HIV-related opportunistic diseases

UNAIDS Technical update

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UNAIDS *Best Practice* Collection

At a Glance

- Opportunistic diseases in a person with HIV are the products of two things: the person's lack of immune defences caused by the virus, and the presence of microbes and other pathogens in our everyday environment.
- A partial list of the world's most common opportunistic diseases and diseases includes:
  - *bacterial diseases* such as tuberculosis (TB, caused by *Mycobacterium tuberculosis*), *Mycobacterium avium* complex disease (MAC), bacterial pneumonia and septicaemia ("blood poisoning")
  - *protozoal diseases* such as *Pneumocystis carinii* pneumonia (PCP), toxoplasmosis, microsporidiosis, cryptosporidiosis, isosporiasis and leishmaniasis
  - *fungal diseases* such as candidiasis, cryptococcosis (cryptococcal meningitis (CRM)) and penicilliosis
  - *viral diseases* such as those caused by cytomegalovirus (CMV), herpes simplex and herpes zoster virus
  - *HIV-associated malignancies* such as Kaposi sarcoma, lymphoma and squamous cell carcinoma.
- Effective intervention against opportunistic diseases requires not only the appropriate drug or other medications for a given medical condition, but also the infrastructure necessary to diagnose the condition, monitor the intervention, and counsel patients. As well, use of drugs and tests must be supported by proper storage, handling and administrative procedures.
- The main challenge of choosing between interventions is to alleviate the morbidity and suffering of those in need while not exceeding the financial and technical capabilities of the health system. Unfortunately, these choices often need to be made *without the help of formal cost-benefit and cost-effectiveness analyses*. This is partly because the information needed to calculate costs is difficult to collect, but also because benefits other than short-term improvements in quality of life are not well understood or easily quantified.
- In places where resources are very scarce, priority should be given to health needs shared by most or all of the population, including those who are HIV-infected. Examples are drugs to relieve pain in terminal patients—including those with AIDS—or for TB. Drugs to treat and prevent TB have a high overall value to society in many countries because they (a) benefit people affected by two epidemics (HIV/AIDS and TB), (b) are proven effective and (c) are relatively inexpensive given the number of people who can benefit.
- Only a few opportunistic diseases and symptoms such as oropharyngeal and vaginal candidiasis ("thrush") or herpes zoster and herpes simplex can be managed effectively through home-based care. Most other opportunistic diseases require diagnosis and treatment which are beyond the capabilities of most community-based groups and NGOs.
- For conditions that can be treated only at a very high cost, the public-health rationale for treatment is weaker, and humanitarian or equity considerations become more important. Examples of such conditions are CMV, MAC, cryptococcal meningitis (CRM), penicilliosis and rarer systemic mycoses.

UNAIDS *Best Practice* materials

The Joint United Nations Programme on HIV/AIDS (UNAIDS) is preparing materials on subjects of relevance to HIV infection and AIDS, the causes and consequences of the epidemic, and best practices in AIDS prevention, care and support. A *Best Practice* Collection on any one subject typically includes a short publication for journalists and community leaders (Point of View); a technical summary of the issues, challenges and solutions (Technical Update); case studies from around the world (*Best Practice* Case Studies); a set of presentation graphics; and a listing of key materials (reports, articles, books, audiovisuals, etc.) on the subject. These documents are updated as necessary.

Technical Updates and Points of View are being published in English, French, Russian and Spanish. Single copies of Best Practice materials are available free from UNAIDS Information Centres. To find the closest one, visit UNAIDS on the Internet (http://www.unaids.org), contact UNAIDS by email (unaids@unaids.org) or telephone (+41 22 791 4651), or write to the UNAIDS Information Centre, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

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Background

People with advanced HIV infection are vulnerable to infections or malignancies that are called "opportunistic" because they take advantage of the opportunity offered by a weakened immune system. Various treatments and prophylaxis—some simple and low-cost, others highly complex and expensive—exist to counter the most common opportunistic diseases, but delivery systems and funding are insufficient in many parts of the world to ensure their universal use.

The worldwide distribution of opportunistic diseases is highly varied. Table 1 shows data on their distribution in six countries from Africa, the Americas, and South-East Asia. Like the following brief overview of the most common diseases and the interventions available for their treatment or prevention, the table is only intended to give a sense of the wide differences from country to country.

Table 2 provides a comparison of costs of treatment and prophylaxis for the most common opportunistic diseases.

Candidiasis

The two main types of candidiasis are localized disease (of the mouth and throat, and of the vagina), and systemic disease (of the oesophagus, and disseminated disease). The mouth and throat variant (oropharyngeal candidiasis or OPC) is believed to occur at least once in the lifetime in all HIV-infected patients.

While OPC is not a cause of death, it causes oral pain and makes swallowing difficult. The symptom of oesophageal candidiasis is pain in the chest that increases with swallowing, and difficulty in swallowing. Disseminated candidiasis causes fever and symptoms in the organs affected by the disease (for example, blindness when it affects the eyes).

Localized disease is treated first with relatively inexpensive topical drugs such as nystatin, miconazole, or clotrimazole. Systemic antifungals agents are usually given only when topical therapy fails.

Systemic candidiasis requires treatment with systemic antifungal agents such as ketoconazole, itraconazole, fluconazole or amphotericin B. A two-week course of ketoconazole 200 mg costs US$ 5.53. Other azole antifungal agents are not available through generics suppliers, and are much more expensive.

Cryptococcosis

Systemic mycoses such as cryptococcosis probably cause about 5% of all HIV-associated deaths worldwide. Cryptococcosis most often appears as meningitis, and occasionally as pulmonary or disseminated disease. Cryptococcal meningitis (CRM) is the most frequent systemic fungal infection in HIV-infected persons. Without treatment, life expectancy is probably less than a month.

Cryptococcosis is relatively easy to diagnose. However, its treatment (either amphotericin B with or without flucytosine, or in mild cases with oral fluconazole) and secondary chemoprophylaxis are often impossible in developing countries because of the high cost and limited availability of the drugs required.

Cytomegalovirus infection (CMV)

Estimates of the incidence of CMV disease vary considerably between geographical locations, but CMV causes significant suffering in HIV-infected persons worldwide. Symptoms include fever and diarrhoea from CMV colitis, dyspnoea from CMV pneumonitis, and blindness caused by CMV retinitis.

Treatment aims to alleviate symptoms, and to prevent blindness, rather than provide a cure. The drugs currently used are ganciclovir and foscarnet, with cidofovir when the first two have failed. They have high toxicity and limited efficacy at a relatively high cost (which is increased by the need for close monitoring), and are not included in the WHO essential drugs list.

Herpes simplex and Herpes zoster

Herpes simplex virus infection (HSV, which causes sores around the mouth and genitals) and herpes zoster virus infection ("zonal" herpes) are not life-threatening but can be extremely painful. Both occur frequently in HIV-infected persons, but as they are not considered AIDS-defining conditions there are few data about their incidence. Note, however, that both can cause encephalitis, which can be life-threatening.

Treatment with aciclovir is only marginally effective in herpes zoster but is sometimes dramatic in HIV-associated herpes simplex with extensive ulceration. Aciclovir is expensive, costing US$ 45.82 and US$ 170.18 for 5-day herpes simplex and 7-day herpes zoster regimens respectively. However, its cost is likely to decrease when it is no longer protected by patent, as is the case in the United Kingdom where generic aciclovir is available. Aciclovir can also be used to treat encephalitis at a cost of US$ 1282.76 for a ten-day intravenous regimen.

Kaposi sarcoma

HIV-associated Kaposi sarcoma causes dark blue lesions which can occur in a variety of locations including the skin, mucous membranes, gastrointestinal tract, lungs or lymph nodes. The lesions usually appear early in the course of HIV infection.

Treatment depends on the lesions' symptoms and location. For local lesions, injection therapy with

vinblastine has been used with some success. Radiotherapy can also be used, especially in hard-to-reach sites such as the inner mouth, eyes, face and soles of the feet. For severe widespread disease, systemic chemotherapy is the preferred treatment.

Most drugs for the chemotherapy of Kaposi sarcoma are included in the WHO essential drugs list. However, since international generic drug suppliers appear to offer only vincristine and methotrexate, the availability of drugs to treat the disease is limited in developing countries.

Leishmaniasis

Leishmaniasis is transmitted by sandflies and currently affects some 12 million people in 88 countries. The most serious of its four forms is visceral leishmaniasis (VL)—also known as kala azar—which is characterized by irregular bouts of fever, substantial weight loss, swelling of the spleen and liver, and anaemia (occasionally serious). Recently, there has been an increase in overlapping of VL and HIV infection. Treatment with pentavalent antimony is relatively expensive, partly because of the cost of drugs but also because hospital admission is recommended (in milder cases, trained health workers may administer the injections or infusions at a patient's home). Even with optimal treatment, mean survival time with this co-infection is only 12 months.

Lymphoma and squamous cell carcinoma

The treatment of lymphoma in HIV-infected persons is controversial. Survival is not greatly increased by expensive chemotherapy, and quality of life is poor during treatment. Drugs used in these regimens are included in the WHO essential drugs list and ought to be available, but this is often not the case as they are not often stocked by generic drugs distributors. Also, only sophisticated health-care systems can handle them safely.

Mycobacterium avium complex disease (MAC)

MAC disease appears to be relatively rare in Africa, but elsewhere it occurs in around 5% of persons with AIDS. Symptoms include fever, weight loss, night sweats, diarrhoea, and wasting.

Recommended drugs for prophylaxis include azithromycin, clarithromycin and rifabutin. For treatment, clarithromycin/ethambutol/rifabutin combination therapy is the only regimen that has been documented to increase life expectancy; even so, in practice a two-drug regimen of a macrolide antibiotic and ethambutol is often used as it reduces the potential for both drug interactions and toxicity and it decreases cost. With the exception of ethambutol, none of these drugs is included in the WHO essential drugs list because of their high cost and the fact they do not cure MAC.

Pneumocystis carinii pneumonia (PCP)

PCP is the most frequent HIV-associated opportunistic infection in industrialized countries, but appears to be less frequent in Africa. The symptoms are mainly pneumonia along with fever and respiratory symptoms such as dry cough, chest pain and dyspnoea. Definitive diagnosis requires microscopy of bodily tissues or fluids.

Severe cases of PCP are initially treated intravenously with trimethoprim-sulfamethoxazole (TMP-SMZ), or clindamycin and oral primaquine. Mild cases can be treated with oral TMP-SMZ throughout. With both of these regimens, toxicity (notably allergic-type reactions) often requires changes in therapy.

Prevention of PCP is strongly recommended for HIV-infected persons with significant immune compromise wherever PCP is a significant health problem for HIV-infected persons, and also after their first episode of PCP. Preventing and treating PCP need not be very expensive: use of no-brand generic products can reduce the cost of drugs for TMP-SMZ prophylaxis to under US$ 12.00 per year.

Toxoplasmosis

This disease is found in about 5% of AIDS patients in the USA, but a greater proportion in Europe. Reliable data on its incidence in developing countries are lacking, but studies have demonstrated that the disease does occur in a significant proportion of AIDS patients. In HIV-infected persons toxoplasmosis mainly appears as encephalitis or as disseminated disease. Diagnosis of toxoplasmosis is by CT scan or MRI scan. Brain biopsies are rarely carried out. If toxoplasmosis is strongly suspected, patients are more likely to be given a trial of therapy, and only if they do not respond to this therapy is a brain biopsy considered.

The disease is treated with pyrimethamine plus sulfadiazine. Primary chemoprophylaxis for PCP with TMP-SMZ, or with dapsone and pyrimethamine, offers protection against toxoplasmosis as well. Secondary chemoprophylaxis is with pyrimethamine plus sulfadiazine and leucovorin. While pyrimethamine is widely available, the drug combination is toxic to bone marrow at the dosage recommended for prophylaxis. Prophylactic leucovorin (also called calcium folinate), which is given to prevent the side effects of pyrimethamine and as secondary prophylaxis, is very expensive.

Tuberculosis

Tuberculosis (TB) is the leading HIV-associated opportunistic disease in developing countries.

The DOTS (directly observed, short course) treatment strategy recommended by WHO treats TB in HIV-infected persons as effectively as it treats those without the virus.

Background

A complete cure takes 6 to 8 months and uses a combination of antibiotics. In addition to curing the individual it also prevents further spread of the disease to others. This is why treating infectious cases of TB has important benefits for society as a whole, and is the mainstay of the WHO's TB control strategy. (See *Tuberculosis and AIDS* in the UNAIDS *Best Practice* Collection for more information.) Isoniazid preventive therapy is recommended as a health-preserving measure for HIV-infected persons at risk of TB, such as those with a positive TB skin test or who are living in areas where the disease is endemic. TB prophylaxis has been shown to increase the survival of HIV-infected persons at risk of TB (see O'Brien and Perriëns in the Selected Key Materials). The case for public funding of TB prophylaxis by developing countries awaits confirmation of its cost-effectiveness compared to treating infectious TB cases. However, given the low incremental cost of isoniazid therapy—US$ 5.15 for a year's prevention according to the 1996 Drug and Price Independent Guide—once a person is identified as HIV-infected, there is a strong case to provide TB prophylaxis for HIV-infected persons whenever financially feasible. (See WHO *Policy Statement on Preventive Therapy against Tuberculosis in People Living with HIV* in the Selected Key Materials.)

Table 1. AIDS-defining opportunistic diseases: Prevalence in six countries[1]

Opportunistic disease or malignancy	Côte d'Ivoire	Brazil	Mexico	Thailand	USA	Zaire[2]	Infrastructure needed [3]
Aspergillosis	3%		3–7%				advanced
Atypical mycobacteriosis	4%		5–6%	2%	4%		advanced
Bacteraemia	7%			4%			advanced
Candidiasis	24%	5%	30%	11%	13%	minimal	
CMV	26%	5%	65–69%	4%	5%	13%	advanced
Cryptococcosis	5%	5%	7–11%	2%	7%	19%	medium
Cryptosporidiosis – Isosporiasis	4%	14%	8%	4%	6.2%	< 2%	advanced
Enteritis, non-specific [4]	12%					13%	minimal
Herpes (systemic)	6%		5%	10%	4%		minimal
Histoplasmosis	3%		5–10%	8%		< 2%	advanced
Kaposi sarcoma	13%	5%	30–43%		21%	16%	medium
Lymphoma	4%	4%	10%		0.7%		advanced
Nocardiosis	5%		< 2%				advanced
Penicilliosis				4–25%			advanced
Progressive multifocal leukoencephalopathy (PML) or HIV encephalitis	6%	11%		7%	0.6%		advanced
Pneumocystis carinii pneumonia	4%	22%	24%	26%	64%	< 2%	medium
Pneumonia	5%	16%				34%	advanced
Toxoplasmosis	21%	14–34%	17%	2%	3%	11%	advanced
Tuberculosis	54%	41%	28%	20%	3%	41%	medium
Others	9%			9%			

Source: Perriëns J, Clinical aspects of HIV-related opportunistic diseases in Africa: tuberculosis and candidiasis. University of Gent, 1994.

[1] Data from autopsy studies, except Brazil (one autopsy and one clinical series), Thailand (two clinical series) and USA (one clinical series).

[2] Democratic Republic of Congo.

[3] Infrastructure needed to diagnose, treat

[4] Clinical diagnosis for non-specific enteritis does not identify the cause. It permits treatment to be carried out, but not necessarily the most effective one.

Table 2. Comparative costs of treatment and prophylaxis for common opportunistic diseases in adults

Opportunistic disease	Drug and dose	Duration	Cost of treatment (in $) course or per-year cost [a]	Source [b]
Candidiasis	Ketoconazole 200 mg once a day	14 days	5.53	IDPIG
	Fluconazole 50 mg once a day	07 days	26.34	BNF
	Itraconazole liquid 100 mg twice a day	07 days	82.92	BNF
Cryptococcosis Acute treatment	Amphotericin B 1 mg/kg daily +/-	14 days	164	
	Flucytosine 100 mg/kg/day orally	14 days	price not available	BNF
	Fluconazole 800 mg orally for 2 days followed by 600 mg daily	see dose	662	BNF
Cryptococcosis Consolidation treatment	Amphotericin 1 mg/kg/day	8 weeks	657	BNF
	Fluconazole 400 mg/day	8 weeks	1685	BNF
	Itraconazole 400 mg/day (liquid)	8 weeks	1238	BNF
Cryptococcosis Secondary prophylaxis	Fluconazole 200 mg once a day	Long term	5493 p.a.	BNF
	Amphotericin 50 mg twice a week	Long term	610 p.a.	BNF
Cytomegalovirus infection Prophylaxis	Ganciclovir 1 g 3 times a day orally	Long-term	21 968	BNF
	Ganciclovir 5 mg/kg once a day	Long-term	12 358	BNF
	Foscarnet 90 mg/kg once a day	Long-term	18 148	BNF
	Cidofovir 5 mg/kg/14 days	Long-term	29 071[c]	
Cytomegalovirus infection Treatment	Ganciclovir 5 mg/kg twice a day	14 days	959	BNF
	Foscarnet 90 mg/kg twice a day	14 days	1160	BNF
	Cidofovir 5 mg/kg once a week	14 days	2236 [c]	
Herpes simplex and zoster	Simplex: Aciclovir 200 mg 5 times a day	5 days	45.82[d]	BNF
	Zoster: Aciclovir 800 mg 5 times a day	7 days	170[d]	BNF
	Encephalitis: Aciclovir 10 mg/kg IV 3 times a day	10 days	1283[d]	BNF
Kaposi sarcoma	Bleomycin 15 units and vincristine 2mg	1 cycle	25.84	BNF
	every three weeks.		33.58	BNF
Mycobacterium avium complex disease Prophylaxis	Azithromycin 1.25 g once a week (American dose 1.2 g)	Long-term	923 p.a.	BNF
	Clarithromycin 500 mg twice a day	Long-term	1860 p.a.	BNF
	Rifabutin 300 mg once a day	Long-term	3176 p.a.	BNF
Mycobacterium avium complex disease Treatment	Clarithromycin 500 mg twice a day	Long-term	1860 p.a.	BNF
	+ ethambutol 15 mg/kg once a day	Long-term	34.68 p.a.	IDPIG
	+/- rifabutin 450 mg once a day	Long-term	4764 p.a.	BNF
Mycobacterium tuberculosis Prophylaxis	Isoniazid 300 mg daily	1 year	5.15 p.a.	IDPIG
Mycobacterium tuberculosis Treatment	Rifampicin 600 mg once a day	6 months	Combined	IDPIG
	Isoniazid 300 mg once a day	6 months	22.72 +	
	Pyrazinamide 2 g once a day	2 months	11.11/course	IDPIG
Pneumocystis carinii pneumonia Prophylaxis	Trimethoprim-sulfamethoxazole 960 mg once a day	Long-term	11.39 p.a.	IDPIG
	Dapsone 100 mg a day	Long-term	3.58 p.a.	IDPIG
	Dapsone 100 mg a day and pyrimethamine 25 mg three times a week	Long-term	10.83 p.a.	IDPIG
Pneumocystis carinii pneumonia Treatment	Trimethoprim-sulfamethoxazole 90 mg/kg/day	21 days	PO 3.93	IDPIG
			IV: 611	BNF
	Clindamycin 600 mg four times a day	21 days	PO 253	BNF
	and primaquine 15 mg once a day		IV 1370	BNF
			PO 0.11	IDPIG

Table 2. (continued)

Opportunistic disease	Drug and dose	Duration	Cost of treatment (in $) course or per-year cost [a]	Source [b]
Toxoplasmosis Treatment	Sulfadiazine 2 g three times a day plus pyrimethamine 200 mg in divided doses then 50 mg daily and calcium folinate 15 mg daily (all oral)	6 weeks 6 weeks 6 weeks	217 4.19 244	BNF IDPIG BNF
	Clindamycin 600 mg orally four times a day plus pyrimethamine and calcium folinate as above	6 weeks	507+ 4.19 + 244	BNF
Toxoplasmosis Secondary prophylaxis	Sulfadiazine 1 g three times a day plus pyrimethamine 25 mg once a day and calcium folinate 15 mg once a day	Long-term Long-term Long-term	944 p.a.+ 16.97 p.a.+ 2125 p.a.	BNF IDPIG BNF
	Clindamycin 450 mg three times a day and pyrimethamine and calcium folinate as above	Long-term	4411 p.a.+ 16.97 p.a.+ 2125 p.a.	BNF

(a) PO—orally; IV—intravenously; p.a. per annum

(b) Sources: IDPIG: International Drug Price Indicator Guide 1996, and BNF: British National Formulary Number 33 (March 1997)

(c) Middlesex Hospital Price (recently released medication not yet in the BNF)

(d) Aciclovir prices given are for branded products, reduced generic prices not in the BNF yet

Doses calculated for an average 60 kg patient. If it is possible for intravenous vials to be used more than once or the reconstituted solution kept, doses have been calculated as the number of milligrams for the treatment course, and then converted into the number of vials (e.g. ganciclovir). When this is not possible, the number of vials for each dose has been calculated (e.g. amphotericin 60 mg would require 2 x 50 mg vials/day).

The Challenges

Lack of advocacy

Because of the large variety of conditions related to HIV and the number of care options, prophylaxis and management of opportunistic diseases (including their diagnosis, treatment and palliation) is a difficult issue to advocate for. Patients and their families may enthusiastically lobby for access to a particular drug they have heard about. However, it is harder to for them to inform themselves sufficiently to advocate in an effective way for a full "package" of equipment, services, laboratory materials, testing kits and staff training needed to deal with the full range of opportunistic diseases.

Representative organizations may have the same problem of insufficient knowledge, or they may have too many other priority issues to focus on this highly technical one. Even medical personnel who, on a technical level, have a clear understanding of what is needed, often do not have the means or motivation to turn this knowledge into effective advocacy.

In some places, it is difficult or dangerous for people living with HIV to carry out their own advocacy openly, or for organizations to do it on their behalf.

Lack of infrastructure

Effective intervention against opportunistic diseases requires not only the appropriate drug or other medicament for a given medical condition, but also the infrastructure necessary to diagnose the condition, monitor the intervention, and counsel patients. As well, use of drugs and tests must be supported by proper storage, handling and administrative procedures. (For a more detailed discussion of HIV-related drugs, see the Technical Update on *Access to Drugs*. Also relevant to this discussion is the Technical Update on *HIV Testing Methods*.)

As can be seen in Table 1, the infrastructure required to prevent, diagnose and manage opportunistic diseases and malignancies can be classified (somewhat arbitrarily) in three levels:

• *Minimal*: diagnosis can be made by observation of symptoms or use of a simple microscope; diagnostic, treatment and palliative procedures are non-invasive; follow-up of patients does not require highly trained staff. Relatively little investment in equipment is required. Successful diagnosis, treatment and palliation (including for terminal patients) chiefly require that staff have sufficient knowledge and experience to recognize symptoms and prescribe drugs that are easily stored, along with equipment for simple microscope work. Home-based care and community health initiatives can be very effective in delivering treatment and follow-up. Examples are oral candidiasis and pulmonary tuberculosis, herpes, and cryptococcal meningitis.

• *Medium*: diagnosis requires X-ray equipment or culture facilities, while diagnostic and treatment procedures require trained staff and well run laboratories. Significant investment in equipment and ongoing operating costs are required. Examples are extra-pulmonary tuberculosis, cryptosporidiosis-isosporiasis, PCP and Kaposi sarcoma.

• *Advanced:* diagnosis requirements include endoscopy and CT scanning; diagnosis and treatment require highly trained and specialized staff; investment in equipment and operating costs is high; patient follow-up may be complex. Examples include toxoplasmosis, MAC disease and CMV.

As one moves from level to level, costs and training requirements increase dramatically.

Lack of information for decision-making

To estimate which interventions and what supporting infrastructure are required to handle HIV-related opportunistic infections and malignancies, decision makers need to know:

• What are the incidence rates of the HIV-related conditions in the area under their responsibility?

• Which regimens are available to treat or prevent the conditions of interest, and at what cost?

• What are the non-drug costs of dealing with opportunistic diseases (such as medical staff time, purchase and operation of diagnostic equipment, storage and transportation of drugs, etc.)?

The main challenge of choosing between interventions is to alleviate the morbidity and suffering of those in need while not exceeding the financial and technical capabilities of the health system.

Unfortunately, these choices often need to be made *without the help of formal cost-benefit and cost-effectiveness analyses*. This is partly because, as described above, the information needed to calculate costs is difficult to collect, but also because benefits other than short-term improvements in quality of life are not well understood or easily quantified. For example, it has been demonstrated that prophylaxis of MAC with azithromycin can lengthen survival, but it is still not clear exactly how much life expectancy is lengthened with it.

The challenge of fairness

Given the lack of complete epidemiological data in many regions and the difficulties of formal cost-benefit and cost-effectiveness analysis, the process of choosing which interventions merit public funding is frequently forced into less methodologically solid—and more political—calculations than most health administrators would like. This brings forward the additional challenge of ensuring equity and non-discrimination in the decision-making process, and re-emphasizes the need for informed advocacy.

In places where resources are very scarce, priority should be given to health needs shared by most or all of the population, including those who are HIV-infected. Examples are drugs to relieve pain in terminal patients and to treat or prevent TB.

The Responses

A complete response to the needs created by HIV-related opportunistic diseases requires a variety of stakeholders to play their part. On the one hand, people infected with or affected by HIV must become aware of (and believe in) the possibilities for managing opportunistic diseases if they are to advocate for them. On the other hand, health systems must be prepared to make decisions about what interventions can and should be offered. In between, NGOs and community-based organizations can have a strong role to play both in advocacy and delivery of care.

Preventing opportunistic diseases

Interventions that prevent the occurrence of opportunistic diseases can result in significant gains in life expectancy and quality of life among people living with HIV. Two useful sources for those wishing more information on this important subject are mentioned in the Selected Key Materials. In France, the book *Prise en charge des personnes atteintes par le VIH* (Care for people with HIV) is widely distributed to physicians and presents a great deal of practical information on the subject. In the United States, guidelines on prevention of opportunistic diseases are jointly published and updated by the US Public Health Service (USPHS) and the Infectious Diseases Society of America (IDSA). These guidelines are also found on the Internet at *http://www.thebody.com/cdcoiguide/guidelines1.html*.

Mobilizing communities

In a variety of settings around the world, community-based groups and NGOs are working to provide home-based care for people with HIV/AIDS. However, it should be realized that only a few opportunistic diseases and symptoms such as oropharyngeal and vaginal candidiasis or herpes zoster and herpes simplex can be managed effectively through home-based care. Most opportunistic diseases require Toxoplasmosis diagnosis and treatment of a complexity beyond the capabilities of most community-based groups and NGOs.

Priorities for public spending

When faced with limited resources, as is the case for most health-care systems, the best framework for decision making is one that takes into account both the costs and the "spinoff" value of interventions for HIV-related opportunistic diseases. The term "spinoff" means that the framework must not only value the benefits of a given intervention for individual HIV-infected patients, but also the benefits for other people—including those not infected with HIV.

The clearest example of a high-priority public intervention against opportunistic infection is probably the diagnosis, treatment and prevention of tuberculosis. Even without exact information on HIV prevalence or the cost-benefit ratios of these interventions in a given setting, their overall value to society can be accepted as high on several counts:

- they benefit people affected by or at risk from two epidemics: HIV/AIDS and TB;
- they are proven effective;
- both the drug costs and associated costs are relatively low given the number of people reached by the intervention.

Even in societies with "minimal" resources and facilities, a basic package of palliative care should be available for persons living with HIV/AIDS, including terminal patients.

For conditions that can be treated but only at a very high cost, the decision to be made is more controversial. Examples are CMV, MAC, fungal infections such as cryptococcal meningitis (CRM), penicilliosis and rarer systemic mycoses such as histoplasmosis and coccidioidomycosis. All have very high treatment and prophylaxis costs. Governments should assess which of these diseases are common in their population, and then decide whether subsidizing the available therapies is warranted. In many cases the only affordable approach is to make available palliative drugs that alleviate the suffering caused by these conditions.

Selected Key Materials

Dormont PJ (ed). *Prise en charge des personnes atteintes par le VIH*, 1996 edition. Paris: Flammarion, 1996. This is a practical, compre-hensive guide to management of HIV, published with the support of the French Ministry of Labour and Social Services. It is widely distributed to physicians in France.

Steward GJ (ed). *Managing HIV*. Sydney: The Australasian Medical Publishing Company, 1996. Part 5 of this book provides a comprehensive overview of how HIV-related opportunistic diseases should be diagnosed and treated.

U.S. Public Health Service (USPHS), Infectious Diseases Society of America (IDSA). *Guidelines for the Prevention of Opportunistic Diseases in Persons Infected With Human Immunodeficiency Virus: A Summary*. Available on the Internet at *http://www.thebody. com/cdc/ oiguide/guidelines1.html.* This overview of prevention of HIV-related opportunistic infections includes therapeutic recommend-ations and guidance on pet ownership, hygienic practices, and avoidance of environmental exposure. A version specific to Latin America and the Caribbean has been published in Spanish.

Kaplan JE *et al*. Preventing opportunistic diseases in human immunodeficiency virus-infected persons: implications for the developing world. *American Journal of Tropical Medicine and Hygiene* 1996; **55**(1):1–11. This discusses how the USPHS/IDSA Guidelines can/should be adapted to fit developing country needs.

Leishmania and HIV: in gridlock. Geneva: WHO/UNAIDS, 1998 (WHO/CTD/LEISH/98.9/UNAIDS). This document is aimed to help decision-makers shape and prioritize strategies to deal with the growing threat of leishmania/HIV co-infection.

Management Sciences for Health. *Managing Drug Supply: The Selection, Procurement, Distribution, and Use of Pharmaceuticals (2nd edition)*. Boston: Kumarian Press, 1998. Comprehensive manual with practical case studies on all aspects of drug selection, procurement, distribution and use.

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