one hand, people think doctors are useless, and on the other, doctors are prescribing wrongly."

A recent survey by the Brazilian Federal Council of Physicians suggests that part of the problem does lie with health professionals themselves, largely as a result of the conditions under which they work. Brazil has an estimated 183,000 doctors, one for every 1,000 inhabitants. But some 65 percent are concentrated in cities, and about 60 percent work for the private sector, creating shortages in overcrowded government hospitals. Because of low salaries (an average of US\$1,300 monthly), one out of four Brazilian doctors works three jobs or more. Nursing staff have similar work patterns, increasing the possibility of transferring resistant strains from one hospital to another. "The bad conditions result in low-quality services," says Dr. Regina Parizi Carvalho, president of the São Paulo Regional Council of Physicians, pointing out that doctors in Brazil examine an average of 16 patients per shift.



Doctors who want to maintain good patient relations may prescribe antibiotics against their better judgement, particularly when they know that cheaper, often substandard drugs can be easily purchased over the counter. (Photo ©Armando Waak/PAHO)

The social conditions of patients also contribute to inappropriate prescribing practices. According to Carvalho, many doctors prefer to prescribe wide-spectrum antibiotics for patients they assume cannot wait for a full diagnosis or are unlikely to return because of transportation time or costs. Moreover, many health workers know that if they do not prescribe a drug, the patient will likely resort to self-medication, buying cheaper over-the-counter drugs that are often substandard or insufficient for a complete treatment.

Others say the problems are exacerbated by the absence of national policies on medication for the poor. A 1998 study by Brazil's Ministry of Health showed that the wealthiest 15 percent of the population consumes 48 percent of the medication dispensed from the country's pharmacies, while the 51 percent that earns US\$600 a month or less consumes only 16 percent. "This is the bottom line," says Dr. Anibal Sosa, director of APUA's Latin America Initiative. "Access to health care is precarious all over Latin America, forcing people to obtain antibiotics on the streets."

Mr. Francisco Caravante, director of the São Paulo Regional Pharmacy Council, agrees that "the lower-income population doesn't get access to proper medication." This can result from poor prescribing practices, scarcity of supply in government clinics, or lack of funds to buy medication. Whatever the cause, infected patients who are unable to get proper medication are more likely to see their health worsen to the point where they are forced to go to the hospital, where they will be exposed to the hardest bacteria of all.

A larger problem is that infectious diseases spread more easily anyway in low-income communities-and in developing countries in general-because of their poorer hygienic conditions associated with poverty.

While most Latin American and Caribbean countries have existing legislation to control the sale of medicines, few have adequate means to enforce it. Given other pressing problems, dealing with antibiotic resistance and controlling drug sales have not been top priorities.

Moreover, according to Dr. Clara of Argentina's APUA chapter, "because of the economic problems, nobody wants to face up to pharmaceutical companies and reduce consumption of antibiotics." Doctors who don't have the time to fully inform themselves about new medicines end up using the latest drugs on the market, reducing the effectiveness of older families of antibiotics. "There is no government control, and something that should be a technical choice by the doctor becomes a commercial choice," says Caravante of São Paulo's pharmacy council.

Even if doctors do wish to educate themselves, the differences between resistant microbes in Latin America and North America can mean a lack of information on less-frequently used antimicrobial drugs. "In certain cases, we've had to take forgotten, more toxic antibiotics out of the cupboard to fight these new resistant strains, and there is no literature about their use," says Dr. Helio Sader, head of the clinical microbiology laboratory at the São Paulo Federal University in Brazil.

Such was the case in the fight to control *Acinetobacter* infections, which occur almost exclusively in hospital patients and which in Brazil were registering 5 percent to 10 percent resistance to antibiotics. In cases in which no other drugs were successful, doctors began to use toxic polymyxins A and E, which can result in kidney failure when administered in high doses.

Increasing costs

Growing antibiotic resistance is also pushing up the costs of treatment, as doctors must increasingly rely on latest-generation antibiotics, often in combination, rather than older, less expensive drugs. In Brazilian hospitals, for example, strains of *Pseudomonas* bacteria, which typically affect patients with weakened immune systems, were registering 25 percent to 30 percent resistance. Physicians had to resort to a relatively new wide-spectrum class of antibiotics called carbapenems, which also happen to be more expensive.



The growth of antibiotic resistance means higher healthcare costs. As less expensive, older-generation antibiotics lose their potency, hospitals and physicians must increasingly resort to newer, more expensive drugs. (Photo ©Armando Waak/PAHO)

A study by Mexico's Spanish Hospital showed a major increase in the use of third-generation antibiotics from 1992 to 1997. Of the hospital's own \$1.5 million total annual antibiotics bill, \$350,000 was found to be inappropriately prescribed. The study concluded that correct control policies and prescribing practices could reduce hospital costs by some \$500,000 a year.

A study by Chile's chapter of APUA found that antibiotic sales in their country rose more than threefold from 1988 to 1997, to some \$46 million. The study attributed the inordinate rise to the lack of adequate control policies. In Brazil, imports of latest-generation antibiotics such as imipenem, cephalosporins, and polymyxins have been rising in the past three years, according to statistics from Brazil's Ministry of Development. Such rising costs are particularly difficult to manage for the cash-strapped countries of Latin America and the Caribbean.

As a result of this growing international problem, the World Health Organization in 1998 advised its member states to develop controls on antibiotic use. In June 1999, the Pan American Health Organization issued guidelines for its own member countries that included the following measures: the creation of surveillance systems; control of antibiotic sales; better training for health personnel on drug dispensing; control of quality of medicines, including generics; and public education campaigns. It also recommended controls on antibiotic use in animal feed, a practice found in countries such as Argentina, Brazil, and Mexico, as well as the United States and Canada, and which research has shown contributes to antibiotic resistance.

To date, 12 Latin American and Caribbean countries have taken concrete steps to curtail the growth of antibiotic resistance, mainly through the creation of surveillance systems. But the Region has a long way to go. In Brazil, for example, Ministry of Health officials do not have an exact count of how many hospitals in their country have functioning microbiology laboratories. They do estimate that only half of Brazilian hospitals have infection control centers.

One bright spot in the Region is the growing number of hospital-based programs, aimed at reducing the use of antibiotics and promoting antiseptic conditions that inhibit the development of antibiotic resistance. Since 1997, PAHO has been working closely with Bolivia, Ecuador, El Salvador, Guatemala, Honduras, Nicaragua, and Peru to implement programs for training microbiologists and physicians to tackle the problem.

So far, only Chile and Cuba have implemented truly nationwide programs to curb antibiotic resistance. Beginning in 1999, Chilean public health authorities began enforcing local drug-dispensing laws, complementing their efforts with a public information campaign. The program succeeded in cutting consumption of antibiotics by 22 percent in dollar terms. Cuba's unified health system has effective surveillance and control of antibiotic dispensing, but even there, according to APUA, resistance to antibiotics has been rising.

Other countries are starting to take positive steps. In Venezuela, the government is currently discussing methods to enforce existing controls on antibiotics sales, while

Peru is obtaining assistance from USAID to do the same. For its part, Brazil last year named a 10-person multidisciplinary task force in the Ministry of Health to develop a set of guidelines for action; their report is expected later this year.

Antibiotic resistance is probably here to stay, experts say. But "what we have to do now is to make sure that resistance doesn't escalate," says Dr. Ronald Jones, researcher and collaborator at APUA. Compared with other parts of the world, particularly the developed countries, Latin America and the Caribbean may be getting a late start in this battle. But if the steps taken so far are expanded, and coupled with strict enforcement of controls on antibiotic sales, the goal of at least slowing the growth of antibiotic resistance is still within reach.

Alexandre Spatuzza is a Brazilian journalist who lives and works in São Paulo.

What you can do

Consumers play a major role in the growth of antibiotic resistance. But they can also do their part to combat the problem by following some basic guidelines:

- Do not "demand" antibiotics from your physician. Antibiotics are useful only against bacterial infections. The common cold and flu are caused by viruses, and antibiotics are ineffective in treating these.
- If your doctor prescribes antibiotics, ask him or her questions about why they are indicated. Also ask about possible side effects and allergic reactions.
- When you do get antibiotics, be sure to take the full course of medication. Incompletely treated infections are prime culprits in the growth of antibiotic resistance.
- Never take "leftover" antibiotics to treat an illness; they may be the wrong type, and there will not be enough for a complete treatment, thus contributing to antibiotic resistance.
- Wash your hands frequently with regular (not antibacterial) soap and warm water. This is the best way to avoid spreading harmful microbes. Keep your hands and fingers out of your mouth, nose, and eyes, the primary portals through which bacteria enter your body.