

BEYOND OUR MEANS?

Millions of people in the developing world are in urgent need of the antiretroviral drugs which suppress HIV and indefinitely postpone symptoms of AIDS. But the vast majority live in the world's poorest countries and cannot afford the US\$5,000 a year that the drugs, medical tests and consultations cost. Why are costs so high and can they be brought down to a level where the developing world can afford to pay for them?

The price of antiretrovirals is not the only factor preventing treatment for AIDS reaching those who need them. In many countries, health care systems are weak, with far too few doctors, nurses and medical facilities. Antiretroviral drugs require laboratories and trained medical personnel to diagnose HIV/AIDS, prescribe and distribute the appropriate drugs and monitor their impact. How easy is it to set up such systems in the countries that most need them?

Beyond Our Means? provides an overview of these and other issues surrounding access to treatment for HIV in the developing world.



The PANOS AIDS Programme

9 White Lion Street London N1 9PD United Kingdom

Tel: +44 20 7278 1111 Fax +44 20 7278 0345 aids@panoslondon.org.uk www.panos.org.uk



PANOS

(c) The Panos Institute, 2000
All rights reserved

The Panos Institute exists to stimulate debate on global development and environment issues.

Since 1986 the Panos AIDS Programme has provided in-depth information on the social, psychological and economic causes and consequences of the epidemic. We are currently widely recognised as a leading international authority on HIV/AIDS.

Panos works globally, from offices in eleven countries. The Panos AIDS Programme focuses activities in Africa and South Asia.

For further details contact:

The AIDS Programme
Panos Institute

9 White Lion Street London N1 9PD UK
Tel: +44 20 7278 1111 Fax +44 20 7278 0345
www.panos.org.uk
AIDS: aids@panoslondon.org.uk
Press: markc@panoslondon.org.uk
General: panos@panoslondon.org.uk

BEYOND OUR MEANS?

The cost of treating HIV/AIDS in the developing world

Introduction	1
Care and Treatment	3
Zambia: Lack of Access	10
Realities in the Developing World	13
India: Conflicting Priorities	19
Bridging the Gap?	21
Senegal: A Lucky Few	28
Who Has the Right?	31
Who Pays?	47
Last Words	50
For Further Research	51
Index and Definitions	53

PANOS

Published with funding from the Rockefeller Foundation and Royal Danish Ministry for Foreign Affairs

Funding for this publication was provided by the Rockefeller Foundation and Royal Danish Ministry for Foreign Affairs. The Panos AIDS Programme also receives regular support from the Swedish International Development Co-operation Agency.

Written by: Martin Foreman, with contributions from Fleur Pollard and Winnie Ssanyu-Sseruma. Additional text by Ranjit Dev Raj, Fara Diaw, Mildred Mpundu. Research by Tsehaynesh Abebe, Alexandra Fischer, Tom Scalway, Bridget Sleaf. Other assistance gratefully received from Javier Hourcade Bellocq, Carlos Correa, Khalil Elouardighi, Richard Laing, Julian Meldrum, Joseph Perriens, Eric van Praag. Editing by Nikki van der Gaag. Cover design: Nicole Heinzl. Layout: Nicole Heinzl and Jennifer Leask. Cover Photograph: Giacomo Pirozzi/Panos Pictures

No opinions expressed in this document should be taken to represent the views of any funding agency or of individual acknowledged as undertaking research or providing assistance. Signed articles do not necessarily reflect the views of Panos or any of its funding agencies.

Copies of this document are sent free to resource-poor non-governmental organisations in the developing world. Copies are available elsewhere for UK£5 / US\$10. Contact the Panos AIDS Programme at the above address.

INTRODUCTION

Across the world, nearly 35 million people are living with HIV, the virus which causes AIDS. [1] The disease is the primary cause of death in Africa and the fourth highest cause of death worldwide.

Almost all those with HIV/AIDS live in the developing world and the disease is most prevalent in communities already weakened by severe poverty, widespread lack of education and the presence of many other diseases. Perhaps 12 million have developed the disease to such an extent that they face death within the next five years from tuberculosis, pneumonia, meningitis or other serious infections that their bodies can no longer resist. Most of these deaths could be prevented if the appropriate drugs and the expertise to monitor their impact were widely available.

Treatment for HIV/AIDS ranges from the emotional support that comes from the presence of a carer, through provision of painkillers and treatment for opportunistic infections, to the antiretroviral drugs which suppress the virus and restore the immune system. Only in a few countries, however, do most people with AIDS* have access to all levels of treatment. The vast majority receive either no medical treatment or only palliative care to reduce pain and suffering.

What needs to be done?

A number of factors lie behind this failure to provide full treatment to those who need it. These vary from country to country, but include lack of political will, unhelpful economic policies (eg taxing medical products), lack of relevant information and lack of appropriate distribution mechanisms.

While these are all important, two other factors stand out. The first is poor infrastructure: inadequate health facilities, including lack of hospital beds and laboratories, lack of trained medical and laboratory staff and non-existent or incomplete drug distribution systems. The second is the high price of drugs. Attempts to reduce these prices have led to often bitter disputes over costs and ownership of patents (otherwise known as intellectual property rights) between manufacturers, governments, international organisations such as the World Trade Organization and the Joint United Nations Programme on AIDS (UNAIDS) and people living with the disease.

* In this paper “people living with HIV” refers to those with the virus, but not needing antiretroviral drugs; “people living with AIDS” refers to people with HIV who require antiretrovirals.

Poor health infrastructures and difficulties in accessing drugs are not unique to HIV/AIDS. The World Health Organization estimates that over one in three people living in the poorest parts of Africa and Asia has no access even to such essential drugs as painkillers. [2] Altogether, the number of people affected by injuries, violence and other diseases and conditions is many times that affected by AIDS; nevertheless, HIV provides a focus for such issues and the provision of greater access to treatment for AIDS will result in improved health care for whole communities and nations.

Why bother?

It may seem that providing access to treatment for HIV/AIDS for all who need it in the developing world is an impossible, and therefore pointless, task. But providing health care, for whatever disease, is essential if the quality of life for the majority of people living on this planet is to be improved. Besides, access to treatment is not simply an abstract question of logistics and economics. As Major Rubaramira Ruranga, a Ugandan ex-serviceman and one of the most articulate voices of those living with HIV, points out, each individual denied treatment is denied hope and a future. Denial of life-giving drugs leads to fear, anxiety and bewilderment. "The problem of care extends from the immediate family to the extended family and eventually stretches to the community, to the nations and finally to the global village." [3]

This booklet provides an overview of the issues surrounding access to treatment for AIDS in order to encourage informed debate, further research and considered action in those communities and nations most in need. Its conclusions are that widespread access to treatment is possible, although highly improbable in the foreseeable future, that a combination of approaches must be taken and that progress is often hindered by different perspectives on the problem.

These are not the conclusions we wish to reach. Since 1986, when Panos published its first report on HIV/AIDS in the developing world, [4] the Institute has consistently argued the disease is both a consequence and a cause of underdevelopment. While recent years have seen wide acknowledgement both North and South that this is the case, the response by many governments and community leaders continues to be too little too late. Now, more than ever, the global community must confront the economic and political realities that prevent full access to treatment, recognise that the costs of providing treatment are many times greater than the sums currently available and put into place mechanisms to meet those costs.

Martin Foreman
Director, Panos AIDS Programme

CARE AND TREATMENT

Care can be defined in many different ways. In the sense of emotional support from others, care is an important aspect of our lives, whatever our state of health. Indeed, care keeps us well; adults in long-term relationships live longer than those who are single [5] and care is an essential element in combatting child malnutrition. [6]

Care can also be defined as meeting the psychological and medical needs of those who are ill. "Care and support for people living with AIDS is available everywhere, even without drugs," says Joseph Perriens, of the UNAIDS Care and Support Team. "It is very important and already in effect where community groups and families actively care for those who are ill." Furthermore, care is essential to AIDS prevention, in that it reduces the fear and hostility that arise from stigma and encourages those who are at risk to come forward for information and counselling.

Yet even when no medical costs are involved, care is not provided to its full extent in many parts of the world. Stigma still prevents many with the disease from receiving the support they need - either because they have been rejected by their family, friends or community, or because fear of rejection prevents them from admitting their situation. Furthermore, the burden of care falls much more on women than on men, suggesting that there are deep wells of physical and emotional support that are as yet untapped.

What HIV does

HIV is a retrovirus* transmitted primarily through sexual intercourse, but also through infected blood and from mother to newborn child. It survives by replicating (reproducing) inside CD4 blood cells - the very cells which normally protect the body against infection. In the first few weeks after entering the body, HIV spreads rapidly and may cause flu-like symptoms and / or a rash which disappear after a few days. Then the viral load - the amount of virus in the blood - falls and for several years most people have no symptoms. During this time, however, viral load slowly rises again and the number of CD4 cells falls, making the individual increasingly susceptible to infections such as tuberculosis that people without HIV are more likely to resist. AIDS is defined

* Technical terms are defined on page 53

as the appearance of one or more of these "opportunistic infections" together with HIV. ("Advanced HIV infection" is sometimes used to refer to a severely weakened immune system irrespective of the presence of other infections.)

People's immune systems respond to the virus in different ways. Younger and healthier people are likely to live longer without symptoms of AIDS than those who are older or malnourished or whose immune systems are already compromised by other diseases. The average period of 10 years between infection and development of opportunistic infections frequently quoted in the industrialised world may be less relevant in Africa or Asia.

HIV/AIDS is incurable; no means has been found to eradicate the virus from the body and restore the individual to complete health. However, where full treatment is available, most people with the disease can lead almost normal lives for indefinite periods of time.

Monitoring the virus

Incurable does not mean untreatable. What treatment should be offered depends on the extent to which the immune system has failed and which, if any, opportunistic infections have appeared. Ideally, the first response to HIV/AIDS takes place soon after infection, when a simple blood test confirms the subject is HIV-positive (has the virus). [7]

Once infection has been proved, tests should be carried out to check the state of infection. Monitoring of HIV is accomplished through two tests: viral load and CD4 cell count. Viral load is measured in copies or logs per millilitre of blood. (A log is a factor of ten and a one log change is the same as a ten-fold change.) The higher the viral load, the more virus is circulating in the body. The CD4 count measures the strength of the immune system. In a healthy adult there are between 700 and 1,500 CD4 cells per cubic millimetre of blood. A count of below 500 is considered a sign of a depressed immune system; below 200 heightens the risk of opportunistic infections; below 100 signifies severe immune damage.

If the initial results are good, such tests need not be more frequent than once a year. Once viral load increases and CD4 count falls, clinicians theoretically have two strategies: (i) antiretrovirals to prevent the spread of HIV, reduce viral load and hopefully increase CD4 cells; or (ii) prophylaxis - treatment to

prevent opportunistic infections; (iii) treatment of opportunistic infections that do occur; and (iv) painkillers such as oral morphine for palliative care (relief of suffering). In fact, if antiretrovirals are successful - as confirmed by three monthly testing of viral load and CD4 count - there will be little or no need for prophylaxis, treatment or painkillers.

Opportunistic infections

Lack of symptoms, reluctance to know one's HIV status - often from fear of the stigma attached - and lack of testing facilities all combine to prevent many people in the developing world from learning they have the virus. It is only when they fall ill and their blood is tested that they discover that they are HIV-positive - and when resources are scarce, that diagnosis may have to be assumed rather than confirmed. In other words, many of those only learn they have the virus several years after they contract it, when their CD4 counts have fallen and viral loads have risen to levels that allow opportunistic infections to appear.

In theory, any infection can be 'opportunistic', but in practice some infections are more common than others in people with AIDS. These include the following: [8]

- candidiasis (also known as thrush), a yeast-like infection seen in over 50% of AIDS cases;
- cryptococcus, another yeast infection, the most serious manifestation of which is meningitis, seen in 9% of people with AIDS;
- cytomegalovirus (CMV), a virus related to herpes which can cause blindness in people with severely impaired immune systems, affecting one in five people with AIDS;
- pneumocystis carinii pneumonia (PCP), a form of pneumonia found in one in four cases; [9]
- tuberculosis, the leading cause of death among people with HIV. [10] (Because the mycobacterium tuberculosis is passed through casual contact, the interaction of HIV/AIDS with tuberculosis has also meant an increase of tuberculosis among the general population in many countries.)
- Non-Hodgkin (also Non-Hodgkin's) Lymphoma, which is ten times more common in people with AIDS than in the rest of the population, is associated with the Epstein-Barr Virus;
- Kaposi's sarcoma (KS), a tumour affecting the skin, lungs or intestines or lymph nodes and seen in 15% of AIDS cases, is associated with Kaposi's

Sarcoma-associated Herpes Virus or Human Herpes Virus 8.

Although not the result of infection, severe weight loss resulting from malnutrition, diarrhoea or poor absorption of food can also be a symptom of AIDS. Other symptoms common in advanced HIV infection include allergies, anxieties, convulsions, nausea, rashes and pain.

Many opportunistic infections are best diagnosed through laboratory tests, following which the appropriate treatment or prophylaxis can be prescribed. Even with such treatments, however, without access to antiretroviral drugs, most people's immune systems weaken so much that they eventually die from a combination of infections. In such circumstances, few people live longer than two or three years after the first opportunistic infection appears.

Each of the above conditions responds to treatment, although the weaker the immune system is, the less effective such treatment may be. UNAIDS provides a list of appropriate drugs for a wide range of opportunistic infections, such as ganciclovir for CMV, miconazole for candidiasis and isoniazid for tuberculosis prophylaxis. [11]

In addition to these Western - also known as allopathic - medicines, traditional forms of healing are practised in many countries. These are chosen by many people with AIDS because they cannot afford the Western versions or because they believe that traditional treatments do alleviate symptoms and may resolve some AIDS-related conditions. However, despite claims from many different countries, there is no evidence that any combination of herbs or other ingredients based on traditional healing can cure AIDS.

Pill after pill after pill after...

Ten years ago, AIDS appeared to be a universal death sentence. Today, for hundreds of thousands of people with the disease in the industrialised world, antiretroviral drugs (ARVs) are a miracle allowing them to lead full, healthy lives. Three types of ARVs are available, targeting the virus at different stages of its life cycle. These are: non-nucleoside reverse transcriptase inhibitors (NNRTIs) and nucleoside analogues reverse transcriptase inhibitors (NRTIs), which both prevent HIV in CD4 cells from converting RNA into DNA*, and protease inhibitors (PIs), which prevent HIV from being released from infected

* Technical terms are defined on page 53

CD4 cells. Other types of antiretrovirals are under development.

Guidelines as to the best time to start taking ARVs vary. They are often prescribed when the CD4 count falls below 350 and are considered essential for counts of 200 or under. The aim of treatment is to reduce viral load and boost CD4 counts. Bringing viral load below 20 copies is usually the goal, although in some cases bringing it below 500 may be seen as successful. Some individuals have undetectable viral loads; however, this does not mean that HIV has been eradicated from their bodies, and people who have stopped taking ARVs in such circumstances have found their viral loads rapidly rise and their CD4 cells fall.

Antiretrovirals are usually taken in a combination of three or more drugs of two different types. This triple or combination therapy, otherwise known as Highly Active Anti-Retroviral Therapy (HAART) presents numerous challenges to both doctor and patient. Doctors must have access to tests for viral load and CD4 counts, as well as being familiar with the range of drugs available, their impact, possible side effects and interactivity with each other. Patients must take a number of pills, sometimes as many as thirty a day, at specific times of day and before, during or after food (to ensure proper absorption by the body, depending on the drug) for an indefinite period, possibly for the rest of their lives. A typical daily intake for an individual on antiretrovirals in the UK, for example, is between six and fifteen pills per day taken two or three times a day. [12] However, the development of pills which have more than one drug, such as Combivir and Trizivir, is reducing both the number and frequency that need to be taken.

Strict adherence to such drug regimens is essential, yet even the most methodical person with none of the problems such as homelessness, poverty or lack of drinking water that beset many with AIDS, can find it a strain to eat, drink and take medicine at exactly the same hour every day for the rest of their lives. In the UK, in one study 51% of respondents said they had not missed a dose in the previous month and 75% had not missed one in the previous week. [13] In other words, even in a wealthy country with strong support networks for those with HIV, in any given week one in four people taking antiretrovirals does not take them as prescribed.

The study showed that failure to follow the exact regimen could result from factors within an individual's control - "I forgot", "I didn't have the drugs with me", "I was asleep" - or from side effects such as nausea. Sixty percent of those taking ARVs reported greater or lesser side effects. In most cases,

attacks of nausea or vertigo are mild and wear off within four to six weeks. Sometimes reactions do not develop immediately but become more severe as time passes. In a few cases, such reactions as severe pancreatitis or liver failure, can be fatal.

Despite such problems, only 15% of those taking antiretrovirals in the study found it consistently difficult or very difficult to follow their drug regimen. In general, those who were least likely to comply with the regimen were younger, less aware about drug resistance (see below) and more likely to be from an ethnic minority, unemployed or living alone.

Combination therapy is not fixed and may change if a particular combination does not succeed in reducing HIV levels or if HIV levels are reduced but side effects are too persistent for the patient to tolerate. Furthermore, specific combinations are seldom successful for more than one or two years; the virus builds up a resistance to one or more drugs, which then have to be changed. Among patients taking antiretrovirals in the North, 10% do not react to standard triple therapy, and this proportion may grow as people live longer with the disease. In such cases, doctors may prescribe up to ten drugs in what is called "salvage therapy" to suppress viral load effectively. Taking all these fac-

Toxicity

As with many other drugs, antiretrovirals are potentially toxic - dangerous to the individual who takes them. In the long term monotherapy (use of a single antiretroviral) is harmful and it is now only recommended to reduce the likelihood that a pregnant mother with HIV will pass the virus to her new-born child. In such circumstances, Zidovudine or Nevirapine is taken for a limited period before and during birth and given to the infant for a short period after birth.

Combination therapy has only been used on a large scale since 1996 and it is uncertain what impact it will have on individuals in the long run. Whatever the problems, however, it is certain that hundreds of thousands of people lead full, healthy lives today who would have died without antiretrovirals. For many people, the risk of toxicity seems a small price to pay in return for the gift of life.

tors into account, overall in the industrialised world, some experts estimate that in the long-term combination therapy may only be effective for 50% to 80% of patients.

Drug resistance

One of the strongest fears of AIDS researchers is that antiretrovirals may keep the virus at bay, but they cannot stop it developing drug resistance. HIV replicates very quickly and with random mutations; the viruses which survive are those which develop a resistance to whichever antiretrovirals the individual is taking. By attacking the virus at different stages in its cycle, combination therapy increases the likelihood that viruses resistant to one type of ARV are killed by another. Taking an inappropriate combination or frequently missing doses can therefore have serious consequences, because the virus then has more opportunity to develop a resistance.

Furthermore, no matter how regularly an individual takes ARVs, over the long term there is the risk of the virus developing "cross-resistance". This occurs when a virus resistant to one drug becomes resistant to others of the same type, because they are made of similar ingredients. It will, however, still be susceptible to other types. Tests are available to detect resistance - and thereby help decide what further treatment to recommend - but they are expensive (\$400-\$800*).

Because it can be passed on with the virus during unprotected sex or through infected blood, resistance is not only a problem for individuals but for the community in which they live. Drug resistant strains of HIV in people who are newly infected have emerged in the United States and Europe, as reports of unsafe sexual activities in these regions increase. [14] Such transmission occurs, at least in part because it is widely believed that people with low or undetectable levels of the virus cannot transmit it, and that because the virus is now treatable it is no longer dangerous. Such beliefs are wrong.

* US Dollars

Zambia: Lack of Access

Zambia is ill-equipped to respond to an HIV/AIDS epidemic that has reached one million people out of a total population of ten million. The health infrastructure is weak and, with an average annual income of \$370, the vast majority of its citizens have no access to antiretroviral treatments and only limited access to drugs for opportunistic infections.

The Ministry of Health claims there are 694 doctors and over 6,000 nurses countrywide, but a source at the University Teaching Hospital (UTH - the country's leading hospital) claims the country has only 200 doctors. Drug shortages are reported from many clinics and a long-running strike has led to patient anger and low morale at UTH.

Meanwhile, the government is unable to meet even the basic annual health budget of \$14 per capita. In 1995 only 40 per cent of all resources spent on health came from the government, with 30 per cent from donors, 15 per cent from the private sector and 15 per cent from individual households; these proportions have not changed radically since then. In 1996, Zambians spent on average \$1.60 a month on health services, including drugs, equivalent to five per cent of the average monthly income of \$33.25. [15]

Uncertain supplies

Very few Zambians can afford antiretrovirals on a regular, long-term basis. Winston Zulu, co-ordinator of the 4,000-strong Network of Zambian People Living with HIV/AIDS (NZP+) used to take three drugs, donated by friends abroad, until the source became unreliable. Clement Mfuzi, a member of NZP+, is concerned not just by the cost of antiretrovirals, but the damage they can do without the supervision of medical personnel. Rather than spend 15 million kwacha (ZK) (\$5,000) a year on such drugs, Mfuzi says, he would spend it on a good diet.

Antiretrovirals led Charles Mukuka (not his real name) into debt in June 1998. "Initially I was allowed to get these cocktails from the clinic on credit. As months went by I felt better and stopped going to the doctor. Then I started los-

ing appetite and weight." Mukuka changed his combination and when he received a bill for ZK5,849,000 (\$1,900), he was forced to sell his car. Soon after, he received another bill for ZK5,000,000 (\$1,650). Then a member of his church got some drugs from a relative in London and his combination changed again. Recently, however, the supply stopped and he has no other source.

Mukuka's bills reflect high prices. The wholesale price for a month's supply of Combivir is ZK488,000 (\$163), but it retails in chemists for ZK900,000 - ZK1.5 million (\$300 - \$500). Other drugs wholesale at ZK250,000 (\$83) and sell to the public for over K600,000 (\$200).

Zulu, Mfuzi and Mukuka are typical of Zambia's urban middle class in that they live in a world where antiretrovirals appear almost within reach. Yet even without antiretrovirals, AIDS is expensive, with illness and death from the disease consuming an average of 200% - 400% of annual household income. [16] In rural areas, ARVs are heard about but never seen, while, although no member of government has talked openly about their HIV status, there is widespread belief and some evidence that political leaders have access to treatment for HIV/AIDS denied to ordinary Zambians. More than one minister has died in a South African hospital and one source at UTH claims that the government buys antiretrovirals for those leaders who need them.

The role of clinics

Although various laboratory tests for HIV and opportunistic infections can be undertaken at UTH - a CD4 count costs US\$20 and viral load costs US\$70 - the hospital does not supply antiretrovirals.

Private clinics, such as the Midlands Medical Centre, which has 10 doctors and 15 nurses on its staff, and claims more HIV/AIDS patients than any other clinic, are the primary importers of ARVs. Boniface Kawimbe, former Minister of Health and proprietor of the Centre, points out only 40 % of his clients who begin treatment can afford to continue after three months.

Kawimbe sees the cost of antiretrovirals as a vicious circle which reduces access and keeps costs high. "If these drugs were affordable, clinics would find it cost effective to order these treatments." As one measure to reduce the

burden, he appeals to the government to remove the five per cent duty on imported drugs. "At the end of the day the cost is passed onto the patients. The high tax also limits the number of imported drugs." Alternatively, Kawimbe suggests, the government should import the drugs in bulk to get discounts, making them more easily accessible. (This is one of the actions taken by the government in Senegal: see p28)

Dr Mushikita Nkandu, a cancer specialist at UTH, dispenses antiretrovirals sparingly through his private practice, hesitating to start patients on treatment if they cannot sustain it. Nkandu also uses nutritional supplements such as imported vitamins and herbal remedies, together with herbs produced locally. Research is underway in collaboration with the Forestry Department to give the herbs scientific authenticity, as well as studying the plants' side effects, toxicity and potency.

Need to standardise

This patchwork whereby some people take antiretrovirals some of the time represents an urgent need to standardise therapy and cost, says Francis Kasolo, Head of Pathology and Microbiology at UTH. Otherwise, "we will end up with a drug-resistant disease. There should also be a serious look at who is prescribing medicines. ARVs are now being prescribed by people who do not understand the virus."

Antiretrovirals are only one problem. Drugs for opportunistic infections are not always available or are too expensive and there are many stories of people unable to access treatment for tuberculosis. Simon Mulenga, one of the founders of NZP+, was more public than most about his situation as a person living with AIDS and TB; to get treatment for tuberculosis, he fought many a battle with the Ministry of Health, even carrying banners in the street demanding treatment, until he died of the disease in July 1999.

Mildred Mpundu

REALITIES IN THE DEVELOPING WORLD

Two primary factors prevent widespread access to treatment for AIDS in the developing world: inadequate health services and lack of drugs. Where the health infrastructure is poor - where there are too few clinics, hospital beds and laboratories, doctors, nurses and technical staff - the disease cannot be properly diagnosed, the correct treatment prescribed or the best care offered. Drugs may be unavailable for several reasons, such as distribution problems or high taxes, but the main reason why antiretrovirals are not widely available in the developing world is the price of the drugs themselves.

In a few countries, the majority of citizens are assured treatment for AIDS by the state, but in most countries medical facilities are routinely understaffed and poorly equipped and drugs as basic as painkillers are frequently unavailable. In the poorest countries only the wealthiest, including the political leadership, have access to a full range of drugs and tests; the urban middle class, with limited financial resources, get hold of any pills they can and impoverished village dwellers agonise on straw beds without clean water or basic painkillers. For most people, there appears little incentive to learn whether one is HIV-positive; even if the disease had no stigma, many would avoid taking the test, since without medication a positive result can appear as nothing more than a death sentence.

Furthermore, access to drugs is not the only problem facing many living with AIDS. Critical to good health, whatever one's HIV status, is clean water and good nutrition, yet 50% of the population in sub-Saharan Africa and 18% in South Asia do not have access to clean water and 32% and 48% of under five year olds in the same regions are under-nourished.

Poor infrastructure

While expensive private facilities may offer standards of care on a level with the best in the West, the quality of a country's public health service depends to a large extent on the money spent on it. In Western Europe and North America, figures of upwards of \$1,500 per person are the norm. In contrast, in most of Africa and Asia annual health expenditure is frequently under \$20 per person. In Latin America, figures range from \$41 in Guatemala through \$359 in Brazil to \$792 in Argentina. [17] Not surprisingly, most countries which

offer their citizens antiretrovirals are in Central and South America. Money pays for doctors, nurses and hospital beds; the less money available, the fewer facilities and staff. In the last twenty years, access to adequate medical facilities in many developing countries has fallen as populations have increased and resources have been squeezed by Structural Adjustment Policies - reductions in government funding as a result of loan conditions imposed by the International Monetary Fund. Whereas in the industrialised world, figures of 200 - 300 doctors and 500 - 1,000 nurses per 100,000 people are common, in sub-Saharan Africa, the average is 16 doctors and 75 nurses. In South Asia, excluding India, the average is 33 doctors and 24 nurses (in India there are 48 doctors per 100,000; the figure for nurses is unavailable); Latin America and the Caribbean average 91 doctors and 136 nurses. [18]

Bed spaces are equally limited. While France and the US have 8.7 and 4.0 hospital beds per 1,000 people respectively, the equivalent figures for Bangladesh, Benin and Botswana are 0.3, 0.2 and 1.6. [19] The number of beds in the Kenyatta National Hospital, Nairobi, Kenya, fell by 30% between 1990 and 1995; in the same period occupancy rose from 100% to 190% [20] - which means that beds were frequently shared or patients were accommodated on stretchers, benches or the floor.

In other words, many, if not most, of the countries hardest hit by HIV/AIDS have under 10% of the medical personnel and bed space considered acceptable in the developed world. Furthermore, since medical facilities are concentrated in towns and cities, in rural areas, where the majority of Africans and Asians live, the proportion of doctors, nurses and hospital beds is much lower.

Although in some cities in sub-Saharan Africa over 50% of hospital beds are occupied by patients with HIV [21], that may not mean that weak infrastructures are collapsing. Between 1992 and 1997 the proportion of people with HIV admitted to the Kenyatta National Hospital (KNH) remained unchanged at 40% and the survival rates of those who were admitted improved, although an increase in the proportion of patients with HIV and a fall in survival rates were expected. [22] What happened, the authors of the KNH study suggest, was a change in the behaviour of those with the disease; those with advanced infection who were pessimistic about the hospital's ability to treat them stayed away, while the less seriously ill still sought treatment.

Such behaviour is a rational response to the epidemic, but it is hardly satisfactory. Furthermore, it does not predict how hospital admission patterns would

change if treatment became widely available. Fewer people might fall ill and need hospitalisation, or hospitalisation might increase as more people see that treatment is available.

Hospitals, Doctors, Patients and HIV

Most people in the poorest countries of the developing world only visit a doctor or hospital when in severe pain or in emergency. A visit to a public hospital often begins queuing with 20 or more others, waiting for staff who may turn up late or not at all. X-rays and other tests may not be available or may be beyond the patient's resources, as may the treatment prescribed.

Patients admitted to hospital face further trials. A bed may be available, but linen, food and cooking facilities must be provided by a friend or relative who will often stay in the hospital as well, sleeping on the floor. Doctors and nurses are usually overworked and underpaid; doctors may ask patients for bribes or spend part of their day running a private practice. And with hygiene often difficult to maintain, many public hospitals are not only ill equipped to care for the sick but are themselves health hazards.

Doctors are often not trained to explain treatments and patients do not expect to ask questions. They may be told to take vitamins, treatment for opportunistic infections and, where available, antiretrovirals, without differentiating between the three or being warned of possible side-effects. In one province of Thailand, it has been reported that 80% of the patients stop the taking the anti-retroviral Didanosine (ddI) within the first two weeks, often because they do not like the side-effects and have not been told how important the drug is. Such a high drop-out rate could be avoided if patients had more information.

Away from hospital, the situation may not be much better. In Uganda, often seen as offering the rest of Africa a model response to HIV, real progress has yet to trickle down to most people with the virus, says Winnie Ssanyu-Sseruma, an activist with AIDS. Most who are diagnosed with the disease have very few choices and have to rely on extended families for finances and care.

With little access to accurate and up-to-date information, many taking anti-retrovirals choose their own combinations, according to what they can afford, or solicit advice from friends or unscrupulous entrepreneurs selling expensive

and sometimes useless or harmful treatments. Unaware of the dangers of resistance, many buy drugs that give them no benefit, or stop therapy if they cannot afford it. As one Ugandan says, "I would love to be able to adhere to medication and know it is the right thing to do, but if one month I am faced with buying my medicine or paying my child's school fees, it will have to be the latter."

The cost of treating opportunistic infections

In the industrialised world, most expenditure on drugs is paid by government or private insurance schemes; in the developing world, most comes from the pockets and purses of ordinary citizens.

The first expenditure for people with HIV/AIDS usually comes with testing for the infection itself. This may be free, at nominal cost or as much as \$5 or \$10. Once the infection is diagnosed, and as long as the individual is not ill, there may be no more expenditure for some time, although many people do not learn they have the virus until they fall ill.

With opportunistic infections come demands for treatment, further tests and, ideally, antiretrovirals. Many opportunistic infections can be treated cheaply with drugs on the World Health Organization's Model List of Essential Drugs [23], which exists in national variations in almost 150 countries. The list identifies key drugs which provide safe and effective treatment for the majority of communicable and non-communicable diseases and which should, ideally, be available in hospitals worldwide. Some are within developing world budgets: candidiasis can be treated with a very cheap gel and a course of regular tuberculosis treatment is between \$15 and \$45 [24] - although that figure rises steeply if it is the drug-resistant form of the disease. Other treatments can be much more expensive; trimethoprim-sulfamethoxazole for pneumocystis carinii pneumonia (PCP) can cost \$611 for a 21 day course, while aciclovir for herpes zoster may be \$170 for a 7 day course. [25]

Overall, the World Bank has estimated the average cost for palliative care for AIDS in sub-Saharan Africa as \$19 and for treatment other than antiretrovirals as \$33 - \$223. The equivalent costs in Thailand are \$19 and \$158 - \$801 respectively. Costs of hospital care in a year for someone with AIDS are estimated as \$218 in Africa and \$673 in Thailand and overall, costs of treatment, without antiretrovirals, \$490 a year in Africa and \$1,657 in Thailand. (all figures in 1996 dollars) [26]

The fact that some treatments are relatively cheap, however, does not mean they are widely available. In many parts of the developing world, poor administration, lack of funds, cash flow problems and corruption can all prevent even the cheapest treatments from reaching hospitals and patients.

The cost of antiretrovirals

In the few countries where antiretrovirals are widely distributed, viral load tests and CD4 counts may be free or available at a nominal cost, although patients may have to travel long distances in order to be tested. Otherwise individuals are likely to be charged the full cost of testing; figures reported from Zambia in May 2000 are \$20 for a CD4 count and \$70 for viral load (p11). The price of antiretrovirals has been falling in many countries in recent years, but by no means far enough to reach the millions of people in the developing world who need them. In May 2000 the typical price for a year's supply of the combination of Lamivudine, Zidovudine and Nevirapine [27] in three countries was:

- \$9,950 in the United States
under 1% of the adult population has HIV; annual per capita expenditure on health is over \$4,000, antiretrovirals are paid for by private or state insurance.
- \$2,365 in Brazil
under 1% of the adult population has HIV; annual per capita expenditure on health is \$360, antiretrovirals are paid for by the government.
(Brazilian government figures for 1999 showed \$4,100 per person spent on antiretrovirals, reflecting both higher prices in previous years and the fact that different combinations are prescribed.)
- \$4,201 in Uganda (with Zalcitabine replacing Nevirapine)
9% of the adult population has HIV; annual per capita expenditure on health is \$14, antiretrovirals are generally unavailable.

The differing figures for Brazil and Uganda reflect widely differing costs in the developing world. In May 2000, a daily dose of Zalcitabine (ddC) ranged from \$0.24 in Brazil to \$3.75 in the Ivory Coast and \$4.17 in Uganda, while Stavudine was \$0.56 a day in Brazil and \$6.19 in Uganda. [28] Other research in April 2000 indicated that the price of Lamivudine (3TC) varied from \$50 for a month's dose for the generic version in India through for the proprietary drug

\$138.70 in Costa Rica to \$208.80 in Malaysia (see p32 for definitions of 'generic' and 'proprietary'). The drug was cheaper in France than in Malaysia or the Philippines. [29]

Black market for drugs

The reasons for such price differences are discussed below (pp31-46). While it is a barrier that only a few with AIDS are able to overcome, price is not the only obstacle preventing people from accessing much-needed medicines. Corruption and mismanagement can divert drugs and testing kits intended for widespread distribution into the hands of those with influence or money.

At other times, the black market appears to benefit those who might not otherwise have access to drugs. Richard Stern, from the Agua Buena Human Rights Association in Central America, notes that antiretrovirals are sold in the street in front of the Guatemalan Security Institute, the government body that distributes ARVs free to a limited number of Guatemalans with AIDS. Some of these, Stern reports, have other sources of medications or are willing to sell duplicate pills for needed cash to people desperate to obtain them.

"Lorena" is a 37-year old Nicaraguan who buys and sells the drugs throughout the region. Lorena herself and her husband both have HIV and this is one of the few options open to her to make a living; "she takes buses, eats only the cheapest food, and is trying to supply a group of impoverished individuals that certainly cannot pay her much more than her expenses". [30]

Some experts see such actions as a double-edged sword, increasing access and prolonging life in the short term, but in the long-term encouraging wastage and mismanagement and threatening drug-resistance and other side effects from medicines taken without adequate supervision. On the other hand, Richard Stern notes, following a court decision in Costa Rica to grant people with AIDS the right to antiretrovirals, "motivation among [people with AIDS] and their families improved dramatically after the Court's decision. Several strong PWA organizations now exist and they provide peer support and education regarding adherence, secondary effects etc. ... A large number of physicians employed by the Public Health service here who previously knew nothing about ARV medications, received training in administration of these medications. Physician morale and interest in the AIDS epidemic and attention to [people living with AIDS] increased significantly." [31]

India: Conflicting Priorities

India is one of the world's giants, with a population of over one billion and many health problems to confront. Although only South Africa has more people living with HIV/AIDS, such is the size of India, that its estimate of 3.7 million HIV-positive people is only a small fraction of its population. Against such a background, for many Indians the real question is not how to make antiretrovirals available, but what priority they or indeed the whole anti-HIV programme should be accorded in an overstretched and fund-starved public health delivery system.

The country's health system is creaking under the strain of the overall burden of disease. In April 2000, the Chairman of the World Health Organization's Commission on Macroeconomics and Health, Jeffrey Sachs, pronounced the 0.7 percent of gross domestic product (the country's annual wealth less foreign investments) spent on public health grossly inadequate. India, Sachs pointed out, did not even have a strategy to tackle the urgent problem of building a health delivery system or to mobilise resources for it.

Despite these problems, India seems better placed to respond to AIDS than many other countries. It has a powerful pharmaceutical industry which manufactures, markets and exports drugs, including antiretrovirals. Competition between indigenous manufacturer CIPLA and multinational Glaxo Wellcome has led to frequent reductions in the price of their brands of Zidovudine, while a month's supply of ciprofloxacin, for drug-resistant tuberculosis, costs \$22 a month - only 7% of the US price of \$325. In March 2000, CIPLA received government permission to manufacture nevirapine, which means that all the components of basic triple therapy (two NRTIs and one NNRTI: (pXX)) will soon be available in India at \$2,500 a year, according to CIPLA chief executive Amar Lulla.

However, such prices remain too high for most people in a country where the average annual income is no more than \$370 a year. Says Chingko Lal Thamsing, a doctor at the only AIDS hospice in the capital, Delhi, antiretroviral drugs are used sparingly because of high costs. "We are not sure how cost-effective these drugs are and even at \$200 a month, costs are too high for the kind of patients who come to us."

Many people with HIV resort to Ayurveda, India's ancient system of medicine

based largely on herbs. According to T K Bejoy, a leading ayurvedic practitioner in southern Kerala state where the indigenous system is highly developed: "Ayurvedic formulations have long been known to boost the immune system and AIDS is clearly described in the ancient texts."

In many parts of India practitioners of Ayurveda and other indigenous systems are the only providers of health care and command the respect of the people in spite of the cheapness with which allopathic drugs are available.

Not all Indians are sceptical of antiretrovirals. Long-standing experts such as I S Gilada of the People's Health Organisation (PHO) in Mumbai (Bombay) claims that the state has a responsibility to provide help, improve on currently available care, develop a rational drug policy to make anti-tuberculosis and other drugs for treatment and prevention of opportunistic infections widely available. Otherwise "it will be, as elsewhere in Asia, survival of the richest for others die early." There is, however, no indication that the government is responding to Gilada's concern.

PHO's strategy is to recommend treatment according to income. Those whose annual salary is more than 300,000 rupees (Rs = \$6,700) should take the full combination of drugs, costing \$4,400 a year. Those who earn between Rs 100,000 and Rs300,000 (\$2,200 - \$6,700) should take two NRTIs and hydroxyuria (not an antiretroviral, but a drug which has shown some success in reducing viral load). Those who earn Rs50,000 - 100,000 (\$1,100 - \$2,200) should "think of taking two NRTIs and hydroxyuria, borrow money, extend life, earn more and repay." If the annual income is below Rs50,000, "do not even think of these medicines, just take treatment for opportunistic infections".

Furthermore, since few Indians weigh close to the standard average weight of 70 kilograms, PHO suggests reduced dosages. "Such dose reduction reduces costs as well as side effects and increases patient compliance."

Gilada's optimism and enthusiasm are well-known, and PHO's advice makes sense to many. Nonetheless, it is likely to be a long time before those Indians who need antiretrovirals get them and India resolves its ambivalent attitudes towards HIV/AIDS and health in general.

Ranjit Dev Raj

BRIDGING THE GAP

In 1998, using 1994 statistics, WHO and UNAIDS compared estimates of the cost of providing antiretroviral drugs to all those living with HIV in fifteen developing countries with the same countries' health budgets [32] Costs ranged from less than 1% of the health expenditure in China (a large country with few cases) to 81 times the health expenditure in Uganda (a relatively small country with a high proportion of cases). Indeed, the \$13 billion dollars that would have been required each year was equivalent to more than three times Uganda's gross national product - the total wealth the country produced in a year.

These figures may overestimate the problem, partly because the price of anti-retrovirals has since fallen and partly because the calculations assumed that everyone with HIV would need the drugs. However, even if the estimates are substantially reduced to take these factors into account, they remain much too high for the worst affected countries to bear.

What has to be paid for?

HIV/AIDS-related costs can be divided into direct and indirect costs:

direct:

- tests
- treatment and prophylaxis for opportunistic infections, including visits to doctors and hospital stays
- antiretrovirals

indirect:

- physical and technical infrastructure (buildings and medical staff), which are shared with other aspects of health care

By estimating the numbers of people needing treatment, the cost of that treatment and the cost of improving infrastructures, the likely overall cost of providing universal access to treatment for HIV/AIDS in a country can be calculated. Such a figure depends on estimates that cannot be gone into detail in a report of this length; nonetheless, the exercise gives an idea of the magnitude of the task.

How many need treatment?

Not everyone who has contracted HIV requires antiretrovirals. Most clinicians recommend waiting until the immune system has begun to weaken before prescribing the drugs. Furthermore, people's immune systems respond to the virus in different ways. Younger and healthier people are likely to live longer without symptoms of AIDS than those who are older or malnourished or whose immune systems are already compromised by other diseases.

Let us assume that in the developing world it takes an average of six years after infection for CD4 counts to fall to 200 - 350, the stage when antiretroviral drugs should be prescribed. This means that in a country where one million people have HIV and on average 100,000 contract the infection each year, the 60% (600,000) who contracted the virus in the previous six years will not yet require antiretrovirals, while the 40% (400,000) who contracted it before that time will. [33]

Without antiretrovirals, up to 25% of the 400,000 (ie 100,000 people) would be expected to die within the first year; with ARVs, that number might be cut to 25,000. In other words, with antiretrovirals, 375,000 would survive to the second year. By that time, however, another 100,000 would have become eligible for treatment, giving a total of 475,000 on ARVs. Assuming that each year a similar proportion survive who would otherwise die, by the third year, 531,000 people would be taking the drugs. The numbers under treatment would continue to rise until the tenth year and only begin to diminish six to ten years after severe declines in the transmission rate.

Per patient costs

The above figures mean that hundreds of thousands of people would require year after year, for an indefinite period, not only antiretrovirals, but regular laboratory tests and outpatient visits; some would require prophylaxis and / or treatment for opportunistic infections and a small minority would occasionally need hospitalisation. These per patient (direct) costs vary from country to country, depending on factors such as average salaries and the cost of imports.

As noted above, the 1996 costs of treatment, without antiretrovirals, were estimated as \$490 a year in Africa and \$1,657 in Thailand. If the cost of antiretrovirals is added, these figures rise considerably, to \$2,800 - \$5,900 a year,

depending on whether the Brazilian and Ugandan prices are used. Assuming an average cost of \$5,000 per person per year, in a country where one million people have HIV, the total cost of providing full access to treatment would be \$2 billion in the first year, \$2.4 billion in the second year and \$2.7 billion in the third year.

Such sums are daunting for a country like Zambia, where one million people are HIV-positive; \$2 billion - \$2.7 billion represents 57% - 76% of its gross national product (GNP - the total wealth it produces in a year). Worldwide, the figure of 12 million people with weakened immune systems represents expenditure in the first year of \$60 billion - a figure that would rise as more people required antiretrovirals. Reducing the cost of treatment to \$3,000 per person brings that figure down to \$36 billion worldwide and \$1.2 billion in Zambia, still far beyond reach for most countries. Meanwhile annual US military expenditure is \$300 billion.

Per country costs

Even if they were available, antiretrovirals cannot be effectively distributed without the systems in place to monitor their impact. That requires the provision and maintenance of adequate buildings (such as outpatient clinics, hospitals and laboratories, including furniture, laboratory equipment etc) and the training costs and salaries of medical and technical staff (doctors, nurses, laboratory technicians) in sufficient numbers to meet demand. As indicated above, health services in the countries worst affected by HIV/AIDS are severely under-resourced. ARV monitoring systems cannot be installed without significant improvements to health infrastructures.

Such improvements would obviously benefit those suffering from all diseases. Conversely, improvements in health care reducing the incidence of other common infections are also a factor in preventing transmission of HIV (eg reducing the incidence of other sexually transmitted infections makes it less likely that HIV will be passed on) and in caring for those who have already contracted the infection (eg reducing the general incidence of tuberculosis makes it less likely that those with AIDS will contract it).

The problem, once again, is cost. Assuming that \$150 - \$200 per person per year was spent on health (one tenth the figure spent in many West European countries), this would represent additional annual expenditure of \$13 billion in

Bangladesh, \$9.7 billion in Nigeria, \$2.1 billion in Uganda and \$1.1 billion in Zambia - figures equivalent to 29%, 29%, 32% and 31% of those countries' GNP respectively. In some cases such costs are less than the costs of providing antiretrovirals at current prices (eg Zambia); in other cases, the cost of antiretrovirals is less (in India increasing health expenditure from \$18 per person per year to \$180 represents almost 15 times the cost of antiretrovirals to those who currently need them). But whichever way the balance falls, the total costs are far beyond what most developing countries can afford.

Step by step

While money from the government or their own pockets gives many people in the developing world access to antiretrovirals and other needed drugs, either within carefully monitored and supported programmes or on their own account, it is clear that extending access to the millions who need them is not simply a question of writing billion-dollar cheques.

The World Health Organization and UNAIDS argue that "ARV treatments must be supported by a functioning health and social system which ensures adequate diagnosis and treatment of opportunistic infections, appropriate pain management, and correct use of and adherence to antiretrovirals to avoid the emergence of drug resistance and transmission of resistant strains." [34]

The agencies' guidelines for introducing antiretrovirals, whether in a pilot programme, such as Senegal's (p28) or nationwide, as in Brazil, includes a step-by-step approach that includes (i) secure financing, (ii) reliable methods of distribution and procurement of drugs, (iii) appropriate institutions and trained personnel responsible for diagnosis and prescription of drugs, (iv) adequate long-term monitoring of the programme, (v) co-operation with community-based organisations, including associations of people living with HIV/AIDS, the private sector, donors and others. [35] These are not simple matters; such basic questions as where are drugs stored, how are health workers trained, what guarantees are there for long-term financing, must be clearly resolved before any effective programme can begin.

Failure to undertake these steps may cause more problems than they resolve. In 1999 an attempt by the Ivory Coast to provide antiretrovirals to some people with AIDS fell into difficulties because the finance and distribution mechanisms were not strong enough to support even the limited numbers (400 - 500)

offered treatment. Senegal has helped fewer people, but the project appears to have a stable base and all sections of the community, including the government, donors, the business community, pharmaceutical companies and people living with HIV/AIDS are actively involved.

Elsewhere in Africa, this step by step approach appears the exception rather than the rule. In South Africa, President Thabo Mbeki has said that providing antiretrovirals for only a proportion of the population is unacceptable. "You cannot discriminate in that way." [36]

In Latin America eight countries - Argentina, Brazil, Chile, Costa Rica, Guatemala, Mexico, Panama and Venezuela - are reported as offering access to treatment to a significant number (10% or more) of people living with HIV/AIDS. In several of these countries access to treatment has been granted only after people living with AIDS and their supporters took their respective governments to court. Even in countries where access is theoretically universal, the public health service often fails to reach people who do not live in the main cities and lack of confidentiality in testing means that many people who need the drugs are unaware of their status and do not claim them.

In Asia, only Taiwan theoretically guarantees full access to treatment to all who need it, while in Thailand, the government has actively encouraged Thai manufacturers to produce generic versions of antiretrovirals to ensure significantly reduced costs in that country.

Meanwhile...

In addition to efforts to make antiretrovirals universally available, other measures need to be taken to ensure that the best possible care and treatment for the disease reaches those who need it. As described above, this means ensuring (i) emotional support, (ii) physical needs such as proper food and assistance are met, (iii) palliative care for relief of symptoms and (iv) treatment for opportunistic diseases. Many health ministries have developed national guidelines which provide advice on how to manage HIV/AIDS, how to make clinical care and referral systems efficient and how to integrate care programmes into existing community health programmes. Nevertheless, many poor communities are still struggling to meet even these basic needs and lack both financial and strategic support, from national, state or province and municipal governments, donors and commercial organisations.

Accurate and widespread information is key to this approach. As one African woman says, "To be informed is empowering. It has enabled me to manage living with the virus. I know how to take care of myself. I know my body, I understand it. I know where to seek support if I need it. I know what kind of support I need. I feel courageous to ask questions. Even to protest. ... All these wouldn't have happened, or might take an awfully long time to happen, if I wasn't informed." [37]

Indeed, Senegal shows, access to treatment for AIDS, at whatever level it is provided, must be integrated not only into national AIDS plans, but into the overall strategy of each government department and large commercial enterprise.. This process must also involve northern governments and the pharmaceutical industry.

What are the benefits?

HIV/AIDS is much more expensive than many other diseases. Malaria affects a much greater number of people and curbs the growth of many developing countries by 1% to 3% a year through illness and death. However, global spending of \$1 billion (eg through the provision of mosquito nets and clearing breeding grounds) would result in savings of \$12 billion in treatment and lost productivity. [38]

Most people would agree that health care should be provided on humanitarian or moral grounds but economists and politicians often ask whether it is cost effective to provide full access to treatment for people living with HIV. In other words, will the money gained from people continuing to work, rather than falling ill and dying prematurely, be greater than the money spent on care and treatment? While malaria prevention and care generates more wealth than is spent, the evidence for AIDS is less certain.

In 1998, WHO and UNAIDS argued that antiretrovirals were not cost-effective in countries where the annual average income is below \$4,000. [39] That figure was based on an analysis that compared the cost of drugs [\$10,000 per year] with savings in wages that would be earned [\$4,000] and health care costs that would be avoided [\$6,000]. Given that the average income of even medium level developing countries is \$3,327, that analysis means that in at least 100 countries, where the vast majority of people with HIV/AIDS live,

it would cost more to treat people than they could repay in labour that would otherwise be lost.

WHO/UNAIDS' figures implied continued high costs of antiretrovirals and no restructuring of health services. A different approach is to look at the impact on the country's gross national product and to assume that costs of up to 4% of GNP are bearable - a percentage that represents an achievable annual increase in production. At 10% of current prices (ie \$500 a year), providing full treatment for 40% of those living with HIV comes within sight of many countries (in Uganda such costs would be \$186 million in the first year, equivalent to 2.8% of GNP), but not all (in Zambia \$200 million in the first year represents 5.7% of GNP). Reducing antiretrovirals to 5% of current prices (\$250 a year) should bring that component of costs within the reach of even the poorest country.

In other words, assuming reasonable national growth is achieved and the cost of AIDS is assumed by the whole nation and not only those who required antiretrovirals, provision of the drugs at 5% of current prices is cost-effective. That measure, however, is only part of the solution, since the problem of addressing infrastructures still has to be addressed. Yet, as was noted earlier, improvements in health services benefit the whole nation in many ways and the costs should not fall on AIDS alone.

Irrespective of the potential financial cost or benefit, there is the argument that treatment should be made available on humanitarian grounds alone - as treatment is made available to the elderly or mentally or physically incapacitated or others who cannot create the wealth necessary to pay for that treatment. If nothing else, human dignity and sympathy and, many would argue, human rights require it.

Senegal: Hope for a few

In one of the first national experiments in Africa, a small number of people with AIDS in Senegal have received antiretroviral drugs since 1998, thanks to a government grant of FCFA 250 million (US\$360,000) a year. This action, which even government officials describe as "timid", was launched on the grounds that "something had to be done".

Senegal is one of the few countries in sub-Saharan Africa where the epidemic appears under control. According to the National AIDS Programme (NAP), approximately 80,000 people are living with HIV, representing one per cent of the total population of 8.8 million. That number "risks climbing to three per cent by 2005 if prevention efforts are not maintained and reinforced," warn Ibra Ndoye, NAP executive director, and Souleymane Mboup, head of the Aristides le Dantec virology and bacteriology service of the University Hospital Centre (UHC) in Dakar, the country's capital.

"We were concerned to know where this would take us, because once treatment has begun, it cannot stop as long as there is life," explains Papa Salif Sow, of the Infectious Diseases Clinic at UHC.

Currently 70 people living with AIDS have been chosen by a national multi-disciplinary committee to receive antiretrovirals, according to strict eligibility criteria. Lack of money prevents the plan being extended to all those who need the drugs (32,000 according to Panos estimates). With costs at FCFA 320,000 (US\$460) per patient a month, 70 is the maximum affordable under the government grant. Currently the service is only available in Dakar, although some people on the programme live outside the capital and travel long distances for tests and consultations.

Some costs are met by patients. A medical and social dossier for each applicant for treatment is examined by a committee which includes representatives of government services, independent medical and psychiatric specialists, social services, as well as lawyers and representatives of associations of people living with HIV/AIDS. Dossiers are identified by number only and the final choice is based on a number of criteria, including income and family responsibilities etc.

Those accepted on to the programme pay according to their means, on a scale between \$32 and \$285 a month.

Yet in a country where the average annual per capita income is \$600 a year, even the lowest rate of patient contribution is too high for some people. Baba Goumbala, Executive Secretary of the National Anti-AIDS Alliance, welcomes the programme, but points out "there are gaps in our social services. Our organisation helps poor people with HIV/AIDS, those who are out of work, who have almost nothing to eat, yet they have to take a number of pills and capsules a day [and in such a situation] side effects are soon exaggerated." If the programme is not adjusted to overcome such situations, Goumbala goes on, "there is a risk of ending up with the wrong pattern of drug-taking and the threat of resistance."

"We believe this is a good experience which should be offered to others," notes Ismaila Goudiaby, co-ordinator of Espace UACAF, an association of people living with HIV/AIDS and member of the eligibility committee. There are five such associations in Senegal, the first of which was founded in 1991; in total they have 200 members, but, Goudiaby says, only four have been accepted by the programme. The five associations are preparing a "telethon" and other activities supported by the public authorities to raise money annually to increase the number of patients.

Meanwhile, the national committee is seeking ways to reduce the cost of participation or other alternatives to allow the number of people benefiting to increase. One idea is to create a foundation called "Espoir" (Hope). "Such a foundation could add to the state's budget, with contributions from public or private companies and other donations," says Salif Sow. Other potential sources of income are taxes on tobacco or alcohol, or putting airport taxes into a treatment fund. "Financial support would allow the individual's monthly contribution to be reduced, perhaps from \$32 to \$14."

The numbers served by the programme are intentionally small. "We said at the beginning that we had to make an experiment, in other words, not to be too ambitious," says Sow. The experiment seems to have been more successful than in the Ivory Coast, where the programme began with 400 or 500 people and ran into difficulties when drugs became unavailable. "We have to continually be sure that the mechanisms are working, through efficient financing, drug

management and biological, clinical and psychological follow-up of the patients in the programme."

Furthermore, the biological follow-up is extremely expensive. A grant from the French National AIDS Research Association (ANRS), allows all the programme participants to be given free viral load and CD4 count tests. These are undertaken in a laboratory built by the Roche Foundation and French government aid.

For the last 16 months the programme has undergone an evaluation which has confirmed that the "wheels were well greased and demonstrated that an African country can start a programme of this type and keep it going," says Sow, who adds that, "if it works in Dakar, we now have to try and expand the sites to the interior of the country."

The programme hopes to expand to 100 participants in the near future, including 40 people currently in a free clinical trial. Training is at the centre of the programme's activities for much of 2000, with a working group set up to train biologists and all doctors and pharmacists in the private and public sectors on the management and prescribing of antiretrovirals. The goal is for patients who currently come to Dakar each month for medical examinations to be seen by local doctors in their home town. Meanwhile blood tests will continue to be taken every six months in Dakar, at the only laboratory in the country capable of viral load and other tests.

Fara Diaw

WHO HAS THE RIGHT?

Although not the most expensive aspect of providing full treatment for AIDS, the cost of drugs, and in particular antiretrovirals, has been the most controversial. Attempts have been made by many stakeholders - people living with AIDS, organisations working in AIDS care, multilateral agencies such as UNAIDS and the World Health Organization, Northern and Southern governments and others - to reduce the cost of such drugs in the developing world. Some pharmaceutical companies insist that they too have been part of this movement, while other stakeholders accuse them of creating the very obstacles that need to be abolished.

In the developed world, drugs are mostly paid for by government or private insurance schemes. Such schemes can pay relatively high prices, but they can also negotiate discounts. In many developing countries, where health insurance schemes are limited, governments may import drugs, but it is usually the individual patient who pays, if s/he can afford them. But irrespective of who pays, the developing world market provides a very small proportion of the manufacturers' global profits.

The price of a drug charged to an individual, insurance company or government health service is determined by a series of factors, including the cost of research and development; manufacture; company overheads, such as administration and marketing; and distributor's costs and commission. Prices are also affected by taxes and fluctuating exchange rates. Finally, one of the most important factors - and the one least mentioned by manufacturers - is the price the consumer can afford or is willing to pay.

The International Federation of Pharmaceutical Manufacturers Associations (IFPMA), which represents confederations of the industry in 55 countries, says that price differences reflect different price and reimbursement systems, macro-economic differences and dynamics, Commercial strategies of individual companies are only one factor in the mix.

Whatever the truth of the cost of drugs, at the heart of the issue lie questions, not of cost, but of ownership: which individual, company, institution or government owns the patent (also known as the intellectual property right) to the drug in question? How far should that patent extend geographically and in time? How much is it worth? And do governments have the right to override ownership of a patent in order to extend it to other manufacturers? These

issues affect not only antiretrovirals and other medicines, but many other products, and reflect many broader controversies over the presumed benefits and disadvantages of global free trade.

From glint in the eye to niche in the market

Research into new drugs takes place in many countries, but the greatest expenditure and activity takes place in the United States. Unsurprisingly, that country's processes and regulations have considerable influence over the acceptability and use of drugs in the developing world.

Creating a new drug takes time, with 15 years from initial idea to bringing the drug to market not uncommon. The usual process is that one or more scientists in a pharmaceutical company, university or national research institute seek funding to prove that a particular chemical formula will have a specific effect on the human body. The idea is reviewed and if funding is approved, pre-clinical (laboratory) tests are carried out, often by government institutions. If these are shown to work, the next stage is to devise and carry out a series of clinical tests (on human beings) to check that the drug is both safe (it does not harm those who take it) and effective (it achieves the proposed result in a significant proportion of those given it).

The company wishing to manufacture and sell the drug applies to the US Food and Drug Administration (FDA). Once the FDA is persuaded that independent analysis confirms the drug's safety and efficiency, official permission is granted to market the drug in question. While this final stage can take years, most antiretrovirals are deemed "Fast Track" and may be approved in as little as six months. Approval is also the licence - recognition that the applicant is the owner of the patent and has exclusive right to market it for a specific period of time. After that period other companies can create "generic" versions of the same drug.

Because most drugs created to treat HIV/AIDS are relatively new, they are "proprietary" - they remain under patent and can only be manufactured by the patent-holder or a licensee. In the United States, the patent for Zidovudine (AZT) runs out in 2005, for Didanosine (ddI) in 2007 and for the various protease inhibitors (the most expensive type of antiretroviral) in 2014. "That's a long way off for 30 million people waiting to have access," says Richard Laing of the Boston University School of Public Health. [40] In fact the

majority of these will die before that date, if access is not achieved, and a similar or greater number may contract the infection in the meantime.

Who funds the research?

The manufacturers of pharmaceuticals, in common with other commercial enterprises, are reluctant to reveal company secrets, but it has been suggested that the cost of manufacturing some drugs may be as little as one hundredth of the price at which they are retailed. The industry claims that such high charges partly reflect the need to recoup the costs of research over the twenty years for which a licence is granted. In the words of the International Federation of Pharmaceutical Manufacturers Associations, "there are hundreds, indeed thousands, of unmet needs that can only be addressed through the innovation that comes from research and development, the risk of which is largely provided by the research-based pharmaceutical, biotechnology and vaccine industries." [41]

Estimates for the cost of research and development (R&D) of a new drug vary widely. In 1998, one US expert suggested the figure was as high as \$500 million [42], a dramatic increase, even allowing for inflation, on a 1987 estimate of \$114 - \$231 million [43]. However, James Love, of the Washington DC-based Consumer Project on Technology, makes several arguments that suggest that actual costs to the manufacturers may be considerably lower. These include the fact that pre-clinical (laboratory) research, which may represent 70% or more of R&D costs, is often paid for by public institutions such as the US National Institutes of Health. [44] Indeed, between 1987 and 1996, a period critical for antiretroviral development, annual US government funding for AIDS research increased almost five-fold to reach \$1.65 billion. [45] Furthermore, the costs of clinical trials, particularly for antiretrovirals, are often subsidised by the government; clinical trials for 14 ARVs reportedly cost an average of \$6 million, and less than \$4 million when subsidies are taken into account. [46] Antiretrovirals typically earn their manufacturers \$200 - \$500 a year.

Other costs are involved in research and development, in particular the costs of drugs which fail to reach market. However, Love claims that data from the US Internal Revenue Service (the tax department) shows that in 1997 research and development for all drugs in the United States, including those which failed to reach market, represented no more than 7.4% of sales income (\$12.9 billion on research and \$175.3 billion in sales). [47] Calculations using R&D figures

from the US Pharmaceutical Research and Manufacturers Association (\$19 billion) suggest that component represented 10.8% of total costs.

Higher - and lower - costs in the developing world

Even if the costs of research are much lower than the industry claims, the price to consumers reflects other factors, such as the time and money needed to produce a drug of suitable quality for mass manufacture. Transnational companies must also maintain large administrations, marketing teams and distribution networks, all of which cost money. Furthermore, as Julian Meldrum of the UK's Body Positive suggests, investment in antiretrovirals by drug companies may become more important if governments lose interest in funding HIV research, although this seems unlikely in the immediate future.

Other elements pushing up the prices of drugs in the developing world include import duties, taxes, registration, distribution costs and dispensing fees. In April 2000, for example, it was reported that the registration fee for new drugs in Russia was \$12,000, "a strong disincentive for a company to enter a market that is not assured" says Richard Laing of the Boston University School of Public Health. [48] In South Africa there is a 14% value added tax on drugs (and condoms). Such charges have led, in some cases, to consumers paying up to five times the manufacturers' selling price for a drug, in comparison with double, as is the norm in the developed world. [49] In 1999, Health Action International and Consumers International found that the cost of 15 out of 18 dosage forms of 11 (antiretroviral and other) drugs were all higher in Africa, Asia and Latin America, in comparison with 10 wealthy countries in the Organization for Economic Co-operation and Development. [50] (These figures have been disputed by the pharmaceutical industry.)

As some factors push the price of drugs up, other factors bring prices down. Chief amongst these is competition. David Scondras of the Boston-based activist organisation Search for a Cure reported that in December 1998 Zidovudine could be bought from the US manufacturer (Glaxo Wellcome) \$0.42 for a 300mg dose, but was on sale in India for \$5.82, representing an increase of 1,285% for tableting, packaging, marketing and transportation. [55] At two doses a day, these figures are equivalent to \$306.60 a year at the manufacturer's price and \$4,248.60 at the retail price. In February 1999, the Indian version of the drug, Zidovir, manufactured by CIPLA, was reduced to Rs15 a dose (\$0.36 = \$260.71 a year), while the retail cost of the Glaxo Wellcome

The Case of AZT - and other drugs

The US patent for Zidovudine (AZT), which is due to expire in 2005, is held by Glaxo Wellcome. In 1991 the company's right to hold the patent, which includes sole rights for manufacturing and marketing the drug for HIV/AIDS, was challenged in court on the grounds that the company had not been entirely responsible for the development of the drug. There were no other antiretrovirals available and, with the support of treatment activists, other drug companies were seeking means of producing alternatives cheaper than the \$3,000 per year per patient that Glaxo Wellcome were charging for the drug.

The suit claimed that, while Burroughs Wellcome (the name of the company before its merger with Glaxo) were first to claim that the drug might be used against the virus, the publicly-owned National Cancer Institute (NCI) was at the time the only laboratory willing and able to screen agents for anti-HIV activity and provide documentation proving that Zidovudine was effective against HIV in pre-clinical trials. Because the NCI were not named as co-inventors, the suit claimed, the patent granted to Burroughs-Wellcome should be declared invalid. The National Institutes of Health (which incorporates the National Cancer Institute) agreed to allow these companies non-exclusive licenses to produce other versions if the NIH's rights to a claim on the patent could be proved. [51]

In February 1996, by refusing to hear appeals against earlier rulings, the US Supreme Court effectively recognised Glaxo Wellcome's claim as sole patent-holder. However, the ruling was only valid in the United States and alternatives to Zidovudine have been produced in Canada, India and elsewhere. In April 1999, the US price was reported as \$239 a month, compared to \$47 a month for the generic equivalent in India. [52]

Other antiretrovirals have also been at least partially developed by public or semi-public institutions. These include Bristol-Myers Squibb ARVs Videx (Didanosine - ddI), which was discovered by the National Institutes of Health, and Zerit (Stavudine - d4T), discovered by Yale University, which reportedly did not give the company an exclusive patent. [53] Meanwhile the US government-run National Institute of Allergy and Infectious Diseases (NIAID), claims that "pivotal to the approval of saquinavir [patent held by Hoffman-La Roche] were data from an NIAID-sponsored clinical trial known as AIDS Clinical Trials Group (ACTG) 229." [54]

product was Rs 49 a dose (\$1.17 = \$851.67 a year). [56] By April 1999, the Glaxo Wellcome version was reported as \$564 a year. [57]

While it may be true that prices fall in markets where there is competition, they are likely to rise again when competition is eliminated (a practice by no means restricted to the pharmaceutical industry or the developing world).

Global Capacity, Consumption and Profit

Of the over 200 countries and territories on the planet, only ten - eight countries in Europe plus Japan and the United States - have pharmaceutical industries with a significant research base. Another twelve industrialised countries and five in the developing world (Argentina, China, India, Mexico and South Korea) have an industry with some innovative capacity. A further six developed and seven developing countries are capable of producing both therapeutic ingredients and finished products, and another 80+ can produce finished products from imported materials. (1991 data) [58]

The pharmaceutical industry is thus heavily grounded in the North, and it is in the North where the industry has by far its greatest sales and profits. In 2002, it is expected that sales of pharmaceutical products will earn \$406 billion globally. \$190 billion (46.7%) of this will come from North America, \$101 billion (24.8%) from Europe and \$46 billion (11.3%) from Japan. The region of the world most in need of antiretrovirals - sub-Saharan Africa - contributes only \$5.3 billion (1.3%) to these sales, while the Indian sub-continent provides 1.8% (\$7.3 billion). [59]

As Richard Laing points out, the leading pharmaceutical industries have annual turnovers equivalent to the gross national product of many nations. Bayer's income in 1998 was \$30 billion, SmithKline Beecham's and Glaxo Wellcome's were both \$13 billion in the same year [60]; in 1997, Luxemburg, Slovenia and Slovakia all had GNPs under \$20 billion, while Panama, Jamaica and Jordan all had GNPs of under \$10 billion. Laing adds that the annual income from a single drug may be higher than the budget of an agency such as UNAIDS (\$70 million in 2000). Drugs are not the biggest earners, but Glaxo Wellcome's Zidovudine alone had sales of \$244 million in 1998. [61] Bristol-Myers Squibb's Zerit earned \$551 million [62] and while Pfizer was reported to earn \$1 billion from Diflucan, a treatment for fungal infections common to people with HIV. [63]

Sales are not the same as profit; nonetheless, pharmaceutical companies are among the most successful in the world. Shareholders in Bristol-Myers Squibb received a 43% return on their shares in 1998, prompting the comment "surely this can drop considerably before incentive is lost?" from Tim Frasca of the Chilean Corporation for the Prevention of AIDS (CChPS). [64] Meanwhile, the company chairman, Charles Heimbold, was reported to have been paid \$146 million in 1997 [65] - the equivalent of a year's supply of antiretrovirals for almost 15,000 people, and considerably more than the company's grant of \$100 million to Southern Africa announced in 1999.

Licensing Free Trade

With such large sums of money at stake, pharmaceutical companies naturally wish to protect their markets. One of the means by which they seek to do so is through protection of their patents under the international Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). TRIPS regulations are intended to bring uniformity to the question of intellectual property rights. They cover questions of copyright (ie the rights of creative artists), trademarks and patents, including the patents of medicinal drugs, and apply to all 137 members of the World Trade Organization (WTO).

TRIPS sets out the minimum standards of protection that must be provided to patents and patent-holders, while allowing nations at different levels of development differing periods of time to implement the necessary legislation. TRIPS also stipulates procedures to enforce intellectual property rights and determines that disputes between members must be resolved according to WTO's dispute settlement procedures. [66]

Among the articles of the Agreement of particular relevance to medicinal drugs are Article 33, which gives the holders of patents a minimum 20 years protection, and Article 27.1, which states that "patent shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced". In other words, governments cannot overrule a patent only on the grounds that it is needed for healthcare.

Taken alone, Article 27.1 implies that patentholders can exercise a worldwide monopoly. However, Article 30 allows governments to provide for exceptions to these exclusive rights, as in the 'Bolar Amendment', a provision in US law

Other Untreated Diseases

Purely commercial considerations are denying hundreds of thousands, perhaps millions of people, access to treatments for diseases other than HIV/AIDS, according to Médecins Sans Frontières (MSF - Doctors Without Borders). Drugs for infections primarily affecting the developing world, which has few financial resources, are either not manufactured or are only available at high cost. Among examples are:

- * no pharmaceutical company makes melarsoprol, a treatment for sleeping sickness, despite the fact that 300,000 contract the infection each year; other drugs for the same disease are also becoming scarce;
- * production of the drug treating neisseria meningitidis, which affects more than 100,000 people a year in Nigeria alone, is uncertain and not guaranteed;
- * only 13 (1%) of 1223 new drugs or drug components marketed between 1975 and 1997 were specifically for tropical diseases.

While short-term solutions to individual problems may be found - eg in 1997 an agreement was reached between MSF and the manufacturers of a drug combating shigella dysenteriae, a particularly virulent form of dysentery, for \$2 a treatment - sustainable long-term solutions may be more difficult. [67]

recognised by the WTO which allows generic manufacturers to prepare to enter a market immediately the patent lapses. Article 31 allows governments to override patents in cases of public interest, national emergency, anticompetitive grounds or other grounds defined by national law; the article also stipulates that the original patent-holder retains the right to manufacture and / or distribute the product, the assigned licence holder must pay a royalty to the original patent-holder and to use the licence predominantly for the domestic market. In other words, this action, known as compulsory licensing, allows governments in specific circumstances to grant the right to manufacture or commercialise a patented drug to another company.

For and Against

Compulsory licensing would seem to resolve many of the issues around the

high price of antiretrovirals. Drugs manufactured in-country could result in reduced production costs and profit margins and provide an element of competition to established brands. In the words of Jim Keon of the Canadian Drug Manufacturers Association, "compulsory licensing can be a very effective tool for a smaller country with an undeveloped pharmaceutical industry and limited resources." [68]

Pharmaceutical manufacturers, however, vigorously oppose compulsory licensing on the grounds that if protection for intellectual property (patents) is weakened, the incentive for innovation and to develop new drugs is lost. "The risk of [research and development] is largely borne by the research-based pharmaceutical, biotechnology and vaccine industries which will invest tens of billions of dollars annually," says the International Federation of Pharmaceutical Manufacturers Associations. [69] Other arguments put forward by the industry include the suggestion that some generic drugs, may be inferior to the originals (if, for example, they use different ingredients to enable the active element to be absorbed by the body). It is also claimed that compulsory licensing is not a sustainable strategy since it requires large-scale resources.

Overall, the industry says, the primary obstacle to access to medicines is the lack of health delivery system and that market exclusivity "does not grant unfettered discretion over pricing, which is a product of intense competition." [70] (The apparently contradictory statement that a drug which only one company makes is subject to competition, refers to competition with other drugs for the same condition.)

Those who argue in favour of compulsory licensing, such as Consumers International and Health Action International, do so on several grounds. Maintaining some drug patents at 20 years effectively means that developing countries will only have access to certain treatments 20 years later than the industrialised world; the ability to produce drugs locally would not only provide better access and therefore health for a country's population, but provide a manufacturing base for its economy. In conclusion, CI and HAI argue, research and development are important, but compulsory licensing protects both licence holders and those who need access to innovative drugs. [71]

Furthermore, those countries in the developing world which have no facilities to produce generic drugs, can import them from neighbours. This means, suggest activist Khalil Elouardighi of ACT-UP Paris [72] and academic Carlos Correa of the University of Buenos Aires [73], governments in such countries

can grant compulsory licenses to companies in the developed world and import the required drugs. Although not explicitly ruled out by TRIPS, such a move is likely to be resisted by nations with strong pharmaceutical industries and there are questions as to the extent to which generic products, which are supposed to be primarily for the domestic market, can be exported to other countries.

Potential Problems

Even supporters of compulsory licensing recognise that it can present problems. Nationally based manufacturers with a monopoly of a generic drug may keep prices high, may be unwilling to manufacture some drugs or may not have the necessary production facilities. In medium-sized or smaller countries, the potential market may not be large enough to warrant production. Manufacturing standards may be poor and, some suggest, the existence of generics could add to the problem of the production of counterfeit drugs. Even where prices are considerably lower than those of proprietary drugs, they may still be out of reach of the majority requiring treatment. (The \$260.71 a year for the Indian version of Zidovudine quoted above is 70% of the country's annual average income, and that drug represents the least expensive of the combination that a person with AIDS should take.)

Key Points From WHO

The World Health Organization "has consistently given five messages to highlight public health concerns in using patents for pharmaceuticals:

1. Patent protection stimulates development of needed new drugs, but countries must ensure a balance between the interests of the patent holders and the needs of society.
2. The Research & Development priority setting for pharmaceuticals and vaccines does not respond to the needs of the majority of people, therefore public involvement is needed to ensure development of new drugs for certain priority health problems.
3. Generic competition should begin promptly upon patent expiration.
4. Preferential pricing is necessary for lower-income countries and should be actively pursued.
5. Health regulations should not create technical barriers to trade." [74]

Born in the USA

The United States has the world's largest and most influential pharmaceutical industry. That industry has consistently lobbied the government to oppose compulsory licensing in other countries, despite the fact that the US itself has used compulsory licences. [75]

In 1999, the US Government was said to be in dispute with a number of countries over pharmaceutical products, including opposition to parallel importing; opposition to patent exemptions or compulsory licensing agreements; opposition to Health Registration Data - registering data on drugs not under patent; proposing extension of patents on particular drugs when the patent has expired; disputes over generic drug substitution and the use of generic names; opposition to national price controls. [76] US pressure on South Africa in 1999 to reject compulsory licensing was widely reported and allegedly included threats to aid programmes. [77]

In a change of heart in May 2000, an executive order from President Clinton promised that United States officials would not stand in the way of developing countries that sought to obtain generic drugs for their citizens. While US Trade Representative Charlene Barshefsky called the order a "very substantial" policy change [78], others pointed out that it was no more than reaffirming the country's support for TRIPS and that no effective change of policy had taken place. Indeed, later that month at the World Health Assembly (WHO's governing body), the US strongly opposed measures proposed by Brazil and Zimbabwe that would have published data identifying the cheapest drugs worldwide.

Nor is the United States the only government that appears to be opposing wider access to treatment. The Swedish government also attempted to block clauses in the WHA resolution that would have opened up the issue, while Act-Up Paris, in a press statement released three days before the Clinton executive order, charged the US and the European Union with a campaign of "disinformation, blackmail, threatened lawsuits, bilateral pressure, economic repressive methods etc... to dissuade poor countries from having recourse to the conditions permitted by the TRIPS agreement and to maintain a monopoly of Western laboratories over the production and marketing of treatments". [79]

Chris Green, of WartaAIDS in Indonesia, argues "there is no evidence that local manufacturers... are any more 'community-minded' than the big multinationals. ... I'd be surprised if compulsory licensing on average reduced consumer prices by even 50%, let alone the 99% needed to make ARV drugs widely accessible" - a point also made by pharmaceutical companies. Green goes on to point out that national manufacturers may be less stable than transnational companies; the number of generic drugs manufactured in Indonesia fell from 225 in January 1998 to 116 in September that year as a result of economic recession. [80]

Despite these qualms, it may be, as some activists claim, that the principal reason behind the pharmaceutical industry's opposition to compulsory licensing is not the threat to research and development that they allege, but the fear that it sets a precedent for similar moves for antiretrovirals and other drugs in countries where substantial profits are at stake.

Furthermore, as noted above, given that the pharmaceutical companies' primary business is in the industrialised world and they make few sales in those developing countries that most need antiretrovirals, compulsory licensing should make little or no difference to their income - and may even increase profit. Production and distribution of a generic drug in a particular country does not automatically result in the multinational patent holder losing all its market and, when a compulsory licence is awarded, the generic company must pay the patent company a royalty. Pharmaceuticals may make more money from compulsory licensing than without it - in particular since no more than 1.3% of their income currently comes from sub-Saharan Africa and 1.8% from the Indian sub-continent,

In summary, compulsory licensing is opposed by the pharmaceutical industry on the grounds that it threatens the profit basis of research and development, but supported by many other organisations and governments who believe that it is essential in extending access to treatment and that it may threaten monopolies but does not threaten profits or development.

Alternatives

The prices of pharmaceutical products can also be brought down by other means:

Preferential Pricing

offering lower standard prices to poorer countries

In essence, the higher prices paid in wealthier countries subsidise the cheaper

prices paid in the developing world. Two potential problems arise from this strategy. The first is that prices may not fall enough. The second is that consistently lower prices in the developing world will put pressure on prices in the North, especially if other countries can use parallel importing (see below) to buy the cheaper drugs. If consumers globally insist on a single price, it is likely to be near Western rather than African or Asian levels.

Preferential pricing is one of UNAIDS' key strategies and lies behind the joint announcement by five leading pharmaceutical companies in May 2000 that they would supply cheaper drugs to the developing world through the agency. The implicit message is that such a strategy reduces prices for those who need them, while making it less likely that the drugs will be diverted to the black market, particularly in the developed world. Manufacturers of some treatments for opportunistic infections such as Flucanazole from Pfizer for cryptococcal meningitis, have also announced price cuts in some parts of the developing world, although there has been disagreement as to the real impact of such moves.

Parallel Importing

bypassing established distribution mechanisms to buy directly from the manufacturer or a third party

Parallel importing occurs when a wholesaler in one country supplies a product, such as a drug, at a lower price than a wholesaler elsewhere. This is possible because the first wholesaler receives a higher discount from the manufacturer or because they carry a lower profit margin or both.

The United States has placed strong pressure on countries wishing to adopt parallel importing, most recently (May 2000) in Israel where, according to the newspaper Ha'aretz, "the US estimates that it stands to lose \$100 million annually and claims that the new law legitimizes violations of intellectual property and patents belonging to drug companies". [82] Ironically, given the practice of free trade within its borders, the European Union was also reported to be placing severe pressure on various Israeli ministries to get them to back down from the law. Meanwhile, foreign pharmaceutical companies reportedly threatened economic sanctions on the country if it began parallel imports.

Therapeutic Value Pricing

regulation of prices by government body

In Australia, an independent body considers the price the government is prepared to pay for new drugs, based on the therapeutic value compared to existing drugs. If the new drug adds a benefit, the government may offer a percentage more for the

Cheaper in Canada

Canada is one country that has made extensive use of compulsory licensing. In 1969 Canadian legislation licensed indigenous companies to manufacture generic drugs on payment of a 4% royalty to the patent holder. According to Jim Keon of the Canadian Drug Manufacturers Association, this lowered drug prices within Canada, saving hundreds of millions of dollars and led to the development of an export industry to less developed countries that could not afford the patented versions. By the mid-1980s, the legislation was under pressure from multinational companies and it was eventually abolished in 1991, partly to comply with the demands of the North American Free Trade Association (NAFTA, comprising Canada, Mexico and the US).

The result has been, Keon claims, rising drug prices and major cash shortages in the country's national health system. [81] Nevertheless, prices of many drugs remain lower in Canada than in the neighbouring United States and many US citizens "border-hop" to buy cheaper drugs as prices in their own country rise dramatically. In the first half of 2000, a number of legislative initiatives were proposed to reduce the cost of drugs in the United States - perhaps the first sign that opposition to pharmaceutical pricing policies was found at home as well as abroad.

new drug. The manufacturers can negotiate the price. Although effective where manufacturers have or expect significant sales, the potential drawback to this approach is that elsewhere such regulation may lead to the drugs in question being withdrawn.

Pooled Procurement / Negotiated Procurement

Costs can be reduced when several small countries negotiate together, as happens in the Caribbean, or when a country negotiates reductions for bulk purchases.

Further suggestions that have been made by activists to increase access to treatment in the South include

Donations

Manufacturers can be encouraged to donate stock within the use-by date on a planned basis to developing countries.

CRADAs

Co-operative Research and Development Agreements are a US mechanism that allow for joint research between private parties and government agencies; patent-holder rights are subject to agreement. It has been suggested that developing country manufacturing companies could enter into these agreements in the same way as ones from developed countries do, ensuring a greater level of production and manufacture in the South. [83]

Can it work?

"Too often, manufacturers who should be working to reduce prices are busy blaming unreliable supply systems; policy-makers in a position to influence drug financing are busy blaming high prices; and health care managers who could improve supply systems are busy blaming inadequate financing. Instead, all parties should be working toward a common solution - each contributing constructively from their own political, technical and economic perspectives," says Michael Scholtz, Executive Director of Technology and Pharmaceuticals at the World Health Organization. [84]

Scholtz's comments reflect a frustration felt by many. It is true that as a result of the various strategies described here, costs have been reduced in a number of countries, but nowhere near the extent that universal access to treatment is available. As discussed earlier, prices need to fall to at least a twentieth of current levels (ie by 95%) to be within the reach of impoverished governments and individuals. Intermediate price cuts - eg to 50% or 20% of current levels - are a step in that direction, but not enough in themselves.

Stephen Chandiwana of the Medical Research Council of Zimbabwe, and a member of the South African President's advisory committee on AIDS, says that if prices are cut to the extent suggested by the May 2000 preferential pricing announcement, only the middle-class would benefit, while others in Zimbabwe warned that corruption would result in many drugs being stolen for the black market. [85]

Compulsory licensing, preferential pricing and parallel importing in themselves are not the complete solution to the problem of providing full access to treatment for AIDS - questions of production capacity, national monopolies and manufacturing standards and the threats of counterfeiting and the black market still have to be resolved - but they are essential components of the solution. Given the relatively small proportion of sales and profits that the pharmaceutical companies generate in

most of Africa and Asia, compulsory licensing in particular would seem to represent on the one hand no threat, and on the other a potential source of income considerably greater than that which they currently receive.

The warmth that greeted the May 2000 announcement was tempered in the following weeks as only the price of only one treatment appeared to fall: Combivir would be available at \$2 a day in the developing world - roughly a fifth of the US price. The announcement was good public relations which threatened to turn sour; if actual price cuts follow, it will be the first indication that the industry is adopting a more sophisticated approach to the problem than blanket opposition to change. Even then, there will still be a long way to go before the needs of those who are ill are fully met.

WHO PAYS?

The money to pay for antiretrovirals or improving health services may come from a variety of sources: national, state, district or municipal governments, foreign governments through aid programmes, commercial institutions, national or private insurance schemes, individuals and families or households. These sources are interlinked - eg insurance schemes depend on contributions from individuals or institutions, national health budgets depend on individual and institutional taxes - and the more widely that costs are spread, the less of a burden is placed on the individuals least able to bear it. Access to treatment for AIDS will only be universally available when wealthier nations and institutions assume a far greater proportion of existing costs and work towards reducing costs wherever possible.

Only when direct costs (antiretrovirals, tests, consultations etc) are reduced to no more \$250 a year will it begin to be feasible for large numbers of the world's poor to pay for their own treatment - and even then that sum is higher than the average annual income in many countries. Whether or not costs can be reduced that far or further depends on the extent to which governments, international agencies and pharmaceutical manufacturers can work together.

Too little, too late

Some Southern governments can subsidise the cost of antiretrovirals to a greater or lesser extent, as can be seen from Brazil and Senegal. Concentration on that aspect of the problem, however, should not distract from the cost of improving health services, which can only be met by governments. And since the governments where the problem is worst do not have the resources to resolve it, the bulk of funding must come from wealthier countries and the institutions, such as the World Bank, that they support.

However, funding at the level required is not on the horizon. In 1999 the industrialised world provided \$350 million for AIDS prevention and care activities [86], a sum which represents one third the total expenditure required in Zambia, a country of ten million people where one in five adults is HIV-positive. Most of this \$350 million went towards prevention; a small proportion went to organisations working in the South, but headquartered in the North. An additional \$590 million was spent by national governments, primar-

ily Brazil and Thailand. Only \$140 million was spent in sub-Saharan Africa - less than \$7 per person with HIV. Apart from Brazil, which spent \$300 million on treatment, including antiretrovirals, in 1999 [87] these sums almost all reflect spending on prevention.

In early 2000, a number of initiatives were underway to significantly step up the industrialised world's response to the epidemic. The World Bank and United States announced an initiative that would increase global expenditure to \$1 billion over five years and several European countries announced rises in their contributions. However, much of this money will go towards prevention, not treatment. Prevention is of course essential, but it does not meet the needs of those whom past prevention campaigns failed to reach. Furthermore, prevention without care is ineffective, because if a community does not take care of people who have a disease - whether AIDS, tuberculosis or any other illness - those with the disease or at risk of contracting it have no incentive to protect themselves or others.

The advent of antiretrovirals has led to different responses in Northern governments. A number of countries fund ARVs on a short term basis to prevent transmission from mother to child, but fewer support long-term antiretroviral programmes. The Danes (who partly financed this report) believe that health infrastructures are not strong enough and the numbers involved are too great to make subsidies of ARVs an effective use of their limited funds. British policy is to prioritise vaccine research rather than antiretrovirals. Others, such as the French, provide funding for ARVs, although the numbers who benefit remain small.

War and Debt

Even if the industrialised world were to spend \$1 billion a year, that sum would match only a small fraction of the cost of antiretrovirals at current prices. And the chances of the United States diverting \$60 billion a year from its military budget to help people with AIDS is remote. There is, however, one source of funding which theoretically matches necessary expenditure in many countries for the first year or two: external debt.

Fifty-two of poorest countries in the world, including 37 in Africa, owe a total of \$376 billion. [88] At \$28.5 billion Nigeria's foreign debt is three times the estimated cost of improving infrastructures and providing treatment to all who

need it at 10% of current costs; Uganda's \$3.7 billion debt is 1.3 times such costs and Zambia's \$6.8 billion debt five times such costs. Although some of this debt is to private banks, the majority is owed to foreign governments, the World Bank and the International Monetary Fund. A number of governments in the North have expressed a wish to cancel their portion of the poorest nations' debts, but the process is proving long and frustrating.

Cancelling or transferring debt is not an instant solution. Debt does not represent cash in hand but money as yet to be earned. Nevertheless, an accelerated approach to debt relief, combined with improvements in health services and reduced costs of drugs, could go a long way towards getting effective treatment to those who need it. The Zambian government, for example, has proposed transferring its \$123 million a year paid in debt servicing (repaying interest, not capital), a sum equivalent to 69% of its social services budget, to HIV/AIDS prevention and care activities under performance indicators agreed with the creditor nations. [89]

Unwilling to Wait

Understandably, those who have HIV are unwilling and those who have AIDS are unable to wait for the results of long-term measures and lengthy negotiations. Thousands of individuals like Leonora in Nicaragua (pXX) and Charles in Zambia (pXX) struggle on a daily basis to find the drugs that will keep them alive; millions more would join them if they could. It is certain, therefore, that the number of people who get hold of antiretroviral drugs will continue to rise. Some will do so through government-sponsored schemes, many others will pay for tablets and powders out of their own pockets, through more or less legal distribution systems. The pharmaceutical industry, WHO, medical experts and governments North and South may disapprove of the practice, citing loss of profit and fears of toxicity and resistance, but such disapproval will not stop those who see their choices as either taking whatever pills they can find or dying an early death. The question now is whether to ignore or prevent such a situation or to build upon it.

Last Words

Abdou Fall, Senegalese Health Minister:

"since use of antiretrovirals began, there has been an increase in the numbers visiting our testing centres. ... there is an even larger need for treatment which will have to be responded to, so that hope can be reinforced and the dynamics of prevention reinforced." [90]

Jeff O'Malley of the International HIV/AIDS Alliance:

"the evidence points overwhelmingly to a focus on opportunistic infections and pain relief as the immediate priorities to save lives and to improve quality of life over the next few years at least." [91]

Jens Van Roey, former programme development officer with UNAIDS:

"priority should be given to access to basic primary health care including such obvious things like oral rehydration sales, antimalarials, antipyretics [for relief of headaches], painkillers and most important tuberculostatics." [92]

International Federation of Pharmaceutical Manufacturers Associations:

"a set of principles that reflect a common vision of how the HIV/AIDS epidemic can be more effectively tackled in developing countries:

- * political commitment by national governments;
- * strengthened national capacity;
- * engagement of all sectors of national society and the global community;
- * efficient, reliable and secure distribution systems;
- * significant additional funding from national and international sources; and
- * continued investment in research and development by the pharmaceutical industry based on internationally-based rules for intellectual property rights." [93]

Chatinkha Nkhoma, Malawian AIDS activist:

"What is good for the goose must be good for the good for the gander. America and Europe felt the need to put into place wide access to anti-retroviral drugs. Why is something different expected of Africa and Asia? Please spare me the old, stale and sour story of being poor and unable to afford them. We can never to hope to conquer AIDS if we do not provide proper treatment for everyone living with AIDS, wherever they live." [94]

FOR FURTHER RESEARCH

www.aegis.com

"the largest HIV/AIDS knowledge base on the world wide web"

www.aidsmap.com

site dedicated to treatment for HIV/AIDS

Consumer Project on Technology

"Intellectual property rights, health care, and electronic commerce"

P.O Box 19367, Washington DC 20036, USA

www.cptech.org

Tel: +1 202 387 8030, Fax: +1 202 234 5176

Global Network of People living with HIV/AIDS (GNP+)

P.O Box 11726, 1001 GS Amsterdam, Netherlands

www.hivnet.ch/gnp

Tel: +31 20 423 4114, Fax: +31 20 423 4224

gnp@gn.apc.org

Health Action International

"an informal network of more than 150 groups involved in health and pharmaceutical issues in more than 70 countries"

c/o HAI Europe, Jacob van Lennepkade 334-T, 1053 NJ Amsterdam, Netherlands

www.haiweb.org

Tel: +31 20 683 3684, Fax: +31 20 685 5002

HAI@HAI.ANTENNA.NL

www.healthgap.org

"Bridging the Gap in Access to Medicines,"

International Council of AIDS Service Organisations

399 Church Street, 4th Floor, Toronto ON, M5B 2J6, Canada

www.icaso.org

Tel: +1 416 340 2437, Fax: +1 416 340 8224

richardb@icaso.org or maryannt@icaso.org

International Federation of Pharmaceuticals and Manufacturers Association

30 rue de St-Jean, PO Box 758, 1211 Geneva 13, Switzerland
www.ifpma.org
Tel: +41 22 338 3200, Fax: +41 22 338 3299

UNAIDS (Joint United Nations Programme on HIV/AIDS)

20 avenue Appia, CH - 1211 Geneva 27, Switzerland
www.unaids.org
Tel: +41 22 791 3666, Fax: +41 22 791 4187
unaids@unaids.org

Médecins Sans Frontières (Doctors Without Borders)

Rue de la Tourelle 39, Brussels 1040, Belgium
www.msf.org
Tel: +32 2 280 1881, Fax: +32 2 280 0173

www.thebody.com

"use the Web to lower barriers between patients and clinicians; demystify HIV/AIDS and its treatment; improve patients' quality of life."

World Health Organisation

20 avenue Appia, 1211 Geneva, Switzerland
www.who.int
Tel: +41 22 791 2111; info@who.ch

World Intellectual Property Organisation

P.O Box 18, CH 1211 Geneva 20, Switzerland
www.wipo.int
Tel: +41 22 338 9111, Fax: +41 22 733 5428
wipo.mail@wipo.int

World Trade Organisation

Rue de Lausanne 154, CH-1211 Geneva 21, Switzerland
www.wto.org
Tel: +41 22 739 5007, Fax: +41 22 739 5792
enquiries@wto.org

INDEX AND DEFINITIONS

AIDS	Acquired Immune Deficiency Syndrome: p1
antiretroviral	a substance that acts against retroviruses: p6
Bolar Amendment	p37
CD4 cells	A type of blood cell, also known as T-helper cells or T-cells; p4
CD4 count	p4
combination therapy	administering more than one drug for a specific disease; p7
compulsory licensing	p38
cross-resistance	p9
direct costs	(in this report) the costs of health care directly attributable to individual patients: p21
DNA	deoxyribonucleic acid: the material in the centre of a cell where genetic information is stored
FDA	(United States) Food and Drug Administration; p32
generic (drugs)	p32
genotype	the genetic composition of an organism
HIV	Human Immunodeficiency Virus
HIV-positive	having contracted HIV / living with HIV
immune system	the mechanisms to protect the body from disease
indirect costs	(in this report) the costs of health care shared among the whole population: p21
infrastructure	the basic structure and system of an organisation; health infrastructure: p21
monotherapy	administering one drug for a disease; p8
opportunistic infections	p5
palliative	relieving symptoms
parallel importing	p43
phenotype	a characteristic feature resulting from a genotype
prophylaxis	prevention of a disease
preferential pricing	p42
proprietary (drugs)	under patent; p32
regimen	drugs for a specific condition and the means and hours of taking them
replicate	reproduce (used of viruses)
retrovirus	a virus which uses RNA to make DNA

RNA ribonucleic acid. An organic compound storing genetic information

TRIPS Agreement on Trade-Related Aspects of Intellectual Property; p37

UNAIDS the Joint United Nations Programme on HIV/AIDS co-ordinates the global response to HIV/AIDS. UNAIDS is sponsored by seven UN agencies: the UN Children's Fund (UNICEF), UN Development Programme (UNDP), UN Educational, Scientific and Cultural Organization (UNESCO), UN International Drug Control Programme (UNDCP), UN Population Fund (UNFPA) the World Bank and the World Health Organization

viral load a measure of the amount of virus in a body; p 3

virus a micro-organism capable of independent life and reproduction within a living cell. Most viruses store the genetic information they need to reproduce in DNA. Retroviruses, such as HIV, store their genetic information in RNA

WHO World Health Organization

WTO World Trade Organization; p37

TAF refers to the listserv Treatment Access Forum, GAF to Gender AIDS Forum. These can be consulted on www.hivnet.ch/e/index-frame.html, following the path Welcome-HealthDev-Topic Specific-Treatment Access or Gender AIDS. Individual TAF messages can be found on www.hivnet.ch:8000/topics/treatment-access/view?XXX, substituting the number of the message for XXX.

- 1 For evidence that HIV is the cause of AIDS, see www.niaid.nih.gov/spotlight/hiv00/default.htm or www.aegis.org/topics/aids_debate.html.
- 2 "The Rationale of Essential Drugs", WHO 8 Dec 1999; www.who.int/medicines/edm-concept.html.
- 3 TAF [813] 10 May 2000.
- 4 AIDS and the Third World, Panos, London and Washington DC, separate editions in 1986, 1987, 1988.
- 5 Human Development Report 1999, UNDP, New York & Oxford, p77; however, some reports suggest that men in relationships live longer than single men and single women live longer than women in relationships.
- 6 "A UNICEF analysis identifies caring as the third underlying factor in preventing child malnutrition." Human Development Report 1999, UNDP, New York & Oxford, p77.
- 7 The initial test indicates the presence of antibodies to HIV, rather than of the virus. However, except in the case of new-borns, when antibodies may have been inherited from the mother, the presence of antibodies is interpreted as presence of the virus itself.
- 8 Some medical experts define 'infections' more narrowly than is used here; nonetheless all these conditions are associated with AIDS.
- 9 Apart from tuberculosis, the frequency of symptoms in this section is from Access to drugs, UNAIDS Technical Update, October 1998, p3.
- 10 Tuberculosis and AIDS: the Dual Epidemic UNAIDS Points of View, 1997, p2.
- 11 Access to drugs, UNAIDS Technical Update, October 1998, pp5-6.
- 12 Taking heart? The impact of combination therapy on the lives of people with HIV (phase 2), Sigma Research, London, 1999, p20
- 13 Taking heart? The impact of combination therapy on the lives of people with HIV (phase 2), Sigma Research, London, 1999, pp24-5.
- 14 "New Deadlier HIV/Multidrug - Resistant Strains Worry 3 Research Teams", Newsday, New York, 22 September 1999, quoted in International AIDS Forum 28 September 1999.
- 15 National Health Strategic Plan 1998 - 2000, Republic of Zambia Ministry of Health.
- 16 Sector Wide Approach to Health: A proposed Health Sector Investment Programme (2001-2005), unpublished paper.
- 17 World Development Indicators 2000, World Bank, Table 2.14.
- 18 Human Development Report 1999, UNDP, Table 9.
- 19 World Development Indicators 2000, World Bank, Table 2.14.

- 20 "The impact of HIV/AIDS on hospital services in developing countries - will service breakdown ensue?", G Arthur and others, *AIDS Analysis Africa*, 10(6) Apr/May 2000, pp15-16.
- 21 "AIDS Devastates Health Sector in Africa," UNAIDS press release 7 May 2000.
- 22 "The impact of HIV/AIDS on hospital services in developing countries - will service breakdown ensue?", G Arthur and others, *AIDS Analysis Africa*, 10(6) Apr/May 2000, pp15-16
- 23 www.who.int/medicines/edl.html.
- 24 Access to drugs , UNAIDS Technical Update, October 1998, p5.
- 25 Access to drugs, UNAIDS Technical Update, October 1998, p5.
- 26 *Confronting AIDS*, World Bank / Oxford University Press, 1997, p177.
- 27 Figures based on research by UNAIDS Care and Support Team, May 2000
- 28 Figures based on research by UNAIDS Care and Support Team, May 2000
- 29 TAF [777] 13 April 2000, Ann Parsons.
- 30 TAF [793] 26 April 2000 and personal correspondence.
- 31 HealthGAP mailing list 27 May 2000, Richard Stern.
- 32 Guidance Modules on Antiretroviral Treatments, UNAIDS/WHO, 1998, module 2, p6.
- 33 In fact, it is likely that proportionately more people will have contracted the virus in recent years and that number initially requiring antiretrovirals would be lower.
- 34 Guidance Modules on Antiretroviral Treatments, UNAIDS/WHO, 1998, Module 1, p9.
- 35 Adapted from Guidance Modules on Antiretroviral Treatments, UNAIDS/WHO, 1998, Module 3, p3.
- 36 San Francisco Chronicle/Examiner Online, quoted in TAF [856] 31 May 2000.
- 37 Suzana Murni, quoted in *Echidno* 19, 1998, reprinted in *AIDS Action Southern Africa Edition*, September - December 1999.
- 38 *New Scientist*, London, 29 April 2000.
- 39 Guidance Modules on Antiretroviral Treatments, UNAIDS/WHO, 1998, Module 2,
- 40 Presentation by Richard Laing, Boston University School of Public Health at AIDS and Essential Medicines and Compulsory Licensing Conference, Geneva, 26-27 March 1999, quoted on TAF [386] 1 April 1999.
- 41 IFPMA statement 26 March 1999.
- 42 Miller H, *Nature*, vol 395, p835 (1998)
- 43 "Cost of innovation in the pharmaceutical industry", J A DiMasi and others, *Journal of Health Economics*, vol 10, 1991, pp107-142.
- 44 Love, J, *Nature*, vol 397, p202 (1999)
- 45 *Wall Street Journal*, 1 May 1996.
- 46 www.cptech.org/ip/health/aids/sizeoftrials.html
- 47 HealthGAP correspondence, 14 June 2000
- 48 TAF [768] 6 April 2000, Richard Laing, Boston University School of Public Health.
- 49 Presentation by Michael Scholtz, Executive Director of Health Technology and Pharmaceuticals, WHO, at AIDS and Essential Medicines and Compulsory Licensing Conference, Geneva, 26-27 March 1999.
- 50 "Patents & Prices A draft discussion document" K Bala & Krian Sagoo, draft discussion document for International Conference on Increasing Access to Essential Drugs in a Globalised Economy, Amsterdam 25 - 26 November 1999.
- 51 'Generic Drug Companies and NIH Denied AZT Patent Appeal', *Antiviral Agents Bulletin*, February 1996, quoted in TAF [303] 8 January 1999.
- 52 Presentation by Richard Laing, Boston University School of Public Health at meeting on AIDS and Essential Medicines and Compulsory Licensing, Geneva, 26 - 27 March 1999, reported in TAF [386] 1 April 1999.
- 53 TAF [460] 11 May 1999, Eric Sawyer, Act Up New York.
- 54 www.niaid.nih.gov/publications/agenda/0396/page4.htm.
- 55 TAF [331] 28 January 1999, David Scondras .
- 56 *Financial Express*, *Indian Express Newspapers (Bombay) Ltd*, 8 February 1999.
- 57 Presentation by Richard Laing, Boston University School of Public Health at meeting on AIDS and Essential Medicines and Compulsory Licensing, Geneva, 26 - 27 March 1999, reported in TAF [386] 1 April 1999.
- 58 1991 figures. *The World's Pharmaceutical Industries: An International Perspective on Innovation, Competition and Policy*, R Balance and others, UNIDO, 1992.
- 59 Information from IMS Health: www.ims-global.com/insight/report/global/report.htm.
- 60 Presentation by Richard Laing, Boston University School of Public Health at AIDS and Essential Medicines and Compulsory Licensing Conference, Geneva, 26-27 March 1999, quoted on TAF [385] 1 April 1999.
- 61 Presentation by Richard Laing, Boston University School of Public Health at AIDS and Essential Medicines and Compulsory Licensing Conference, Geneva, 26-27 March 1999, quoted on TAF [385] 1 April 1999
- 62 www.sec.gov/Archives/edgar/data/14272/0000014272-00-000002-index.html.
- 63 TAF [746] 15 March 2000, Eric Sawyer, Act Up New York.
- 64 TAF [404] 16 April 1999, Tim Frasca.
- 65 philanthropy-journal/giving/bizleaders1222.cfm (no longer active) 22 December 1998, quoting the *New York Times* and quoted in TAF [460] 11 May 1999.
- 66 The full text of the agreement is available on the World Trade Organization website, www.wto.org, which was being reformatted as this report went to press.
- 67 "Access to Essential Drugs in Poor Countries: A Lost Battle?" Bernard Pécoul and others, *Journal of the American Medical Association*, 27 January 1999, vol 281, no 4, pp361-367.
- 68 Address to meeting on AIDS and Essential Medicines and Compulsory Licensing, Geneva, 26 - 27 March 1999, quoted on TAF [414] 20 April 1999

- 69 "Public Health and Compulsory Licensing" IFPMA statement 26 March 1999, quoted on TAF [400] 14 April 1999.
- 70 "Public Health and Compulsory Licensing" IFPMA statement 26 March 1999, quoted on TAF [400] 14 April 1999.
- 71 Points taken from Statement of Consumers International delivered by Ellen 't Hoen on Agenda item 12 of the 52nd World Health Assembly: Revised Drug Strategy, quoted on TAF [492] 22 May 1999,
- 72 TAF [541] 30 June 1999.
- 73 Integrating Public Health in Patent Legislation in Developing Countries, Carlos Correa, University of Buenos Aires January 2000, unpublished.
- 74 Michael Scholtz, Executive Director Health Technology and Pharmaceuticals WHO, Presentation at Conference on Increasing Access to Essential Drugs in a Globalized Economy, Amsterdam, 25 - 26 November 1999.
- 75 TAF [387] 8 April 1999, Evelyne Laissu.
- 76 Open letter to Charlene Barshefsky, US Trade Representative from James Love, Ralph Nader and Robert Weissman, quoted on TAF [606] 8 October 1999.
- 77 TAF [395] 13 April 1999.
- 78 "US Pledges AIDS Drug Help for Southern Africa" Reuters report 10 May 2000.
- 79 "OAU et SIDA: Act Up-Paris appelle les pays Africains à entrer en résistance contre l'industrie pharmaceutique" Press release reproduced on SAFCO [53] 7 May 2000.
- 80 TAF [527] 23 June 1999.
- 81 Address to meeting on AIDS and Essential Medicines and Compulsory Licensing, Geneva, 26 - 27 March 1999, quoted on TAF [414] 20 April 1999.
- 82 Ha'aretz 31 May 2000
- 83 TAF [457] 10 May 1999, Thomas Poe, director, World Center for Clinical Research.
- 84 Presentation at Conference on Increasing Access to Essential Drugs in a Globalized Economy, Amsterdam, 25 - 26 November 1999.
- 85 Financial Gazette, 18 May 2000.
- 86 "Funding of AIDS efforts not keeping pace with epidemic", UNAIDS press release, 22 April 1999.
- 87 The AIDS epidemic: situation in December 1999, UNAIDS, p10.
- 88 Figures from the Jubilee 2000 debt cancellation campaign;
www.jubilee2000uk.org/faq.html.
- 89 Times of Zambia, 23 May 2000.
- 90 SAFCO [74] 24 May 2000.
- 91 TAF [336] 5 February 1999.
- 92 TAF [343] 19 February 1999.
- 93 IFPMA Press Release, 11 May 2000.
- 94 Personal communication.