**Polypill holds promise for people with chronic disease**

Efforts are under way to make medicines for chronic diseases more accessible to people in developing countries.

A “polypill” containing a fixed-dose of aspirin, a statin and one or two blood-pressure-lowering drugs, has enormous potential in developing countries, where the rate of cardiovascular disease is rising rapidly, according to an expert working party.

No fixed-dose combination pill of this kind has been widely marketed anywhere in the world to date, and the full benefits of such a pill remain unclear until it can be put to the test in upcoming large-scale clinical trials in India and New Zealand.

“Combination pharmacotherapy offers the potential to decrease the incidence of cardiovascular disease worldwide, perhaps especially in people who have never had a cardiovascular event,” concluded the Combination Pharmacotherapy and Public Health Research Working Group, convened by the Centers for Disease Control and Prevention in the United States.

The report, which was published in the Annals of Internal Medicine in October 2005 (Vol. 143, pp. 593–599), came up with the dramatic finding that combining several anti-hypertensive drugs at low doses is likely to be more effective and have fewer side-effects than high-dose therapy with a single drug.

However, more research is needed on the side-effects and bioavailability as well as tolerability and adherence to combination pills. “Combination pharmacotherapy may prove especially effective in the developing world, where studies may precede those done in wealthier countries,” the report concluded.

The study’s findings provide a timely boost to efforts to improve access to treatment for chronic diseases in developing countries. Chronic diseases are often associated with developed countries, but their prevalence is increasing in many low- and middle-income countries, according to the recent WHO report, Preventing chronic diseases: a vital investment.

Only 20% of chronic disease deaths occur in high-income countries — while 80% occur in low- and middle-income countries and these deaths occur in equal numbers among men and women, the report said.

Deaths from infectious diseases, maternal and perinatal conditions, and nutritional deficiencies combined are projected to decline by 3% over the next 10 years globally. However, over the same period deaths due to chronic diseases are projected to increase by 17%.

A recent study carried out in Andhra Pradesh found that noncommunicable and chronic diseases are the leading causes of death in this rural state of India. One of the authors of the study, Dr Bruce Neal, Director of the Cardiac and Renal Division at the George Institute for International Health, in Sydney, said that the health delivery system was in urgent need of “reorientation” to enable the implementation of evidence-based strategies to address the challenge of noncommunicable diseases.

Neal told the Bulletin: “While many lower-income countries have made very substantial advances in the treatment and prevention of acute communicable conditions and in the management of maternal and child health, the development of comprehensive strategies to combat noncommunicable diseases is essential.”

Menaka Seni, 60, felt so strongly about the need for more awareness of chronic diseases in her native India and other countries that she agreed to tell her story in the recent WHO report, Preventing chronic diseases: a vital investment. Seni, a widow, has had diabetes and high blood pressure for 28 years. This year doctors found a clogged heart vessel and she underwent a coronary bypass operation. Since then, she has changed her diet and lifestyle, by eating more fresh fish, fruit and vegetables and by taking more physical exercise.
Infectious diseases remain a leading cause of death in sub-Saharan African countries, but some African countries including Kenya, Nigeria and South Africa are facing a high prevalence of chronic and noncommunicable diseases.

"Coronary heart disease is a huge problem in Africa and is reaching epidemic proportions. This is related to urbanization with people eating more fast food, smoking more and exercising less," said Shan Biesman-Simons, Director of Nutrition and Education for the Heart Foundation in South Africa.

Nigeria is also taking the problem of chronic disease seriously. President Olusegun Obasanjo said his country would be facing a time bomb if it did not act now to address the problem of chronic disease.

"We cannot afford to say 'we must tackle other diseases first — HIV/AIDS, malaria, tuberculosis — then we will deal with chronic diseases.' If we wait even 10 years, we will find that the problem is even larger and more expensive to address," Obasanjo wrote in the WHO report, Preventing chronic diseases: a vital investment.

Access to doctors and appropriate treatment is a major problem in many developing countries. "In the public sector in South Africa it can be very difficult for people to get access to medicines," Biesman-Simons told the Bulletin.

"They may have to travel long distances to get to a clinic, then they may have to wait in a queue all day, and they still may be sent home without the correct treatment," she said.

Poor education is another problem area, both for the medical profession and the general public. Biesman-Simons gave the example of rheumatic heart disease, often called the disease of poverty, which can develop into rheumatic fever, which in turn can lead to heart damage.

"Thousands of young people in South Africa are waiting for expensive heart valve replacement operations and have a poor quality of life and this could have been avoided if they had been diagnosed and treated appropriately at the start," Biesman-Simons said.

Jacqui Wise, Cape Town
News

Polypill study, set up by the George Institute for International Health, will randomize 1000 patients with established cardiovascular disease to a polypill-based approach or to standard care. The patients will be followed for two years.

A similar study of 600 patients is to start in New Zealand next year, led by Anthony Rodgers of the University of Auckland. Patients with a definite indication for all medicines, such as following a heart attack or stroke, will be randomized to polypill or conventional care. The main outcome measures will include compliance, blood-pressure and cholesterol levels.

Fixed-dose combinations are now a core component of care for people with HIV/AIDS, tuberculosis and malaria. As well as improving clinical outcomes, they simplify distribution of multiple medications, which can be an important advantage in resource-limited health-care settings.

Some public health experts say another way of improving access to medicines and treatment for chronic disease would be through public-private partnerships (PPPs). A report by a team from the London School of Economics and Political Science, led by Dr Mary Moran, found that PPPs have driven the recent considerable increase in research activity into so-called neglected diseases, such as malaria and tuberculosis.

After a time when few new therapies were introduced, there are now over 60 drug research projects under way. Three-quarters of these are conducted under the auspices of PPPs and should result in six or seven new drugs being developed by 2010.

There are no PPPs working in the area of chronic disease, a situation Rodgers, who is director of the Clinical Trials Research Unit at the University of Auckland, in New Zealand, wants to change. Rodgers is involved in early consultations to set up a PPP to make treatment for chronic diseases more accessible to people in need.

“We desperately need a not-for-profit organization that enables public-private partnerships to make new medicines more available. Not just new technologies like the polypill, but also health-care delivery solutions.”

Jacqui Wise, Cape Town

Best defence against avian flu is to fight the virus in Asia

The spread of avian flu to Africa and Europe has triggered panic as misconceptions abound over the nature of the threat this poses to human health.

Farming practices, long-held lifestyle traditions and poverty-line economics all make recent outbreaks of avian flu in Asia a far bigger global public health threat than the westward spread of the disease into Europe’s poultry flocks.

For many rural Asian communities, backyard chickens and very small-scale poultry farms are part of the landscape. Children play in the same yard where the household’s flock scratch and where chickens that die are typically eaten in order not to waste a valuable source of protein.

Combinations may prove especially effective in the developing world where studies may precede those done in wealthier countries.

Research Working Group.
Every infection of poultry has serious consequences for the farmers concerned. Flocks must be culled in a wide radius around the area of infection and every person in contact with infected live or dead poultry is at risk of contracting the disease.

Whilst most western Europeans would get no closer to poultry than peeling away the shrink-wrap cover on a pack of supermarket chicken breasts, in Asia most of the 67 confirmed deaths from the H5N1 avian flu virus have been attributed to direct contact with infected birds, such as the slaughter, de-feathering, gutting and preparation of chicken and duck. All 130 known human cases of H5N1 have occurred in Asia.

In Asia, bird flu outbreaks have been reported over the last two years in Cambodia, China, Indonesia, Japan, Kazakhstan, Lao People's Democratic Republic, Malaysia, Thailand and Viet Nam, the latter having borne the brunt of human infections with 42 WHO-confirmed deaths out of 92 cases since December 2003.

Many governments in the region are posed with a dilemma over how much scarce public funds should be poured into the fight against avian flu. Governments in the region have been making efforts to educate the population about preventive surveillance measures, but misconceptions abound about the disease, both in poultry and humans.

Education campaigns in the affected countries are still not getting through to the individuals most at risk. Common misconceptions that owners of poultry have include the mistaken belief that it won't happen to them, that chickens frequently fall sick and that this time is no more serious than any other time, according to Peter Cordingley, WHO's spokesman for the Western Pacific Region, in Manila.

"Worse than any misconceptions, though, is the continuing ignorance in Asia, the fact that after two years people still know so little about risky practices. The latest case in Thailand confirmed by WHO was a woman who apparently cleaned out the muck from a poultry shed where her husband's chickens had died mysteriously, and this was 50 km or so from Bangkok," he said.

Dangerous misconceptions also exist at government level including "the belief early on by some governments that the outbreaks could be covered up and fixed, thus protecting the poultry industry without endangering public health and that vaccinating poultry is a quick, inexpensive and effective way of preventing or responding to outbreaks. Vaccination may stop the spread of the virus but does nothing to eliminate it. Culling is the only option, backed up, where appropriate, by vaccinating," said Cordingley.

China, where H5N1 avian flu originated, is grappling with a resurgence of the disease among poultry and has confirmed the first two human cases of infection with the virus on 17 November.

National government policy is at odds with what happens at the grassroots level because of patchy reporting at local level of outbreaks elsewhere in the country. Local level officials also fear incurring the ire of their superiors by being open about suspected or confirmed outbreaks and are reluctant to deal with the economic consequences of any decision to announce an outbreak and cull poultry.

"There has to be even greater public awareness. Even though bird flu is not new to China and has been widely reported over the last two years, news of every outbreak does not reach everyone and one of the biggest dangers is that this might lead to a sense of complacency," said Roy Wadia, WHO's spokesman in China. "But now that you've got confirmed human cases, people are taking more and more notice, and even getting scared."

"The central government sees the overall problem in getting the right messages out, but it's a big country with a way of life that has existed for thousands of years. People and animals live in very close quarters in rural areas, and backyard farmers move their flocks when they hear there's a chicken cull under way. The other issue is one of compensation," Wadia added.

There are also powerful and potentially harmful misconceptions about what medical options there are to prevent or treat human cases of either H5N1 avian flu or a reassorted avian flu pandemic strain.

"The public may perceive seasonal flu and avian flu to be the same and may also wrongly believe that influenza vaccine could prevent human beings from contracting avian flu," said a spokeswoman for the Department of Health's Centre of Health Protection in Hong Kong SAR.

"The public may perceive seasonal flu and avian flu to be the same and may also wrongly believe that influenza vaccine could prevent human beings from contracting avian flu," said a spokeswoman for the Department of Health's Centre of Health Protection in Hong Kong SAR.

"If the situation is not brought under control in the backyard farms in this part of the world, the virus will continue to spread around the world year after year. Asia is ground zero and still represents the greatest threat to global public health."

Peter Cordingley, a spokesman for WHO's Office for the Western Pacific Region based in Manila.
Quake victims reach help too late to save crushed limbs

The Pakistani government and WHO have appealed for US$27 million, but raised just under half of that for the area’s immediate health-care needs.

When Mazhar Ali, 22, was finally airlifted to the District Headquarters Hospital, Manshera, a frontline hospital for the injured of the devastating 8 October earthquake in northern Pakistan, doctors told him it was too late to regain full use of his arm.

Ali was brought by helicopter to the hospital from his home in the remote mountain village of Paras in Balakot, one of the areas worst hit by the earthquake. He is one of countless patients who were airlifted from that area to hospital since the earthquake.

He said he had no one to talk to and had no idea where his family members were, but that he was lucky to be alive. “I don’t have any place to go. Our house … completely collapsed and four members of my family have died,” Ali said.

“We didn’t know whether we would survive. We relied on burning wood we had gathered from our collapsed roof to warm ourselves. We had no food except for corn [on the cob],” he said, looking at his paralysed right arm with an expressionless face.

More than 600 public health experts and scientists from 100 countries agreed that there is an urgent need for financial and other resources for the countries which have already been affected by avian flu as well as for those which are most at risk.

Participants outlined a global action plan to control avian flu in animals and limit the threat of a human flu pandemic. To date, 36 Member States have reported to WHO that they have influenza pandemic preparedness plans in place.

Since May 2005, outbreaks of H5N1 disease have been reported among poultry in China, Kazakhstan, Romania, Russia and Turkey. Mongolia has reported outbreaks of H5N1 in wild, migratory birds and in October 2005, H5N1 was reported among migrating swans in Croatia. Experts fear the disease may spread further to south-western Europe and Africa, as birds migrate south for the winter.

But public health experts agree that Asia, where the only known human bird flu cases have occurred, is the region that poses the greatest immediate risk to global animal and human health.

“Europe is quite rightly taking measures to control the spread of the virus in poultry and to stock up on antiviral drugs in case of human infection, but the best defence for Europe or anywhere else against avian influenza is to help fight the virus in Asia,” said Cordingly.

Cordingly added: “If the situation is not brought under control in the backyard farms in this part of the world, the virus will continue to spread around the world year after year. Asia is ground zero and still represents the greatest threat to global public health.”

Jane Parry, Hong Kong SAR

Dr Mohammad Shoaib attends to Mazhar Ali’s right arm in the hospital in Manshera.
have appealed for US$ 27 million and so far raised 45% of that for immediate health-care needs.

Ali suffered a crush injury to his right arm after his family home collapsed on him. Relatives rescued him from the rubble of their home the same day, and Ali spent seven nights in the open in freezing winter temperatures with the rest of his family before he could be taken by helicopter to the hospital to have his injury treated.

While waiting to get airlifted to help, his right arm developed compartment syndrome. At the hospital, the orthopaedic surgeon, Dr Mohammad Shoaib said that because of a prolonged disruption of blood flow to the nerves and muscles of his right arm, his arm would not regain full movement.

Many victims of the earthquake suffered crushed limbs and developed similar deformities to those experienced by Ali because they did not receive surgery soon enough. “Those who did present early could not be operated because we did not have [operating] facilities to take care of trauma patients,” Shoaib said.

Once they received surgery, at best these patients regained some movement after the long wait, and, at worst, their gangrenous limbs had to be amputated.

Although the District Headquarters Hospital, Mansehra was built recently, it did not offer orthopaedic services before the quake. After the earthquake, the hospital walls developed cracks and the building was declared unsafe for use. Doctors and nurses had to provide first aid to thousands of patients in the open. “Patients were lying on the floor, on the road and in beds in the open. For the first few days, power supply remained disconnected as well as the phone service,” Shoaib said. “There were no bandages, so we used ordinary cloth we purchased from the cloth shops”.

Dr Ishtiaq Ali Khan, a general surgeon at the hospital, said that shortly after the quake hit a constant stream of patients arrived at the hospital seeking help. He and his colleagues were under immense strain because they did not receive any outside help — including supplies of life-saving drugs and equipment — for the first few days.

They called their colleagues in Lahore to come to help them. Four days later they and their colleagues set up an operating theatre. Thanks to local donors as well as UN agencies, international nongovernmental organizations (NGOs) and donor governments, the hospital received more supplies of medicines and equipment.

Since then, they have performed more than 500 major operations and more than 9 000 injured people have been seen to by local, national and international health-care workers at the hospital. Several wards have been set up in tents, the latest one by international NGO Médecins sans Frontières.

“We were all very exhausted and simply unable to cope with the growing number of patients needing immediate surgical interventions.” Dr Ishtiaq Ali Khan, a general surgeon.

More and more people have been leaving their devastated villages to seek refuge in tents in towns like Mansehra. Due to poor sanitation and hygiene, and inadequate supplies of clean drinking-water in these camps, the number of diarrhoea cases is increasing. This camp has sprung up outside a hospital and patients are receiving care in the open air.
surgical interventions,” Khan said, describing the first few days. About a month after the earthquake struck the workload started to decrease, he said.

In the nearby town of Balakot, close to the earthquake’s epicentre, makeshift field hospitals have been established by Pakistan’s army, by relief workers sent by the United Arab Emirates as well as by international NGOs, such as Oxfam and Save the Children.

According to Pakistan’s government, more than 50 temporary field hospitals and mobile clinics are currently operating in the eight quake-hit districts, including Muzaffarabad where the 400-bed Combined Military Hospital collapsed, killing over 200 patients.

The shortage of doctors, nurses and other health-care workers in the affected areas is a major challenge that is hindering efforts to provide much-needed primary health care including vaccination services.

As a result, cases of vaccine-preventable diseases, such as measles, are on the rise. After crush injuries, acute respiratory tract infections are the second-leading reason for contacts with doctors in health facilities reporting to the Disease Early Warning and Surveillance (DEWS) system, said Haroon Afridi, an epidemiologist at the Aga Khan University, Karachi.

“Before the earthquake, there was no DEWS in this area. It is now slowly developing,” Afridi says. The winter has just begun to set in, and doctors said there were starting to see more cases of diseases associated with malnutrition, lack of shelter and clean water than of crush injuries.

Khabir Ahmad, Maniehra

Growing awareness of skin disease starts flurry of initiatives

More needs to be done to address skin diseases in developing countries. Skin diseases in developing countries have a serious impact on people’s quality of life, causing lost productivity at work and school, and discrimination due to disfigurement. Skin changes may also indicate the presence of more serious diseases that need treatment.

In the past, such conditions were ignored or given low priority by health authorities because they did not, on the whole, kill people, and they often did not present in tertiary care centres.

But now there is a big push at both national and international levels to train health workers in developing countries to improve diagnosis and treatment of dermatological conditions.

Professor Rod Hay, Head of the School of Medicine and Dentistry, Queen’s University Belfast, said the change is very welcome. Hay is Chair of the International Foundation for Dermatology, a non-profit organization based in Chicago, the United States, linked to the International League of Dermatological Societies, that aims to improve dermatological care in developing countries. He said: “There is better recognition of the extent of the problem, helped by the fact that the first signs of certain diseases, including HIV/AIDS, leprosy and onchocerciasis, tend to appear as skin problems.”

Dr José Figueroa-Munoz, who is currently a medical officer in WHO’s Stop TB Department but was previously a fellow of the St John’s Institute of Dermatology in London, United Kingdom, agreed that there is now better acknowledgement of skin diseases and the impact they have.

“Most of these diseases have always been there, and in many cases they are so common that they are part of the local culture,” Figueroa-Munoz said. “But there is now more realization that even though many people do not see these diseases as a problem, they could still be having an important impact on general health.”

For example, skin diseases that cause severe itching at night can reduce someone’s productivity during the day at work, or their ability to pay attention in school. In many communities, people with visible skin disease suffer discrimination when applying for jobs, or, if a woman has a disfiguring skin disease, she may never marry.

“Factors such as these have an impact on people’s quality of life,” Figueroa-Munoz said, “and for this reason it is important to treat skin diseases and educate communities about how to prevent them”. There is plenty of evidence that skin diseases are much more common in developing countries than in the developed world. Surveys have shown that up to 60% of people in both rural and urban areas in developing countries suffer from skin diseases. By contrast, one study in the United Kingdom estimated that 28% of people had a treatable skin disease.

In contrast to the situation in developed countries, malignant melanoma and non-melanoma skin cancers are rare in the indigenous populations of most developing countries, and among those with pigmented skins in general. The exception is the very high risk of skin cancers in albinos.

The last few years have seen a flurry of new initiatives targeted at treatment of skin disorders in developing

Inside a village school classroom in Nigeria many children show signs of skin disease due to onchocerciasis on their legs. Infected children cannot pay attention to classes because they are constantly scratching.
countries, many of them fostered by the International Foundation for Dermatology. At the international level, recognition of the problem is continuing to grow; Hay points out that the Disease Control Priorities Project of the World Bank/WHO/Fogarty International Center is due to publish its second report this month, which includes a chapter on the priorities relating to skin diseases in developing countries.

At a workshop in September 2004 organized by the International Foundation for Dermatology, Hay made the case that it was time to strengthen community dermatology programmes for developing countries. Many skin conditions are due to infections, he concluded, and could be treated with simple remedies if these were used in the right way. Poor training is one factor contributing to the huge amount of time and resources being poured into treating skin disease badly, he said.

Delegates attending the workshop identified several areas for action. First, they called for more up-to-date evidence on common treatments for scabies that can be adopted by whole communities. Second, because antiretrovirals are now more commonly available in developing countries for the treatment of HIV/AIDS, they wanted a simple diagnostic scheme that would allow health-care staff to recognize people who were potentially infected with HIV from changes in their skin or mucosal surfaces.

Their third recommendation was for better training for health-care staff on treatment of common skin conditions, such as pyoderma, ringworm, tropical ulcer, infected sores and diabetic foot.

Finally, the delegates called for better promotion of existing examples of good practice that could be rolled out to other communities.

Hay said one example of good practice that could be usefully transferred to other settings is provided by the Regional Dermatology Training Centre (RDTC) in Moshi, the United Republic of Tanzania, which the International Foundation of Dermatology established, in collaboration with the Government of the United Republic of Tanzania, in 1997. The centre provides training for primary care doctors from across Africa, who can return to their own countries and train others.

The International Foundation of Dermatology, which will be based in London from January 2006, has helped with similar projects, based on a short-course educational model, in the state of Guerrero, Mexico, and in Mali (see article on pp. 935–941). Figueroa-Munoz, Munoz said. “This is important to treat skin diseases and educate communities about how to prevent them.”

Dr José Figueroa-Munoz, Medical Officer in WHO’s Stop TB Department.

Hay agreed. He said: “The core to tackling these problems is proper training at primary care level. Many of these conditions have comparatively simple treatments, and these are often not that expensive. Treatment will confer significant gains to both personal and public health.”

Sharon Kingman, London