



WORLD HEALTH ORGANIZATION

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Essential Drugs Monitor

The Essential Drugs Monitor is produced and distributed by the WHO Department of Essential Drugs and Medicines Policy (EDM). It is published in Chinese, English, French, Spanish and Russian, and has a global readership of some 300,000 to whom it is free of charge. The Monitor carries news of developments in national drug policies, therapeutic guidelines, current pharmaceutical issues, educational strategies and operational research.

WHO's Department of Essential Drugs and Medicines Policy seeks to ensure that all people – wherever they may be – are able to obtain the drugs they need at a price that they and their country can afford; that these drugs are safe, effective and of good quality; and that they are prescribed and used rationally.

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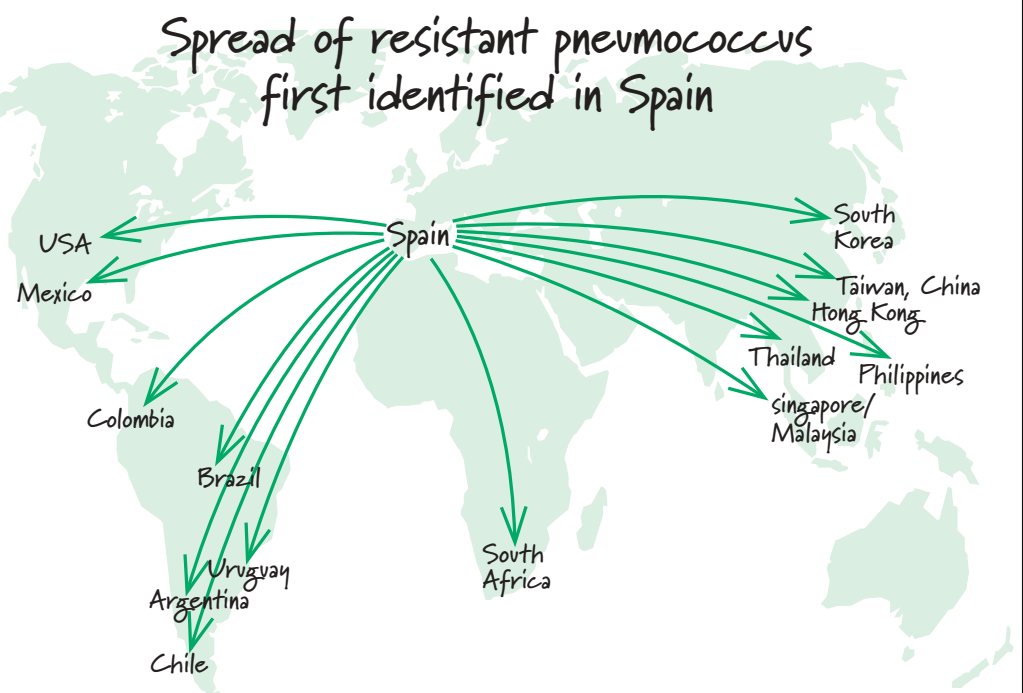
EDITORIAL

Antimicrobial resistance: a global threat

Twenty years ago physicians in industrialised countries believed that infectious diseases were a scourge of the past. With industrialisation came improved sanitation, housing and nutrition, as well as the revolutionary development of disease-fighting antimicrobials. Populations living in those nations were not only enjoying an unprecedented decrease in mortality and morbidity but a corresponding increase in life expectancy. In the developing world – where poverty and ongoing civil disturbance offset often modest health gains – people could nevertheless look forward to a time when an increased quality of life might one day lead to a relatively disease free future. The tools were there. Confident in the available pharmacopoeia, the major drug manufacturers turned away from intensive antibacterial research and concentrated their energies on seeking cures for heart disease and other chronic conditions. Since the 1980s significant breakthroughs have been largely confined to the development of antiviral agents targeting the ever-widening HIV epidemic.

But tragically, and even before developing countries were able to fully benefit from medical advances, we face a major risk that diseases considered vanquished in industrialised countries, will once again become killers stalking society, bringing an ever present threat of sudden death and disability. The risk that threatens to turn back the clock to a darker age in industrialised countries and to block health progress in the developing world is antimicrobial resistance.

As early as half a century ago – just a few years after penicillin was put on the market – scientists began noticing the emergence of a penicillin/resistant strain of *Staphylococcus aureus*, a common bacterium in the human body's normal bacterial flora. Resistant strains of gonorrhoea, dysentery-causing shigella (a major cause of premature death in developing countries) and salmonella rapidly followed. From that first case of resistant staphylococcus, the problem of antimicrobial resistance has snowballed to a serious public health concern with economic, social and political implications that are global in scope, and



Source: K. Klugmann, South African Institute of Medical Research

cross all environmental and ethnic boundaries. Multi-drug resistant tuberculosis (MDR/TB) is no longer confined to any one country or to those co-infected with HIV, but has appeared in locations as diverse as Africa, Asia and Eastern Europe, among health care workers and in the general population. Penicillin resistant pneumococci are likewise spreading rapidly, while resistant malaria is on the rise, disabling and killing millions of children and adults each year.

In 1990 almost all cholera isolates in New Delhi, India, were sensitive to the cheap, first-line drugs furazolidone, ampicillin, co-trimoxazole and nalidixic acid. Now, formerly effective drugs are largely useless in the battle to contain cholera epidemics.

Although most drugs are still active, the lengthening shadow of resistance means that many of them may not be for long. In the case of tuberculosis, the emergence of multi-drug resistant bacteria means that medication that once cost US\$20 must now be replaced with drugs a hundred times more expensive.

Pathogens develop resistance to antimicrobials through a process known as natural selection. When a microbial population is exposed to an antibiotic, more susceptible organisms will succumb,

leaving behind only those resistant to the antimicrobial onslaught. These organisms can then either pass on their resistance genes to their offspring by replication, or to other related bacteria through "conjugation" whereby plasmids carrying the genes "jump" from one organism to another. This process is a natural, unstoppable phenomenon exacerbated by the abuse, overuse and misuse of antimicrobials in the treatment of human illness and in animal husbandry, aquaculture and agriculture. Disease – and therefore resistance – also thrives in conditions of civil unrest, poverty, mass migration and environmental degradation where large numbers of people are exposed to infectious diseases, with little in the way of the most basic health care. Our challenge is to slow the rate at which resistance develops and spreads.

This Monitor examines the growing spread of antimicrobial resistance and its underlying causes. It reports on the actions of WHO and others to raise awareness of the issue and to counteract this serious menace to public health. And it looks at what you, the reader, whether you are a policy-maker, health care professional, health advocate or member of the public, can do to help tackle the problem. □

NEWSDESK

First conference on consumer adverse reaction reporting

➤ DAVID FINER*

The First International Conference on Consumer Reports on Medicines was held in Sigtuna, Sweden, from 29 September–1 October 2000, with some 70 participants from 35 countries. The Conference sought to call attention to the experiences of consumers as a crucial, untapped force in pharmacovigilance, beneficial for drug safety, but also in terms of consumer empowerment in its own right.

Direct consumer reporting of adverse drug events is indeed credible but also controversial in some camps. Yet it is the only system based on the end-users themselves.

The Conference was organized by the Swedish organization KILEN (Consumer Institute for Medicines and Health) in cooperation with the Dag Hammarskjöld Foundation, Health Action International, People's Health Assembly 2000, the Uppsala Monitoring Centre, the Swedish Consumers' Association, and the Sigtuna Foundation. Participants included experts from the medical and pharmaceutical professions, drug regulatory authorities, the consumer movement and WHO.

Presentations of existing consumer reporting systems/initiatives were made by representatives from Australia, the Netherlands, Sweden, Switzerland and the UK.

A consensus report from the Conference states that general reasons for considering consumer reports on medicines relate to the need to promote principles of equity, therapeutic advances, accountability and responsiveness. Also, existing physician-based systems have serious deficiencies, which might to some extent be compensated for by the establishment of consumer reporting. Foremost among these limitations are the small proportion of practising physicians (often less than 5%) who contribute data. Input from existing systems relates primarily to new drugs, despite the fact that new problems can emerge with older drugs even after decades of use.

Consumers give more complete picture

Delegates heard that benefits of consumer reporting of adverse drug effects include an earlier accumulation of signals, covering a wider spectrum of organ systems and adverse events. Consumers provide more informative, vivid and complete accounts of unwanted experiences and situations, about which physicians are not informed and so cannot report, such as self-treatment with over-the-counter drugs or herbals.

With so many excellent reasons for direct consumer reporting, why, one might ask, is it not already established? It is because in most countries, consumer reports are simply not eligible for inclusion in the existing physician-based systems, and because consumers lack power and knowledge.

The Conference recommended that, prior to wide-scale implementation, consumer reporting on medicines system/s should be piloted in regions or with patient groups, and handled by an independent body at arm's length from government and industry. In aggregated form, reports should be made available to all interested parties, including the mass media. The data would also be related to the current data from the 59 national physician-based schemes in the Uppsala Monitoring Centre (a WHO Collaborating Centre for International Drug Monitoring). Appropriate arrangements should be made to enable hospitalised patients as well as participants in clinical drug trials to file reports.

Expert analysis needed

The principle of the subject's freedom to report should be laid down in Guidelines for Good Clinical Practice accepted by the European Commission and in clinical trial protocols, subject to approval by ethics committees and analogous bodies. Confidentiality agreements concluded between an industrial sponsor and a clinical investigator should never be allowed to impede reporting of adverse effects by participants. Provided there is proper feedback and careful expert analysis of reports, it will not necessarily be more difficult to eliminate mischievous, misleading or ambiguous reports than has been the case in professional-based systems.

A system of consumer reporting on medicines might be supported from public funds, drug licensing fees or research organizations, including the European Union. Its value will depend to some part on enlisting support from existing systems, allaying unjustified concerns and countering possible misunderstandings.

Delegates warned that while developing consumer empowerment, one must also seek to counter potentially harmful influences, such as current efforts to extend Direct-to-Consumer-Advertising of prescription drugs from New Zealand and the USA to the rest of the world. □

* David Finer is a medical writer and was Chairperson of the Conference.

Further Conference information can be found on the Web at: www.kilen.org

A world of difference: grim statistics on maternal health in developing countries

A woman living in Africa has a lifetime risk of dying from complications related to pregnancy 200 times greater than a woman living in a wealthy industrialised country, according to research findings reviewed in the *WHO Bulletin**.

WHO data show that of the more than 500,000 maternal deaths every year, over 99% are in developing countries and less than 1% in the industrialised world. The main causes of these deaths are unsafe abortion, haemorrhage, infections, high blood pressure and obstructed labour. A quarter to a third of all deaths of women of reproductive age are the result of complications of pregnancy or childbirth.

"The poor fare far worse than the rest of society on all reproductive health outcome indicators. But poverty is not an insurmountable barrier to health when there is a high level commitment to investing in health," a *Bulletin* article states. "Gender-based discrimination is an important determinant of poor reproductive health. Women suffer the major burden of sexual

and reproductive ill-health because they also suffer discrimination in access to basic needs, health services and the exercise of human rights."

Another *Bulletin* article reviews data suggesting that making abortion safer could save the lives of many thousands of women a year. □

* *Bulletin of the World Health Organization*, May 2000 (available on the Web at: <http://www.who.int/bulletin/>). For subscription details contact: World Health Organization, Marketing and Dissemination, CH 1211 Geneva 27, Switzerland.



Hopefully a trouble-free pregnancy for this woman in Haiti. But women in the developing world have an unacceptably high risk of dying from pregnancy-related complications

Photo: WHO/PAHO/A. Wook

Doctors revise ethical guidelines on medical research

The World Medical Association General Assembly has sent a strong signal to all involved in medical research that rich populations should not exploit poor populations by testing on them new treatments from which they will never benefit. The Assembly held in Edinburgh, Scotland, in October 2000, approved a revised Declaration of Helsinki. Initially drawn up in 1964, the Declaration has since become the most widely accepted guidance worldwide on medical research involving human participants. Commenting on the changes, Dr Anders Milton, chairman of the Association, said: "Research should not be carried out in countries in development just because it is cheaper and the laws are more lax. The same ethical rules should apply wherever research is being conducted".

The new Declaration emphasises in much clearer terms than ever before the duty that doctors owe to participants in medical research. It says that freely given informed consent, preferably in writing, should be obtained from all participants. People who cannot give informed consent should be included in research only under exceptional conditions.

Strengthening participants' rights

The Declaration specifies that doctors participating in research have an obligation to declare any financial or other potential conflict of interest. Research is justified only if the populations to be studied stand to benefit. The Declaration states that every patient entered into a study should have access to the best treatment identified by that study once it is completed. Furthermore, testing of any new treatment should be done against the best current method, where that exists, and not against a placebo. This would mean that people in developing countries would at least get access to the best current treatment if they agree to take part in research into new treatments.

The revised Declaration of Helsinki will be distributed to WHO, national bioethics commissions, patients' representatives groups and other relevant stakeholders. The full text is on the World Medical Association's Web site: www.wma.net □

Source: *BMJ* 2000;321:913

NEWSDESK

New course targets better community drug use

At a time when the majority of medicines are purchased directly by consumers without prescription, community education is vital, and a new course is setting out to meet the needs of those with a critical role to play in this much neglected area. Just how neglected was shown by a WHO global survey on public education in rational drug use¹, which revealed a shortage of expertise, support and funds for this type of work, in spite of its public health and economic benefits.

Developed by WHO's Department of Essential Drugs and Medicines Policy and the University of Amsterdam, in collaboration with experts world wide, the course, Promoting Rational Drug Use in the Community, was held for the first time in October 2000 in Bangkok. Enthusiastic participants learned how to effectively identify and prioritise community drug use problems; choose and develop appropriate intervention strategies and communication channels; pretest materials; evaluate impact; and fundraise and network for support and sustainability.

Anyone who came looking for "quick fixes" would have been disappointed. Participants learned that interventions must take into account the social and economic context in which health- and medicine-seeking behaviour take place, and be developed with community input. The course emphasises that change is usually incremental. So programme objectives may start with awareness training, move on to knowledge acquisition, and then finally on to behavioural change. Twenty-five participants, from 14

countries, valued the help given to identify clear objectives, based on realistic expectations of impact on future work.

The skills and experiences of everyone on this highly participatory course proved a major resource. Teaching methods were group activities, field work, presentations and discussions. Participants spent the final two days preparing a detailed plan of action to tackle an important community drug use problem in their home country. They also took home a set of session materials and a small core communications library. But from their comments it was evident that course members were leaving Thailand with much more. As one participant put it, "I realise that in my professional life I have only been looking at half of the picture...". Another said the course would "help me use scarce resources to implement the most appropriate/feasible and needed interventions." And for a third it was "a great experience, well planned and well organized".

After such initial success the course is set to become a regular event, with the next one being held in Entebbe, Uganda, from 11-24 November 2001. □

Reference

WHO. Public education in rational drug use: a global survey. EDM Research Series No.24. Geneva: World Health Organization; 1997. WHO/DAP/97.5.



Creating a message that counts – participants working on a poster during the course

WHO's Emergency Library Kits

Library Kits containing essential documents related to public health in emergencies are now available from WHO. Intended to provide technical guidance to field-operating agencies, the Kit includes 120 documents – guidelines and reference manuals produced by WHO, other UN organizations and external publishers. The contents will be updated regularly.

Packed in a metal trunk that converts into a bookcase, the Emergency Library Kit costs approximately US\$1,320, plus transport charges. □

For further information contact: World Health Organization, Department of Emergency and Humanitarian Action, 1211 Geneva 27, Switzerland.

Welcome new HIV/AIDS resource for francophone Africa

A new HIV/AIDS information network for Central and West Africa has been launched – the first network of this type in French. Known as SAFCO (SIDA en Afrique du Centre et de l'Ouest), it will encourage discussion and the electronic exchange of information on HIV/AIDS-related issues. The service is particularly welcome because there is a scarcity of such information and technical material in French in Africa, the continent hardest hit by the virus.

As well as information exchange, SAFCO aims to: strengthen advocacy efforts; improve information about current projects; promote prevention measures; reinforce access to care and treatment; disseminate the results of international conferences and support their implementation.

SAFCO, with over 700 members, is a UNAIDS supported initiative. One of its main strengths is that it is a public cross-sectoral and inter-community information forum. It has input from both the "grassroots" – concerned individuals, government representatives, NGOs, educators, investigators, practitioners and others – and from national and international institutions. □

Joining the SAFCO network is free of charge, just send a message to: safco@hivnet.ch

Next Promoting Rational Drug Use in the Community Course

If you would like to know more about the course in Entebbe, Uganda, from 11-24 November 2001, please complete and return this form. Alternatively, further details and an application form can be printed out directly from the EDM web-page at: <http://www.who.int/medicines/organization/par/secondcourse.html>. Course fees are US\$2,950, which covers tuition, course materials and accommodation. The deadline for receipt of applications is 1 October 2001.

Name _____

Occupation _____

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WHO list of comparator products

Multisource (generic) drugs need to meet the same quality, safety and efficacy standards as the original brand name or innovator product. WHO has now published a list of globally recognised comparator products, to help regulators identify the product against which bioequivalence and interchangeability of generic versions can be assessed.

The list includes 147 drugs from the WHO Model List for which a comparator product has already been identified. It names the manufacturer who is the innovator, and the national market where that manufacturer considers that the product meets the best safety, quality, efficacy and labelling standards. A second list gives the remaining essential drugs for which a comparator product has yet to be selected. □

The information is available in WHO Drug Information Volume 13, No.3, 1999.

APUA's small grants programme

The Alliance for Prudent Use of Antibiotics (APUA) has initiated a small grants programme, which provides chapters with seed money of US\$1,500 for projects designed to curb antibiotic resistance and to promote the rational use of these drugs.

APUA's national chapters form a global network of health care practitioners and scientific groups working to control antimicrobial resistance. They provide information and tailor the Alliance's message to local customs and medical practices, and the small grants programme is intended to encourage these efforts. Projects submitted for grants are evaluated according to their objectives, collaborative components and management plans. To date grants are helping to support research and education in seven developing and transitional countries. □

For further information contact: The Alliance for Prudent Use of Antibiotics, P.O. Box 1372, Boston MA 021171372, USA. E-mail: ccogli01@tufts.edu

NEWSDESK

Leading organizations' new guidelines on ethics

At a time of increased focus on ethical issues in the pharmaceutical sector, UNAIDS and the European Medicines Evaluation Agency are among many organizations producing their own guidelines.

UNAIDS and vaccine research

In the case of the Joint United Nations Programme on HIV/AIDS (UNAIDS) the ethical guidelines cover HIV vaccine research for those giving trial AIDS vaccines. It is widely thought that developing such a vaccine offers the best hope of controlling the AIDS epidemic, especially in developing countries. But experts say it will be a lengthy and complex process, because of the scientific and ethical challenges involved in clinical trials among human volunteers.

The guidance document, which

addresses some of these ethical challenges, took over two years to draw up. It was based on a series of consultations organized by UNAIDS and which involved representatives from 33 countries. The meetings took place in Brazil, Thailand and Uganda (countries that are participating in HIV vaccine trials) as well as in Geneva and Washington. They involved lawyers, activists, NGOs, people living with HIV/AIDS, social scientists, ethicists, epidemiologists, health policy specialists, and agencies and institutions involved in vaccine development.

There was consensus on most, but not all, issues. The most contentious area was the level of treatment that should be offered to participants in vaccine trials who become infected with HIV, not through the trials (vaccines cannot cause HIV infection) but through eventual behavioural exposure. According to the UNAIDS document, "Care and treatment should be provided, with the ideal being to provide the best proven therapy, and the minimum to provide the highest level of care attainable in the host country" under the circumstances in which the trial is conducted.

With resources in industrialised and developing countries so different, however, not every country can expect to provide the same level of care.

The document contains 18 "guidance points"

reflecting a number of issues, including:

- ▶ international ethical responsibility to support vaccine trials;
- ▶ the obligation to provide an effective vaccine to populations where trials are conducted and to other populations in need;
- ▶ the need to strengthen ethical review capacity in developing countries;
- ▶ the importance of social and behavioural aspects of testing, and future use of an HIV vaccine.

Collective responsibility

The guidelines identify responsibilities for the "sponsors" of vaccine trials. In modern vaccine development programmes, sponsors are not usually a single pharmaceutical company. Instead, there tend to be multiple sponsors, with one or more corporations, one or more national governments, and one or more international agencies.

The guidelines highlight the importance of involving communities early in the design, development, implementation and distribution of results of HIV vaccine research. They are designed as a framework to enable communities to decide what is appropriate for them.

Agency acts to ensure integrity, independence, transparency

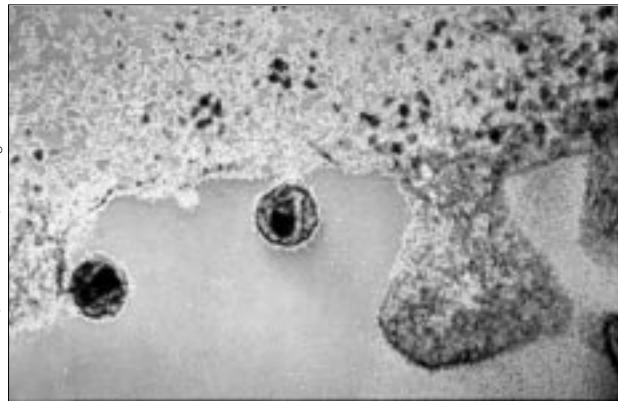
The European Medicines Evaluation Agency is to have a code of conduct giving specific guidance on conflicts of interest, gifts and confidentiality.

The Code applies to management board, scientific committee and working party members, European experts listed by the Agency, all Agency staff and by analogy all visiting staff. Three categories of interest are listed: financial interests, work carried out for the pharmaceutical industry in the previous five years, and other links, such as grants for study or research, or fellowships endowed by industry in the previous five years.

Anyone with direct interests in the pharmaceutical industry has to end them to remain with the Agency. If there are indirect interests they must be neutralised, for example by preventing someone from taking part in certain tasks.

In general staff have to discourage gifts of anything more than token value which can be shared openly with colleagues. Any gifts of a personal nature must be returned, and staff must not use items with pharmaceutical company logos at work.

The Code states that invitations to predominantly leisure events cannot be accepted, and at meetings or on missions staff should normally pay for their own meals. Invitations from individual pharmaceutical companies, suppliers, etc. should not be accepted. In addition no payment may be accepted for speeches, lectures or publications directly related to Agency activities. Permission to speak at conferences will be refused "if networking or gaining influence must be assumed to be the major objective of the organizer". Invitations from congresses or meetings organized by pharmaceutical companies are unacceptable. □



The AIDS virus. Development of a vaccine is considered to be the best hope of controlling the AIDS epidemic. Guidelines are now in place to address the complex ethical issues involved in testing such a vaccine

Africa's strategy on traditional medicine

The Strategy for Traditional Medicine for the African Region (2000–2001) is being developed by the WHO Regional Office for Africa. Its aim is to assist Member States to integrate traditional medicine into health systems and services, and to promote appropriate and rational use. In December 1999, WHO held a consultative meeting on the Strategy, which brought together 23 experts from 15 countries for three days of intensive debate in Harare, Zimbabwe.

Combatting priority diseases

Participants recommended that action plans be developed to implement the Strategy at regional and national levels, so that by 2020 traditional medicine will be an integrated component of the minimum health care package in African

countries. Much discussion focused on ensuring the protection of the intellectual property rights of indigenous knowledge in traditional medicine, and the cultivation and conservation of native medicinal plants. Delegates asked WHO to provide technical and financial support for developing traditional medicinal products to combat priority diseases, such as malaria, hypertension, diabetes and HIV/AIDS-related conditions.

Closing the meeting the WHO Regional Director for Africa, Dr Ebrahim Samba, said he wanted to see the continued use of African herbal plants and traditional medicines to treat diseases. He hoped that such traditional medicinal products would eventually be exported, after clinical trials have proved their efficacy and safety. Dr Samba stressed the

economic importance this could have for Africans.

As a follow-up to the December consultative meeting, WHO's Regional Office for Africa organized the African Forum on the role of traditional medicine in health systems, in Harare in February 2000. Over 100 participants from throughout the region held wide ranging discussions, reviewed current and needed research on these medicines, and identified local production issues. Recommendations from the meeting included: ensuring adequate legal and regulatory frameworks to promote traditional medicines; establishing or strengthening traditional medicine practitioners' associations; and increasing collaboration among healers, scientists and doctors. □

Electronic HAI-Lights

HAI-Lights has become the first HAI-Europe publication designed to be read and used electronically. All of the information included in the newsletter's August 2000 double issue appears in easy to find links shown on the cover page. HAI-Europe has been working towards a Web-based version of the regional newsletter for some time, due to members' demand for faster information and more accessible material.

It is planned to link the newsletter's content to a Web site search function so that articles on various issues can be retrieved quickly and easily.

Access the August issue of HAI-Lights at: <http://www.haiweb.org/pubs/hailights/aug2000/>

The entire newsletter is also available in a downloadable text format. You can choose Word for either PC or Mac to read or print out the issue's complete contents or a specific section. □

NEWSDESK

French set to curb drug spending

The French Government has warned that the rate of growth of pharmaceutical spending is still far too high, and that it is deciding which products will have price or reimbursement cuts, or be removed from the list of reimbursable products.

Speaking at a press conference in May 2000, Labour and Solidarity Minister, Martine Aubry, said that health care expenditure was still rising strongly, particularly in the pharmaceutical sector, which increased by 6.3% in 1999. While projections for 2000 are for a cut of 0.7% this is far higher than the target set by Government of 2%. Addressing the Social Security Accounts Commission shortly before her press conference, Ms Aubry said that it was "absolutely necessary" to bring pharmaceutical expenditure into line with Government targets.



An elderly patient in France, where the Government is acting to reduce rising pharmaceutical expenditure

She singled out "unjustifiable prescribing", saying that some products were quickly capturing a sizeable share of the market more because of what she termed "aggressive commercial policies towards doctors than because they are advances in public health". "Information arrives in doctors' surgeries from pharmaceutical companies and only from them" she continued. "I am not criticising the industry. It does its job, which is to sell and sell even more. But she said that she did not want doctors to be "left alone to face the industry". The Government intends to supply doctors with independent information on the correct use of medicines. While encouraged by increasing generic substitution, Ms Aubry said that she wanted to see more generic products on the market soon.

The French pharmaceutical industry association, SNIP, has criticised the Government's target of a 2% increase in pharmaceutical spending in 2000. The Government cost-containment initiatives (prescribing guidelines, computerization of doctors' surgeries, the encouragement of generics and reimbursement review) were necessary, SNIP stated, but had failed to bring spending into line with the 2% limit. □

Source: Scrip, No.2543, 26 May 2000.

Indian training course highlights pharmacists' evolving role

A group of community and hospital pharmacists and pharmacy students from the Bengal area benefited from a break in routine when in September 1999 they spent two days looking at broader issues affecting their profession. Twenty-six participants held wide-ranging discussions on subjects including their changing role, the structure of the country's pharmaceutical industry and the patent situation. Run jointly by the Community Development Medicinal Unit, Calcutta, and the Indian Pharmaceutical Association, Bengal Branch, the training course, Good Community Pharmacy Practice, was so successful that it is planned to repeat it every year.

Upgrading knowledge and skills

In the varied programme, a session on formulations marketed in India although banned by the Government generated animated debate. So too did the topic of clinical waste management – an area new to many of the participants. The second day began with a discussion on how best to respond to symptoms of common ailments, followed by tips on improving drug dispensing, and medical stores management.

Although maybe not of immediate relevance to the job description of most participants, two sessions provided plenty of food for thought. One was on the scientific principles of pharmaceutical inventory management. The other covered the structure of the pharmaceutical industry in India, recent changes in national drug policy and the Indian patents scenario. □

For further information contact: Community Development Medicinal Unit, 47/1B Garcha Road, Calcutta-700 019, West Bengal, India, or see: <http://education.vsnl.com/cdmudocu/CDMUHome.htm>



Participants engrossed by a demonstration of special dosage forms

A World Health Report with a difference

The World Health Report 2000 – *Health Systems: Improving Performance*¹ is an expert analysis of the increasingly important influence of health systems in people's daily lives. In recent decades, health systems have contributed enormously to better health for most of the global population. But they have the potential to achieve further improvements, especially for the poor. As Dr Brundtland, WHO's Director-General, comments in her introduction to the *Report*, "The poor are treated with less respect, given less choice of service providers and offered lower-quality amenities. In trying to buy health from their own pockets, they pay and become poorer."

To date very little has been done to unravel the complex factors that explain good or bad performance by individual health systems. Given equal resources, why do some succeed where others fail? Is performance simply driven by the laws of supply and demand, or does another logic apply? Why is dissatisfaction with services so widespread, even in wealthy countries offering the latest interventions? If systems need improvement, what tools exist to measure performance and outcomes?

These are some of the questions that the *Report* addresses, as it presents the results of the first ever analysis of the world's health systems. It provides an index of performance based on three fundamental goals: improving the level and distribution of health, enhancing the responsiveness of the system to the legitimate expectations of the population, and assuring fair financial contributions.

As the *Report* argues, good performance depends critically on the delivery of high-quality services. But health systems must also protect citizens from the financial risks of illness and meet their expectations with dignified care. The publication shows how the achievement of these goals depends on the ability of each

system to carry out four main functions: service provision, resource generation, financing and stewardship. Chapters devoted to each function offer new conceptual insights and practical advice on how to assess performance and achieve improvements with available resources.

The analysis revealed a number of problems common to many countries. Among them are that:

- ▶ many health ministries focus on the public sector and often disregard the frequently much larger private sector health care;
- ▶ in many countries, some if

not most physicians work simultaneously for the public sector and in private practice. This means that the public sector ends up subsidising unofficial private practice;

- ▶ many governments fail to prevent a "black market" in health, where widespread corruption, bribery, "moonlighting" and other illegal practices flourish. The black markets, which themselves are caused by malfunctioning health systems, and health workers' low incomes, further undermine those systems;
- ▶ many health ministries fail to enforce regulations that they themselves have created or are supposed to implement in the public interest.

The *Report* aims to stimulate debate about better ways of measuring health system performance and overcoming such problems. By shedding new light on what makes systems behave in certain ways, WHO also hopes to help policy-makers understand the many complex issues involved, weigh their options and make wise choices. □

Reference

1. WHO. The world health report 2000 – health systems: improving performance. Geneva: World Health Organization; 2000. Available from: Marketing and Dissemination, World Health Organization, 1211 Geneva 27, Switzerland. Price: Sw.fr.15/US\$13.50, and in developing countries Sw.fr.10.50. The full report is available on the Web at: <http://www.who.int/home/reports.html>

Celebrating the Chinese version of the Monitor

The Essential Drugs Division of China's State Drug Administration has seen its hard work rewarded as the first two issues of the *Monitor* in Chinese have rolled off the printing presses, to an enthusiastic reception.

Ten thousand copies of each issue have been printed and distributed, free of charge, to Government departments, medical institutes and experts in the pharmaceutical sector. While these first issues contain a selection of key articles from recent editions, future copies will reproduce the text of the most recent *Monitor*. □



NEWSDESK

New public health channel piloted in Africa

WorldSpace Foundation and SATELLIFE have announced a new health service that will provide a steady stream of material to assist medical professionals in Africa in the diagnosis, prevention and treatment of prevalent diseases. The service, called the Public Health Channel, aims to overcome the barriers of poverty, geography and unreliable communications infrastructures, to help stop the rise of diseases such as malaria, tuberculosis and HIV/AIDS.

"The ability to widely disseminate information about the treatment and prevention of HIV/AIDS and other diseases is the reason the WorldSpace system was created," says Gracia Hillman, WorldSpace Foundation President.

"The goal of SATELLIFE's information services is to connect the health practitioner in the developing world with a range of high-quality information resources in a cost-effective manner,

by making use of the most affordable, efficient and appropriate technology", states SATELLIFE Executive Director, Holly Ladd. "The Public Health Channel will employ the technology of the WorldSpace system to exponentially increase the amount of information health practitioners throughout Africa can access – information that most health practitioners in the United States and Europe take for granted."

The Public Health Channel will be launched in four countries: Ethiopia, Kenya, Uganda and Zimbabwe. After an initial test period, the project will expand to other African countries, as funding becomes available. WorldSpace receivers will be placed in hospitals, medical schools, medical libraries, health clinics, health ministries and research settings.

WorldSpace receivers provide crystal clear digital audio channels, and can also serve as a modem, downloading text-based material and dynamic images from

the AfriStar satellite directly to computers. The WorldSpace system transcends the difficulties of unreliable telephone systems at a fraction of the cost of most Internet-based projects.

WorldSpace Foundation works with NGOs and other humanitarian groups to bring life-saving information to people who are disadvantaged by poverty, rural location and the digital divide. □

SATELLIFE is an international not-for-profit humanitarian organization. Its mission is to improve health by improving connections between professionals in the field, through electronic communications and information exchange in the areas of public health, medicine and the environment. Particular emphasis is on areas of the world where poor communications, economic conditions or natural disasters limit access.

SATELLIFE produces two e-mail publications, *HealthNet News* and *HealthNet News-AIDS*, which feature materials from 21 journals, including the *British Medical Journal*, *Lancet* and *East African Medical Journal*.

SATELLIFE also operates and maintains several global electronic discussion groups on subjects relevant to developing countries. (See Netscan page 32 for more information on SATELLIFE's services).

WorldSpace Foundation is a non profit organization created in 1997. Based in Washington DC, USA, its work encompasses Africa, Asia-Pacific, Latin America and the Caribbean. It has 5% of the channel capacity of the three WorldSpace Corporation satellites for non commercial social development and distance learning programming.

Drug donations problem in Venezuela

Months after devastating floods and landslides left up to 30,000 people dead or missing and 200,000 homeless, the Bolivarian Republic of Venezuela was being inundated again by a flood of unusable medical aid. Harrowing television pictures of the disaster in December 1999 in the coastal states of Vargas and Falcon, near Caracas, sparked a massive humanitarian response, and tonnes of medicines arrived from around the world.

However, health workers helping the victims say that huge quantities of medical aid remain stockpiled in warehouses, and up to 70% will have to be incinerated. A report by the Government's Pharmacological Production Service says many products cannot be used because they are out of date, unnecessary, have been partially used, or have no Spanish labelling. As a result, the Government has already had to spend at least 10m bolivars (approximately US\$16,000) to hire extra

staff and increase working hours simply to classify what has been received.

Dr Francisco Griffin, Director-General of the Production Service, said he thought some companies had deliberately sent expired products, considered as toxic waste, to evade the cost of having to deal with them themselves. In 1996 WHO published interagency guidelines on drug donations¹ in response to increasing reports of such problems being caused by inappropriate donations.

However, Dr Griffin accepted that the Service had not anticipated such a massive international response to the landslides. When the disorganized nature of the donations and the "titanic work" required to sort through them became clear, advertisements were belatedly posted on the Web sites of international organizations asking only for specifically requested products.* □

Source: BMJ 2000;320:1491.



Calm waters on Lake Maracaibo for this auxiliary health worker doing her rounds, but floods in Venezuela in 1999 caused massive devastation

*There are signs that countries are beginning to speak out, to avoid receiving unnecessary drugs when faced with disasters. For example, Mozambique required all donations to be consistent with WHO's Interagency guidelines when areas of the country were flooded in February and March 2000.

Reference

1. WHO. Interagency guidelines for drug donations. Geneva: World Health Organization; 1996. (Second edition published 1999).

Update on drug donations

A study carried out by Community Initiatives Support Services International has investigated the benefits and problems of donated drugs at 24 mission health facilities in Kenya and Tanzania between 1997 and 1998. It found that:

- On average health facilities received four deliveries of donated drugs per year.
- Approximately a quarter of all donated drugs had a shelf-life of less than one year.
- A quarter of donated drugs were antibiotics.
- Three-quarters of the health facilities had sent a list of drugs required to the donor, but only half received drugs from that list.
- When donated drugs were not requested by the health facility it was more likely that good drug donation practices were not adhered to.

While nurses were the most likely health workers to be in charge of pharmacies and of selecting, prescribing and dispensing drugs, donors usually decided the quantity of each drug to send.

Researchers concluded that:

- Donated drugs are more appropriate when the recipient, not the donor, decides which drugs are sent.
- As nurses play a central role in drug donations they must understand the principles of good donation practices.
- There is still a need to promote the essential drugs concept and use of essential drugs lists by both donors and recipients. □

For further information on the study contact: Dr Eva Ombaka, The Pharmaceutical Programme, World Council of Churches/Community Initiatives Support Services International, P.O. Box 73860, Nairobi, Kenya.

Source: Practical Pharmacy, No. 14, 1999.

Oxfam campaigns to lower drug prices

Oxfam, the international development agency, is launching a campaign on access to medicines, with a focus on the issue of affordability. Oxfam has drawn on its programme experience and local research to produce a number of reports looking at the determinants of drug prices, and at policies that can bring them down. It is paying particular attention to the influence of World Trade Organization intellectual property rules and to the policies of the pharmaceutical industry, and makes policy recommendations to the main actors.

The British-based organization is seeking to raise public awareness on the issues as part of a broader international campaign to make the world trading system work more to the advantage of poor communities and poor countries. Oxfam has humanitarian and development programmes in over 70 low-income countries. It is also a prominent NGO advocate on international economic development issues, including trade and debt. □

For more information visit Oxfam's Web site at: www.oxfam.org.uk or e-mail: <tradecampaign@oxfam.org.uk>. Alternatively, write to George Tarvit, Campaign Department, Oxfam, 274 Banbury Road, Oxford, OX2 7DZ, UK.

ANTIMICROBIAL RESISTANCE

Antimicrobial resistance: the facts

Over the past decade, there has been a dramatic upsurge world wide in the spread of drug-resistant microbes. Major infectious diseases such as tuberculosis, pneumonia and malaria are becoming increasingly difficult and expensive to treat, as microbes develop resistance to many of the medicines available. How widespread is the problem? How does drug resistance develop? And what is WHO doing to contain this threat? Rosamund Williams, Coordinator, Anti-infective Drug Resistance and Containment at WHO explains.

Antimicrobial resistance is on the increase – threatening our ability to treat some of the infectious diseases that cause most deaths. Diseases such as tuberculosis (TB), which was once thought to be under control, are becoming increasingly difficult to treat as medicines become less effective – steadily depleting the arsenal of drugs available.

Infectious diseases still account for 45% of deaths in low-income countries and for almost one in two premature deaths worldwide. And most of these deaths (about 90%) are due to no more than six diseases: acute respiratory infections (mainly pneumonia), diarrhoeal disease, HIV/AIDS, TB, malaria and measles. Antimicrobial resistance is today challenging our ability to treat effectively at least four of these infections: acute respiratory infections, diarrhoeal disease, malaria and TB.

a year in the United States alone, are almost always caused by drug-resistant microbes. Foodborne infections are also on the increase – promoting growing concern about drug resistance in pathogens such as *Salmonella* and *Campylobacter*. Meanwhile, tropical diseases, such as leishmaniasis (see box p.8) and African trypanosomiasis, which haunt the poor and marginalised communities of the world, are becoming increasingly difficult to treat among people also infected with HIV. Treatment with the usual (and sometimes only) drug is increasingly ineffective.

How widespread is the problem?

Drug resistance is a global problem – affecting both developing and developed countries. Its spread is helped by the enormous increase in global travel and trade. Documented examples include:

- cases of drug-resistant gonorrhoea acquired by tourists visiting South-East Asia and transmitted among communities in Australia;
- outbreaks of multidrug-resistant TB in Western Europe traced back to Eastern European countries where TB control is poor;
- two outbreaks of MRSA (methicillin-resistant *Staphylococcus aureus*) hospital infection in Canada involving patients who acquired the strain in India.

In addition, cases of drug-resistant malaria occur among travellers returning to developed countries from malaria-endemic countries where resistance is high. These drug-resistant infections will not spread in developed countries provided there are no mosquito vectors. But global warming could change all that.

resistance is high. These drug-resistant infections will not spread in developed countries provided there are no mosquito vectors. But global warming could change all that.

What is antimicrobial resistance?

When antimicrobial resistance occurs, it is the microbe (bacterium, virus, fungus or protozoan) that is resistant; not the drug, nor the patient. Species of bacteria that are normally resistant to penicillin, for example, can develop resistance to these drugs either through mutation (vertical

transmission) or through acquisition from other bacteria of resistance genes (horizontal transmission). This dual means of acquiring resistance explains why the resistance trait can spread rapidly and replace a previously drug-susceptible population of bacteria.

Are antimicrobial drugs to blame?

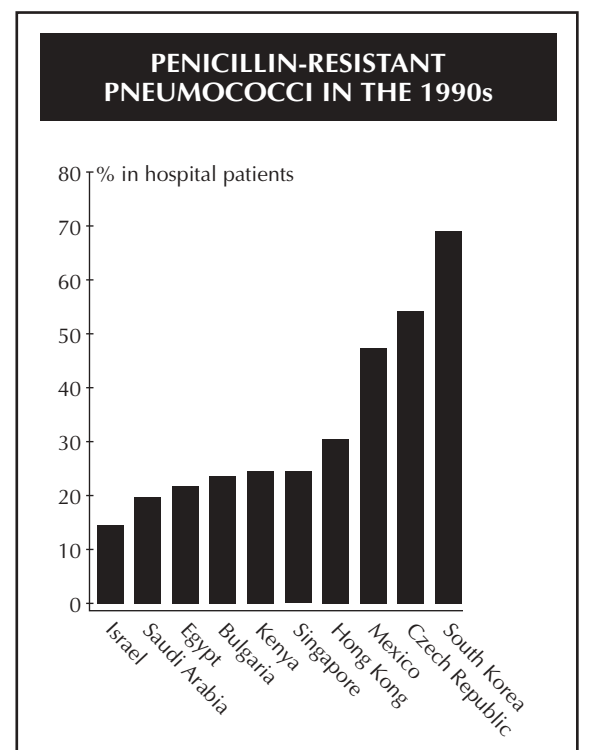
No. Antimicrobial drugs do not cause resistance. But the process is accelerated when antimicrobials are misused. What happens is that natural selection – a natural biological process – favours the survival of microbes that develop resistance genes by chance when exposed to antimicrobials. All uses of antimicrobials – both appropriate and inappropriate – apply a selective pressure on microbial populations. However, the more antimicrobials are used, the greater this pressure will be. Thus it is critical to gain maximum benefit from the curative effects of antimicrobials – especially in developing countries, where they are not only misused, but often under-used due to financial constraints. At the same time, it is also essential to minimise the opportunities for resistance to emerge. In practice this means using antimicrobials both widely and wisely – neither too little, nor too much, and never inappropriately. Inappropriate prescribing practices – including the wrong choice of drug and incorrect dosage or length of treatment – poor compliance with treatment, and the use of low quality (sometimes counterfeit) drugs all contribute to the emergence of drug-resistant microbes.

How does resistance develop?

If a person develops an acute infection such as pneumonia with a drug-susceptible strain of *Streptococcus pneumoniae*, for example, and is treated promptly with penicillin, the bacteria will

be killed and the infection resolved before resistance has time to emerge. However, in the treatment of chronic infections such as TB and HIV/AIDS – especially if treatment compliance is poor – drug-resistant mutants have time to emerge and multiply and replace the drug-susceptible population of microbes. Under these circumstances, it is likely that the treatment outcome will be poor.

So why is it that the microbes involved in acute infections have also become resistant to many of the first-line

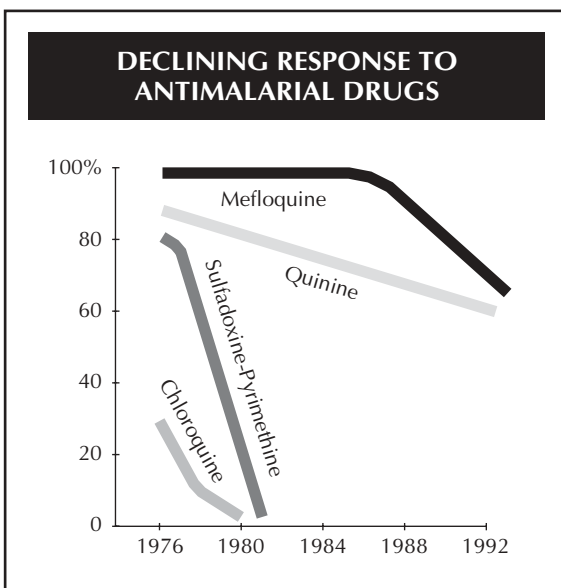


Source: Collected from published data

drugs available? The problem is that antimicrobial drugs not only kill the microbe being targeted, they also “treat” other normally harmless microbes (“normal flora”) in the body as well. For example, *Streptococcus pneumoniae*, as well as causing otitis, pneumonia and meningitis, is also carried by many people, especially children, as part of their normal throat flora, without causing any symptoms. So every time they take an antimicrobial – for whatever reason – their streptococci are exposed. If a mutant emerges, it will have a selective advantage and can spread to other people. A similar process occurs when salmonella bacteria are exposed to antimicrobials incorporated into animal feed. While these bacteria may not cause the animal any harm, they can be spread to humans through the food chain.

What is multidrug-resistance?

There are many different classes of antimicrobials, and microbes have devised ways to resist the action of each and every one. In addition, a single microbial cell can carry resistance genes to a whole series of totally unrelated antimicrobial drugs. Over

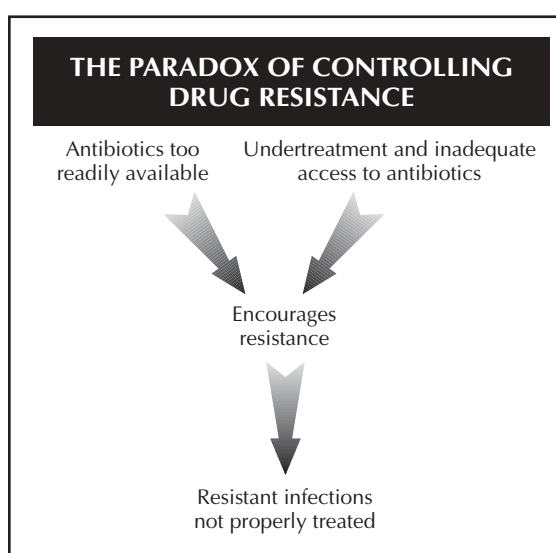


Source: The Southeast Journal of Tropical Medicine and Public Health, Mekong Malaria, Volume 30, Supplement 4, p 68, 1999

Chloroquine, for example – once the first-line treatment for malaria – is no longer effective in 81 of the 92 countries where the disease is a public health problem. In some regions, over half of all cases of streptococcal pneumonia are resistant to penicillin. And over 20% of new TB cases are now multidrug-resistant.

To make matters worse, resistance is already emerging to anti-HIV drugs. There are reports of resistance to all currently marketed antiretroviral drugs. And resistance is also widespread among sexually-transmitted infections, such as gonorrhoea, that enhance the spread of HIV.

But the problem does not end there. Hospital-acquired (nosocomial) infections, which account for 40,000 deaths



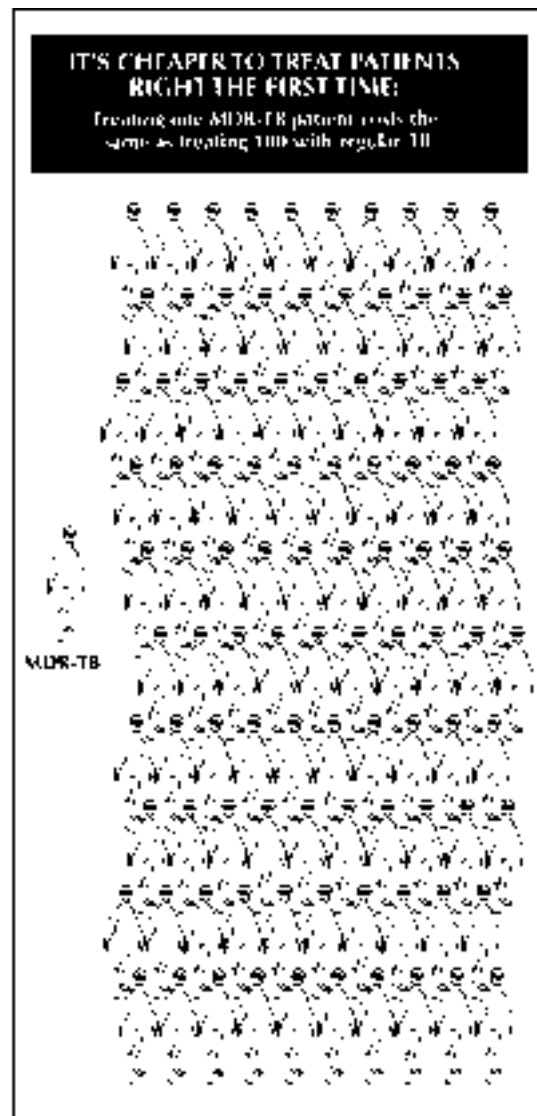
Source: World Health Organization/CDS

...cont'd on page 8

ANTIMICROBIAL RESISTANCE

Antimicrobial resistance... cont'd from pg. 7

time, the dysentery-causing bacterium *Shigella*, for example, has become resistant to each successive class of antimicrobials used in treatment. As a result, it has a string of genes, each



Source: World Health Organization/CDS

coding for resistance to a different antimicrobial. To make matters worse, this string of genes can be transmitted from one bacterial cell to another. Thus a previously susceptible *Shigella* can, in one fell swoop, acquire five or six resistance genes.

Why is antimicrobial resistance spreading so fast?

Although mutations are rare events (about one in a million bacteria may show a mutation which might lead to resistance), microbes multiply very rapidly – thereby enabling a single mutant to rapidly become dominant. Microbes also spread readily from person to person. Thus one patient infected with a resistant strain may be an important source of spread, not only of the infection, but of a resistant infection. This is demonstrated in hospitals, where one patient infected with MRSA, for example, is often the source from which many others become infected or colonised.

Thus in taking action to contain resistance, both the *emergence of resistance* and the *spread of resistant strains* need to be considered.

TACKLING THE PROBLEM

Can antimicrobial resistance be halted?

No. But it can be contained. Antimicrobial resistance is a natural biological phenomenon – the response of microbes subjected to the selective pressure of antimicrobial drug use. The main priority should be to prevent infection in the first place. After that, containment of the problem is the best we can aim for. And since it is antimicrobial use that drives resistance, the focus of any containment strategy should be on minimising any unnecessary, inappropriate or irrational use of antimicrobial drugs. Many groups of people play a role in determining how and where antimicrobials are used:

- patients and the general public;
- all groups of prescribers and dispensers;
- hospital managers and health care professionals;
- users of antimicrobials in agriculture;
- national governments;
- pharmaceutical, diagnostic and “surveillance” industries;
- international agencies, NGOs, professional societies.

All of these groups need to be engaged in developing and implementing a resistance containment action plan.

What is WHO doing?

WHO has taken the lead in developing a Global Strategy for the Containment of Antimicrobial Resistance. The strategy is designed to reduce the emergence of resistance and slow the spread of resistant infections, in an effort to reduce the mortality, morbidity, and high costs

RESISTANCE CAN BE EFFECTIVELY TREATED

Ideal drug usage involves:

- The correct drug
- Administered by the best route
- In the right amount
- At optimum intervals
- For the appropriate period
- After an accurate diagnosis

Problems occur in both developed and developing countries when antimicrobials are:

- Not equitably available
- Used by too many people
- To treat the wrong disease
- In the wrong dosage
- For the wrong period of time
- Not in the correct formulation or strength

Antimicrobial resistance is not a new or surprising phenomenon. All micro-organisms have the ability to evolve various ways of protecting themselves from attack BUT over the last decade or so:

- Antimicrobial resistance has increased
- The pace of development for new and replacement antimicrobials has decreased

RESISTANCE MEANS THAT:

- People can't be effectively treated
- People are ill for longer
- People are at greater risk of dying
- Epidemics are prolonged
- Others are at greater risk of infection

Source: World Health Organization/CDS

The example of leishmaniasis

Leishmaniasis is an insect-borne disease that is showing resistance to the highly toxic, heavy metal-based antimonials at rates of 64% in some developing nations. Currently, visceral leishmaniasis – otherwise known as Kala-azar – afflicts 500,000 people each year in 61 countries in East Africa, India and the Mediterranean basin. The sandfly-transmitted parasite attacks the spleen, liver and bone marrow and is characterised by fever, severe weight loss and anaemia. Left untreated, the disease is fatal. Drug-resistant leishmaniasis results when treatment courses are too short, interrupted, or consist of poor-quality or counterfeit drugs. Once infected, victims remain vulnerable to potentially fatal flare-ups throughout their life. As with most infectious diseases, resistant strains flourish in areas where poverty is high, surveillance is low and treatment frequently inconsistent due to limited medical access, inadequate diagnosis, the availability of parallel-market drugs, and political discord. Active monitoring procedures that could reveal the true extent of the disease are hindered by lack of available funds and civil unrest. In one study, WHO researchers conducting a house-to-house search discovered that the actual rate of infection was 48 times that which had been initially reported.

In the State of Bihar in north-western India, up to 70% of cases are non-responsive to current treatments, while in Bangladesh, Brazil – and particularly Sudan (where 90% of all cases originate), resistance continues to grow. In developed Mediterranean nations, drug-resistant leishmaniasis is spreading as the number of patients co-infected with HIV increases. Those infected with HIV or who are immuno-suppressed in any way (as a result of cancer treatments or organ transplants) are likewise vulnerable. Any kind of immuno-suppression can potentially increase the number of parasites in the blood, thereby giving rise to the likelihood of transmission through the bite of the sandfly. This cycle facilitates a destructive spiral of greater resistance, higher parasitic levels and increased infection-producing potential.

War, globalisation, increased travel and climatic change places this parasitic infection solidly in the category of emerging diseases with rapidly-evolving resistance.

Source: WHO. *Overcoming antimicrobial resistance*. Geneva: World Health Organization; 2000.



A female patient with *Leishmania aethiopica* infection

Photo: WHO/TDR

associated with antimicrobial resistance. The strategy is based on published evidence, expert opinion, and the deliberations of other expert bodies. It includes a review of the factors responsible for the emergence and spread of resistance and of the interventions that have been tested or proposed to address the problem. The strategy provides a framework of interventions for implementation. It also highlights the gaps in current knowledge and the many outstanding research needs. Foremost among these is the need to develop new drugs to combat drug-resistant infections, and to develop a new environment of incentives and public-private partnerships to address the challenges of antimicrobial resistance. □

For further details contact: Dr Rosamund Williams, Communicable Diseases Cluster, Anti-infective Drug Resistance and Containment, World Health Organization, 1211 Geneva 27, Switzerland.

ANTIMICROBIAL RESISTANCE

Who contributes to misuse of antimicrobials?

➤ KATHLEEN HOLLOWAY*

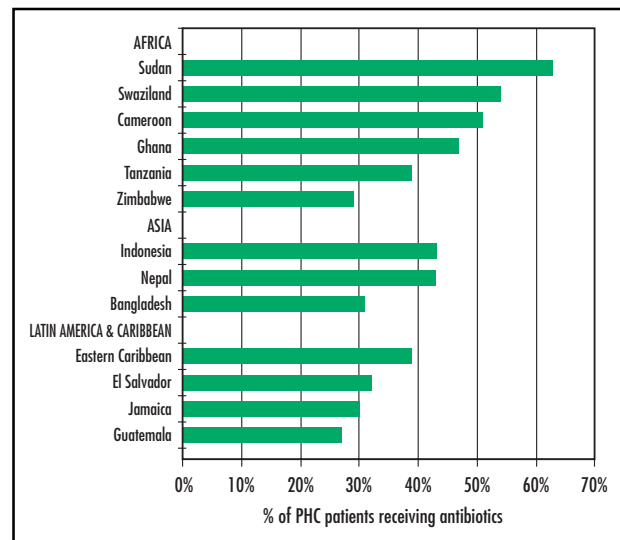
Antimicrobial resistance is a natural consequence of antimicrobial use, which kills the sensitive organisms leaving the resistant ones to survive and multiply (selection of resistance). Overuse and misuse of antimicrobials do not help patients, they merely add to the problem of resistance and waste resources.

Prescribers

There is a wide variation in the prescribing of antimicrobials and other drugs. In primary health care 30–60% of patients receive antibiotics (see Figure 1), perhaps twice what is clinically needed. Misuse is common and may take the form

information, leading to uncertainty about the diagnosis and the most appropriate drug(s), and fear of poor patient outcome
 ➤ patient demand
 ➤ earning a living through selling medicines.

Figure 1
Percentage of primary health care patients receiving antibiotics



Source: *Managing Drug Supply*, 2nd ed. Quick JD, Rankin JR, Laing RO, O'Connor RW, Hogerzeil HV, Dukus MN, Garnett A, eds. Hartford CT: Kumarian Press; 1997.

of incorrect dosage or inappropriate prescription. In Tanzania, 91% of antibiotics were prescribed with incorrect dosage¹ and in India over 90% of prescriptions did not have dose specifications.² Inappropriate prescription of antibiotics has been reported to occur for viral respiratory tract infections in 97% of cases in China³ and 81% of cases in Ghana.⁴ Inappropriate prescription of antibiotics for childhood diarrhoea commonly occurs, as reported in Pakistan. Here private general practitioners were found to prescribe significantly more antibiotics (41% of paediatric cases) than paediatricians (36% of paediatric cases) in the public hospitals.⁵ Hospital prescribers are often the role models for primary health care prescribers. Unfortunately, antimicrobials are misused just as much in hospitals as in primary health care, as shown in Table 1.

Why do providers prescribe antimicrobials too often and unnecessarily? There are many causes including:

➤ lack of knowledge or

Many prescribers in developing countries have little access to good quality information about diagnosis and drugs. Standard treatment guidelines are often unavailable and health workers are often unsupported and unsupervised. Frequently, drug company representatives are doctors' only source of information. Such information may well be biased, particularly with regard to how effective their company's drug is compared to rival drugs of the same class. Uncertainty of the diagnosis, fear of poor patient outcome, (and in industrialised countries, fear of litigation), lead to over-prescription of antibiotics. In many developing countries, the diagnostic process is often inadequate to arrive at

a diagnosis with any certainty (Figure 2).

Patient demand or prescriber perception?

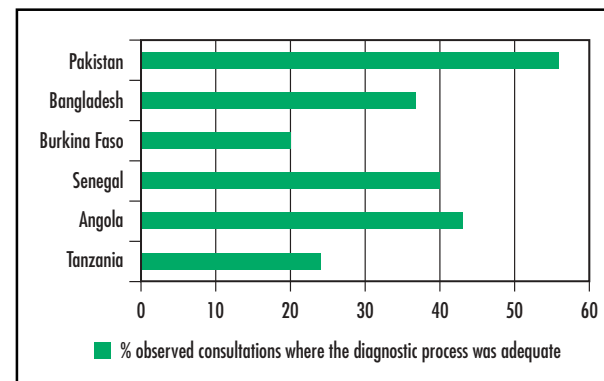
Even if prescribers are certain of their diagnoses (and none of them will be all

the time), they are still greatly influenced by patients' demands. Many traditional practitioners are now prescribing allopathic medicines instead of herbal or other kinds of medicines because this is what patients want. In Tanzania 60% of health workers admitted to prescribing inappropriate drugs demanded by socially influential patients, to avoid being labelled "difficult".⁶ Many people in India believe in 'tonics' and will not return to a doctor unless he or she prescribes according to their wishes. Even though doctors may know that 'tonics' are ineffective, they prescribe them because they are dependent on the patient returning for their livelihood.⁷ In Europe, over 50% of mothers interviewed in a study expected to receive antibiotics for most respiratory infections.⁸ Prescribers citing patient demand as a cause of irrational prescribing has been reported in many countries. And patient demand for specific drugs has been widely observed by researchers. However, the degree to which prescribers are influenced by their patients is unknown and probably varies according to the skills and confidence of the prescriber. There is some evidence that it is a prescriber's perception of patient demand, rather than actual patient demand, during the consultation process that may affect the prescribing decision.^{9,10}

Effects of dispensing doctors

Many prescribers, as well as drug retailers, earn their living by selling medicines and not by charging a consultation fee. It has been shown in many countries that prescribers who earn money from dispensing medicines consistently prescribe more drugs than those who do not make money from dispensing. In a study in Zimbabwe¹¹ dispensing doctors prescribed antibiotics to 58% of their patients compared to non-dispensing doctors who prescribed antibiotics to 48% of their patients. In China, after the 'socialist market economy' reforms of the late 1970s, drug sales became an important source of income for providers, including health worker salary supplements. Once drug sales formed part of health worker salaries, greater polypharmacy was observed, and the average prescription was found to cost two to six times the average per capita daily income.¹² Selling high cost items, such as antibiotics, may earn dispensing prescribers more profit, but unfortunately many patients cannot afford such drugs and may buy incomplete courses. In a study in the Philippines 90%

Figure 2
Adequacy of diagnostic process



Sources: Thaver et al, *Social Science and Medicine* 1998. Guyon et al, *WHO Bulletin* 1994. Krause et al, *Tropical Medicine and International Health* 1998. Bitran, *Health Policy and Planning* 1995. Bjork et al, *Health Policy and Planning* 1992, Kanji et al, *Health Policy and Planning* 1995.

of antibiotic purchases were for 10 or fewer capsules, which in most circumstances would be less than a full course.

In conclusion, antibiotics are often prescribed irrationally (over-prescription and inappropriate prescription) and this contributes to the development of antimicrobial resistance. However, prescribers may have very rational reasons for prescribing irrationally and it is not just a question of lack of knowledge. Only by understanding the reasons underlying inappropriate prescribing can one design effective interventions to change such behaviour. □

* Dr Kathleen Holloway is a Medical Officer in the Department of Essential Drugs and Medicines Policy at the World Health Organization.

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Table 1
Inappropriate use of antibiotics in teaching hospitals

Country	Inappropriate use (%)	Type/department
Canada 1977	42%	Surgical ward – injections, antibiotics
	50%	Gynaecology ward
	12%	Medical ward
USA 1978	41%	All patients
Australia 1979	86–91%	Prophylaxis
Canada 1980	30%	Paediatric medical cases
	63%	Paediatric surgical cases
Australia 1983	48%	All departments
Kuwait 1988	39%	Paediatric inpatients
Australia 1990	64%	Patients on vancomycin
Thailand 1990	91%	All departments
South Africa 1991	54%	Gynaecology inpatients
	22–100%	Unrestricted antibiotics
Thailand 1991	41%	All departments
	79.7%	Surgical prophylaxis
	40.2%	Documented infection

Source: Hogerzeil HV. *British Journal of Clinical Pharmacology* 1995;39:1–6.

ANTIMICROBIAL RESISTANCE

Problems from antimicrobial use in farming

➤ KLAUS STÖHR*

Following their success in human medicine, antimicrobials have been increasingly used to treat disease in animals, fish and plants. They also became an important element of intense animal husbandry because of their observed growth enhancing effect, when added in sub-therapeutic doses to animal feed. Some growth promoters belong to groups of antimicrobials (for example, glycopeptides and streptogramins), which are essential drugs in human medicine for the treatment of serious, potentially life-threatening bacterial diseases. These include *Staphylococcus* or *Enterococcus* infections.

The widespread use of antimicrobials in farming is of serious concern as some of the newly emerging resistant bacteria in animals are transmitted to humans, mainly from food of animal origin or through direct contact with farm animals. Treating disease caused by these resistant bacteria in humans is more difficult and costly and, in some cases, available antimicrobials are no longer effective. The best-known examples are diseases caused by the foodborne pathogenic bacteria *Salmonella* and *Campylobacter* and the commensal (harmless in healthy persons and animals) bacteria *Enterococcus*. Research has shown that resistance in these bacteria is often a consequence of using certain antimicrobials in agriculture.

More studies are needed, however, as the impact of the widespread distribution of non-metabolised antimicrobials through manure and other effluents into the environment is still unknown. And information is also scarce on the type and amount of antimicrobials used in the expanding aquaculture sector. Based on the lessons learned from species living on land, there is an urgent need to review current practices to identify potential hazards. This also applies to other uses of antimicrobials, in plant protection and in industry, for example.

Scale of use

The total amount of antimicrobials used in food animals is not precisely known, although it is estimated that about half of the antimicrobials produced globally are used in farming, particularly in pig and poultry production.

In Europe, all classes of antimicrobial licensed for disease therapy in humans are also registered for use in animals, a situation comparable with other regions in the world, although comprehensive registration data are much more difficult to obtain. National statistics on the amount and pattern of antimicrobial use, in human medicine or anything else, exist in only a few countries.

An average of 100 milligrams of antimicrobials are used in animals in Europe to produce one kilogram of meat for human consumption. Statistics from other regions are scarce, but increased meat production in many developing countries is mainly due to intensified farming, which is often coupled with greater antimicrobial use for both disease therapy and growth promotion.

Factors contributing to overuse

➤ Education on antimicrobial resistance and prudent antimicrobial use is lacking amongst dispensers and prescribers of antimicrobials, and in

many countries, people who are inadequately trained dispense them. One study reported that more than 90% of the drugs used in animals in the United States in 1987 were administered without professional veterinary consultation. Inappropriate doses and combinations of drugs are frequently used in animals. And antimicrobials administered to animal flocks and herds in their feed causes problems of inaccurate dosing, and the inevitable treatment of all animals irrespective of health status.

- Empiric treatment predominates because of the widespread lack of diagnostic services, particularly in developing countries. In many places, it is uncommon to submit clinical specimens and samples from sick animals, due to the costs involved, time restrictions and the limited number of laboratories.
- Drug sales constitute a significant portion of veterinarians' income in some countries and may lead to unnecessary prescribing.
- In many countries, including several developed ones, antimicrobials are available over-the-counter and may be purchased without prescription.
- Inefficient regulatory mechanisms or poor enforcement, with lack of quality assurance and marketing of substandard drugs, are important contributory factors. Discrepancies between regulatory requirements and prescribing/dispensing realities are often wider than in human medicine.
- Antimicrobial growth promoters are not considered drugs and are licensed, if at all, as feed additives.
- As in human medicine, pharmaceutical industry marketing of antimicrobials influences veterinarians' and farmers' prescribing behaviour and use patterns. There are currently few countries with industry codes or government rules for overseeing advertising practices for antimicrobials for non human use.
- There is a significant increase in intensive animal production, particularly in countries with economies in transition where all the factors listed here are present. When animal production appears to benefit from the use of antimicrobials, economic incentives may take precedence over the possible transfer of resistance to humans, and the potential negative impact on human health.

Examples of the consequences of overuse

◆ Shortly after the licensing and use of fluoroquinolone, a powerful new class of antimicrobials, in poultry, fluoroquinolone-resistant *Salmonella* and *Campylobacter* isolations from animals, and soon afterward from humans, became more common. Community and family outbreaks, as well as individual cases, of Salmonellosis and Campylobacteriosis resistant to treatment with fluoroquinolones have since been reported from several countries.

◆ With the emergence of vancomycin-resistant strains of *Staphylococcus* and *Enterococcus* bacteria in many hospitals around the world, the question arose if the use of those antimicrobial agents in agriculture could have compounded the worsening problem. Vancomycin-resistant *Enterococci* were isolated in animals, food and non-treated volunteers in countries where vancomycins were also used as growth promoters in animals. By 1997 all European countries had banned vancomycin, and after this the prevalence of resistant *Enterococci* in animals and food, particularly in poultry meat, fell sharply.

How to tackle the problem

WHO, the UN Food and Agriculture Organization, the Office International des Epizooties and 14 other international governmental and nongovernmental organizations and professional societies have developed a framework of recommendations to reduce the overuse and misuse of antimicrobials in food animals for the protection of human health. (For further information see: http://www.who.int/emc/diseases/zoo/who_global_principles.html).

What the various stakeholders need to do

Responsibilities of regulatory and other relevant authorities

All antimicrobials used in food animals should be reassessed in relation to their propensity to cause antimicrobial resistance in bacteria which can be transmitted to humans. Priority should be given to those products considered most important in human medicine.

After the licensing of veterinary antimicrobials, surveillance of resistance to antimicrobials belonging to classes considered important in human medicine should be conducted. In this way emergence of antimicrobial resistance will be detected in time to allow corrective



A butcher's stall in the Dominican Republic. There is increasing evidence of the problems caused by feeding antimicrobials to farm animals

ANTIMICROBIAL RESISTANCE

Farming... cont'd from pg. 10

strategies to be implemented as part of an efficient post-licensing review.

Authorities should ensure that all antimicrobials for disease control in animals are classified as prescription-only medicines.

Distribution/sales/marketing

Enforcement policies should be designed to ensure compliance with laws and regulations on the authorisation, distribution and sale, and use of antimicrobials. They should aim at preventing the illicit manufacture, importation, and sale of antimicrobials, and at controlling their distribution and use.

Special attention should be paid to the distribution and sale of counterfeit, sub-potent and misbranded veterinary antimicrobials. Enforcement action should be taken to stop such distribution and sale by relevant authorities, in coordination with the exporting country, if appropriate.

Antimicrobial growth promoters

Use of antimicrobial growth promoters that belong to classes of antimicrobial agents used (or submitted for approval) in humans and animals should be terminated or rapidly phased-out in the absence of risk-based evaluations.

Surveillance of antimicrobial resistance

Programmes to monitor antimicrobial resistance in animal pathogens, zoonotic agents (for example, *Salmonella* spp. and *Campylobacter* spp.), and bacteria known to be indicators of antimicrobial resistance (for example, *Escherichia coli* and *Enterococcus faecium*) should be implemented on bacteria from animals, food of animal origin and humans.

Surveillance of antimicrobial use

Information on the amounts of antimicrobials given to food animals should be made publicly available at regular intervals, be compared to data from surveillance programmes on antimicrobial resistance, and be structured to permit further epidemiological analyses.

Prophylactic use of antimicrobials

Use of antimicrobials for prevention of disease can only be justified where it can be shown that a particular disease is present or is likely to occur. The routine prophylactic use of antimicrobials should never be a substitute for good animal health management.

Prophylactic use of antimicrobials in control programmes should be regularly assessed for effectiveness and whether use can be reduced or stopped. Efforts to prevent disease should continuously be in place, aimed at reducing the need for the prophylactic use of antimicrobials.

Education and training

Veterinary undergraduate, postgraduate and continuing education should be evaluated to ensure that preventive medicine, prudent antimicrobial use and antimicrobial resistance are given high priority. The effectiveness of this training should be continuously monitored.

Education strategies emphasising the

Promoting resistance?

➤ JOEL LEXCHIN*

The Autumn 1996 issue of *Health Horizons*, the magazine of the International Federation of Pharmaceutical Manufacturers Associations, ran a two-page feature entitled "International Mobilization Against New and Resistant Diseases." This article highlighted the efforts being made by international organizations and the pharmaceutical industry to deal with the threat of increasing antibiotic resistance. What the article didn't mention was that some in the industry can also play a role in promoting bacterial resistance to currently available medications.

According to one company, ciprofloxacin is "an appropriate choice for your [doctors'] patients at risk." This was the message in an advertisement that appeared in the 3rd October 2000 issue of the *Canadian Medical Association Journal*. "Appropriate" for whom? To answer that question readers had to notice a small asterisk after the word "risk" and then look down to the bottom of the page, where in small print they found the definition. "Appropriate" for what? Once again in small type was the answer; ciprofloxacin should be used in "challenging" respiratory tract infections. Challenging was never defined. In the same advertisement the company claimed that it supports the appropriate use of antibiotics.

Advertisements that do not give clear information or that give it in print that requires the use of a magnifying glass are not supportive of appropriate use of medications. The message in the ad for ciprofloxacin is that doctors should feel free to use this medication as a first line agent any time they are worried about their patients, or think that there is something unusual going on. Ciprofloxacin is a good first choice for a limited number of problems but not for most respiratory tract infections. The Australian Schedule of Pharmaceutical Benefits restricts the use of this antibiotic in these situations and the same is true in some Canadian provinces.

Another recent Canadian journal advertisement, this time for azithromycin, had a young baseball pitcher, his face determined, ready to release the ball with the message "tough on acute otitis media, easy on kids." The message in this case was that doctors and their young patients need a powerful medication to deal with otitis media and that azithromycin fits the bill. However, this does not reflect the growing consensus

that otitis media, at least in children older than two years, should not be treated with antibiotics unless the child fails to improve after 48 hours.

What these advertisements do is to promote, as first line choices, the use of antibiotics that should be kept in reserve, and promote the use of antibiotics for conditions that will probably resolve without any intervention. Both situations represent inappropriate use of antibiotics and clearly have the potential to lead to increased resistance.

The other common feature of these advertisements is that they are for new, expensive antibiotics; drugs that can generate large profits for companies, if sales volumes are large. What doctors do not see is advertising for older, less expensive antibiotics, even though these drugs are the ones that are the most appropriate. When was the last time there was an ad for penicillin for streptococcal pharyngitis or for trimethoprim for a urinary tract infection?

This scenario is not limited to Canada, the situation is, if anything, worse in other parts of the world. The Medical Lobby for Appropriate Marketing (MaLAM) has received a number of examples of inappropriate antibiotic promotion in developing countries. Advertisements in 1994 and 1995 in the Philippines advocated the use of lincomycin for tonsillitis/pharyngitis and clindamycin in upper respiratory tract infections. The most likely cause of any of these conditions is a viral infection where antibiotics are useless. Once again, antibiotics are being advertised for conditions that do not require them.

1997 advertising claims in India for clarithromycin used the words "paediatric suspension... speed, ... strength, ... spectrum, ... safety" without any qualification. In MaLAM's opinion it would have been reasonable for readers

of this ad to interpret those words to mean that clarithromycin has clinically important advantages over alternative antimicrobials and thus was a first line antibiotic for common childhood infections. As MaLAM pointed out, authoritative sources did not recommend clarithromycin as the treatment of choice for paediatric otitis media, pharyngitis or sinusitis. The parallels with the Canadian example of the advertisement for ciprofloxacin are clear; the advertisements are encouraging the overuse of second-line drugs.

A couple of American studies, spanning almost a quarter of a century, make the point that the concern about promotion leading to the misuse of antibiotics is more than just a theoretical problem. The first of these, published in the early 1970s, showed that more appropriate use of the antibiotic chloramphenicol was related to infrequent use of journal ads to learn about usefulness of new drugs, and disapproval of detailers as sources of prescribing information for new drugs.¹ The second study came out in 1996. In this case, researchers presented a group of primary care doctors with three case scenarios, two of which involved infectious diseases, and asked them to choose between four treatment options of equal efficacy but with widely varying costs. The more credibility that doctors attached to information coming from sales representatives the higher the physician's cost of prescribing.²

In many cases in developing countries doctors lack sources of objective information about antibiotics. These doctors are totally reliant on promotional material from companies, with all of the biases that this material entails. In the mid 1980s physicians practicing in a peripheral health centre in Sri Lanka where polypharmacy, multiple antibiotic therapy and the use of mixtures of unproven efficacy were common, were totally dependent on, and positive towards, drug information from drug companies.³

Drug companies are now racing to bring out new, more powerful antibiotics to combat drug resistance, and we should welcome these medications. But if the industry is sincere about wanting to do something about resistance then it should start by monitoring its promotional practices more closely. □

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importance and benefits of prudent use principles must be developed and implemented to provide relevant information on antimicrobial resistance for producers and stakeholders. Emphasis must also be given to the importance of optimising animal health through implementation of disease prevention programmes and good management practices.

The public should be informed of the human health aspects of antimicrobial use in food animals, so that they can support efforts to control antimicrobial resistance.

Research

Stakeholders should identify research priorities to address public health issues of antimicrobial resistance from antimicrobial use in farming. Governments, universities, research foundations and industry should give high priority to supporting research in these areas. □

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ANTIMICROBIAL RESISTANCE

Antibiotic use and bacterial resistance to antibiotics in children in a Vietnamese community

In 1999 a household survey was conducted in one agricultural district in sub-tropical north Viet Nam. This district has 32 community health stations, one district hospital, three licensed private pharmacies, a few private practitioners, about 16 drug outlets and 362 villages. The researchers randomly selected 200 children, aged 1–5 years, within 166 households, from the 225 households in five villages (out of 67 villages where there is a surveillance programme). Nasopharyngeal and throat specimens were collected from each child, and their carers were interviewed to obtain drug use information. Researchers explained the purpose of the study to each household and obtained permission to collect the specimens.

A standardised questionnaire was developed, piloted and then used by four experienced local interviewers. They asked questions about the types of antibiotics which had been used, how long for, where they were purchased, and what they knew about them. At the same time, microbiologists from Hanoi University collected nasopharyngeal (posterior nares) and throat (tonsillar) swabs. The swabs were immediately placed in charcoal transport medium, and transported to the laboratory for culture,

species identification and susceptibility testing.

Ignoring treatment guidelines

It was found that 82% of the children had at least one symptom of acute respiratory infection during the four weeks prior to interview, and that of these children 91% had been treated with antibiotics. Thus, 75% of all the children (both with and without symptoms) had

Figure 1
Antibiotic consumption amongst children

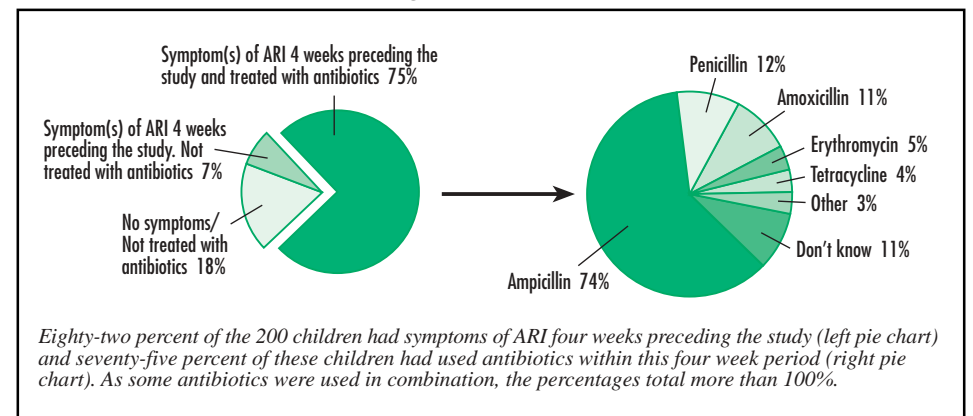


Table 1
Prevalence of antibiotic resistant (R) and intermediate susceptible (I) strain of *H. influenzae*, *S. pneumoniae* and *M. catarrhalis*

Antibiotics	<i>H. influenzae</i> n = 74		<i>S. pneumoniae</i> n = 62		<i>M. catarrhalis</i> n = 27	
	R	I	R	I	R	I
Ampicillin	18%	6%	–	–	19%	30%
Chloramphenicol	24%	0%	25%	3%	15%	4%
Ciprofloxacin	6%	6%	0%	80%	0%	19%
Erythromycin	4%	49%	23%	3%	–	–
Gentamicin	0%	2%	3%	95%	0%	0%
Loracarbef	2%	0%	–	–	0%	4%
Penicillin V	24%	60%	6%	5%	54%	31%
Tetracycline	32%	32%	88%	2%	13%	0%
Trimethoprim/ Sulphonamide	44%	3%	32%	12%	59%	19%
Vancomycin	–	–	2%	2%	–	–

Number of susceptibility tested strains susceptibility tested (n). Antibiotic not tested (–).

been treated with antibiotics. On average antibiotics were given for 3.9 days and ampicillin was the commonest choice; this is contrary to the national treatment guidelines, which recommend cotrimoxazole for acute respiratory infection.

When deciding which antibiotic to use, 67% of carers used a pharmacy, 11% decided themselves, and 22% followed a doctor's prescription. The carers were asked what drug information they paid attention to when treating their children, and replied as below:

daily dosage	87%
how to take the drug (e.g. with water)	52%
total dosage	12%
contraindications	8%
expiry date	3%
antibiotic resistance	1 person

Eighty percent of the antibiotics were purchased from small shops and pedlars, 18% from community health stations and 2% from a national hospital pharmacy.

A disturbing level of resistance

One hundred and sixty-three isolates from 145 children were susceptibility tested. The carrier rate for *S. pneumoniae* was 50%, for *H. influenzae* 39%, and for *M. catarrhalis* 17%. In 74% of the 145

children resistant pathogens were found. Resistance to one or more antibiotics was shown in 68% (50/74) of *H. influenzae* isolates, 90% (56/62) of *S. pneumoniae* isolates, and 74% (20/27) of *M. catarrhalis* isolates. The prior consumption of ampicillin or penicillin was associated with a significantly greater ampicillin or penicillin resistance, odds ratio 2.3 ($p < 0.05$). Multi-drug resistance to a combination of trimethoprim/sulphonamide, tetracycline, chloramphenicol, penicillin V and ampicillin was found in 26% of *H. influenzae* isolates. Multi-drug resistance was found in 31% of *S. pneumoniae* isolates. Almost all *S. pneumoniae* isolates were resistant to both tetracycline and trimethoprim/sulphonamide and about half were resistant to chloramphenicol and/or erythromycin.

The authors conclude that there is a serious public health problem in the Vietnamese community. A majority of children will suffer acute respiratory infection symptoms within any one month. They will be treated inappropriately with antibiotics, which are contributing to significant levels of resistance. □

Source: Larsson M, et al. Antibiotic medication and bacterial resistance to antibiotics: a survey of children in a Vietnamese community. *Tropical Medicine and International Health* 2000;5(20):711–721.

Working to decrease costs of anti-TB drugs

➤ MARCOS ESPINAL, RAJESH GUPTA, MARIO RAVIGLIONE*

Among infectious diseases tuberculosis (TB) remains a leading cause of adult mortality.¹ Over the last decade, the rising spectre of multidrug-resistant TB (MDR-TB) began

to threaten global TB control efforts. MDR-TB is defined as disease caused by *Mycobacterium tuberculosis* resistant to at least isoniazid and rifampicin, the two most powerful anti-TB drugs. There is evidence that short-course chemotherapy with first-line anti-TB drugs used to treat drug-susceptible cases is not as effective

to cure MDR-TB cases.² In some areas of the world (especially countries of the former Soviet Union and eastern Europe), rates of MDR-TB among new and previously-treated cases are so high that they are considered “international public health emergencies” given the possibility of international spread.^{3,4}

To respond to the challenge, WHO and several partners have launched pilot projects to manage MDR-TB within programme conditions in settings of limited resources. However, one of the greatest obstacles to providing treatment to patients infected with MDR-TB has been the high cost of the second-line anti-TB

ANTIMICROBIAL RESISTANCE

**Anti-TB drugs...
cont'd from pg. 12**

drugs needed for the management of MDR-TB.⁵ Over the last three years, open market prices for these second-line anti-TB drugs have been as high as US\$15,000 for an 18-month treatment regimen. In contrast, the first-line anti-TB drugs needed for management of drug-susceptible TB cost as little as US\$11 for a six-month treatment regimen.⁶ In order to decrease the cost of these drugs, the WHO Working Group (specially created to deal with MDR-TB) has negotiated with both the research-based and generic pharmaceutical industry. Negotiations have resulted in a preferential price decrease in the cost of treatment regimens of up to 90% in comparison to the open market price. These preferential prices were partially achieved through global procurement of drugs. Consolidating the market into a single-demand source not only allowed for some market forces to arise, but also for industry members to conduct more accurate demand forecasts that, previously, had been very difficult.

At the same time, in order to protect against the misuse of drugs and creation of resistance to these drugs (the last line of chemotherapeutic defence against TB), these preferentially priced drugs are only released to those projects adhering to standard scientific guidelines as determined by an independent body called the

Green Light Committee.⁷ This Committee, housed in WHO, is currently comprised of six institutions: Centres for Disease Control and Prevention, Harvard Medical School, Médecins Sans Frontières, the National TB Programme – Peru, Royal Netherlands TB Association and WHO (serving as a permanent member and secretariat). Most of the work conducted by the Green Light Committee is performed via videoconference, teleconference and e-mail. All decisions are made by consensus.⁸

Overall, the process has worked well due to the joint efforts of all institutions involved. Pilot projects have benefited from the procurement process and the negotiations, which, by virtue of the mechanism described, guarantee that high-quality anti-TB drugs provided at preferential prices are used in the best possible, controlled manner. This method of procurement helps to ensure the scientific integrity of the pilot projects and should be explored for use in other infectious diseases, including HIV/AIDS. □

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A patient in Tanzania suffering from TB, a disease which is becoming increasingly common and increasingly resistant to drug treatments

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Photo: WHO/C. Harber

How Chile tackled overuse of antimicrobials

➤ LUIS BAVESTRELLO AND ANGELA CABELLO*

In 1998, the Pan American Infectious Diseases Society and the Pan-American Health Organization carried out a study in Chile on trends in antimicrobials use during the previous 10 years.¹ The study revealed a significant increase in antibiotic consumption, expressed in terms of DDD (defined daily dose) per 1,000 population per day over the 10 years, based on annual sales data for antibiotics in terms of both grams consumed and units of sale.² Noteworthy findings included increases in sales of amoxicillin (+ 498%), oral cephalosporins (+ 309%) and oral fluoroquinolones (+ 473%) between 1988 and 1997. The only antibiotic with declining consumption was chloramphenicol (-18%). See Tables 1 and 2.

These findings were submitted to the Chilean Ministry of Health, and meetings arranged to study what to do about the problem. Health Ministry staff met with scientific associations, the body regulating drug manufacture and prescribing, the Institute of Public Health and the

Table 1
Percentage increases in consumption of selected antibiotics and groups of antibiotics, 1988-1997

Antimicrobial	1988 DDD/1000 pop. per day*	1997 DDD/1000 pop. per day	Variation % increase
cloxacillin	0.39	0.417	7
ampicillin	0.54	0.613	14
amoxicillin	0.87	5.204	498
clavul. amoxicillin	0.0025	0.414	16460
cotrimoxazole	0.965	1.163	20
cephalosporins	0.064	0.262	309
fluoroquinolones	0.049	0.281	473

* Defined Daily Dose per 1,000 population per day

Committee on Health of the National Congress. Professional organizations of physicians and chemists, and the National Department of Consumer Affairs were also consulted, with a view to informing the general public before adopting any potentially unpopular measures. This was necessary because people were accustomed to purchasing antibiotics without a prescription, and even

individual tablets in Chile's pharmacies.

Hitting the headlines

At the end of September 1999, after this consultative process, the Ministry of Health acted to control antibiotics, by making them available only through chemists and on prescription. Compliance with the measure was encouraged by distributing leaflets in private chemists,

displaying posters and by extensive coverage on radio and television news programmes. In addition, the attention of the pharmaceutical chemists responsible for the technical management of pharmacists was drawn to the increase in antibiotic consumption over the previous 10 years.

...cont'd on page 14



These children playing happily in Chile stand to benefit from the country's actions to minimise antimicrobial resistance

Photo: WHO/PAHO/C. Greggero

ANTIMICROBIAL RESISTANCE

Chile... cont'd from pg. 13

Three months after the Ministry's action an evaluation study showed a downturn in consumption. This further study, entitled "Preliminary evaluation of the impact of the measures to regulate outpatient consumption of antimicrobials in Chile", involved a comparison between the same two quarters of two years, one immediately before the introduction of the measure, the other immediately after. The study showed a decline in consumption of 36% in amoxicillin, 56% in ampicillin and 30% in erythromycin between the last quarter of 1998 and the same quarter of 1999.

Expenditure dropped by US\$6,483,883 between 1998 and 1999, representing a saving for the population as shown in Table 4.

Studies reveal that the Ministry of Health's control measures introduced after consultation with scientific, professional and consumer associations, and with Parliament, had a clear impact on

Table 2

Annual sales of packs of antimicrobials in private pharmacies in Chile, by antimicrobial group, 1988-1997

Year	Macrolides	Penicillin: broad spectrum	Penicillin: M-R Spectrum	Cephalosporin	Cotrimoxazole	Tetracycline	Chloramphenicol	Fluoroquinolone
1988	765,800	3,199,000	3,488,600	1,409,800	836,500	392,600
1989	798,400	3,373,700	3,797,800	185,200	1,457,000	851,400	457,100
1990	989,235	3,633,271	3,379,425	214,084	1,478,396	870,288	398,428
1991	1,053,390	4,104,949	3,354,194	221,457	1,717,625	1,028,031	402,170
1992	1,118,807	4,368,913	3,240,031	247,261	1,578,412	914,297	278,566
1993	1,435,275	5,151,850	3,289,910	322,135	1,752,653	883,301	298,809	240,167
1994	1,400,078	5,090,712	3,250,074	367,539	1,543,922	844,178	276,392	269,452
1995	1,615,879	6,213,139	3,548,893	505,036	1,532,223	1,016,890	320,594	307,376
1996	1,818,824	6,858,590	3,676,448	537,154	1,550,226	979,917	341,639	335,728
1997	2,076,073	7,799,949	4,035,888	563,902	1,692,889	1,055,055	330,348	414,625

... = No data available

Source: International Marketing System

the sale and consumption of antibiotics in Chile. As a result, in Chile antibiotics may now only be purchased by prescription. This has reduced self-medication and the concomitant threat of microbial resistance.

Table 3

Changes in consumption by DDD/ 1000 pop./ per day between the last quarter of 1998 and the same quarter of 1999 (immediately after the introduction of the Ministry of Health regulation)

Antimicrobials	4 th quarter 1998	4 th quarter 1999	Variation (%)
clarithromycin	0.366	0.446	21.8
azithromycin	0.342	0.353	3.2
erythromycin	0.536	0.370	-30.9
amoxicillin	4.639	2.943	-36.5
ampicillin	0.391	0.182	-53.4
clavulanic amoxicillin	0.459	0.443	-3.5
cloxacillin	0.424	0.338	-20.3
phenoxymethylpenicillin	0.184	0.111	-39.7
cotrimoxazol	0.913	0.633	-30.7
tetracycline	0.499	0.340	-31.8
ciprofloxacin	0.317	0.386	21.8

Table 4

Dollar sales of groups of antimicrobials by private pharmacies in Chile, 1998-1999

Group of antimicrobials	1998	1999	Difference(US\$)
macrolides	14,763,740	12,448,627	2,315,113
broad spectrum penicillins	13,747,242	11,227,954	2,519,288
oral cephalosporin	4,488,543	4,193,849	294,694
fluoroquinolone	4,075,818	4,115,261	-39,443
med.-nar. spect. penicillin	4,121,100	3,275,517	845,583
cotrimoxazole	2,316,260	1,767,612	548,648
Total	43,512,703	37,028,820	6,483,883

Source: International Marketing System

This Chilean example shows that given political will, determination, consultation and public education, effective measures that save lives – by promoting rational use of antibiotics – and money are possible. □

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Nepal: an economic strategy to improve prescribing

A pre-post with control study was conducted in 33 health facilities (10-12 per district) in three districts in Eastern Nepal¹. In 1992 all three districts charged the same flat fee per prescription, covering all drugs in whatever amounts. In 1995 the control district charged the same fee, but the other two districts had instituted new fee systems. One district charged a single fee per drug item (1-band item fee), whatever the drug, but covering a full course of the drug. A second district charged a higher fee per expensive item (e.g. antibiotics and injections) and a lower fee per cheap item (e.g. vitamins), each fee covering a full course of the drug. All the fees were priced so as to cost patients about 25% of average daily household income for two drug items. Prescribing was monitored in all health facilities before and after the

fee systems were changed.

Table 1 shows that both item fees were associated with significantly better prescribing quality than the prescription fee. The percentage of patients receiving antibiotics decreased and the proportion of prescriptions conforming to standard treatment guidelines increased in both item fee districts as compared to the prescription fee district. The 1-band fee was associated with a greater reduction in cheap vitamins and tonics, and the 2-band fee with a greater reduction in expensive injections. □

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Table 1

The effects of different kinds of user fee on prescribing quality in Nepal

Fees system	Control flat fee / Px n=12	1-band fee / drug item n=10	2-band fee / drug item n=11
Av. no. items/Px	2.9 → 2.9 (0%)	2.9 → 2.0 (-31%)	2.8 → 2.2 (-21%)
% Px with antibiotics	66.7 → 67.5 (+0.8%)	63.5 → 54.8 (-8.7%)	60.7 → 54.3 (-6.4%)
% Px with injections	23.4 → 20.0 (-3.4%)	19.8 → 16.1 (-3.7%)	21.8 → 14.9 (-6.9%)
% Px with vitamins or tonics	27.0 → 22.1 (-4.9%)	26.5 → 8.4 (-18.1%)	23.5 → 15.8 (-7.8%)
% Px conforming to STGs	23.5 → 26.3 (+2.8%)	31.5 → 45.0 (+13.5%)	31.2 → 47.7 (+16.5%)
Av. cost / Px (NRs)	24.3 → 33.0 (+35.8%)	27.7 → 28.0 (+1.1%)	25.6 → 24.0 (-6.3%)

Px = prescription

ANTIMICROBIAL RESISTANCE

Containing drug resistance through hospital infection control

> NIZAM DAMANI*

Hospitals are a crucial component of the antimicrobial resistance problem world wide, because highly vulnerable patients often require prolonged antibiotic therapy, and the problem of cross infection arises.

Every hospital should make containment and control of multi-resistant micro-organisms a high priority, and it requires a team approach. The first step is to establish an active and effective infection control committee with responsibility for formulating, implementing and auditing an infection control programme throughout the hospital.

The microbiology laboratory's role

A good diagnostic microbiology laboratory service is essential. Laboratories should use internationally recognised protocols to identify organisms and antibiotic sensitivity, and their range of diagnostic facilities should cover non bacterial and unusual infections. Close liaison with clinicians, the infection control team and the drug and therapeutics committee is essential. Laboratories should serve as an important source of local surveillance data both for the hospital and the community.

Antibiotic prescribing: a crucial element

Hospital drug and therapeutics committees should be responsible for the promotion of rational prescribing, drug use monitoring and cost containment. They must regularly review antibiotic use, conduct audits and give doctors feedback to influence prescribing habits. Committees should also approve the use of newer antimicrobial agents, which should be restricted to agreed clinical conditions.

Doctors must be trained to take responsibility for rational prescribing and to justify their antimicrobial use. Their prescribing policy must be evidence-based and should reflect local antibiotic resistance surveillance data. This can be achieved by having a written hospital formulary, and an antibiotic policy that is regularly updated and has broad input and consensus among all involved.

Infection control measures

Barrier precautions are vital to prevent the spread of multi-resistant micro-organisms in hospitals. These include isolating patients with multi-resistant organisms, and ensuring that staff adheres to hand hygiene procedures and use of appropriate personal protective equipment. It is important for infection control measures to be based on the local epidemiology and be tailored to

suit individual needs.

Hospitals should have a written disinfectant policy with procedures to ensure adequate decontamination of equipment and the environment. Internationally recommended sterility checks must be carried out on a regular basis. As multi-resistant organisms can survive in the environment for prolonged periods, and may act as a reservoir for infection, the hospital environment should be kept clean, dry and dust free.

Therapeutic devices, such as urinary and intravenous catheters, are not only responsible for the majority of hospital-acquired (nosocomial) bacteraemias, but also for cross infection/outbreaks of multi-resistant organisms. Urinary catheters should be inserted only when necessary and removed when no longer required. All hygiene precautions must be followed. The use of antibiotics should be restricted to patients who show clinical signs of infection.

The majority of primary blood stream infections are associated with the use of intravascular devices. Again the best prevention is to insert an intravascular line only if necessary and to keep it in place for a minimum period. The routine use of antibiotics to prevent

catheter-associated and intravenous line infection is not recommended.

A universal challenge

The control and containment of multi-resistant micro-organisms represents a universal challenge requiring national and international efforts, as ease of long distance travel no longer limits spread. Every hospital should devote adequate resources to an infection control programme or health and health care resources could suffer. □

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No one is more vulnerable to multi-drug resistance than people admitted to hospital wards

Photo: WHO/FAHO/A. Wack

Changing prescriber behaviour

TRAINING AND TREATMENT GUIDELINES IMPROVE PRESCRIBING IN UGANDA

A randomised controlled trial to test the impact of standard treatment guidelines (STGs) plus training and supervision on rational prescribing was carried out in 127 health units in Uganda. Prescribing was monitored in all facilities both before and after the interventions. In a control group of 42 health units, no intervention was introduced. In a second group of 42 health units, the national standard treatment guidelines were disseminated but no training or supervision was conducted. In a third group of 29 health units, the national standard treatment guidelines were introduced and on-site training on therapeutic problems conducted. In a fourth group of 14 health units, the same was done as for the third group but, in addition, four supervisory visits were conducted over a six-month period.

Table 1 shows how prescribing changed in the different groups. Prescribing quality, (as judged by the percentage

of prescriptions conforming to standard treatment guidelines) did not improve when only guidelines were disseminated, but greatly improved if dissemination was accompanied by training and supervision. The intervention used was not only directed at antibiotic prescribing, but other aspects of prescribing also. This may account for why the changes in prescribing quality (percentage of prescriptions

conforming to treatment guidelines) were much greater than for antibiotic use alone (percentage of prescriptions containing antibiotics). □

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Kafuko J.M, Zirabumuzaale C, Bagenda D. Rational drug use in rural health units of Uganda: effect of national standard treatment guidelines on rational drug use. Final report. Kampala: UNICEF, Uganda; 1996.

Table 1
Randomised controlled trial in Uganda

Randomised group	n	% prescriptions containing antibiotics	% prescriptions conforming to STG
Control group	42	53.0 → 58.0% +5.0%	24.8 → 29.9% +5.1%
Dissemination of STG	42	51.6 → 57.8% +6.2%	24.8 → 32.3% +7.5%
STG + on-site training in therapeutic problems	29	51.7 → 50.7% -1%	24.0 → 52.0% +28.0%
STG + on-site training in therapeutic problems + 4 supervisory visits in 6 months	14	54.3 → 54.3% 0%	21.4 → 55.2% +33.8%

ANTIMICROBIAL RESISTANCE

Prioritising interventions to contain antimicrobial resistance

➤ KATHLEEN HOLLOWAY*

Just as there are many actors and activities that contribute towards antimicrobial resistance, so there are many potential strategies to contain the growth and spread of resistance. The WHO Global Strategy to contain resistance, (which will be published in 2001 and will be available on the Web via <http://www.who.int/emc/amr>), identifies 64 interventions in total. Of these, 44 interventions are aimed at improving the use of antimicrobial drugs in humans at the national level or below, (i.e. excluding interventions concerning animal use, new vaccine and drug development and international measures).

Critical decisions

No country in the world is implementing all of these recommended interventions and most would find it impossible to do so. Therefore, all countries will need to prioritise the interventions and choose which ones to implement first and which to implement later. Developing countries in particular will need to prioritise and choose only those interventions that, in their local contexts, are both feasible and likely to have the greatest impact. This article discusses the problem of how to choose which interventions will be both feasible and have a significantly large impact. Two methods are

described. The first method was used in two WHO Regional Offices and one country, whilst the Global Strategy was being developed. From the problems encountered using the first method, a second method was developed and used at WHO Headquarters in finalising the present draft of the Global Strategy.

THE REGIONS' PRIORITISATION PROCESS

Step one: deciding who participates in the process

A list of participants was agreed locally. In the Regional Office for the



A pharmacy in Colombia. Ensuring good dispensing practices is seen as a high priority in the fight against antimicrobial resistance

Photo: WHO/PAHO/A-Woak

Table 1
Agreed list of interventions to contain antimicrobial resistance

Target group	Recommended interventions
A Patients and the public	<ol style="list-style-type: none"> 1. Education on appropriate use 2. Education on hygiene 3. Discourage self-medication
B Prescribers and dispensers	<ol style="list-style-type: none"> 1. Training 2. Guidelines and formularies 3. Monitoring and supervision 4. Regulation of professionals 5. Educate prescribers about promotion
C Health systems	<ol style="list-style-type: none"> 1. Therapeutic committees 2. Infection control committees 3. Guidelines for antimicrobial use 4. Antimicrobial use surveillance 5. Laboratory network and epidemiological resistance surveillance
D Government policies, strategies and regulations	<ol style="list-style-type: none"> 1. National AMR task force with budget 2. Drug policies e.g. essential drugs list, standard treatment guidelines 3. Registration of all drug outlets 4. Antimicrobials by prescription-only 5. Dispensing of antimicrobials by licensed staff only 6. Quality assurance system 7. Drug licensing to include resistance data 8. Undergraduate and postgraduate training on AMR 9. Access to evidence-based drug information 10. Cut perverse rational drug use economic incentives 11. Monitor and supervise drug promotion 12. Monitor and link AMR and drug use data
E Pharmaceutical industry	<ol style="list-style-type: none"> 1. Incentives for industry to do research and development 2. Monitor and supervise drug promotion 3. Production according to Good Manufacturing Practice standards
F Non-human antimicrobial use	<ol style="list-style-type: none"> 1. Surveillance of resistance and use 2. Phase-out growth promoters 3. Educate farmers and vets

Eastern Mediterranean (EMRO) and the Regional Office for South-East Asia (SEARO), participants were WHO staff members. In Nepal they were from the Ministry of Health, academic institutions and local NGOs. All health disciplines concerned with antimicrobial use and/or resistance were invited, including all those concerned with communicable diseases, health systems, essential drugs and primary health care.

Step two: developing a list of interventions

EMRO participants developed a list of interventions starting from those recommended in the WHO draft Global Strategy. SEARO and Nepali participants also agreed to use this list (see Table 1).

Step three: voting on the proposed interventions

Each intervention was scored according to:

- (1) the importance or relevance of any impact it might have, and
- (2) the feasibility of implementation.

It was agreed that "relevance" would take into account whether an intervention would impact on the diseases of particular concern locally, and that "feasibility" would take into consideration both cost of implementation and the political context. The scoring was as follows:

- 0 = not feasible or no relevant impact
- 1 = medium feasibility or medium relevant effect
- 2 = good feasibility or very relevant effect

Step four: collating the voting data

All the participants' scores for likely relevant impact and feasibility for each intervention were added up and then plotted on a matrix. Interventions that were likely to have the greatest impact and be feasible appeared in the top right-hand

corner of the chart and were judged to be of highest priority. Those interventions that appeared in the bottom left-hand corner of the chart were judged less feasible and relevant. For example, in a group of 11 people, the maximum score an intervention could receive for either importance or feasibility was 22 (11 participants awarding a maximum of two points). The points plotted on the matrix would therefore be 22 for importance and 22 for feasibility.

Diverse views

The graphs below (figures 1–3) indicate the priority given to different interventions. Comparison shows how the various regions agreed and disagreed on which interventions should have highest priority. The reasons for differences in the priorities between these three groups may have been due to different priorities in different areas, but were also in large part due to the different expertise of participants in the different groups. For example, in SEARO there was no one specialising in health systems or drug regulation, in Nepal microbiologists were poorly represented, as were agriculturalists in both EMRO and SEARO.

The most feasible and important interventions agreed by everyone included:

- training of prescribers and dispensers, and the use of guidelines and formularies;
- establishing infection control committees, guidelines for antimicrobial use, and surveillance of antimicrobial use in hospitals;
- developing national drug policies, essential drugs lists and standard treatment guidelines;
- ensuring undergraduate and postgraduate training on antimicrobial resistance;

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➤ ensuring drugs are produced according to Good Manufacturing Practice standards.

The least feasible and important interventions agreed by everyone included:

- ensuring that antimicrobials are dispensed by licensed staff and only with a prescription;
- cutting perverse economic incentives to prescribe antibiotics – for example the problem of dispensing prescribers earning more money from selling antibiotics than from other drugs;
- monitoring and linking data concerning antimicrobial resistance and antimicrobial use;
- monitoring and supervising drug promotion both for human and animal use;
- phasing out growth promoters in animal use.

PRIORITISING INTERVENTIONS FOR THE WHO GLOBAL STRATEGY

As a result of the diverse views obtained from the regions, a different process of prioritisation was conducted for the draft Global Strategy, in order to produce some concrete practical advice for Member States.

Experts in the fields of drug use,

clinical microbiology and other related disciplines from all over the world were invited to a workshop in Geneva. Participants were divided into three working groups, with each considering interventions aimed at a particular target audience:

- Group 1: Prescribers and dispensers
- Group 2: Hospitals
- Group 3: Health systems

For each target audience, the interventions were prioritised according to their relative merits and ranked according to sequence and importance of implementation. This complex task required consideration of multiple factors relating to each intervention including:

- overall importance of the intervention to improving the appropriate use of antimicrobials and containing antimicrobial resistance;
- likely impact, allowing for the expected cost of implementation;
- complexity of implementation, considering the capacity of various health care systems and political realities;
- time required for implementation and the expected lag period before outcomes could be expected;
- the accuracy with which most health care systems could assess the efficacy of each intervention;

the interrelationship between various interventions, including the need to undertake some interventions in a logical sequence.

As a result of this process, interventions were ranked as high, medium and

low, and consideration was given to whether the ranking would vary according to a national health system's level of development.

Once interventions for each target

...cont'd on page 18

Figure 1
Prioritisation of interventions by the 11 members of EMRO antimicrobial resistance task force

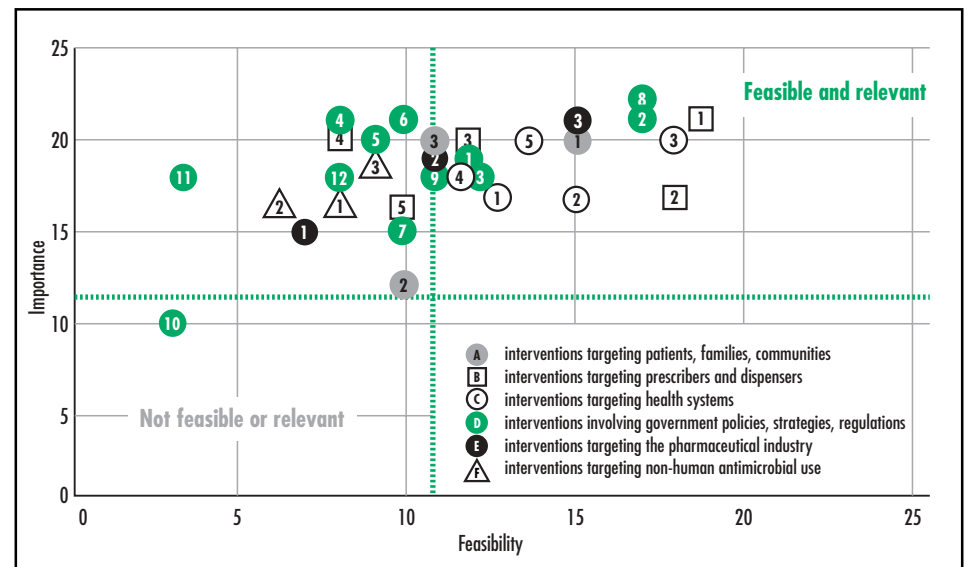


Figure 2
Prioritisation of interventions by 15 health officials in Nepal

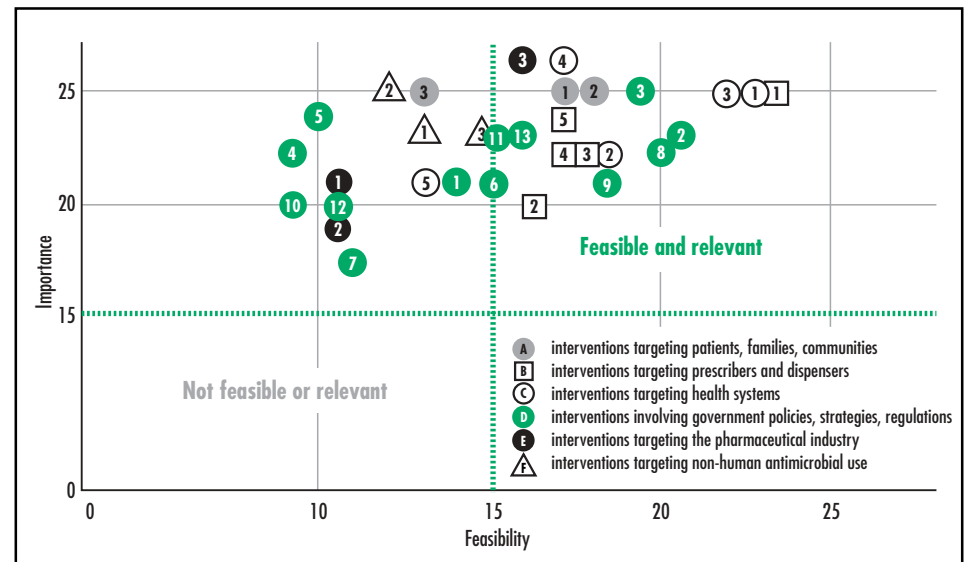
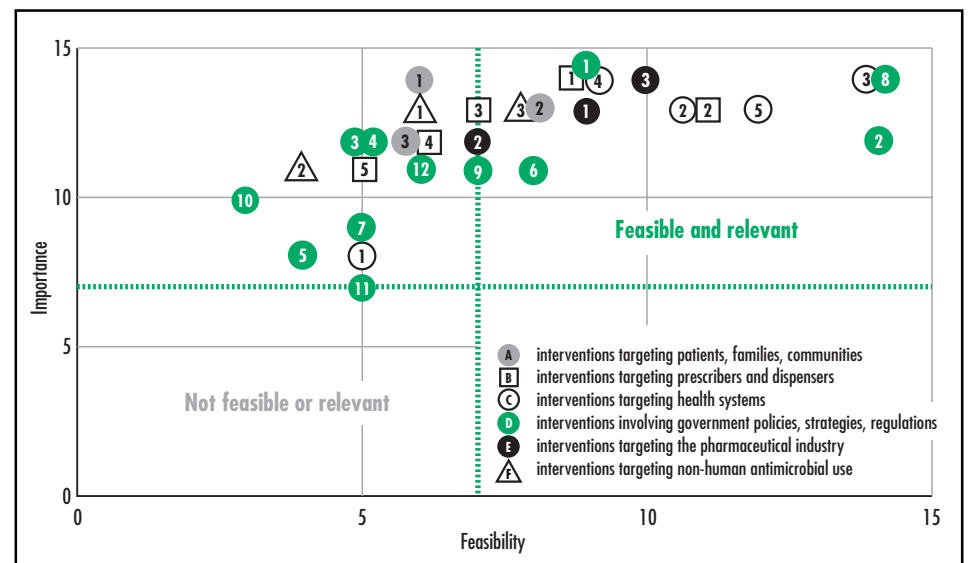


Figure 3
Prioritisation of interventions by 7 staff members of SEARO



The figures should be viewed in conjunction with Table 1, as the different shapes and colours on the three graphs each represent one of the six target groups (A–F) listed in the Table. For example, a green circle signifies D – interventions involving government policies, strategies and regulations. The numbers within each shape correspond to the different recommended interventions in each of the target groups. So there are 12 green circles on the map numbered 1 to 12, corresponding to the numbered list of interventions under D in Table 1. Their position on the graph is dependent on the scores participants awarded them. For example, D10 – cutting perverse rational drug use economic incentives – appears in the bottom left-hand corner of the graph, showing that it received the lowest scores for both importance and feasibility.

The dotted green cross lines signify where the average score (1 point for both importance and feasibility awarded by each person in the group) would appear.

Priorities in the WHO Global Strategy for Containment of Antimicrobial Resistance

Although all interventions were classified into fundamental, high, medium and low, only the first two categories are shown below. Within the two priority groupings shown here, interventions are not ranked.

Fundamental interventions

Make containment of antimicrobial resistance a national priority including:

- ◆ creating a national task force;
- ◆ allocating resources to implement interventions to contain antimicrobial resistance;
- ◆ developing indicators to monitor and evaluate the impact of an antimicrobial resistance strategy;
- ◆ designating or developing reference microbiology laboratory facilities. These would coordinate effective, epidemiologically-sound, surveillance of antimicrobial resistance among common pathogens in the community, hospitals and other health care facilities.

High priority interventions

1. Patient education on:
 - ◆ the importance of measures to prevent infection such as immunization, vector control, use of bed-nets;
 - ◆ simple measures that may reduce transmission of infection in the household and community, such as hand washing, food hygiene.
2. Prescriber and dispenser (including drug seller) education on:
 - ◆ the importance of appropriate antimicrobial use and containment of antimicrobial resistance;

- ◆ disease prevention (including immunization) and infection control issues.
3. Targeted undergraduate and post-graduate education programmes for all prescribers, dispensers and other health care workers, and veterinarians, on accurate diagnosis and management of common infections.
 4. Development, updating and use of standard treatment guidelines and treatment algorithms to foster appropriate use of antimicrobials.
 5. Infection control programmes with responsibility for effective management of antimicrobial resistance in hospitals.
 6. Diagnostic laboratories that provide:
 - ◆ microbiology laboratory services which are appropriately matched to the level of the hospital (e.g. secondary, tertiary);
 - ◆ appropriate diagnostic tests, bacterial identification, antimicrobial susceptibility tests of key pathogens, with adequate quality assurance, and timely, relevant reporting of results.
 7. Limiting the availability of antimicrobials to prescription-only status, except in special circumstances where they may be dispensed on the advice of a trained health care professional.
 8. Ensuring that only antimicrobials meeting international standards of quality, safety and efficacy are granted marketing authorisation.

ANTIMICROBIAL RESISTANCE

Prioritising interventions... cont'd from pg. 17

audience were ranked, the interventions were then ranked according to their overall importance and timing (sequence) of implementation, without consideration of their target audience. This was done by all the participants in a plenary session (see box). It was recognised that some priorities might vary depending on the health care system in which they would be implemented. However, this did not impact to any significant extent on the priority given to the majority of very high priority interventions.

Although it was not planned to address issues relating to consumers and drug promotion at this workshop, in fact they were also considered. This was because participants, particularly in Group 1, felt that prescribers and dispensers could not be considered separately from consumers.

INTERVENTIONS FOR MAXIMUM IMPACT

Comparison of the priorities identified at country, regional and international levels shows many similarities. The interventions agreed by everyone to be both high priority and feasible are:

1. training prescribers and dispensers, and using guidelines and formularies;
2. establishing infection control committees and guidelines for antimicrobial use;
3. developing national drug policies, essential drugs lists and standard treatment guidelines;
4. ensuring undergraduate and postgraduate training on antimicrobial resistance;
5. ensuring that drugs are produced according to good manufacturing practice standards and are of adequate quality.

Interestingly, regional staff felt that surveillance of antimicrobial use in hospitals was feasible and important, and gave it higher priority than the experts invited to Geneva did. On the other hand, while the Geneva group felt that restricting antimicrobials to prescription-only status was very important, regional staff felt that it was not feasible.

There is no hard evidence as to which interventions are most important and have the greatest impact, and expert opinion varies. Nevertheless the two different processes of prioritisation identified the five interventions listed above. Everyone agreed that these interventions were feasible and would have the greatest impact on antimicrobial resistance if adequately implemented. □

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A leaflet from the UK's public education campaign on the correct use of antibiotics

Department of Health, UK

Useful websites on antimicrobial resistance

APUA-Alliance for the Prudent Use of Antibiotics
<http://www.antibiotic.org> (see also EDM No.24 p.20)

AR InfoBank-WHO Antimicrobial Resistance Information Bank
<http://oms2.b3e.jussieu.fr/arinfobank>

BUBL Catalogue of Internet Resources – Infectious Diseases
<http://bubl.ac.uk/link/i/infectiousdiseases.htm>

Center for Adaptation Genetics and Drug Resistance
<http://www.healthsci.tufts.edu/labs/Sblevy/home.html>

Center for Complex Infectious Diseases
<http://www.ccid.org/>

Centers for Disease Control, Drug Resistance Homepage
<http://www.cdc.gov/drugresistance/>

CIA. The global infectious disease threat and its implications for the United States. 1999
<http://www.odci.gov/cia/publications/nie/report/nie99-17d.html>

EARSS-European antimicrobial resistance surveillance system
<http://EARSS.rivm.nl>

Eurosurveillance
<http://eurosurv.org/>

Global Polio Eradication Initiative
<http://www.polioeradication.org>

Infectious Disease News
<http://www.slackinc.com/general/idn/idnhome.htm>

International Society for Infectious Diseases
<http://isid.organize-it.com/>

Johns Hopkins University – Infectious Diseases
http://www.hopkins-id.edu/index_id_links.html

Karolinska Institute, Sweden
<http://micf.mic.ki.se/Diseases/>

National Foundation for Infectious Diseases, USA
<http://www.nfid.org/>

Project Icare: Intensive Care Antimicrobial Resistance Epidemiology
<http://www.sph.emory.edu/ICARE/>

Roll Back Malaria
<http://www.rbm.who.int/>

Stop TB Initiative
<http://www.stoptb.org>

The Hot Zone: Emerging Infectious Diseases Reports and Web Sites
<http://www.qis.net/~edwardmc/eid.htm>

UK Public Health Laboratory
<http://www.phls.co.uk/>

US National Center for Infectious Diseases
<http://www.cdc.gov/ncidod/eidtopics.htm>

Washington University Infectious Disease Division, USA
<http://www.id.wustl.edu/>

WHO Communicable Diseases Home Page
<http://www.who.int/health-topics/idindex.htm>

WHO/TDR (Special Programme for Tropical Disease and Research)
<http://www.who.int/tdr>

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ANTIMICROBIAL RESISTANCE

Pioneers of antimicrobial resistance

Paul Ehrlich, 1854-1915



A German medical scientist renowned for his pioneering work in haematology, immunology and chemotherapy, Ehrlich won the 1908 Nobel Prize for his discovery of the first effective treatment for syphilis. As well as his research into early chemotherapy, Ehrlich also developed "side chain

theory" a hypothesis that provided the first plausible description of the body's own immunological response to destructive pathogens.

Louis Pasteur, 1822-1895



Considered one of the greatest French biologists of the nineteenth century, Pasteur devoted his life to solving practical problems in industry, agriculture and medicine. Pasteur was the first to discover that fermentation and putrefaction only took place in the presence of living organisms. With

further research he developed the technique of pasteurization that not only revolutionized the dairy industry, but food processing as well.

Selman Waksman, 1888-1973



A Ukrainian-born biochemist, Selman Waksman played a major role in initiating a calculated, systematic search for antibiotics among microbes. His discovery of streptomycin – effective in the treatment of tuberculosis – garnered him the Nobel Prize in 1952.

Sir Alexander Fleming, 1881-1955



Honoured with a Nobel Prize for his discovery of penicillin, Fleming transformed medical science with the development of the world's first antibiotic. While working with *Staphylococcus* bacteria in 1928, the Scottish bacteriologist noticed a bacteria-free circle around a mould

growth contaminating a culture of staphylococci. Upon further investigation he discovered a substance that prevented bacterial replication even when diluted 800 times. In 1943 he was elected fellow of the Royal Society and knighted in 1944.

Robert Koch, 1843-1910



A 1905 Nobel Prize honoree, Koch was the first scientist to identify the organism that causes tuberculosis, Koch is considered the founder of modern bacteriology because he successfully isolated several disease-causing bacteria and discovered the animal vectors of a number of major diseases including anthrax. Through his many experiments, Koch discovered how to obtain microorganisms from animals, and how to culture those same samples. It was Koch who discovered that cholera is primarily a water-borne disease.

John Enders went on to demonstrate the safety of cultured viruses in producing immunity, and proved that measles could be prevented through vaccination.

John Enders, 1897-1985



American microbiologist and Nobel laureate John Enders led a research team which developed a technique for growing viruses in cultured cells. He showed that poliomyelitis viruses grew in both brain and cultured tissues and in this way caused cell destruction.

John Enders went on to demonstrate the safety of cultured viruses in producing immunity, and proved that measles could be prevented through vaccination.

LETTERS TO THE EDITOR



Private sector prescribing

Editor,

When I worked as a pharmacist in the public sector I found it relatively easy to promote rational use of drugs through adherence to the essential drugs list, standard treatment guidelines and formularies. However, now employed in the private sector, I find these tools difficult to use because of prescribers' resistance to what they see as restrictions upon them.

Obviously the forces driving the private sector are unlike those in the public sector. For example, cost containment is not a priority, as the consumer (generally those dissatisfied with the public health care system) pays for services, mainly through some form of health insurance. My question is, in the private sector is it really possible to rationalise medicines' use and still have a good income? I would be interested to hear readers' views.

—Dr Atieno Ojoo, P.O. Box 13576, Nairobi, Kenya.



A simple solution to outpatient record keeping?

Editor,

In developing countries the idea of keeping medical records in hospital

offices is impractical, and often impossible to implement. Here in Tanzania's Dodoma region the Out Patient Service has adopted my suggestion of patients keeping a "health booklet". The booklet is in fact a primary school exercise book, widely available and priced at around US\$0.06. As the booklet is the patient's property, a sense of ownership means it is usually well kept and made available whenever requested.

The system's advantages are that it can provide a full patient history, particularly useful in cases such as hypertension, diabetes, asthma or allergy. Also data are recorded chronologically, whereas before we often had to sort through numerous pieces of paper and put them in date order. When there is a shortage of hospital cards and files, the booklet can also be used as an in patient file or as a growth chart for the under-fives. As senior doctors can comment on and change previous diagnoses and treatments, the system can help in improving junior colleagues' skills and prescribing practices.

Lack of supplies and of motivated staff should convince hospital managements to rely more on user commitment, and let patients document their own medical histories.

—Dr Massimo Serventi, Paediatrician, Dodoma General Hospital, Box 1498, Dodoma, Tanzania.



Substandard chloroquine in Ghana

Editor,

Countries in tropical Africa account for more than 90% of total malaria incidence and the great majority of malaria deaths, with children the most vulnerable to the disease. Chloroquine is one of the most frequently used drugs in prevention and treatment. But in recent years in some endemic areas certain strains of *Plasmodium falciparum*, one of the parasites responsible for malaria, has become resistant to chloroquine. Among the reasons cited for this is the manufacture, sale and use of substandard chloroquine formulations. In Ghana we have completed an eight-year study to discover the scale of the problem, and it has reinforced concerns about the quality of chloroquine available here.

Thirty-eight samples of chloroquine phosphate tablets and 57 samples of syrups, manufactured locally by different firms, were tested in the Ghana Standards Board's laboratories between 1992 and 1999. All the samples were analysed according to *British Pharmacopoeia* assay methods. The *Pharmacopoeia's* specification for the content of chloroquine phosphate in tablets ranges between 92.5% and 107% of the label claim. In Ghanaian produced tablets 250 mg of chloroquine is the norm and for syrup the

acceptable level is between 118.75 and 131.25 per 5ml.

Of the 38 tablet samples analysed, four contained levels of chloroquine phosphate below the minimum requirement, with one sample at 38.9%. Of the 57 samples of syrup 10 contained levels of active ingredient below the minimum required.

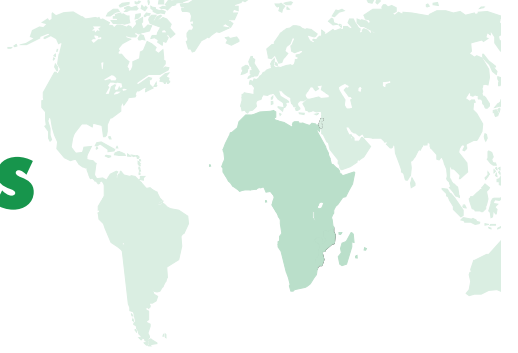
We conclude that during the eight-year study period some malaria sufferers were exposed to significant amounts of substandard chloroquine phosphate in both tablets and syrups. However, lessons have been learned, and steps taken to improve matters. One local manufacturer had to withdraw affected batches of drugs and had his factory closed until an effective quality assurance scheme was in place. Local manufacturers supplying the Ministry of Health must now have their products tested and certified by the national quality control laboratory. The Food and Drugs Board is implementing measures to assure drug quality in manufacture, supply and distribution. And during 1999 an association of drug manufacturers was formed, pledging to comply with WHO Good Manufacturing Practices.

—Charlotte Ohene-Manu and Jonathan Martey, Ghana Standards Board, Drugs and Cosmetics Department, P.O. Box MB, 245, Accra, Ghana.



NATIONAL DRUG POLICY

Meetings give impetus to Africa's essential drugs programmes



Essential drugs programme managers in Africa have met to debate a range of pharmaceutical issues and move forward their agenda to ensure access to essential medicines. At two critical meetings they endorsed the Intensified Essential Drugs Programme for the African Region, and made numerous policy recommendations.

The first meeting, in South Africa in March 2000, brought together managers from 16 anglophone countries. They called on health authorities to adopt good procurement practices for essential drugs. Authorities should capitalise on economies of scale, and make pricing information available to prescribers, dispensers, consumers and health insurance companies, to enable them to make informed decisions. Participants also proposed that governments should encourage local production of essential drugs, and remove taxes on both the drugs and their raw materials.

The managers endorsed the idea of joint bulk purchasing of drugs for priority health problems, and urged WHO to provide more information to Member States on the benefits and limitations of such schemes. However, they insisted

that local industries should not be put at an undue disadvantage in the bidding process.

Delegates emphasised that easy access to reliable information on pharmaceutical suppliers and pricing was vital to achieve optimal quality at affordable prices. A Web site should be established, coordinated by WHO, to make such information freely available and keep it updated.

Participants also wanted information disseminated on the concept and benefits of harmonisation of drug regulatory activities, and the promotion of common minimum standards. This would generate confidence in the quality of services. Public health needs rather than commercial interests should drive the harmonisation process, delegates stressed. In addition, Member States should strengthen the capacity of drug regulatory agencies and grant them some degree of autonomy, to ensure effectiveness

and efficiency.

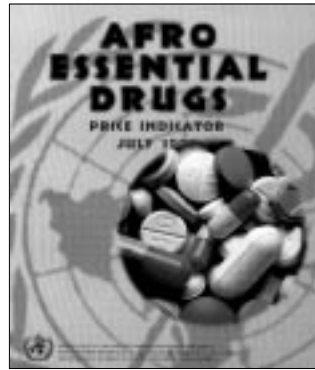
Rational use of drugs was high on the agenda. Participants recommended that Member States develop strategies and incorporate rational use principles in health workers' training curricula. Pharmacotherapeutics committees were seen as a way to improve rational use by prescribers and dispensers, and should be introduced at all levels of care.

Acknowledging the role of traditional medicines in African health care, programme managers urged WHO to give support to countries in deciding how best to use them within health systems.

In August 2000 it was the turn of 38 essential drugs programme managers from 20 francophone countries to spend time reflecting on their work and planning ahead. Meeting in Lomé, Togo, they recommended: the creation of Directorates of Pharmacy and Medicines; quality control laboratories; pharmaceutical

inspection services; and the legislation and regulations necessary to ensure drug quality. As in South Africa there was much discussion on improved pricing policy. Participants called for complementarity between the public and private sectors, the creation of autonomous central medical stores, promotion of local production, and state and community co-financing to improve drug supply and access. They also discussed integrating drug policy programmes in health development plans, creating rational drug use strategies, and improving staff training.

At both meetings WHO requested countries to specify the activities they would carry out to implement the Intensified Essential Drugs Programme, so that the Organization can make detailed plans for supporting them. But important work is already underway. The WHO Regional Office for Africa is running training in good manufacturing practices, and the *AFRO Essential Drugs Price Indicator* has been launched. Countries continue to receive support in implementing national drug policies, assessing drug regulatory capacity in Member States and reviewing pharmaceutical legislation. □



The *AFRO Essential Drugs Price Indicator* – one of the welcome initiatives introduced by the *AFRO Intensified Essential Drugs Programme*

Brazil: WHO's Director-General speaks out for generics

Dr Gro Harlem Brundtland, WHO's Director-General, has made a major speech in Brazil strongly supportive of generic drug strategies. Testifying before the country's Parliamentary Commission on Investigation of Medicines in April 2000, she discussed national drug policies, essential drugs and the importance of generics in promoting affordability of medicines.

Saying that there are no "simplistic solutions and no magic bullets", Dr Brundtland explored how people living in poverty might get sustainable access to drugs at affordable prices. She spoke

of pharmaceutical companies' moral obligation to contribute to the solution, but also said that protective tariff barriers and distribution margins for drugs should come down. Dr Brundtland highlighted the need for political acceptance of the concept of "equity pricing", especially for newer essential drugs of vital public health importance. Equity pricing means that the poor would not have to pay the same price for life-saving drugs as those who are better off. She urged governments of industrialised countries to lead in its establishment. While developing country governments must facilitate access by "improving financing, importation, purchasing and distribution systems for medicines, vaccines and medical equipment", Dr Brundtland continued.

Brazil's National Drug Policy highlights generic drug prescribing and use, and stipulates mandatory adoption of generic names in all public purchases. The Director-General said that promoting generics can help meet the objectives of health sector reforms by improving affordability, reducing

cost, increasing choice and helping to rationalise both the selection and use of pharmaceuticals.

Relevance for the private sector

Dr Brundtland told Commission members that policies advocating generics – which are frequently only associated with the public sector – can be just as beneficial in the private sector, because they promote efficiency within pharmaceutical markets. She stressed the importance of this in developing countries, where up to 90% of drug consumption is through the private sector. She added that generic strategies involve much more than legal mandates; "they need support and enforcement, must respond to the concerns of involved parties and provide adequate economic incentives".

More countries adopt the strategy

Dr Brundtland spoke of the progress made to date. In Latin America, several countries have already enacted legislation relevant to generic strategies, but in most cases implementation is limited. Overall, however, the results indicate that lower prices have resulted where solid and

transparent legislation exists. The Director-General pointed out that in the USA generic drugs represent half of the market in volume. One of the European Union's three major policy regulations on pharmaceutical pricing and reimbursement is to enhance competition by making the market more transparent and encouraging generics. And many hospitals in developed countries have lists of approved drugs which identify products by generic name.

In conclusion, Dr Brundtland said that WHO has, for a long time, been encouraging drug policies based on the promotion of generic drugs of assured quality – a cost-effective strategy in containing drug expenditure. She told Commission Members that WHO is, therefore, in favour of so called "early workings" of patented drugs for generic manufacturers, to encourage competition and give impetus to research for improved products. This includes the use of patented drugs for research and testing, which necessitates prompt registration and early production of generic drugs, the Director-General said. Countries with variations of early workings provisions include Argentina, Australia, Canada, Hungary, Israel and the USA. □



A young patient in Brazil, where generic drugs are rapidly increasing their share of the pharmaceutical market

NATIONAL DRUG POLICY

Launch of the Australian National Medicines Policy

➤ ANTHONY SMITH*

Australia has gained a reputation as an innovative country for its work on the quality of use of medicines, and for its recently established National Prescribing Service. It may therefore come as a surprise to learn that, until recently, Australia had no formal, comprehensive, endorsed National Medicines Policy. The reasons are historic rather than political.

For more than 50 years, acceptable quality, safety and efficacy of medicines have been assured through the work of the Therapeutic Goods Administration.

Equity of access to medicines is provided through the Pharmaceutical Benefits Scheme which, by a system of graduated co-payments, allows access to medicines for all including the poorest members of society – in the extreme at no cost to the consumer. This Scheme has operated for half a century.

While the pharmaceutical industry may have some ambivalence about its relationships with government, financial incentives have been provided to enhance industry's viability, both in Australia and as a presence in the South-East Asia/Western Pacific region.

In line with the prototype policy elaborated by WHO, rational use (or quality use, as we chose to call it) of medicines became the fourth component of Australian policy in 1992. Therefore, our Medicines Policy evolved over a long period in contrast to that of many countries who have devised theirs over a period as short as a few months.

At last, and primarily through the work of the Australian Pharmaceutical Advisory Council (APAC), all this activity has come together in the National Medicines Policy which was formally launched by the Joint Parliamentary Secretary for Health, Senator Grant Tambling, on 10 December 1999.

APAC was a good vehicle for the development of the Policy document as its membership reflects the partnership approach which has become central, particularly, to the Quality Use of Medicines Programme in Australia. Consumers, the pharmaceutical industry, government and health professionals are all represented on APAC. The document reflects all of their views including, most recently, those relating to the community role of complementary medicines (Australia has a Federal Government Office for Complementary Medicines and a



Photo: WHO, H. Anand

Aborigines in Kalgoorlie, Australia. Adoption of the National Drug Policy has formalised the country's efforts to provide quality medicines for all

separate evaluation committee for these products).

As a country we have been very fortunate that several of the essential ingredients of a National Medicines Policy have been in existence for so long.

Nevertheless, our comprehensive policy has finally won the endorsement of Government and with this endorsement goes the expectation that continuing resources will be made available to ensure that we can implement strategies in the many areas which are currently less than ideal. It would have been good to have had this policy and its endorsement a long while ago!

The Australian Medicines Policy document may be accessed and downloaded from: <http://www.health.gov.au:80/haf/docs/nmp2000.htm> □

* Anthony Smith is Professor of Clinical Pharmacology, Newcastle University Mater Misericordiae Hospital, Waratah NSW 2298, Australia.

Progress on drug policy in FYR Macedonia

The Former Yugoslav Republic of Macedonia launched its National Drug Policy development process in February 2000, with the support of WHO/EURO and WHO Humanitarian Assistance Office, Skopje.

Five working groups were created to develop different elements of policy: legislation and regulations; drug selection; drug information; rational drug use; supply and economic strategies; and human resource development. By October the groups were ready to move to the next phase of the process – combining the different drafts to produce one comprehensive document. Macedonia is now deciding on future activities and a time frame for policy implementation. □

NEWSDESK

World Health Assembly 2000: drug debates focus on HIV/AIDS

A comprehensive resolution on HIV/AIDS was among the highlights of the World Health Assembly, held in Geneva in May 2000. Ninety-five percent of the 34 million people living with HIV/AIDS are in developing countries. And it was these countries' representatives who successfully campaigned for WHO to increase its role in advising on the best treatment options, and how to overcome drug pricing and access problems. During discussions on the Revised Drug Strategy delegates also stressed the need for WHO to support broader approaches to drug financing, and to address the growing dangers of unregulated sale of medicines on the Internet and counterfeit drugs.

Among its provisions resolution WHA53.14 on confronting the HIV/AIDS epidemic requests the Director-General to: support the implementation of drug price monitoring systems in Member States, to promote equitable access to care, including essential drugs; promote rational use of drugs by strengthening Member States' capacity to implement drug monitoring systems; and continue to develop methods and support for monitoring the pharmaceutical and public health implications of trade agreements.

Numerous delegates stressed the need for WHO to retain its independent voice when advising countries on the complex subject of health-related aspects of trade.

At one of the many side meetings during the Assembly, public health advocates from Health Action International, Médecins Sans Frontières and Consumer Project on Technology held a joint briefing for Member States on improving access to essential drugs. And they added

their voices to support for WHO's role in providing global pricing information on quality medicines for people living with HIV/AIDS.

Tackling counterfeit drugs

A well-attended technical briefing on drug quality at the Assembly focused on counterfeits. The presence of senior health officials, and representatives from Interpol, the pharmaceutical industry and NGOs reflected the multi-faceted nature

of the problem. The audience was told of highly sophisticated operations in which criminals take advantage of cross-border loopholes. Supplies, production, shipping re-labelling, financing and distribution of these drugs are often handled in different countries.

The meeting called for closer cooperation between law-enforcing agencies, legislative bodies and the pharmaceutical industry. Saying that there was "an urgent need for action", Dr Yasuhiro Suzuki, Executive Director of WHO's Health Technology and Pharmaceuticals Cluster, referred to the "deadly combination of demand for cheap drugs and fat profit margins" that makes counterfeiting drugs so attractive to criminals and such a threat to society. □

Bridging the digital divide

Only a small fraction of global health research expenditure goes to research into diseases and health issues that affect the poor, such as malaria, killer childhood diseases and nutrition. One step towards changing this is to facilitate research in the countries that have first-hand experience of these problems. Now WHO and the Open Society Institute (part of the Soros Foundation network) have teamed up with information providers ISIO and SilverPlatter, and other partners to do just that. They will provide

medical and health research institutions in Africa, Central Asia and Eastern Europe with Internet access to quality scientific information from around the world.

The project's first year pilot phase will enable scientists at leading research institutions in Armenia, Ghana, Mali, Mozambique, Mongolia, Uganda, Tanzania and Uzbekistan to access information in digital format. In this way integration of the world scientific community through electronic communication will advance. WHO will be among those

negotiating with service providers in the eight initial countries to provide high-speed connection to the Internet. Research staff in the countries will receive comprehensive training to ensure maximum benefit from the project. It is anticipated that by the end of its second year between 30 and 40 countries will have joined the project, which is part of the wider United Nations programme "Health InterNetwork". This aims to improve public health world wide by facilitating the flow of health information using Internet technologies. □

ACCESS

WHO and partners – taking the initiative to make a healthier world

There are several important and new international health initiatives involving WHO in global partnerships that are addressing some of the most pressing health problems of our time. Here we focus on some of them, beginning with WHO Director-General Gro Harlem Brundtland's call for a concerted global effort to tackle diseases of poverty, made in October 2000.

Opening a meeting of 200 health and advocacy experts from 70 countries in Winterthur, Switzerland, Dr Brundtland said that although the world had long known that illness and poverty are closely linked, recent data show a much more devastating economic impact on developing country economies by a few infectious diseases, particularly malaria, HIV/AIDS and tuberculosis. But a number of effective health interventions exist that dramatically reduce mortality of these killers, she emphasised. "Quite simply, if we can take these interventions to scale – and by that I mean to a global scale – we have in our hands a concrete, result-oriented and measurable way of starting to reduce poverty." Dr Brundtland said that a concerted global effort was needed that would involve a process, a road to follow, a framework for thinking and a set of values to underpin it all.

The forum followed recent announcements by the G8 leading industrial nations of targets to reduce the burden of malaria and tuberculosis by 50% within 10 years, and to reduce the spread of HIV/AIDS by 25% within the same time period. It also comes after the creation of a new policy framework by the European Commission intended to focus the European Union's aid effort on reaching those targets.

ACCESSING VACCINES

Every year, nearly three million children die from diseases that could be prevented with currently available vaccines. The Global Alliance for Vaccines and Immunization (GAVI), formed in 1999, is a coalition of international organizations, with a mission to ensure that every child is protected against vaccine-preventable diseases. It wants to close the growing gap in the number of vaccines available to children in industrialised and developing countries. GAVI is working to:

- improve access to sustainable immunization services;
- expand the use of all existing cost-effective vaccines;
- accelerate the development and introduction of new vaccines;
- accelerate research and development efforts for vaccines and related products specifically needed by developing countries;
- make immunization coverage an integral part of the design and

assessment of health systems and international development efforts.

Since its inception the Alliance has received a great deal of interest from developing countries wanting to benefit from its work. On 20th September 2000 the Global Vaccine Fund, one of the financial tools used by the initiative, announced that it will be giving more than US\$150 million worth of vaccines and funding over five years to improve immunization rates in Africa, Asia and Latin America. According to estimates more than 100,000 lives will be saved every year due to initial grants to 13 countries.

For further information check: www.who.int/vaccines/aboutus/gavi.htm

ROLLING BACK MALARIA

When she became WHO's Director-General in 1998, Dr Gro Harlem Brundtland decided that malaria would be one of the Organization's top priorities. She instigated Roll Back Malaria, a partnership involving a wide range of organizations at country, regional and global levels. The initiative's goals include:

- support to endemic countries in developing their national health systems as a major strategy for controlling malaria;
- efforts to develop the broader health sector – all providers of health care to the community. This includes the public sector health system, civil society, NGOs and private health providers (including drug vendors and traditional healers) and others;
- encouragement to obtain the necessary human and financial investments for health system development.

In recent months Roll Back Malaria has received a major boost from the African summit meeting, which set the agenda for the continent's efforts to beat the disease (see report on page 23).

Find out more at: www.rbm.who.int

ERADICATING POLIO

The Polio Eradication Initiative is on track to certify global eradication of the disease in 2005, with more than 190 countries and territories which will have interrupted poliovirus transmission by the end of the year 2000. This is an initiative that began in 1988, but it is entering an

intensive final phase in order to mop up the final pockets of the virus.

In September 2000, a broad spectrum of leaders from business, governments, UN agencies and humanitarian groups, met at the United Nations in New York to galvanise the necessary financial resources and political will for the Initiative to ensure it meets the 2005 deadline. Over 250 participants pledged to help overcome the challenges: poliovirus was still circulating in up to 20 countries at the end of 2000, and US\$450 million in new funding is needed to conquer the disease in those places. The 20 high-risk countries also present some of the most difficult logistical challenges to polio eradication, including populations that are geographically isolated and, in a handful of countries, living in the midst of severe civil conflict. Emphasising the urgency of the task, UN Secretary-General, Kofi Annan, said that "our race to reach the last child is a race against time. If we do not seize the chance now, the virus will regain its grip and the opportunity will elude us forever".

A recent milestone

The WHO Western Pacific Region was certified polio-free on 29 October 2000 by an independent panel of international public health experts. The Region includes 37 countries and areas ranging from tiny islands to China with a population of 1.2 billion people. The Regional Certification Commission on Poliomyelitis Eradication confirmed that no new cases of indigenous polio have been detected in the Western Pacific in the last three years, despite excellent surveillance for the virus – the major benchmark for certification.



A sight that will soon disappear? A polio victim learns to walk with callipers

For more news on the Polio Eradication Initiative check: www.who.int/vaccines-polio/

STOPPING TB

Tuberculosis (TB) remains the largest killer of young people and adults in the world, and the problem is growing with the spread of HIV/AIDS and drug resistant strains of the disease. Stop TB is a global movement to accelerate social and political action to stop the unnecessary spread of TB around the world. Its mission is to ensure that every person with TB has all the necessary information and access to treatment and cure. Stop TB is a partnership working with public and private organizations from the local to the global level. Donors, research institutions, industry, international agencies, governments and NGOs are all playing a role in:

- linking TB control to health sector development;
- linking TB control to poverty alleviation;
- linking TB control to relevant aspects of socioeconomic development;
- promoting a more client-centered approach for wider coverage and compliance by partnering with community-based groups and others.

For further information check: www.stoptb.org/stop.tb.initiative/index.html#StopTB

One of Stop TB's partners is the Global Alliance for TB Drug Development, a not-for-profit venture that is accelerating the discovery and development of new drugs to fight the disease by drawing upon best practice and resources from the public and private sectors (see page 19). The Alliance aims to fill a gap in TB drug development by using a lean research and development operating model that outsources projects to public or private partners. It will survey all TB drug development and selectively intervene when its actions will help move a drug candidate towards registration and use in therapy. In this way the Global Alliance will build a portfolio of projects with varying levels of funding, management and ownership.

Further information is available at: www.tb Alliance.org/home.cfm

IMPROVING INJECTION PRACTICES

Injections are predominantly needed for the treatment of severe diseases, mostly in hospital settings. Nevertheless, they are overused to administer medications in many countries because of an ingrained preference for injections among health workers and patients. In developing countries up to 50% of injections are administered with re-used syringes and needles. Such unsafe practices have been linked to the transmission of many

ACCESS

pathogens between patients, including the hepatitis, HIV, Ebola and dengue fever viruses, and the malaria parasite.

The Safe Injection Global Network (SIGN) is a coalition of several public and private partners, including WHO, UNICEF, UNAIDS, NGOs, governments, universities, health workers and industry. Formed in Geneva in October 1999, it aims to unite the partners' strengths and skills to work together on injection safety. Because there have been few integrated programmes that link community and health systems to promote safe injection use, SIGN is coordinating the launch of pilot projects in five countries. Results of the pilot projects' evaluation should be available by 2002, and will enable the Network to identify and adopt successful strategies to counter unsafe injections.

Positive developments

SIGN's annual meeting, held in Cairo in October 2000, showed that there has already been progress. For example, Pakistan has set up a national "SIGN" group, Tanzania has launched an education campaign for the public and health workers, and Burkina Faso has made significant improvements in injection safety recently. Participants reviewed the previous year's activities, exchanged information and coordinated their advocacy and public awareness activities.

New technical guidelines on preventing infection from injections are being prepared, and a provisional document open for comments from the public will be available on the SIGN Web site: www.injectionsafety.org □

New drugs needed to fight TB

More than 120 tuberculosis (TB) and public health experts, government and industry representatives, researchers and donors discussed TB drug development at a two-day workshop in Cape Town, South Africa, in February 2000. They met because of the urgent need for new drugs to ensure shorter TB treatments and to fight the increasing resistance to existing drugs. Basic TB drugs are already 20–30 years old, and few new drugs have been marketed in recent years.

TB experts, including WHO representatives, described the need for new TB drugs, researchers presented promising state-of-the-art research methods and findings, and drug companies explained the difficulties of drug development.



Credit: WHO

Mixed panels discussed the pharmacoeconomics of the TB drug market, which is predicted to be US\$700 million for treating 10,000,000 TB patients worldwide by 2008. The general opinion was that the size of this market should enable the development of at least one or two new drugs.

But some participants argued that there was a reluctance to develop drugs for a market where most of the people are poor, and where developing countries, institutional buyers and agencies working on TB demand low prices. A guaranteed off-take or market would be a strong incentive for manufacturers. There was a view that "corporate awareness" of the problem is increasing. Some companies have specific TB projects, others are considering "donating" the licensing rights of economically less viable second-line TB drugs to public bodies.

Not only money...

Many participants warned that low cost drugs or even donations are no guarantee of solving the TB problem, as managerial problems in many countries with mid level economies have meant that they have only achieved 50–60% cure rates. Poor patient adherence after the first two months of a six-month treatment period increases the risk of drug resistance.

The meeting discussed accelerating the development of new TB drugs to improve prevention and treatment of the disease. It also decided to develop a dedicated Global Alliance for TB Drug Development, with partners from academia, industry, major agencies, NGOs and donors worldwide.

From vision to fruition...

By October 2000 the participants' push for a Global Alliance for TB Drug Development became a reality with its launch by WHO's Director-General, Dr Gro Harlem Brundtland, at a meeting in Bangkok. And in February 2001 the Alliance opened its head office in Cape Town, South Africa, to coordinate and fund research in tuberculosis in developing countries.

The main aim is to find a major new treatment for TB by 2010, specifically a drug that is more effective so that it needs to be used for a shorter time, reducing the treatment period by at least 50 per cent, and so increasing adherence.

The Alliance will not set up its own research institutions but will support existing projects, particularly in developing countries, and coordinate their findings. The first funding allocations will be made in April 2001. □

For further information on the Global Alliance for TB Drug Development see page 22.

Beating malaria: leaders pledge action at historic summit

Malaria, a disease that is preventable, treatable and curable, kills one million people a year in Africa, with nine out of 10 cases occurring in the sub-Saharan region. Now, the first summit of African heads of state to focus on the disease has committed to intensive efforts to halve malaria mortality by 2010. Held in Abuja, Nigeria, in May 2000, the summit was attended by representatives of forty-four of the fifty malaria-affected countries in Africa. Also present were officials from United Nations agencies and major international donors. The meeting culminated in the signing of the Abuja Declaration and the Plan of Action in which the leaders resolved to initiate sustainable actions to strengthen health systems, so that by 2005:

- at least 60% of those suffering from malaria have prompt access to, and are able to correctly use, affordable and appropriate treatment within 24 hours of the onset of symptoms;
- at least 60% of those at risk of malaria, particularly children under five

years of age and pregnant women, benefit from the most suitable combination of personal and community protective measures. These include insecticide treated mosquito nets and other accessible and affordable interventions, to prevent infection and suffering;

- at least 60% of all pregnant women who are at risk of malaria, especially those in their first pregnancies, have access to chemoprophylaxis or presumptive intermittent treatment.

Commitment, targets and resources

The Heads of State called upon all countries to undertake and continue health systems reforms that will promote community participation in rolling back malaria, and so increase sustainability. Diagnosis and treatment of malaria should be available as peripherally as possible (including home treatment), and accessible to the poorest.

Amongst other things the signatories to the Declaration pledged to: prevent

re-emergence of malaria; provide reliable information on the disease to decision-makers at all levels; and to reduce or waive taxes and tariffs for mosquito nets, insecticides, anti-malarial drugs, and other goods and services needed for malaria control strategies.

Hidden costs reinforce urgency

The summit's importance was reinforced by simultaneous publication of a report showing that the cost of malaria is substantially greater than economists previously estimated. According to the report,¹ the disease results in a loss of economic growth of more than one percentage point per year.

Previous estimates have looked only at immediate short-term financial implications, such as the loss of labour and the costs of treatment and prevention.



The world's biggest bednet was erected at Abuja as a symbol of the 225 African children who die every two and a half hours from malaria

Photo: WHO/RBM

But the longer-term costs are even more devastating to the country, the report argues. □

Reference

1. Gallup JL, Sachs JD. Economics of malaria. Centre for International Development, Harvard University and the London School of Hygiene and Tropical Medicine. (Forthcoming). Executive summary available on the Web at: <http://www.malaria.org/jdsachseconomic.html>

ACCESS

NGO meetings on drug access

Following their successful conference on compulsory licensing held in Geneva in March 1999 (see EDM-27), Médecins Sans Frontières, Health Action International and the Consumer Project on Technology have organized two more meetings on one of today's most topical issues. A conference entitled Increasing Access to Essential Drugs in a Globalised Economy – Working Towards Solutions, brought together 350 people from 50 countries in Amsterdam in November 1999. Health advocates and public health professionals from developing countries,



Intense concentration on the faces of delegates at the Nairobi meeting, which tackled complex and controversial issues

representatives from domestic and international NGOs, the pharmaceutical industry, international organizations, national governments and academics all contributed their ideas on how to achieve access to essential medicines. After two days intensive work, the Conference culminated in the drawing up of the Amsterdam Statement, which includes a recommendation for the World Trade Organization to create a Standing Working Group on Access to Medicines. The Group would work within the WTO to consider the impact of trade policies on people in developing and least developed countries. It would provide a public health framework for the interpretation of key features of WTO agreements, and WHO and other international organizations would support the activities of the Working Group.

Among the many thought-provoking speeches, Dr Gro Harlem Brundtland, WHO's Director-General, told delegates that "Making a difference requires the often painful work to build consensus among stakeholders that can move things in the right direction. Health products and health services are tradable. Health products such as pharmaceuticals are produced, marketed and sold across the globe – benefiting some but failing to reach too many. So the rules that regulate this trade are key", she told delegates.

The Director-General listed WHO's five key public health messages on international trade agreements and pharmaceuticals (see box).

Moving on to Africa

The NGO campaign on access to essential drugs gathered further momentum in Nairobi in June 2000. The Kenyan capital was the venue for the East Africa Access to Drugs Conference, where representatives from 21 countries met to devise a regional strategy.

The presentation of a new study showing that East Africans pay more than Europeans for life-saving drugs¹ was one of the conference highlights. Among the many examples cited in the study is that of the antibiotic, ciprofloxacin, which was found to be twice as expensive in Uganda as in Norway. Another example is fluconazole, a treatment for AIDS-related meningitis. In Thailand, where generic competition has lowered prices, fluconazole costs only US\$0.30. However, the same drug costs US\$18.00 in Kenya, where it is patent protected.

Participants argued that the reasons medicines are expensive in East Africa include high tariffs, taxes and lack of generic competition as well as strong patent protection. Discussion focused on strategies to enact legal safeguards to remedy the current situation. Delegates heard that, within existing international trade rules, such safeguards include parallel importing (the right to shop around for the best prices of branded products) and compulsory licensing (granting limited production rights to generic producers).

Another report presented at the meeting on patent protection and medicines in Kenya and Uganda², calls on governments to ensure these safeguards, and to include Ministry of Health representatives and health professionals when negotiating and adopting trade agreements. □

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1. Myhr K. Pharmaceutical pricing: law of the jungle. Amsterdam: Health Action International; 2000.
2. Boulet P. Patent protection of medicines in Kenya and Uganda. Geneva: Médecins Sans Frontières; 2000.

Further information on this series of meetings on access to essential drugs can be found at: www.haiweb.org

Five key messages from WHO on trade agreements and pharmaceuticals



First, patent protection is a necessary and effective incentive for research and development for needed new drugs. Essential drugs are a public good and not simply just another commodity. Patents must therefore be managed in an impartial way to benefit both the patent holders and the public.

Protectionism has never benefited public health. WHO supports governments to enact national legislation which can draw advantage from more open trade and a better regulated international system. And we support governments in incorporating the safeguards that have been built into the WTO TRIPS Agreement to protect the rights of the public.

Second, priority-setting for research and development in the pharmaceutical market is imperfect. There are also striking market failures when there is such desperate demand for products that are available – but not within reach of those in need.

WHO has initiated, with other partners, innovative mechanisms to stimulate research and development in areas of high public health need, such as malaria and tuberculosis. Through its Medicines for Malaria Venture (MMV), the Global Alliance for Vaccines and Immunization (GAVI) and other initiatives, WHO is actively encouraging public sector financing for critical public health problems and neglected tropical diseases.

Third, WHO strongly supports development of mechanisms for preferential low prices for essential drugs in lower-income countries. Lower-income countries simply cannot be expected to pay the same price for essential drugs as the wealthier countries.

For governments, industry, and other stakeholders, there is a range of measures which might be used to achieve preferential pricing. But where there is an abuse of patent rights, where patented essential drugs are unavailable or where a national emergency exists, recourse to compulsory licensing is a legitimate measure consistent with the TRIPS Agreement.

Fourth, WHO supports implementation of the TRIPS Agreement to ensure prompt availability of generic drugs upon patent expiration. WHO has long promoted use of generic drugs of assured quality. Experience from countries with "generic-friendly" policies clearly demonstrates that the market competition created by these policies increases affordability of medicines, stimulates true innovation within the research-based industry, and encourages increased production efficiency by the generic industry.

Finally, trade agreements should not create barriers to trade. An important WTO principle is that technical regulations, standards and assessment procedures should be based on international standards, guides and recommendations. In the area of pharmaceuticals, WHO norms, standards and guidelines represent such international consensus. So we will actively promote these guidelines".

Trade and access: Ugandan groups push for progress

The title of a workshop held in Kampala, Uganda, in February 2000, certainly conveyed the spirit of the event and the breadth of subjects addressed. "Advocacy and Campaign for Better Trade, Access to Essential Medicine and Promoting Rational Drug Use in Uganda" was the result of collaboration between Uganda's Consumers Protection Association, Action Aid Uganda, Health Action International and Médecins Sans Frontières.

Participants left this lively meeting in February 2000 determined to push for better trade policy, improved health services and increased consumer awareness of pharmaceutical issues. They agreed that access to drugs is a crosscutting issue, and that to be more effective they

need to network and to create awareness of key issues using various media. Discussions also highlighted the importance of involvement in legislation review and formulation (particularly the draft bill on intellectual property rights), and participation in Uganda's National Drug Policy review. Delegates were urged to campaign for improved infrastructure. Only when this is in place can important developments get underway, such as offering incentives to open drug outlets in poor rural areas. □

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This ambulance may be stuck in the mud in Uganda, but the description could not apply to campaigners pushing for improvements in the pharmaceutical sector

ACCESS

Transforming drug supply in Dar es Salaam

➤ KARIN WIEDENMAYER,
DEO MTASIWA*

In 1990 the inadequacy of the pharmaceutical supply system in Dar es Salaam, commercial capital of the United Republic of Tanzania, was evident. There was chronic shortage of drugs at health facilities, supply was erratic as was Government funding, drug supply management was poor and use of drugs irrational. Despite a national policy to provide drugs free of charge, unofficially patients often had to pay for them. Drugs were purchased from the national Central Medical Stores, which was seen as inefficient, unreliable and poorly stocked. Drug quality was questionable and pharmacy premises were often unsuitable – hot, humid and cluttered with piles of drugs, some of them expired. Pharmacists tended to have low professional visibility and not to be involved in hospital committees. At a time when studies showed that patients equated availability of drugs with good quality of care¹, a survey of user patterns in Dar es Salaam in 1990 reported that “the majority of patients complained that usually health facilities do not have drugs at all”.

Ten years on and the picture is very different. Dar es Salaam has a decentralised supply system with drug requisition at district level and local procurement from a newly restructured Medical Stores Department, financed by cost-sharing schemes and Government contributions, and based on the National Drug Policy. How was this achieved?

The structural and functional rehabilitation of Dar es Salaam’s Government health facilities, based on primary health care principles, started in 1990 with an intergovernmental agreement between Switzerland and Tanzania, with the Swiss Tropical Institute as the executing agency. The overall goal of the Dar es Salaam Urban Health Project, created at this time, was, and remains, to improve the health status of people in the Dar es Salaam region. As regards drug supply, the main aim was to improve resource administration at all levels of care, to create a reliable, efficient and sustainable drug management system, addressing both effective supply and rational use of essential drugs.

The Project serves three districts each with one district hospital, one or two health centres and a total of about 60 dispensaries in urban and semi-rural areas. In 1990 the population of Dar es Salaam was estimated at 1.5 million and the current population is approximately 2.5 million.

THE BACKGROUND: DRUG SUPPLY HISTORY IN DAR ES SALAAM

During the late 1960’s the number of health units in Tanzania increased considerably. This increase and the economic crisis of the late 1970’s led to a drug crisis in the public health sector. The lack of drugs was caused by: the acute shortage of foreign currency; an increase in access to health units; people’s greater awareness of modern medicines; and wastage of drugs due to poor planning, procurement, storage, distribution and transport,

as well as irrational use.

In 1984, the Government created the Essential Drugs Programme to provide essential drugs to health facilities. The Programme introduced a prepacked drug kit system, which partially improved the situation for health centres and dispensaries, but not for the hospital sector. And the foreign financed and operated (by WHO, the Danish International Development Agency and the United Nations Children’s Fund) drug kit system did not help to improve management of the drug sector’s infrastructure.

In the early 1990s, when the Dar es Salaam Urban Health Project began, Tanzania started to restructure the economy towards a market-oriented environment. In the health sector this translated into the appearance of the private profit oriented sector and the introduction of user fees. In 1991, Tanzania formulated the National Drug Policy, which aimed to improve the whole pharmaceutical sector, and ensure a regular supply and rational use of essential drugs throughout the country. Later, the Health Sector Reform Action Plan 1996–1999 covered decentralised district-based drug supply and management, liberalised drug procurement, quality assurance, and equitable access and affordability of drugs. Here we highlight the main elements of the Health Project’s work and how against this background, it has transformed drug supply in the region.

BUYING DRUGS: WHICH, HOW MUCH AND WHERE?

Drug need quantification was initially done by morbidity and later by the consumption method. Drug selection was based on the National Essential Drug List. Drug kits for the Dar es Salaam Health Project were procured through restricted international tender. The kit system was centrally and externally organized, donor funded, supplied and imported from overseas, with little or no involvement or

commitment from the recipient side. The project bypassed the national procurement system, the former Central Medical Stores being unreliable and inefficient. Later the organization was restructured and became an autonomous department within the Ministry of Health, under the responsibility of an external management team. In 1996, the new Medical Stores Department was operating efficiently, and it was considered appropriate to start using the existing local drug procurement infrastructure. The Department’s performance has been good overall, with an adequate product range, appropriate pricing, good quality and service, and sufficient provision for emergency situations. The Medical Stores Department has become the backbone of the Project’s supply system.

Drug kits are a good but not optimal solution. Because of their predetermined contents (selection and quantity) certain items were regularly out of stock, others were piling up and some even expired before redistribution. Quantification was therefore introduced at the health facilities and ordering is now done by decentralised requisition, i.e. the indent system has gradually replaced the push system with prepacked kits. A recent study on quality of care showed a significant improvement in drug availability. For example, the level of availability of four key drugs rose to 95% in 1998 compared with 64% in 1992.

DISTRIBUTION AND STORAGE

Initially drug kits were delivered monthly to the three district hospital pharmacies. From there, subsequent distribution to the hospitals, health centres and dispensaries was the responsibility of the district pharmacist, who supervised all peripheral distribution and monitoring. Delivery of drugs from the district stores to the hospital posed no problems as they were on the same premises. From the district hospitals the kits were distributed by vehicle to health centres and dispensaries on a monthly basis. Logistics were more problematic and deliveries were often delayed due to lack of transport, distance and road conditions. Health workers inspected the kits on arrival and documented receipt. All reorganized facilities had adequate and secure drug storage areas. Functioning cold chain equipment was also available, however, storage conditions in district stores were inadequate, with high temperatures and humidity affecting drug quality. Pile-ups and expired drugs that were not disposed of took up valuable space. Storage and

inventory management was done haphazardly and did not follow good practice. Bin cards were unavailable, drug flow monitoring was difficult and documentation was poor.

By 2000, full decentralisation to the districts was complete, on structural, administrative and operational levels. Pharmacy premises have been reorganized, and hospital and district pharmacies have been physically separated. The separation of these premises considerably facilitates storage and inventory practice, as well as drug flow monitoring, which have consequently improved. District pharmacies are located within the newly constructed district medical offices, at a distance from the district hospitals.

KEEPING TRACK OF DRUGS: MONITORING AND DOCUMENTATION SYSTEM

The Project implemented a disease and drug monitoring system. Forms were developed for data collection on morbidity, drug consumption and kit distribution. However these were not used routinely, little evaluation was done, and little attempt made to give health facilities feedback on the data. Follow-up of drug consumption, distribution and performance monitoring was almost impossible. Drug flow could not be traced and accountability was difficult to enforce.

To improve this situation, a Pharmacy Plan of Operations and a Monitoring/Supervision Form were drawn up with all pharmacists. Operational objectives/activities, implementors, a timeframe, reporting channels and evaluation outputs were defined. Several documents and forms have been standardised, incorporated in the documentation system and used in all health facilities. Today, pharmacy management tools are available and are to varying degrees integrated into district and hospital operational plans. Documentation and monitoring of drug flow have improved.

Security of drugs has always been a

...cont’d on page 26 ➤



Delivering drug kits to a dispensary in Dar es Salaam

ACCESS

**Dar es Salaam...
cont'd from pg. 25**

major concern. Not all drugs used to reach the intended patient. Pilferage and misappropriation was a significant problem that is hard to quantify. Despite there being sufficient drugs, some patients still complained about not receiving drugs or of occasionally being forced to pay. Internal monitoring also indicated that drugs, particularly antibiotics, were used by health staff for their own and their families' treatment. However, increased supervision, professional ownership and accountability are improving the situation. Good inventory practice and drug monitoring have helped reduce pilferage. Each health facility has a Health Board, so involving the concerned community, which has also helped to reduce the problem.

QUALITY OF DRUGS

The main mechanism used for quality assurance of drugs is supplier selection and contract conditions with the Medical Stores Department. However, there is no formal reporting system for drug quality problems. Pharmacists and patients have to learn that they have a right and a duty to complain and follow-up on substandard drugs. Since 1997, operations and management at the National Pharmacy Board have been restructured in order to enforce drug regulation and quality assurance. More recently a new quality control laboratory has begun operating.

**BEING IN CHARGE OF DRUGS:
HUMAN RESOURCES AND TRAINING**

At the beginning, the Project's pharmacists generally had limited management skills – a major reason why the drug supply system functioned poorly. Today, each district has a district pharmacist operationally responsible for supervision of district health facilities, including district hospitals. Hospital pharmacists are more involved in the usual drug supply management activities, such as quantification, procurement, storage and distribution of drugs, as well as in some clinical activities within hospital committees and in drug information. However, pharmaceutical management capacity, particularly at district level, remains weak and should be strengthened. Decentralisation needs to be founded on capacity-building at local level.

With the focus on general district management in the Project's early years, training for pharmacists did not receive the necessary attention. Human resources were neglected. Only much later were the district pharmacists and pharmacy technicians consulted, and invited to discussions and activities aimed to improve the drug supply system. Pharmacists have therefore mainly been responders to change rather than reformers themselves, even though policy implementation and operational planning in part depend on them.

Ten years later pharmacists are more involved, visible and in control. They have gained some self-confidence and a

voice. Pharmacists are part of the hospital and district health management team. One pharmacist received training in the UK and all pharmacy staff participated in the training programme on rational prescribing (see below).

PROMOTING RATIONAL USE

All efforts put into a well functioning drug supply system can be futile if not followed by rational use of drugs by prescribers, dispensers and patients. From its inception, the Project has emphasised the importance of promoting rational drug use. In 1994, a programme was started to improve prescribing. A general quantitative drug use indicator study clarified the drug use situation. A concurrent qualitative study investigated motivations and underlying causes of prescribing habits and constraints within the system. Problems identified were overprescribing of antibiotics and injections, low availability of the national Standard Treatment Guidelines and incorrect prescribing according to norms. Based on these findings, interventions were selected and implemented to improve prescribing and quality of care. They include new Standard Treatment Guidelines, a Drug Information Manual, concurrent training, continuing education and supervision.

Since printed material alone has shown very little effect on prescribing practices, continuing education and supervision are necessary tools to assure sustained impact. Training sessions were conducted in all districts. Within five months a total of 328 Project prescribers (80%) in the three districts' health facilities were trained. Unfortunately, despite the existence of approved tools and an agreed schedule, planned activities for continuing education and supervision are not yet conducted in a systematic way.

PAYING FOR DRUGS

After liberalisation of the health sector, a 1995 study identified that about 35% of the population used public health facilities as first contact. It was estimated that drug expenditure for essential drugs to all public health facilities of the City Council amounted to between US\$0.7million and US\$1.1million a year. This represents a yearly per capita drug expenditure of about US\$1 to 1.5, which is in line with the generally accepted figure for essential drugs coverage in Africa³. A recent study concluded that drugs account for 40% of the total governmental and external health expenditures at Dar es Salaam level.

From 1992 until 1996, the City Council health facilities were supplied with essential drugs financed by an untied non-reimbursable allocation from the Swiss Government. In 1993, the Tanzanian Parliament allowed health services to be charged for. Cost sharing was introduced in Dar es Salaam public hospitals as in the rest of the country. A pilot Bamako-type project successfully implemented full cost-recovery of drugs in a few Dar es Salaam public dispensaries. The donor contribution gradually decreased and ended in 2000 with that phase of the

Project. The budget gap has been filled by Tanzanian Government contributions and cost-sharing schemes.

Currently, all dispensaries and health centres operate a Bamako-type model of a drug revolving fund. Hospitals have introduced 50% to 80% cost-sharing and are supported with donor and, unfortunately irregular, Government contributions. User fees allowed donor contributions to gradually decrease. Government funding is still essential for hospitals, cost-sharing exemptions, staff costs etc., and needs to continue to complement user fees or future insurance schemes. The system is no longer dependent on donor funds. Long-term sustainability will require continued political will and Government funding, together with further improvements in drug supply management and accounting.

REVIEW OF EXPERIENCE

The objective of drug availability has been achieved with large investments and is one of the Project's recognised accomplishments: visible, appreciated by patients and health workers, and valuable for the health care system. This has contributed greatly to the credibility of Dar es Salaam's health care delivery system and the willingness of patients to share the cost of services.

Professionally defined quality of care relating to drugs (availability, prescribing practice, drug quality) has improved, whereas community perceived quality of services (dispensing practice, patient care, affordability) is less enthusiastic.

Achievements

- The Project has a functional drug supply system in place that assures continued availability of essential drugs at Dar es Salaam public health facilities. The drug supply system is decentralised and integrated as part of the general district management structure within a reformed health organization in the framework of health sector reform. Pharmacists have gained a voice, are more involved, better informed, more interested in their work and more present in the system.
- A purchase agreement with the Medical Stores Department constitutes the basis for local procurement of drugs. Drugs are of good quality since most are bought from a reputable non profit international procurement agency. Storage and inventory practice has improved. Monitoring and documentation tools are available and partially used. The indent system (drug requisition) has been introduced and kits are gradually being phased out.
- Drugs are financed by full drug cost-recovery at dispensaries and health centres, and by cost sharing at hospitals. Attendance rates have changed little, and exemption policies are in place. The budget gap is filled with Government and donor contributions. Financial sustainability seems possible provided there is continued

political support, and improvements in management and accounting.

- A programme to promote rational drug use has been implemented, with Standard Treatment Guidelines and training of all prescribers in the districts.

Shortcomings

- Management capacity is still insufficient (storage, inventory management, documentation, monitoring of drug flow) particularly at district hospital level. Supervision needs to be strengthened and accountability reinforced.
- The human resource potential of pharmacy staff should be strengthened further (knowledge, skills, motivation and involvement). Quality of care in terms of attitude and patient care needs improvement.
- Rational drug use needs further promotion to improve prescribing behaviour (continuing training and supervision). Dispensing of drugs needs attention (training of drug dispensers). There is a great need to educate patients about drug use.
- Dialogue with the private sector is minimal.

Summary of development and achievements of Dar es Salaam Urban Health Project drug supply

Drug related activities	1990	2000
Selection	Appropriate	↑
Procurement	Foreign kit import	↑↑ <small>(kits being phased out)</small>
Distribution	Deficient	↑↑
Storage	Poor	↑↑
Monitoring and documentation	Poor	↑
Quality assurance & security	Poor	↑
Promotion of rational drug use	Irrational use	↑
Management	Poor	↑
Training	None	↑
Financing	Donor dependent	↑↑ <small>(reduction in dependence)</small>

Indicators	1990	2000
Availability	Poor	↑↑
Affordability	Free	*
Quality	Poor	↑↑
Rational use	Poor	↑
Sustainability	No	↑↑
Quality of care	Poor	↑

↑↑ significant improvement

↑ some improvement

* Cost-sharing/full cost recovery with little change in attendance rates, exemption policy

LESSONS LEARNT

The Dar es Salaam Urban Health Project's drug supply experience was and is a learning process. An efficient,

...cont'd on page 27 ➤

ACCESS

Why do the poor pay more? Survey reveals disparity in drug prices

What effect is an increasingly globalised economy with tighter intellectual property systems having on developing countries' efforts to make essential drugs available and affordable? A Consumers International and HAI survey in 1999 addressed this crucial question. The survey examined retail prices of 16 drugs in 36 countries – 10 advanced economies and 25 developing ones in Africa, Asia and Latin America, plus one from the Commonwealth of Independent States.

For the study the drugs were grouped into three categories according to their patent status: those still under patent in some countries; drugs whose patents will expire soon or have recently expired; and multisource drugs with several companies' products available in all the countries. The drugs are all widely prescribed.

HAI partners and Consumers International members visited leading retail pharmacies in the 36 capital cities seeking information on the:

- availability and retail prices of the proprietary or brand name product of the 16 drugs;
- total number of products which include the originator's brand, branded generics and generics of each of the 16 drugs available in the pharmacy;
- retail prices of the originator's brand and the package size. Where several products of the drug were available, the prices of the next two best-selling products in addition to the proprietary brand or top-selling brand.

- prices of each package size in the national currency and then converted to US dollars.

In line with the results of other studies reported at the Nairobi Conference (see page 20), the survey found a very wide variation in retail prices in the countries surveyed. Among its most striking findings were that:

- in some developing countries retail prices were higher than in developed countries. This was the case for 15 out of 18 dosage forms of 11 drugs (those for which comparable data exist);
- proprietary brand forms of several of the multisource drugs surveyed are the only products available in many of the African countries. This is even though low priced generic equivalents are available in the world market, in countries not offering patent protection to pharmaceuticals;
- survey differences in the retail prices of proprietary drugs are much wider (range 1:16–1:59), than those for prices of generic equivalents (range 1:7–1:18);
- variations in the retail prices of multisource drugs in developing countries are much wider than the variations in the developed countries.

While the study did not analyse the sources of price variations, researchers suggest that the small difference in prices in the industrialised countries may in part be due to co-marketing arrangements by manufacturers, parallel importing, reference pricing and drug pricing policies. Other studies have shown that producer/

importer prices vary between countries. And that import duties and distribution costs, pharmacy margins and local taxes also vary greatly between countries, but particularly from one developing country to another, so contributing to price differentials.

This wide range in proprietary drug prices in developing countries (1:4–1:59) is shown in the Table, with India having the lowest prices for six out of nine dosage forms. Consumers International and HAI argue that the Indian situation proves that competition is possible in the pharmaceuticals market and that it brings prices down. They say that India underscores the need for national policies on intellectual property systems with provisions to enable national firms to begin production of new drugs as quickly as possible. Indian firms could do this by

reverse engineering (a practice for discovering the manufacturing process of a product starting from the finished product), as the country's legislation did not provide patent protection for products, the authors state.

The report advocates that provisions for compulsory licensing and parallel imports should be in all national legislation on intellectual property rights as permitted by TRIPS. It states that this will help developing countries ensure regular access to good quality essential drugs at affordable prices. □

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Price comparison of 8 proprietary brand drugs in developing countries in the study

Generic name	Retail price of 100 units in US\$				Ratio of lowest to highest price
	Country		Country		
	Lowest	Price	Highest	Price	
Acyclovir 200mg	Togo	50	Indonesia	371	1:7
Acyclovir 800mg l	India	94	South Africa	790	1:8
Atenolol 25mg	India	03	Cameroon	53	1:18
Ciprofloxacin 500mg	India	15	Mozambique	740	1:49
Diclofenac 50mg	India	02	Argentina	118	1:59
Nifedipine 20mg	India	03	Peru	96	1:32
Omeprazole 20mg	Zambia	30	Brazil	477	1:11
Ranitidine 150 mg	India	02	South Africa	116	1:58
Zidovudine 100mg	Pakistan	81	Argentina	316	1:4

Dar es Salaam... cont'd from pg. 26

reliable and sustainable drug supply system depends on a variety of internal and external factors, and many components and actors determine its success. In retrospect we learnt the following lessons:

- Initially there was mainly an external materials injection, i.e. provision of drugs, which increased their short-term availability. Human resources, infrastructure such as pharmacy premises, and drug supply management skills were neglected. The provision of drugs was important, as



Photo: K. Wiedenmayer

Training prescribers in rational use of drugs

a visible symbol of development, to gain people's confidence and satisfy politicians, but it was not sustainable by itself.

- There was insufficient effort to involve, train, empower and motivate **pharmacy staff**. To have had pharmacy staff proficient in drug supply management from the beginning would have been extremely important for improving allegiance and cooperation, including early capacity-building and training. Emphasis needed to be placed on improving skills, increasing motivation and changing attitudes. Supportive supervision and monitoring as well as continued education are important tools.
- In order to follow-up, monitor and evaluate the quantitative and qualitative outcome of a high investment drug supply system over 10 years, a detailed **baseline assessment** with structure, process and outcome **indicators** should have been conducted at the beginning of the project. However only some rather randomly and informally collected information was available, which

makes evidence-derived outcome measurement difficult.

- An efficient national **Medical Stores Department** has proven to be one of the main pillars for the drug supply system, providing drugs of good quality at affordable prices. Thus externally organized tendering and import from overseas could be replaced by local and professional bulk purchasing, clearing, distribution and storage of essential drugs.
- The Tanzanian **National Drug Policy** has been an important tool and framework for the development of a more efficient, equitable and sustainable drug supply system for the Dar es Salaam Project.

A TENTATIVE OUTLOOK

A drug supply system cannot be managed in an isolated way but needs to be considered as part of a larger socio-cultural, political and economic context and environment. It is also part of an organization, the supporting health system, from which it cannot be isolated. Each sub-system, such as drug supply, is

a resource for and in interrelation with other sub-systems that have to be coordinated. For the new drug supply system, which developed over nearly 10 years, to be sustainable active consolidation is necessary. New structures and processes need to be kept alive, to be implemented and to become established, to avoid falling back into old patterns. Active consolidation involves strengthening as well as internal and external support. This translates into careful monitoring, supportive supervision and continuing education. A key assumption is a stable and supportive political environment. □

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DRUG INFORMATION

Introducing Pakistan's first Drug Helpline for professionals and patients

➤ AYESHA AHMED*

Providing independent drug information to health professionals and consumers through specially designated drug information centres is a relatively new concept in Pakistan. Although many countries automatically incorporate such centres in hospitals, in Pakistan they are rare. Those that exist, such as at the Aga Khan Medical University Hospital and Jinnah Post-Graduate Hospital, Karachi, and Lahore's Children's Hospital, are only for use by health professionals. But recently The Network-Association for Rational Use of Medication in Pakistan has established a Drug Information Helpline, the first of its kind in the country. Catering to the needs of doctors and patients, it is not hospital based but is run from The Network's office in Islamabad.

Meeting a need

As elsewhere, the available sources of drug information for Pakistan's health professionals, apart from pharmaceutical companies, are the standard pharmacology textbooks, and local and international compendia. These are not only cumbersome but soon become outdated. Busy physicians have little time to go through these sources and may rely mostly on industry information about medicines.

Although patient information leaflets supplied by the manufacturer accompany each medicine, the consumers' sources of information about drugs are mainly their prescriber and word of mouth. But prescribers have little or no time to tell people about possible adverse/side-effects, precautions or drug interactions, as there are usually other patients waiting. They may also be unaware of some details if the drug company does not provide complete information. Sales representative may minimise the importance of side-effects and precautions, for example. This creates a situation where there is insufficient information for the doctor and even less for the consumer. In the vast majority of cases people discuss their medicines with others showing similar symptoms, leading to abuse of medicines and the use of completely inappropriate drugs.

The Network's efforts

Since it became involved in the health sector nine years ago, The Network, a not-for-profit organization, has been committed to protecting consumers from harmful effects of medicines caused by lack of knowledge and misinformation. Through its publications, especially the *Drug Bulletin*, The Network has been catering to the information needs of health professionals and consumers, but on an individual level there was no system to deal with specific requests. The Helpline has filled this gap. Started with initial

support from WHO, it aims to give adequate, objective and up-to-date information on request.

A comprehensive service

A pharmacist, trained at the WHO Collaborating Centre for Drug Information, The National Poison Centre in Penang, Malaysia, runs the Helpline.

Consumers and health professionals access the service by phone, fax, mail and e-mail. Working hours are quite short, 9am–5pm Monday to Friday, mainly due to financial and staffing constraints.

The Helpline provides information on drug dosage, formulations, effects and adverse reactions, and probable drug interactions with food and with other allopathic medicines used together. The service does not offer any help with disease diagnosis or with prescribing medication to consumers, nor does it provide information on herbal or homeopathic medicines.

Requests from health professionals and consumers are dealt with in different ways. Consumers have to supply additional information about their prescribers and their prescriptions. Requests are documented on a standard form (see right) and scheduled on the basis of their urgency and the available resources – all are answered as quickly as possible. Different queries about the same drug by the same person are recorded as one. For example: if a request comes in for misoprostol and the doctor has asked for its availability, drug interactions, contraindications, precautions and side-effects, staff complete only one form and the various categories are marked on it.

Our resources

The Centre uses the latest version of MICROMEDEX, the standard updated database. It has the Drug Index and the poisoning information database, Poison Index. In addition, the *Australian Prescriber*, *Prescribe International*, *Drug and Therapeutics Bulletin*, *Worst Pills Best*

Pills, *American Hospital Formulary Service*, *Physician's Desk Reference*, *USP Drug Information*, *WHO Drug Information*, *British National Formulary* and *Ellenhorne's Medical Toxicology* are available. Information is also gathered from the electronic discussion groups Essential Drug (E-Drug) and International Network of Drug Information Centres (INDICES).

Much in demand

Although it is early to assess its contribution to rational drug use, the service is catering to the needs of eleven hospitals, both Government- and non Government-run. Analysis after 12

months in operation showed that 47% of users were health professionals including doctors, pharmacists and paramedic staff, and 53% consumers. The most frequently asked questions concern side-effects, availability and cost of medicines, followed by drug dosage regimen, drugs of choice, drug interactions and drug use during pregnancy. Approximately 95% of questions are answered by telephone, and the rest receive written replies.

Spreading the word

The Helpline has printed separate publicity brochures in English and Urdu and posters in the local Urdu language. Each hospital in Islamabad and Rawalpindi was

Ref No.

The Network's Drug Information Helpline

Administrative Record:

Requestor (Name):

Date:

Profession (Please tick the right option):

Time:

Doctor Pharmacist Nurse

Status: New Follow up

Paramedic Medical/ Pharmacy students

Method of communication:

Public

Verbal Written

Address of the requestor:

Tel:

Patient Information:

Age:

Diagnosis:

Sex:

Allergies:

Weight:

Medication being used:

Occupation:

Laboratory values:

Marital Status:

Additional Information:

Request:

Drug Information:

General product information

Drug interaction (unknown/drug/laboratory/disease/food)

Pharmacokinetics/Pharmacology

Side effects/Adverse effects/Contraindication

Therapy Evaluation/Drug of choice

Teratogenicity/Genetic effects

Dosage/Regimen recommendation

Poisoning/Toxicology

Pharmaceutical (formulation)

Pregnancy/Lactation/Infant risks

Others

Compatibility/Stability/Administration (rate/method)

Search Conducted (Source and utility, record specific data):

Findings/ Evaluation:

Response:

Responder:

Method of response: Verbal, Written

Date:

Time:

Time spent:

Follow Up:

Effective

Additional Comment:

Required additional help

Unsatisfactory

DRUG INFORMATION

contacted separately, with a letter and promotional materials sent to the Medical Superintendent or Executive Director. Doctors and other health staff received publicity materials at seminars about the service, which were held at all hospitals. The *Drug Bulletin* and our Urdu publication featured articles, as did the national daily English and Urdu newspapers when the Helpline was launched.

Educational activities

The drug information Helpline has regular input in The Network's *Drug Bulletin* and the Urdu publication *Sarfeen Aur Sehat*. As well as providing articles on specific drugs, the service also passes on the information it has on drug use trends, who is accessing the Helpline and the types of requests it is receiving.

Money matters

The service's major constraint is lack of finance. Eventually, we want to create a national service, but for this we need more staff. At present answering queries and promoting our service are the major activities, and one person is sufficient to run the Centre. But we need to publicise our work in other cities; we need money to travel to them, and more staff to handle the increased number of queries. We want to open at least 12 hours a day or even become a round-the-clock service. Resources and equipment also need to be updated. At present we have older editions of the core titles and our subscription to MICROMEDEX, one of our major information sources, must be renewed in 2001. Moreover, we want to improve the service by using the

Iowa Drug Information Service too.

Currently our dedicated phone-line is sufficient for people calling from within Islamabad and Rawalpindi. But it is inconvenient for people calling from outside the cities, mainly because it is expensive to call during the peak daytime hours. A separate toll free telephone line would solve this problem.

Proving our value

Since the Helpline started as a small pilot project in Islamabad in November 1999, it has proved popular with doctors and consumers. Now it is facilitating several hospitals, including major Government-run ones. We now believe that if information services are based within hospitals, doctors and patients could access them quicker. It could also

boost the profile of hospital pharmacists and give them an opportunity to become a more integral part of the health team.

Independent and objective drug information is essential for achieving rational drug use. If it is to be effective, this information has to be tailored to the level and specific needs of the enquirer. But this is a complex process. By starting small, with what we had, we have shown that Helplines can be successful. We intend

to form a network of such services, based within hospitals, and once we have shown our value nationally, we hope to attract the funding to ensure sustainability. □

* Ayesha Ahmed is the pharmacist in charge of the Helpline. For further information contact: The Network For Consumer Protection, 40-A, Ramzan Plaza, G-9 Markaz, Islamabad, Pakistan. Tel: + 92 51 2296802, fax: + 92 51 2291552, e-mail: helpline@best.net.pk

UK's new bulletin fills patient information gap

For many years the UK's Consumers' Association has been providing professionals and consumers with impartial information about health. Now, as more patients want to be involved in the increasingly complex decisions regarding their health care, the Association is introducing a new information service. It will reinterpret the information it gives to doctors and pharmacists in its *Drug and Therapeutics Bulletin* in a new bulletin for health care consumers. The doctor- or pharmacist-supplied leaflet will be accurate, concise, easy to read and up-to-date.

The Association acted because although there is a plethora of health and medical information available, especially on the Internet, many patients do not have access to it or cannot find the right information when they need it. Also, it was felt that the quality of Internet information is mixed and can be heavily biased towards commercial sources. The

Consumers Association decided there was still a dearth of high-quality, impartial information about drugs and medical treatments designed expressly for patients.

The new information bulletin will cover one topic per leaflet, for example, antibiotic resistance or weight loss. It will give background information for the newly diagnosed patient, and advice and recommendations that match the "parent" *Drug and Therapeutics Bulletin*. Pilot issues were tested with patients and health professionals. The Association hopes local health authorities will purchase the bulletin and make it available, free of charge, in doctors' surgeries and community pharmacies. An electronic version should follow soon. □

For further information contact: Philip Taylor, Consumer's Association: Drug and Therapeutics Bulletin, 2 Marylebone Road, London NW1 4DF, UK. Tel: + 44 20 71 830 7608, fax: + 44 20 71 830 7664, e-mail: taylorp@which.co.uk



One of the posters produced by the Service as part of its publicity campaign

Transparency in US drug approval system – a lesson for others?

It is common practice for manufacturers to selectively make clinical trial results of new drugs available only as abstracts or in meeting presentations, rather than publishing full length journal articles. This creates a problem for those wanting complete information. However, it is the companies' data, and the release of some results may have a negative impact on sales. But even when manufacturers do give a more complete report, the boundaries may be blurred between what is science – publication of peer reviewed journal articles – and what is basically drug promotion. An independent assessment of the drug becomes impossible.

A partial solution can be found in the transparency of the US drug approval process, at least for drugs approved there. The Freedom of Information Act gives public access to Food and Drug Administration (FDA) reviews of the clinical trials and other data submitted by manufacturers as part of a new drug application.

These reviews are referred to as approval packages and are available for many drugs approved since 1997 on the FDA's web site at <http://www.fda.gov/cder/foi/nda/index.htm>. Approval packages typically contain pharmacology/toxicology, biopharmaceutics and pharmacokinetics, and statistical reviews of the data submitted in a new drug application. The FDA Medical Officer also writes an overall assessment of a drug's safety and efficacy, based on the reviews and the clinical trials submitted in the application.

Transcripts of FDA Advisory Committees are also valuable in that they can reveal members' concerns about a drug's safety and efficacy. Committee members are outside experts who make recommendations to the Agency about a drug's approval that are not always followed. Meetings are conducted under the Federal Advisory Committee Act to ensure that the public has access to the workings of the government. Transcripts are found at <http://www.fda.gov/foi/electr.htm> on

the FDA's web site, although not all drugs go before FDA Advisory Committees.

Copies of approval packages and Advisory Committee transcripts for drugs approved prior to 1997 can be obtained from the FDA through a request under the Freedom of Information Act. Access to these documents is not limited to US citizens and US non-profit organizations are granted a fee waiver when the requested information is shared with the public. Procedures for making a Freedom of Information Act request can be found at <http://www.fda.gov/opacom/backgrounders/foiahand.html> on the Agency's web site.

Since January 2000, FDA reviews of new drugs are available on the FDA's web site at least one day before Advisory Committee meetings. About 30% of the drugs approved by the FDA go before an Advisory Committee. Legal hearings have been taking place to decide if safety and efficacy data can be considered confidential commercial information that is

exempt from public disclosure under the Freedom of Information Act until a drug is approved.

The selective publication of clinical trials by manufacturers can influence the perception of a new drug's therapeutic value by only making available evidence that is most favorable to the drug. It now appears necessary to wait until a drug's approval package is publicly available from the FDA before independent recommendations or formulary decisions can be made about new drugs. Controlled access to published clinical trial results by manufacturers and the lack of transparency in the drug approval process in other countries remain problems. □

Source: E-Drug electronic discussion group message from Larry D. Sasich, Research Analyst, Public Citizen Health Research Group, 1600 20th Street, NW, Washington DC, 20009, USA. Fax: + 1 202-588-7796, e-mail: lsasich@citizen.org, Web Site: www.citizen.org/hr

DRUG INFORMATION

Going from strength to strength – Iran's Drug and Poison Information Service

➤ SHEKOUFEH NIKFAR, MOHAMMAD ABDOLLAHI, ABDOLMAJID CHERAGHALI*

Parmacotherapy has become increasingly complex, as patients receive more and more drugs to manage their diseases. New prescription drugs are being introduced at a bewildering rate^{1,2,3}, and people hear of them through the media, and increasingly through Internet. Patients request these drugs before their doctors have a chance to build their knowledge base on them. Advertising has also increased demand for non prescription and herbal drugs, nutritional therapies and even homeopathic remedies. Studies showed that drug- and poison-related problems existed in the Islamic Republic of Iran, as in many countries, and the lack of a drug information centre was evident. To go some way to meeting the needs of health professionals and consumers⁴, we opened the first Drug and Poison Information Centre in Tehran, in February 1997. Three and a half years of hard work later, what have we achieved?

The Centre has 10 staff, two doctors, two pharmacists and the rest are specialists in pharmacology and toxicology. Conveniently located in the city centre, we open from 8 a.m. to 8 p.m. Users can leave a message on the answer machine after working hours, or submit queries by post or e-mail. We answer requests by phone or in writing. Staff complete a standard request form, covering: name, address, occupation, education, patient history, the question, category of question, the answer and the references used. The staff member also records age, weight, sex, diagnosis, allergies and current medications, together with any other relevant details of the conversation. The request form is countersigned by the supervisor who reviews the responses. If we suspect that a caller has had an adverse reaction to medication, we report the incident to the National Adverse Drug Reaction Centre, with which we collaborate very closely.

We are rigorous about quality, and an internal committee at the Centre reviews response forms regularly, looking at the references used, and the clarity, accuracy and completeness of answers.

Fast, efficient and increasingly popular

We analysed 31,931 enquiries to assess the type of users, questions asked and references used between February 1997 and January 2000. Most questions were answered verbally (85%), 3% were answered only in writing and 12% were answered verbally and followed up with a written response. Ninety percent of the questions took less than 15 minutes to answer, while 10% took more than 15 minutes, up to a maximum of two days. The number of enquiries rose from 6,500 in our first year to 16,898 between February 1999 and January 2000. The number and type of questions received by the Centre are given in Table 1. The majority concerned problems involving therapeutic use (indication and efficacy), poisoning, pregnancy and lactation, and adverse effects. Among poisoning cases most enquiries concerned drugs (70%), followed by other chemicals (20%) and herbals or natural toxins (10%).

Physicians (26%), pharmacists (25%) and patients or their relatives (25%) were the most frequent users, while nurses (8%), dentists (6%) and other health professionals (5%) use us to a lesser extent.

Physicians mainly asked about drug dosage and therapeutic use, while specialists were interested in the comparative efficacy and toxicity of drugs, particularly new ones. Most pharmacists wanted to know about formulations, interactions, identification of foreign products and substitution. Nurses commonly asked us about pharmacokinetics, dosage and compatibility of intravenous drugs.

Table 1
Categories of enquiries at the Drug and Poison Information Centre from February 1997 to January 2000 (n=31931)

Enquiries	Number	Frequency (%)
Therapeutic use	5109	16
Poisoning	4470	14
Pregnancy and lactation	3832	12
Adverse effects	3512	11
Dosage	3193	10
Drug abuse	3098	9.7
Therapeutic comparative efficacy	2554	8
Interaction	2235	7
Substitution	1277	4
Precautions	958	3
Identification of foreign product	639	2
Contraindications	639	2
Metabolism	319	1
Pharmaceutical compatibility	96	0.3

Table 2
Distribution of drug-related questions according to anatomical therapeutic chemical classification system from February 1997 to January 2000

Drug class	Number	Frequency (%)
Central nervous system	6386	20
Gastrointestinal system	4790	15
Systemic anti-infectives	4151	13
Systemic hormonal preparations	3832	12
Cardiovascular system	3831	12
Genitourinary system	3193	10
Dermatological system	1916	6
Respiratory system	1914	6
Antineoplastic/ immunosuppressive drugs	957	3
Blood and blood-forming organs	319	1
Various	642	2

Significantly 10% of the patients contacting the Centre said they did so because their doctor or pharmacist had failed to provide any information about the uses and effects of prescribed medications. Forty percent considered the information provided to be unclear or in some way inadequate, and 50% wanted a second opinion, to verify the accuracy of information provided by the physician or pharmacist.

Table 2 gives a breakdown of drug-related questions according to anatomical therapeutic classification. Questions about drugs acting on the central nervous system (mostly antidepressants and anticonvulsants) were the most common, followed by requests concerning gastrointestinal drugs (mostly acid lowering agents), systemic anti-infectives (mostly fluoroquinolones, cephalosporins and penicillins), systemic hormonal preparations (mostly sex and thyroid hormones, then antidiabetics), cardiovascular drugs (mostly β -adrenoceptor blockers and antihypertensives), drugs affecting the genitourinary system (mostly drugs for impotence and erectile dysfunctions),

dermatological drugs (mostly drugs used for acne and alopecia), respiratory drugs (mostly antiasthmatic agents). There are also questions concerning drugs used for specific disease groups like hepatitis, cancer, immune disease, coagulation factors deficiency and thalacemia.

The references we use most are the DRUGDEX (used in 48.9% of queries), POISINDEX (16%), TOMES (8%) and EMERGINDEX (7%) databases. Among our textbooks Briggs' *Drugs in Pregnancy and Lactation* is used most often. Other frequently used textbooks

were Martindale's *The Extra Pharmacopoeia*, followed by Kathzung's *Basic and Clinical Pharmacology*, Merck *Manual*, Harrison's *Principles of Internal Medicine*, American Hospital Formulary Service *Drug Information Source* and Ellenhorn's *Medical Toxicology*. The bibliographic databases of IOWA Drug Information, Medline and useful Internet sites are also used regularly to search medical literature (Table 3).

More than an enquiry service

Drug and poisoning information requests take up most time. But in our efforts to educate and promote rational use of drugs we do far more than wait for questions to come to us. As Table 4 shows the Centre participates in pharmacy and therapeutic committees; gives workshops, seminars and lectures as part of its training and education programme; produces information newsletters, pamphlets and review articles; conducts literature searches; provides mass media

Table 3
The most frequently used references at the Drug and Poison Information Centre from February 1997 to January 2000 (n=31931)

Reference name	Number	Frequency (%)
DRUGDEX Micromedex international health care series	15615	48.9
POISINDEX Micromedex international health care series	5109	16
TOMES Micromedex international health care series	2554	8
EMERGINDEX Micromedex international health care series	2235	7
Briggs Drugs in pregnancy and lactation	1596	5
Martindale The extra pharmacopoeia	734	2.3
Kathzung Basic and clinical pharmacology	639	2
Merck manual	639	2
Harrison Principles of internal medicine	638	2
AHFS Drug information source	638	2
Ellenhorn Medical toxicology	447	1.4
MEDLINE	416	1.3
IOWA drug information services	319	1
Others	352	1.1

DRUG INFORMATION



● Drug and Poison Information Centres

New drug and poison information centres are being set up throughout Iran

information to help increase rational use of drugs; and reports to the Adverse Drug Reaction Centre. As the Service's popularity has grown so too has the variety of organizations we assist.

The Centre tries to ensure that the literature it produces meets the needs of users. So, when we do quality checks on our responses we also assess the need for education materials on particular topics. For example, we were receiving questions from young men about the effects of anabolic drugs that might be used for body building. We immediately increased our dissemination of information on this subject in seminars, the mass media and our newsletters.

As our drug and poison information pamphlets are so popular, the Centre has created a subscription service, which includes over 20,000 health professionals. They regularly receive literature promoting rational drug use, often based on our most interesting queries.

We want as many Iranians as possible to have access to drug information, not only those living in the capital. So we have established new drug and poison information centres – more than 15 to date – all with access to a computer and references (see map). The Tehran Centre supports them

by providing reference materials and funds.

After our first assessment of the Centre we are optimistic about its future. Questionnaires distributed to health professionals during seminars showed that they thought our service has an impact on prescribing practice, and in most cases users were satisfied with their consultation. The increased rate of enquiries and users are other positive indicators.

Now we want to build on success. The Centre is preparing more reference materials for health professionals and expanding its e-mailing of information on specific diseases to patients. We are doing more evaluation of Internet

sources for patients. We are also considering having a computer-based system to assist in analysing information, and documenting the Centre's activities and effectiveness.

Staff believe they could be even more effective if health professionals' training and continuing education covered the role and use of drug information centres. We also want to see more training in applied toxicology, to reduce the large number of poisoning queries we receive.

Our work with the public is very important, particularly given our findings on the lack of information patients receive about their prescribed medicines, and people's increased exposure to advertisements and media-provided information. Correct, unbiased and practical drug and poison information is one of the best ways to neutralise the effect of drug promotion and reduce drug-related adverse effects.

Our analysis of queries has shown that too little of this exists in Iran and underlines the Centre's crucial role in the health care system and the community. □

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1. Johnson JA, Bootman JL. Drug-related morbidity and mortality. *Arch Intern Med* 1995;155:1949-1956.
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3. Rodriguez C, Arnaud JM, Vidal X, Laporte JR. Therapeutic consultation: a necessary adjunct to independent drug information. *Br J Clin Pharmacol* 1993;135:46-50.
4. Hemminki E, Herxheimer A. Should drug information be an integral part of health care? *J R Coll Physicians Lond* 1996; 30:104-6.

Table 4
Percentage of time spent on Drug and Poison Information Centre activities from February 1997 to January 2000

Activity	Frequency (%)
Providing drug and poisoning information	30
Producing newsletters and pamphlets	14
Providing seminars and giving lectures	10
Reporting to the Adverse Drug Reaction Centre	10
Preparing review articles	9
Providing workshops, training and education	8
Establishing new drug and poison information centres	7
Participating in pharmacy and therapeutic committees	5
Conducting literature searches	4
Providing mass media information	3

RESEARCH

Burkina Faso: study shows value of qualitative monitoring

While prescribing practices have been studied in various developing countries, most research has limited evaluation to numerical analysis, such as the number of drugs prescribed or the percentage of prescriptions containing an antibiotic. But a study carried out in Burkina Faso¹ used both qualitative and quantitative indicators to investigate the rationality of drug prescriptions at outpatient consultations. The study results demonstrate the importance of a multifaceted research approach, and add to the evidence that greater efforts must be made to improve prescribing practices globally.

Specially trained medical students and nurses observed a total of 313 outpatient consultations in nine health centres in three rural districts. Data on 2,815 drug prescriptions were also analysed. These had been copied from patient registers two months before observation began, in order to compare prescribing habits in observed and unobserved consultations.

During the two-week study period 366 prescriptions for 793 drugs were given out and an average of 2.3 drugs was prescribed per visit. A total of 33.1% of prescriptions contained antibiotics and 24.6% contained injections. Of the drugs prescribed, 88.0% were on the essential

drugs list, but only 59.3% of prescriptions conformed to standard treatment guidelines. In all other prescriptions at least one drug was not indicated or the dosage was wrong. Errors in dosage occurred significantly more often in children under the age of five, mostly in terms of dangerous overdosing. Seven out of 21 pregnant women received drugs contraindicated in pregnancy. In two-thirds of all cases the

patients received no information on how long a prescribed drug had to be taken. Prescribing was similar in both the observed and the unobserved consultations.

The study concludes that a significant proportion of patients probably received ineffective or even harmful prescriptions, although the interpretation of quantitative indicators alone would have led to a positive evaluation of prescribing practices.

Only by correlating prescriptions to patients' diagnoses was it possible to detect problems of false dosage and contraindications, and to identify certain risk groups. So while quantitative drug use indicators have proved very useful for a rapid and economic assessment of general drug use habits, in-depth studies may be necessary from time to time. Additionally this methodology allowed the identification of special risk issues and risk groups, so helping to determine the focus of further interventions. □

Reference

1. Krause G et al. Rationality of drug prescriptions in rural health centres in Burkina Faso. *Health Policy and Planning* 1999;14(3):291-298.

Science shopping in the Netherlands

A move to bring science out of the "ivory tower" and into the service of a wider public has been proving very successful in the Netherlands. The idea for Science Shops originated in the 1970s, and today there are more than 30 such research information centres, affiliated with 11 universities and covering a wide field – from health to literature. Financed by the universities, the Shops may work free of charge for non profit social organizations needing help with community-based research. One of them is the Science Shop for Medicines attached to Utrecht University's Faculty of Pharmacy, which

receives many of its research questions from patients' associations, consumer organizations and women's groups.

When a question comes in, the Science Shop looks for a staff member in the Pharmacy Faculty whose work ties in to the topic, which generally concerns pharmacotherapy or pharmacoepidemiology. Then, under supervision, a student does a literature review and receives study points for the work. The study is usually written up as a short report or brochure, available from the Shop for a nominal charge. While a literature review is usually what is required, other types of research, such as surveys, interviews and

drug analyses are also possible. In recent years many questions have been asked about the use of drugs for psychiatric disorders and about women's health issues.

As well as collaborating with the other research information centres at Utrecht University, the Science Shop for Medicines often works with Groningen University's Medicines Shop and the country's seven Health Shops. □

For further information contact: Science Shop for Medicines, Sorbonnelaan 16, Postbus 80082, 3508 TB Utrecht, the Netherlands. Tel: + 31 30 253 7309, fax: + 31 30 253 9166, e-mail: wewi@far.ruu.nl

COURSES & MEETINGS

Lebanon hosts drug policy seminar

The many issues surrounding drug procurement, production, regulation and use, and how best to develop, implement and evaluate a national drug policy were hotly debated at a seminar held in Lebanon in October 2000. The event was organized by Boston University's Centre for International Health and the Inter-Ministerial Council for Health Reform in Lebanon, in collaboration with WHO.

The seminar's workshop format combined lectures, in-depth discussion of case studies and small-group exercises, plus several field visits to health facilities and community pharmacies. The meeting attracted policy-makers and senior managers responsible for pharmaceutical systems in developing and transitional countries, and senior officials of funding agencies throughout the region.

Previous seminars have been held successfully in Africa, India and the USA.

For information on future seminars contact: Dr Richard Laing, Associate Professor of International Health, Boston University School of Public Health, 715 Albany St, T4W, Boston MA 02118, USA. Tel: + 617 414-1444, fax: + 617 638-4476, e-mail: richardl@bu.edu

Community-based health education and health promotion course

A 10-week course to update managers, project and field staff on new developments in health education and health promotion will run from 30th April 2001 at Leeds Metropolitan University, UK. The course provides skills in research, planning, management and evaluation of programme's education and promotion components. Its flexible structure allows participants to follow a topic of particular interest, and the chance to apply their new skills to a problem from their own work-setting.

Applicants should have field experience/training in a subject area relevant to health promotion and a good working knowledge of English. The fee for academic tuition, course materials and field visits is £3600. In addition students will have to pay travel, subsistence and accommodation expenses.

For further information contact: Overseas Admissions Tutor, Health Education, Queens Square House, Leeds Metropolitan University, Calverley Street, Leeds, LS1 3HE, UK. Tel: + 44 113 2831915, fax: + 44 113 2831916, e-mail: health-promotion@lmu.ac.uk or john@hubble.co.uk

Zimbabwe hosts rational use course

The next INRUD/MSH/EDM course on Promoting Rational Drug Use will be held at Victoria Falls, Zimbabwe, from 26 August – 8 September 2001. Topics will include identifying drug use problems, developing and evaluating interventions and developing public and prescriber educational materials and campaigns. This highly participatory course is intended for physicians, pharmacists, health programme managers, policy-makers, researchers and others interested in improving the use of drugs.

For further information contact: PRDU course, NDTPAC, Directorate of Pharmacy Services, Ministry of Health and Child Welfare, Box CY924, Harare, Zimbabwe. Tel: + 263 4 730970 or + 263 4 795353, e-mail: inrudzim@healthnet.zw

Diploma in Drug Evaluation and Pharmaceutical Sciences

Today's potent drugs, combined with the complex issues of their production and use, have created a growing need for evaluation of their safety and efficacy.

For such evaluation wide-ranging expertise is required in the areas of chemistry, pharmaceuticals, pharmacology and toxicology, clinical medicine, and legal and ethical considerations.

The new Graduate Diploma in Drug Evaluation and Pharmaceutical Sciences offered by the University of Melbourne, Australia, offers a systematic overview of these areas and how they affect drug evaluation. The course is aimed at pharmacists, research nurses, scientists and those involved in regulatory affairs.

For further information contact: Mrs Nicola Cash, Drug Evaluation Unit, Austin and Repatriation Medical Centre, Studley Road, Heidelberg Vic 3084, Australia. Tel: + 61 3 9496 3420, fax: + 61 3 9459 3510, e-mail: nicola@austin.unimelb.edu.au



NETSCAN

Catch up on the Australian Prescriber

For the first time the Internet version of the journal *Australian Prescriber* is available in PDF format, with Acrobat reader software provided. Back issues of the journal (from 1994) are also available on the Web site at <http://www.australianprescriber.com>

Read INRUD News on the Web

INRUD News, the twice-yearly journal of the International Network for Rational Use of Drugs (INRUD) is now available on the Web. Published twice a year, over 3,000 copies of the journal are distributed free of charge worldwide. Contents include updates on INRUD global activities, news from country and support groups, meeting and workshop reports, research briefs, and references to articles on rational use of drugs.

You can subscribe to *INRUD News*, and read current and previous issues by clicking on the newsletter icon at <http://www.msh.org/inrud>

Lancet's electronic research archive

The *Lancet* has launched an experimental electronic research archive (ERA) in international health. This self-archive will be owned by authors and administered by the *Lancet*. Access will be unrestricted through the ERA Web site: <http://www.thelancet.com/newlancet/eprint>

The objective is to create a searchable electronic public library of research in international health. It is hoped to cover all issues relevant to medicine in the

developing world, and the *Lancet* is appealing for support in its effort to make knowledge accessible to all members of the international health community.

SATELLIFE Information Services' new automatic response

There is a new and easy way to learn about the free information services that SATELLIFE makes available to health professionals, particularly those in the developing world. Send a request to autoinfo@usa.healthnet.org inserting no text in the body of your message and leaving the subject line blank. You will soon receive details of SATELLIFE's services.

For further information see page 6. You can also visit SATELLIFE on the Web at: <http://www.healthnet.org>

Drug Price Indicator Guide updated

The *International Drug Price Indicator Guide*, available on Management Sciences for Health Manager's Electronic Resource Centre Web site at: <http://erc.msh.org> has been updated. Data for the 1996, 1998, 1999 and 2000 editions are on line. Search capabilities have also been improved, and new features added.

To obtain a print version of the 1999 *Guide* contact: the MSH Bookstore. Fax: + 1 617-524-2825, e-mail: bookstore@msh.org

Children and medicines

The United States Pharmacopoeia has posted "References for Children and Medicines" with abstracts on its Web site: www.usp.org This is a 47-page document with references primarily relating to behaviour, ethics and rates of use. Send suggestions for additions to Patricia J. Bush, e-mail: pjb@usp.org

Ordering WHO books on pharmaceuticals?

Check out WHO priced publications on pharmaceuticals at: <http://www.who.int/dsa/cat98/phar8htm>

No Free Lunch

No Free Lunch, which is dedicated to evidence-based health care, has created a listserv, called nofreelunchserve. The list is intended to serve as a forum for the exchange of ideas and information.

Subscribe at: <http://www.nofreelunchserve.pairlist.net>

International Digest of Health Legislation on-line database

The International Digest of Health Legislation contains a selection of national and international health legislation, mainly official publications and other documents forwarded by WHO Member States. Some texts are summarised, while only the titles are given for others, but where possible

links are provided to other Web sites containing full texts of the legislation.

You can query a database by selecting a country, a subject, a volume, and by looking for a specific keyword. Check out the site at: <http://www.who.int/idhl>

HIF-net at WHO

HIF-net at WHO is an e-mail discussion list for people who want to improve access to reliable information for health workers in developing and transitional countries.

To join, send an email message to the list moderator at: INASP_Health@compuserve.com

In the body of the message, say you want to participate in HIF-net at WHO and add a few lines about your professional interest in health information. This will be used as your HIF Participant Profile. Your name will be added to the list and the WHO server will automatically send you a welcome message with details on how to participate.

For an information sheet on HIF-net at WHO, send an e-mail to: majordomo@who.int leave the subject line blank, and in the message-box type: info_hif-net

Messages to the whole list should be sent to hif-net@who.int

Health Information Forum (HIF) is run as an activity of the INASP-Health Programme, a cooperative network of partners which aims to improve global access to information and knowledge.

Contact: Dr Neil Pakenham-Walsh, Programme Manager, INASP-Health, 27 Park End Street, Oxford OX1 1HU, UK. E-mail: INASP_Health@compuserve.com

Web site: <http://www.inasp.org.uk>



NETSCAN

Now HIV/AIDS information in French

The SAFCO (SIDA en Afrique du Centre et de l'Ouest) network has been set up to encourage discussion and the electronic exchange of information on issues related to HIV or AIDS in francophone Africa. To subscribe send a message to: safco@hivnet.ch (see page 3 for more details).

**What's new on EDM's homepage?**

The Department of Essential Drugs and Medicines Policy's homepage is continuing to expand and become more user friendly. As well as introducing the essential drugs concept, national drug policies, and the work of WHO and EDM, many more of the Department's documents can

be viewed and downloaded.

Among recent highlights are the addition of *Operational Principles for Good Pharmaceutical Procurement* (see below) and *Quality Assurance of Pharmaceuticals. A Compendium of Guidelines and Related Materials. Volume 2. Good Manufacturing Practices and Inspection*. The *WHO Medicines Strategy: Framework for Action in Essential Drugs and Medicines Policy 2000-2003* is now available electronically, as is the document *Essential Drugs used in the Care of People Living with HIV: Sources and Prices*. Some documents in EDM's Health Economics and Research Series can also be downloaded.

The complete English, French and Spanish versions of the *Monitor* (from number 23 onwards) can be found in PDF format.

Check us out at: <http://www.who.int/medicines>

**Pharm-policy e-discussion group**

Discussions in this group cover pharmaceutical policies, particularly those involving intellectual property, technology transfer and pricing. Anything significant gets on this discussion group within 24 hours: <http://lists.essential.org/mailman/listinfo/pharm-policy>

**New Medline search tool**

BioMail periodically does a user-customised Medline search and sends all matching articles recently added to Medline to the users' e-mail address. Medical researchers and biologists wanting regular updates from journal articles will benefit from the service, which is free of charge. It will be particularly useful for countries where access to the Internet is

not yet widely available. If people have a permanent e-mail address, but only sporadic access to the World Wide Web, they only need to fill out a BioMail form once and they will receive new references from Medline continually.

Find out more at: <http://biomail.sourceforge.net/biomail/>

Links to other free alert sites:

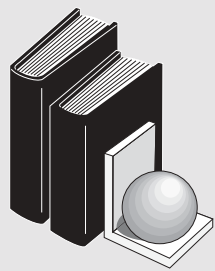
Pubcrawler is another Medline alert service, available through the Department of Genetics, Trinity College, Dublin, Ireland: <http://www.pubcrawler.ie>

PubMed Query tool: Biotechnology Computing Facility, Arizona Research Laboratories, USA, at: <http://bcf.arl.arizona.edu/query/add.html>

JADE: also a Medline alert service, The National Center for Emergency Medicine Informatics in the USA: <http://biodigital.org/jade/>



PUBLISHED LATELY

**Important**

The Department of Essential Drugs and Medicines Policy cannot supply the publications reviewed on these pages unless stated otherwise.

Please write to the address given at the end of each item.

Intellectual Property Rights, the WTO and Developing Countries. The TRIPS Agreement and Policy Options, C.M. Correa, 2000, 254 p.

The structure of international trade is being fundamentally altered by the various agreements which the World Trade Organization polices. This book cuts through the sometimes daunting technicalities of one of the most important of these agreements, that dealing with intellectual property rights. The publication clearly explains what the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) is about and its main provisions.

The author is particularly concerned to explore the Agreement's implications for developing countries. These relate to the future of local research and development, access to advanced technology, commercial

exploitation of their natural resources and welfare effects. The book uses Latin American and Caribbean experience to illustrate the problems that have arisen with implementing TRIPS.

Throughout, Correa indicates concrete options available at national level to implement the TRIPS Agreement's provisions in a manner consistent with development objectives and public policy concerns. (See also page 36).

Available from: Zed Books, 7 Cynthia Street, London N1 9JF, UK. Price: £16.95, plus £2.50 postage and packing.

Handbook on Antimicrobial Therapy, (revised edition), The Medical Letter on Drugs and Therapeutics, 1998, 205 p.

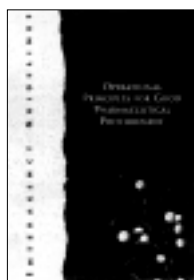
This comprehensive handbook on antibacterials, antifungal and antiviral drugs includes first-choice and alternative drugs for every indication, doses and adverse effects. In addition there are chapters on the safety of antimicrobial drugs in pregnancy, advice for travellers and drugs for HIV infections. The non profit publication also includes price lists for commonly used oral antibacterial drugs.

Available from: *The Medical Letter on Drugs and Therapeutics*, 1000 Main Street, New Rochelle, N.Y. 10801-7537, USA. Fax: +1 914 632 1733. Price 1-9 copies US\$14 each, 10-99 copies US\$11.20 each, 100+ copies US\$8.40 each. Special rates are available for subscribers to the journal, *The Medical Letter on Drugs and Therapeutics*.

Operational Principles for Good Pharmaceutical Procurement, Interagency Guidelines, World Health Organization, WHO/EDM/PAR/99.5, 2000, 24 p.

Pharmaceutical procurement is a complex process and problems are common. This document from the Interagency Pharmaceutical Procurement Group sets out four strategic objectives and 12 operational principles for good procurement. These will be reproduced in full in EDM-30.

Available, free of charge, from: Department of Essential Drugs and Medicines Policy, World Health Organization, 1211 Geneva 27, Switzerland.

**Référentiel pour l'harmonisation des procédures d'enregistrement des médicaments essentiels génériques dans les pays de la zone franc et pays associés, (Pharmaceutical Sector Collaboration between CFA and Associated Countries), World Health Organization, WHO/EDM/DAP/99.2, 1999, 25 p.**

This guide on harmonization of registration procedures is intended to facilitate the introduction of essential drugs on to the markets of Communauté financière africaine (CFA) and associated countries, and thus improve the availability and affordability of pharmaceuticals. The guidelines, adopted at a seminar in Ouagadougou in February 1999, cover generic drug registration and marketing authorisation.

Available, free of charge, from: Department of Essential Drugs and Medicines Policy, World Health Organization, 1211 Geneva 27, Switzerland.

HIV Testing: A Practical Approach, Healthlink Worldwide, 1999, 48 p.

HIV testing is an essential part of all HIV prevention and care programmes, to ensure safe blood supplies and determine HIV status. And appropriate counselling, education, care and follow-up support are an essential part of any HIV testing programme.

HIV testing: a practical approach provides clear information for policy-makers, planners, and health personnel involved in counselling and HIV testing. An update of the 1994 publication, *Practical issues in HIV testing*, it reflects recent developments, and lessons learned over the last six years. Topics covered include: considerations before beginning an HIV testing programme; technical aspects of testing, testing individuals

and surveillance; and implementing blood screening programmes.

In addition, the publication provides examples of programmes in Africa, Asia and Latin America, and experiences from people who have had HIV tests. A useful resource list and detailed technical information on the characteristics of some of the most commonly used tests are also given.

Available from: *Healthlink Worldwide*, Cityside, 40 Adler Street, London E1 1EE, UK. E-mail: publications@healthlink.org.uk Price: £7.50/US\$15. Single copies are free of charge to indigenous organizations in developing countries.

Counterfeit and Substandard Drugs in Myanmar and Viet Nam, World Health Organization, EDM Research Series No. 29, WHO/EDM/QSM/99.3, 1999, 55 p.

This report presents the results of two studies, done in Myanmar and Viet Nam, to obtain independent information on the counterfeit drugs problem, and so help to develop measures against counterfeiting. The research study involved collecting background information on the status of drug regulation and also samples of 500 products, which were subjected to laboratory quality testing. Two hundred and fourteen of these were selected for investigation, with a portion of each sent to the drug regulatory authorities in the manufacturing country for analysis.

The report shows that the prevalence of substandard drugs is generally a much greater problem than counterfeit drugs in both countries. Products which had passed laboratory tests were sometimes found to be counterfeit (deliberately mislabelled products, for example). The report concludes that laboratory tests alone are insufficient to determine whether a product is counterfeit. Any investigation requires adequate resources, planning, and undercover work, and must be undertaken in collaboration with drug regulatory authorities and manufacturers.

Available, free of charge, from: Department of Essential Drugs and Medicines Policy, World Health Organization, 1211 Geneva 27, Switzerland.

PUBLISHED LATELY

Narcotic and Psychotropic Drugs. Achieving Balance in National Opioids Control Policy. Guidelines for Assessment, World Health Organization, WHO/EDM/QSM/2000.4, 2000, 37 p.

WHO estimates that by the year 2020 approximately 70% of the annual 20 million new cancer cases will occur in developing countries, where most patients are diagnosed in the late stages of the disease. It is at this time that pain is most prevalent. But cancer pain is frequently untreated and, even when it is, relief is often inadequate. While health worker training and increased access to palliative care services can help, the publication focuses on solving the problem of inadequate availability and use of pain medications, particularly opioid analgesics, in developing countries.

The authors state that opioid analgesics, such as codeine and morphine are "absolutely necessary" for the management of cancer pain and that for moderate to severe pain there is no substitute for opioids in the therapeutic group of morphine. But, because of their potential for abuse, opioids are classified as narcotic drugs.

The International Narcotics Control Board, WHO and national governments report that opioids are not sufficiently available for medical purposes. Reasons for this include the low priority of pain care in health systems, greatly exaggerated fears of addiction, overly restrictive national drug control policies and problems in procurement, manufacture and distribution of opioids. The publication presents guidelines for governments to determine whether their national drug control policies have the legal and administrative framework to ensure medical availability of opioid analgesics, as recommended by the International Narcotics Control Board.

Available, free of charge from: Department of Essential Drugs and Medicines Policy, World Health Organization, 1211 Geneva 27, Switzerland.

Beyond Our Means? The Cost of Treating HIV/AIDS in the Developing World, The Panos Institute, 2000, 59 p.

This report looks at the controversial and complex issues surrounding access to HIV/AIDS treatments in developing countries. It states that at least 12 million people in the developing world are in urgent need of the antiretroviral drugs which can suppress HIV and indefinitely postpone symptoms of AIDS. But the vast majority of these people live in the world's poorest countries, and while providing such treatment is theoretically possible, it is highly improbable in the foreseeable future, according to the authors.

A number of factors lie behind this failure to provide full treatment to those in need. These vary from country to country, but, according to the publication, include lack of political will, unhelpful economic policies (such as taxing medical products), lack of relevant information and lack of appropriate distribution mechanisms. The authors believe two other factors are critical. The first is weak

health care systems – poor infrastructures, inadequate facilities, including lack of hospital beds, laboratories and trained staff. The second factor is a combination of the high cost of antiretroviral and other drugs, and disputes over patenting and licensing rights for these products.

The publication provides an overview of the issues surrounding access to treatment for AIDS, in order to encourage informed debate, further research and considered action. It is intended primarily for policy-makers, AIDS organizations and medical personnel.

Available from: The Panos AIDS Programme, 9 White Lion Street, London N1 9PD, UK. Tel: + 44 20 7278 1111, fax: 44 20 7278 0345. Available on the Panos Web site: www.panos.org.uk Price: £5/US\$10. Copies are available, free of charge, to resource-poor NGOs in developing countries.

Integrating Public Health Concerns into Patent Legislation in Developing Countries, C. Correa, South Centre, 2000, 124 p.

This publication presents options for the design and implementation of public-health sensitive patent policies in developing countries. It is particularly concerned with the TRIPS Agreement (Trade-Related Aspects of Intellectual Property Rights) which covers protection of pharmaceutical products and processes. World Trade Organization member countries are obliged to comply with the minimum standards of the Agreement. But, the author points out, they also have considerable room to develop their own patent and other intellectual property laws in response to the characteristics of their legal systems and development needs. Topics

covered include patentability requirements, special cases in pharmaceuticals, disclosure, exceptions to exclusive rights and compulsory licensing.

The publication is primarily intended for policy-makers, particularly ministries of health and government lawyers responsible for drafting TRIPS compliant national legislation. For further details see page 36.

Available, free of charge, from: South Centre, Case Postale 228, 1211 Geneva 19, Switzerland. Also available on the South Centre Web site at: www.southcentre.org/publications/publichealth/toc.htm

Guidelines for the Regulatory Assessment of Medicinal Products for Use in Self-Medication, World Health Organization, WHO/EDM/QSM/00.1, 2000, 32 p.

Reclassification of medicinal products from sale on prescription only to non prescription (over-the-counter) sale is increasingly common. Drug regulatory and health authorities have to consider the types of medicinal products for which reclassification is appropriate, safe and rational in the interest of public health.

The Guidelines suggest criteria and methods which drug regulatory agencies can use to determine the suitability of medicinal products for use in self-medication. They are also intended for marketing authorisation holders applying for the classification of a prescription product to be changed to non prescription sale. Guidance is given on documentation for new active substances, never marketed as prescription medicines, to accompany applications for self-medication marketing authorisation.

Available from: World Health Organization, Marketing and Dissemination, 1211 Geneva 27, Switzerland. Price: Sw.fr.10, US\$9, and in developing countries Sw.fr.7.

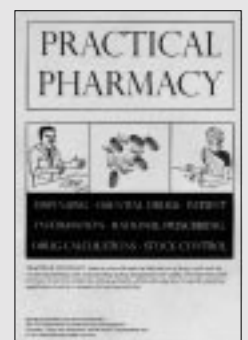
Updates on new formularies, treatment guidelines, essential drugs lists, drug bulletins and newsletters

The Department of Essential Drugs and Medicines Policy produces a global index of formularies, therapeutic guides and essential drugs lists, which is available free of charge. (Please note that we are unable to supply copies of the publications themselves. Requests should be addressed direct to the countries concerned). Some recent additions are:

- ◆ India, Himachal Pradesh: *List of Essential Drugs*. 1999. Department of Health and Family Welfare, Government of Himachal Pradesh. Drugs by generic name, divided into 29 therapeutic groups.
- ◆ Médecins Sans Frontières: *Essential Drugs: Practical Guidelines*. New editions of this useful manual for doctors, pharmacists, nurses and medical auxiliaries are available. A first edition in Portuguese, and second editions in English and Spanish, will soon be followed by a second edition in Arabic.
- ◆ Nepal: *Standard Treatment Schedules for Health Posts and Sub-Health Posts*, 3rd ed., 1999. Ministry of Health. Now available in English and Nepali. Includes principles of appropriate prescribing and dispensing, and advice for patients.
- ◆ Russia: *Formulary 2000* (Russian Formulary System). 2000. Health of Men Foundation, Moscow. Guidelines for doctors on drug use. Approved and recommended by the Russian Federation Ministry of Health. In Russian.
- ◆ South Africa: Treatment Guidelines from South Africa's Department of Health include:
 - *National Guideline on Management and Control of Asthma in Children at Primary Level*. 1999.
 - *National Guideline on Primary Prevention and Prophylaxis of Rheumatic Fever and Rheumatic Heart for Health Professionals at Primary Level*. 1999.
 - *Hypertension: National Programme for Control and Management at Primary Level*. 1998.
 - *Diabetes: National Programme for Control and Management of Diabetes Type 2 at Primary Level*. 1998.
- ◆ South-East Asia: *Essential Drugs for Primary Health Care*, 3rd edition. 2000. WHO Regional Office for South-East Asia. The manual provides community health workers and auxiliary health personnel with guidelines on the use of 34 essential drugs. It also advises on treatment and referral requirements for 22 common medical problems.
- ◆ Zimbabwe: *EDLIZ. 4th Essential Drugs List and Standard Treatment Guidelines*. 2000. Ministry of Health and Child Welfare. Fewer drugs on the list (from 600 down to 250) and updated advice for Zimbabwe's health workers.

Drug bulletins and newsletters

- ◆ Introducing *Essential Drugs in Brief*. Anyone involved in national drug policy implementation who wants a quick update on the latest WHO activities carried out with and for countries should subscribe to the bulletin, *Essential Drugs in Brief*. The bulletin, which will be published twice a year, shares information on the latest country support provided or coordinated by EDM's extended Drug Action Programme team through country, regional and Headquarters' offices.
- ◆ And a new look for the *WHO Pharmaceuticals Newsletter*, which has been redesigned and has had some content changes. Articles will be restricted to subjects more directly related to drug quality assurance and safety. Some more general information, such as new developments, guidelines, and regulations of a general nature, will be published only in the quarterly journal *WHO Drug Information*. The WHO Collaborating Centre is now providing the Safety of Medicines section for International Drug Monitoring. The Centre's *Adverse Reactions Newsletter* is being discontinued.
- ◆ With WHO support the Delhi Society for the Promotion of Rational Use of Drugs (DSPRUD) launched its *Medical Newsletter* in July 1999, to help health care professionals update existing knowledge about drug therapy. Distributed free of charge to doctors, the *Newsletter* contains a digest of various published articles, which include drug reactions, news and review articles.
- ◆ WHO/EDM is also supporting *Spectrum*, India-WHO Essential Drugs Programme Newsletter, which covers the activities of the Delhi Society for the Promotion of Rational Drug Use and the Essential Drugs Programme.
- ◆ *Practical Pharmacy* packs. Complete sets of *Practical Pharmacy* are now available to developing countries, free of charge, while stocks last. This newsletter for health workers of all levels includes easy-to-read information on basic aspects and skills of pharmacy work. Contact: Echo International Health Services Ltd, Ullswater Crescent, Coulsdon, Surrey CR5 2HR, UK. Tel: + 44 20 8660 2220, fax: + 44 20 8668 0751.

**Globalization, Patents and Drugs: An Annotated Bibliography, 2nd ed., World Health Organization, Health Economics and Drugs, EDM Series No.10, EDM/PAR/01.1, 2001, 52 p.**

The impact of globalisation and trade agreements on access to drugs is an increasingly important issue. This annotated bibliography is intended for those in the health sector with no particular legal background, who want an overview of the issues and arguments involved. It directs readers to key reports, books and articles from technical and scientific journals, subdivided into general

articles and country specific studies. The document concludes with a section on useful Web sites.

Available, free of charge, from: Department of Essential Drugs and Medicines Policy, World Health Organization, 1211 Geneva 27, Switzerland.

TRADITIONAL MEDICINE

Research focuses on traditional antimalarials

With modern pharmaceuticals often unavailable and unaffordable in the areas most affected by malaria, and drug resistance increasing, the use of herbal antimalarials is very common. But there has been almost no research into their clinical effectiveness.

Developing a strategy for more evidence-based use of traditional medicines against malaria, has led WHO's Special Programme for Research and Training in Tropical Medicine to team up with the UK's Global Initiative for Traditional Systems of Health. They have formed a Research Initiative on Traditional Antimalarials, and in November 1999 the two groups co-sponsored a meeting in Moshi,

Tanzania, to move the process forward.

Delegates included biological and social scientists, doctors, traditional healers and policy-makers from Africa, Asia, Europe and the Americas. They developed four specialist groups to implement a research strategy which will contribute to malaria control programmes. The topics covered by the groups are: policy, advocacy and funding; pre-clinical studies; clinical development; and repellance and vector control.

Future plans include updating the Research Initiative's database of traditional treatments for malaria, and regulatory guidelines for traditional medicines and natural products, case studies of their use, clinical efficacy, safety, screening and clinical evaluation. □

Source: TDR News, June 2000.



Research into herbal antimalarials aims to improve the plight of sufferers, such as this patient in Congo

India: protecting its heritage of medicinal plants

The Indian Government is setting up a programme to protect and promote its rich tradition in herbal medicines. One of the main aims is to prepare standardised formulations of traditional medicines that will undergo the same regulatory procedures, including clinical trials, as modern pharmaceuticals.

A new Department for Indian Systems of Medicines and Homeopathy has been set up and a Biodiversity Bill is going through Parliament. This will establish a National Biodiversity Board to oversee access to and use of medicinal plants, as well as applying for patents when appropriate.

Clinical trials

A pilot project will begin in the Western Ghats region, where experts will study and document medicinal plants. A small formulations unit will process plants into medicines, which will then undergo clinical trials to international standards. This work will form part of a digital database of India's traditional knowledge, which will be included in the World Intellectual Property Organization's patent classification system, and made available to patent offices world wide. The Government hopes the move will help to prevent patents being granted on traditional Indian plants and remedies.

The pilot programme will be run

by a non profit NGO assisted by an advisory panel of international experts, and it is hoped that other international organizations will become involved.

Drawing on local knowledge

One of the programme's key elements is the involvement of local people, who will be employed to identify, document



Crushing and storing medicinal plants at a processing plant in Kanizcode, India

and cultivate the plants, and participate in running the formulations unit and therapeutic centre. There are plans to involve local schools, and to set up a home for the elderly who will be encouraged to pass on their knowledge of local plants and their uses. □

Source: Scrip No.2547, 9 June 2000.

WORLD TRADE

Delhi Declaration on trade issues

Abalancing of rights and obligations under the TRIPS Agreement was one of the main demands of the *Delhi Declaration* released at the end of a two-day workshop on trade issues held in New Delhi in October 1999. In a hard-hitting statement the 65 delegates called for strong, clearly defined compulsory licensing provisions; protection of traditional knowledge from all forms of patenting; and strengthening of existing anti-monopoly practices by developing countries.

Participants argued that as international trade agreements contribute to widening the socioeconomic and technological gap between developed and developing countries, it is necessary to have an alternative framework, incorporating greater self-reliance.

As well as the TRIPS (Trade-related Aspects of Intellectual Property Rights) Agreement the national and international experts present also addressed issues such as food security, competition policies and electronic commerce.

The International Brainstorming Workshop on World Trade Organization Agreements and People's Concerns was organized by the Centre for Study of Global Trade System and Development and the National Working Group on Patent Laws. □

Copies of the *Delhi Declaration* are available from: Centre for Study of Global Trade System and Development, A-388, Sarita Vihar, New Delhi 110 044, India. Tel/fax: + 91 11 694 7403, e-mail: wgkeayla@del6.vsnl.net.in

Fears over new regional patent agreement

A new agreement on patent protection for medicines could endanger people's health in some of Africa's poorest nations, according to Médecins Sans Frontières. The organization has urged countries not to ratify the Bangui Accord, created last year by 15 French-speaking African nations. In these countries, patents are granted through the African Intellectual Property Organization (OAPI), which acts as a patent office for all its Member States. Patents are granted and regulated according to the Bangui Agreement (signed in 1977), which was recently revised to comply with WTO rules, increasing patent protection from 10 to 20 years.

A report¹ issued jointly by WHO, UNAIDS and MSF says the new treaty, which has not yet come into force, could lead to increased prices for medicines. This is because the new Bangui Agreement is more stringent than the TRIPS Agreement and provides little come back in case of patent abuse, the report states. Compulsory licences are only available provided that the patented drug can be manufactured locally, yet there is little manufacturing capacity in the region. Parallel imports are

only possible between OAPI Member States whereas lower prices might be found in other parts of the world.

OAPI counters that in revising the Bangui Accord Member States have affirmed their conviction that bringing intellectual property rights into line with the TRIPS Agreement will attract investors and stimulate technology transfer. In an Information Memo* the Organization says that its critics need to look elsewhere for the reasons why many Africans lack access to essential drugs.

Under WTO rules, the so-called "least-developed countries" – 10 of which are covered by the Bangui Accord – have until January 2006 to change their patent systems. But if the Accord is ratified by at least 10 members, countries will find themselves forced to change their systems immediately. So far eight nations have ratified. □

Reference

1. MSF/WHO. Revue of the pharmaceutical policy in Cameroon – Medicine patents in francophone Africa. Joint Mission MSF-WHO-UNAIDS. Geneva: Médecins Sans Frontières and World Health Organization; 2000. (Available in English and French).

* The Information Memo is available on the web at: <http://www.oapi.wipo.net/>

WORLD TRADE

Patents from a public health perspective

➤ CARLOS CORREA*

The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) requires all WTO Member Countries to adapt their laws to the minimum standards set forth by the Agreement, within established transitional periods. Developing countries face a special challenge in conforming to international trade obligations, particularly the TRIPS Agreement which covers intellectual property rights of pharmaceutical products and processes.

The way in which countries reform their legislation may have a significant impact on public health policies, and particularly on access to drugs. Any property rights system must strike a balance between creating incentives for innovation, and people's need for availability and affordability of protected goods. So when they draw up their own intellectual property rights rules, it is important that developing countries realise the scope they have – within the framework of international treaties – to produce their own patent laws.

The TRIPS Agreement does not establish a uniform international law or even uniform legal requirements. World Trade Organization Member Countries must comply with the Agreement's minimum standards. But countries may legitimately adopt regulations that ensure a balance between the minimum standards of intellectual property protection and the public good. Moreover, they can adopt measures which are conducive to social and economic welfare (Article 7 of the Agreement). These include steps necessary to protect public health, nutrition and the public interest in sectors of vital importance for socio-economic and technological development. Countries can also adopt measures to prevent the abuse of intellectual property rights (Article 8.1 and 8.2).

In those countries that are bound to introduce patent protection for pharmaceuticals as a result of TRIPS, patents will only be available for products for which a patent application was filed after 1 January 1995. This means that other products (including those already applied for or patented in other countries, or marketed before that date) will remain in the public domain. The exception is where the national law permits retroactive protection of the so-called "pipeline" products, as is the case in Brazil.

Scope for national differences

Given diverse national objectives, it is not surprising that different countries' patent systems diverge, in some cases significantly. There is no single "patent system". Moreover the solutions adopted in particular countries have changed over time. They treat specific patent issues –

including eligibility requirements, scope of protection, exceptions to exclusive rights and compulsory licences – in quite different ways. In drawing up their own intellectual property rights rules, policy- and law-makers in developing countries need to be aware of this. They will be most successful in meeting their own needs if they can draw on the experiences of national systems worldwide.

Some countries – particularly developed countries – have opted for legal systems that confer strong patent rights. They have done so in order to protect revenues from their already established technological base and to promote investment in technological innovation. Considerable debate exists in such countries, however, on the level and scope of protection which are optimal to foster innovation without unduly restricting the free circulation of ideas and stifling competition. A growing concern is voiced in some countries on the shortcomings of the examination process and the proliferation of low quality patents. Moreover, the economics of patent law is still an uncertain area, for which a robust theoretical framework and empirical evidence are lacking.

Checks and balances

Countries with less advanced technologies may prefer to promote the transfer of those technologies needed for development, and to preserve and enhance competition. They do so in order to secure access to goods, services and technologies on the most favourable market conditions. Even in countries with the strongest intellectual property rights protection, national laws provide for checks and balances, to protect against possible abuse of the powers conferred by protection.

Policy-makers should consider cross-cutting issues when they design a national patent system, for example: protection of public health and the environment; promotion of competition and technology transfer; protection of consumers; and support for small local inventors. Countries should also respect inventors' rights to a reward for contributions to technical progress. Other regulatory measures affecting public health, such as those relating to medicines' registration, must be carefully considered, so that there is a consistent legal framework that improves access to medicines.

Health-sensitive approach

A health-sensitive approach to patent legislation might address short-term emergencies that justify different temporary measures (for instance, medicines' supply in cases of epidemics or natural disasters). Or the approach may be part

of an integrated medium- or long-term patent policy. In some cases, a country may – within limits permitted by its international obligations – opt for different levels of protection in different areas of intellectual property. The level would depend on its competitive position and the expected role of national and foreign investors and technology suppliers. It may, for instance, be possible to emphasise protection for information technologies, through high levels of copyright protection for computer programmes and databases. At the same time lower levels

more than 880 million people lack access to health care. Of the more than 33 million HIV-positive people in the world, 95% live in developing countries, and most of them cannot afford required drugs. To deal with this dramatic situation, an integrated approach to the deeply inter-related issues of national health policy, pharmaceutical policy and patent policy is required. None of these policies can be framed or implemented in isolation.

If developing countries are not to be disadvantaged by new trade rules, they



Taking the medicine in Guatemala. International trade agreements don't just affect people in the rich industrialised nations

of protection may be given in areas where local industrial and technological capabilities are low, and unlikely to be significantly improved through a high standard of patent protection.

The way in which such options are implemented should be consistent with the country's level of development, particularly its research and manufacturing capabilities in the pharmaceutical sector. The options followed by a large developing country with significant capabilities may differ from those preferred by a small economy which is totally or substantially dependent on foreign supplies of pharmaceuticals. Likewise, patent laws may evolve as a country develops. It should be remembered, however, that problems of access to drugs caused by poverty and low income are common to most developing countries.

Considering options

The protection of public health is one of the most pressing issues in developing countries. A large part of the global population still lacks access to essential drugs. In the poorest parts of Africa, for instance, over 50% of the population lack that access. An estimated 1.5 billion people are not expected to survive to age 60, and

must look at options for designing and implementing public-health-sensitive patent policies. There must be a balance between the public and private interests involved, including the rights of states, patients and suppliers of health-related goods and services. □

* Carlos Correa is Director of the Masters Programme on Science and Technology Policy and Management at the University of Buenos Aires, Argentina. He is a specialist in global intellectual property law, and was involved in the negotiations on TRIPS during the Uruguay Round of trade negotiations. Further information on legal options for drawing up TRIPS-compatible national legislation can be found in Professor Correa's new books, *Integrating public health concerns into patent legislation in developing countries*, and *Intellectual property rights, the WTO and developing countries*. (See Published Lately pages 33 and 34).

Other useful documents include *Globalization and access to drugs. Perspectives on the WTO/TRIPS Agreement*. Health Economics and Drugs, EDM Series No. 7, and *Globalization, patents and drugs: an annotated bibliography*, Second edition. Health Economics and Drugs, EDM Series No. 10. Both documents are available, free of charge, from: Department of Essential Drugs and Medicines Policy, World Health Organization, 1211 Geneva 27, Switzerland.