HIV/AIDS Prevention *and* Care *in* Resource-Constrained Settings

A HANDBOOK FOR THE DESIGN AND MANAGEMENT OF PROGRAMS

Editors

Peter R. Lamptey, MD, DrPH
Executive Vice President/COO
HIV/AIDS Prevention and Care Department
Family Health International
Arlington, VA U.S.A.

Helene D. Gayle, MD, MPH
Senior Advisor for HIV/AIDS
Bill and Melinda Gates Foundation
Seattle, WA U.S.A.

Coordinators:
Kristen Ruckstuhl, MA
Madaline Feinberg, MA

Consulting Editors:
John-Manuel Andriote, MS
Catharine P. Farrington, MS

preview CHAPTER 25

Management of HIV Disease and its Complications in Resource-Constrained Settings

INTRODUCTION

The disease burden attributable to HIV infection will probably continue to increase for at least another decade. The impact of the disease is especially severe in the countries least equipped to deal with it: More than 90 percent of HIV-infected people live in resource-constrained settings.

This chapter focuses on providing health care for people living with HIV/AIDS (PLHA) in resource-constrained countries. Most health facilities in these areas lack the resources to offer high-quality medical care to the general public—much less meet the complex demands of HIV/AIDS-related morbidity and mortality. Antiretroviral treatments and other expensive diagnostics and treatments for HIV-related illnesses are rarely available or accessible. The challenge of improving PLHA's quality of life requires a more comprehensive or holistic approach—an approach that meets the medical, psychological and social needs of people and families living with HIV.

HEALTH CARE FOR PEOPLE INFECTED WITH HIV

Care for PLHA should cover all stages of HIV, from asymptomatic infection through end-stage disease, bereavement and care for survivors in the family. The composition and emphasis of such a comprehensive approach changes—as do the medical, psychological and social needs of PLHA and their families—between early-stage infection emphasis on counseling to help cope and change behavior and late-stage emphasis on palliation and social support. But at all stages medical interventions are needed to prevent or treat opportunistic infections and HIV-related illnesses.

CONTINUUM OF CARE

Providing the different elements of comprehensive care to complement and strengthen each other demands coordination and collaboration. This should include timely referrals between home or community and hospital (and vice versa) and effective discharge planning, as well as follow-up at each level to ensure a continuum of care.

Clinical Guidelines

Differences in clinical presentation and variations in the ability of health systems to diagnose and manage HIV-related illnesses mean that the clinical approach to medical problems of people infected with HIV varies from country to country. But there is a need for generic guidance, with updated information on diagnosis and management to help countries develop or update their national guidelines.

Management of HIV-Related Problems

Managing the health problems of a person infected with HIV differs according to his/her degree of immune deficiency. Health problems with a relatively intact immune system include skin disorders such as herpes zoster, lymphadenopathy or pulmonary tuberculosis. At later stages of infection there are chronic diarrhea and serious opportunistic infections, wastage and neuropsychiatric disorders.

Prophylaxes for Opportunistic Infections

Cotrimoxazole can significantly reduce hospitalization and mortality for symptomatic HIV-infected people. Studies have also shown that isoniazid (IHG) treatment is effective and feasible preventive TB therapy for PLHA in areas where TB is very common.

CLINICAL MANAGEMENT OF TB

An HIV-infected person is 10 times more likely to develop TB than an uninfected person. In resource-constrained countries, more than 30 percent of people infected with HIV will develop TB—and the disease can occur at any point in the course of the infection. The highest priority for TB control is the diagnosis of sputum smear-positive pulmonary TB cases. Early diagnosis and good adherence to treatment are the best ways to prevent further spread.

IMPROVING ACCESS TO ESSENTIAL DRUGS

Regular and adequate availability of essential drugs will ensure proper management of most opportunistic infections and HIV-related illnesses during both early and later palliative stages of disease.

Increasing Access to Antiretroviral Drugs (ARVs)

Antiretroviral drugs (ARVs) are increasingly used in resource-constrained countries and even more in medium-income countries. The challenge is, therefore, how to use these medicines in the most efficient and safest manner. Guidelines are available to help countries with limited resources.

ARVs to Reduce Transmission of HIV

Recent studies demonstrate that the concentration of HIV in blood—and by extension, genital secretions—determines the efficiency of the sexual transmission of HIV within discordant couples. These observations and extensive work with macaques suggest that ARV therapy can reduce transmission, although it is too early to be certain.

DIAGNOSIS AND MANAGEMENT OF HIV INFECTION IN CHILDREN

Without affordable antigenic tests, it remains difficult to diagnose HIV infection in infants. But clinical tools are available to build management capabilities to treat HIV-infected children.

HIV INFECTION IN WOMEN

The vast majority of women infected with HIV are of reproductive age, and are at particular risk of stigmatization, abandonment by their partner/family or becoming victims of violence. They are also less likely than men to receive early clinical care. Gynecological examination is essential as such symptoms may be the first sign of infection, allowing for comprehensive management. In making reproductive decisions, infected women should be given information and counseled about their pregnancy options, including contraception. During pregnancy, they should have a wide range of care services, including preventive therapies, interventions to prevent mother-to-child transmission (MTCT) of HIV and follow-up care and counseling.

HEALTH SECTOR REFORM AND HIV/AIDS

Many countries are introducing health reforms to improve the quality and effectiveness of services delivered at lower levels of the health care system. These countries have found that decentralizing authority and responsibility of service planning and provision has often led to better health care quality and effectiveness. The countries believe that the rapidly increasing number of people seeking care can be more effectively managed in the new, decentralized format.

FUTURE CHALLENGES

In recent years, progress in the treatment of PLHA has been made mainly in industrialized countries. The challenge now is to look at ways to introduce new treatment regimens into resource-constrained settings and maintain quality comprehensive care.

table of contents CHAPTER 25

607 **INTRODUCTION**
611 **HEALTH CARE FOR PEOPLE INFECTED WITH HIV**
611 Continuum of Care
612 **CLINICAL GUIDELINES**
615 **MANAGEMENT OF HIV-RELATED PROBLEMS**
617 Prophylaxes for Opportunistic Infections
618 TB/HIV Dual Infections
618 TB Diagnosis
618 TB Treatment
619 HIV Testing in TB Patients
620 Prevention of TB
620 TB Prophylaxis in HIV-Infected People
621 BCG Vaccination and HIV Infection
621 **IMPROVING ACCESS TO ESSENTIAL DRUGS**
621 **IMPROVING ACCESS TO ANTIRETROVIRAL DRUGS (ARVS)**
621 What Should *Not* Be Done with ARV Treatment
622 How to Improve Adherence to Treatment
622 ARVs to Prevent Transmission of HIV
624 **HIV INFECTION IN CHILDREN**
624 Diagnosis and Management of HIV Infection in Infants
624 Monitoring Pediatric HIV Infection
624 Management of Opportunistic Infections
625 Prophylaxis against Opportunistic Infections
625 Vaccinations
625 **HIV INFECTION IN WOMEN**
625 Gynecological Problems
625 HIV Infection in Pregnancy
626 **HEALTH SECTOR REFORM AND HIV/AIDS**
627 **FUTURE CHALLENGES**
627 **RELEVANT CHAPTERS**
627 **REFERENCES**
628 **RECOMMENDED READING**

INTRODUCTION

HIV infection has risen from 22nd to fourth place as a cause of disease-adjusted life-years lost to disease in the last 10 years—and experts fear the disease burden attributable to HIV infection will continue to increase for at least another decade.[1] The impact of the disease is especially severe in the countries least equipped to deal with it: Ninety percent of HIV-infected people live in resource-constrained settings. Wherever HIV has emerged, communities and individual societies have mounted care and prevention efforts. While the adequacy of those responses and activities have frequently been less than optimal, the foundation has been laid for an integrated system of prevention and care services.

UNAIDS and WHO advocate supporting four major areas to advance care and support for PLHA: (1) Voluntary counseling and testing for HIV (VCT); (2) Access to health care; (3) Psychosocial support; and (4) Help for families affected by HIV.

This chapter focuses on the provision of health care for PLHA in resource-constrained countries, where most health facilities lack the resources needed to offer high-quality medical care to the general public—much less provide the complex treatment of HIV/AIDS-related morbidity and mortality.

Affected communities, in coordination with health facilities, have developed innovative approaches to meet the broad clinical, psychosocial and welfare needs of PLHA and their families through community-based programs.

In recent years, HIV/AIDS-related morbidity and mortality has declined more than 50 percent in industrialized countries—thanks largely to highly active antiretroviral treatment (HAART).[1] Prophylaxes against opportunistic infections and early detection and adequate treatment of these infections also helped the decline. Despite their high cost—more than US$10,000/year—HAART regimens may reduce overall health-care costs for HIV-infected people in industrialized countries, because patients need less hospitalization and treatment of HIV-related complications and can return to their jobs. In addition to its dramatic effect on the clinical management of patients, HAART has improved PLHA's quality of life, offering a new perspective on living with HIV. The challenges are now focused on choosing the right antiretroviral drugs (ARVs), monitoring their side effects and efficacy (by viral load and CD4 lymphocyte testing), treatment counseling and support for patients to obtain maximum adherence with ARV drugs.[2,3]

But in situations where HAART and other expensive diagnostics and treatments are not available or accessible, AIDS still has a devastating impact on patients and their family members. The challenge is to improve their quality of life. This requires a comprehensive, holistic approach. Patients with HIV/AIDS-related illnesses face many problems. Not only do they suffer from medical conditions such as diarrhea, fever, skin lesions, cough and weight loss but they also have many psychosocial and material needs. These include fear of loss of support from family members, friends, employers or the authorities if their serostatus becomes known; and income depletion due to increased spending on medical

needs, traditional practitioners and transportation. PLHA often express the need for spiritual support, household help and assistance in disclosing serostatus to a partner. Incomes are further depleted by despair-driven care seeking, which often leads to paying healers who make false claims. Listening to patients' needs and trying to address them is the key to improving their quality of care; it forms the basis of various community care responses, often at minimal expense. (See Chapter 3 for more information on the socioeconomic impact of HIV/AIDS and Chapter 23 for more information on psychosocial support.)

The absence of expensive treatments, including ARVs, should not be an excuse to neglect patients. Certainly, HIV-infected patients in resource-constrained settings should have access to ARVs, but they are not a panacea: Even when available, there are many obstacles to the safe and effective use of ARVs, especially if the health care infrastructure is very weak.[4,5] When they are used, ARVs should be introduced progressively and in a supervised way, while at the same time strengthening the quality of health care to accommodate these new and complex interventions.

HEALTH CARE FOR PEOPLE INFECTED WITH HIV

HIV comprehensive care includes three basic components:

1. Counseling and testing for HIV infection.
2. Health care (including nursing, psychological and medical care).
3. Impact alleviation for HIV-affected families (social support).

Care for PLHA should cover all stages of HIV infection, from asymptomatic infection to end-stage disease, bereavement and care for family survivors.

Awareness of HIV serostatus allows for early access to HIV-specific health care services. Ideally, people should be informed of their serostatus through VCT provided in a confidential manner (the advantages, planning and implementation of which are discussed in Chapter 23). HIV care must respond to both medical and psychosocial needs. Various studies in developed and resource-constrained countries have shown that the needs of PLHA are comprehensive and interrelated. The needs might be clinical and concern HIV-related illnesses; they might be emotional and spiritual (such as coping with infection in a stigmatizing environment); or they might be social (maintaining a nutritional and economic balance when repeated health expenditures deplete family incomes, planning to secure basic support for survivors including orphans, etc.). These needs must be met if the goal is improvement of quality of life for PLHA.

The composition of and emphasis within such a comprehensive approach will change as the disease progresses. Early-stage infection requires emphasis on counseling and behavioral change; late-stage disease should emphasize palliation and social support. Medical interventions are needed at all stages to prevent or treat opportunistic infections and HIV-related illnesses.

Continuum of Care

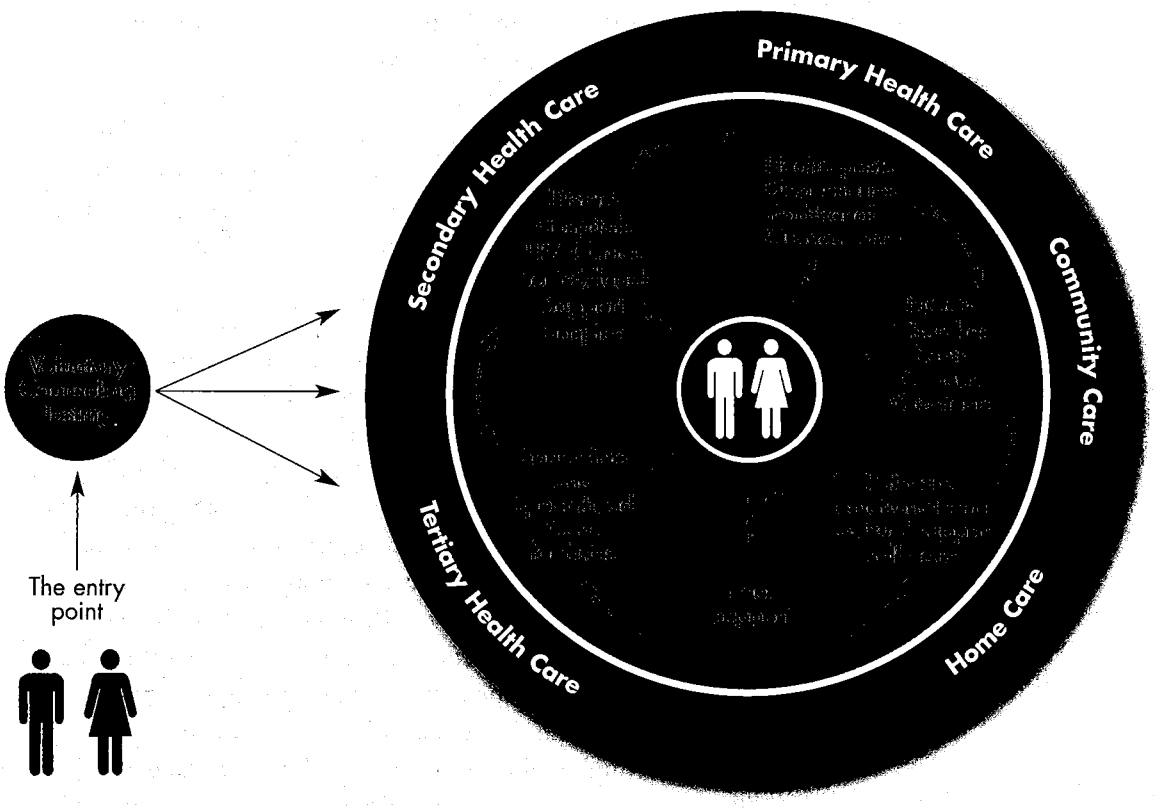
At all stages, the different elements of comprehensive care should complement and strengthen one another. For example, managing a clinical condition will be easier and more effective if worries about infecting a partner and planning for the family's future can be addressed through referral to counseling services that provide social or legal support.

The different elements of comprehensive care need not come from the same institution, but can be provided through networking with other services, institutions and projects in the community, including urban neighborhoods. Comprehensive care should include timely referrals between home or community and the hospital (and vice versa), effective discharge planning and follow-up at each level in order to ensure a continuum of care.

Functional and confidential referral systems must be in place to build on previous care efforts. Patients who have already disclosed their serostatus to one health care provider may not immediately disclose the fact that they are HIV-infected to a second. This is as important for medical referrals from a central hospital to a community health center as it is for psychosocial referrals between a counselor and a spiritual worker, or between a welfare officer and a home-based care program. Such coordination permits a continuum of care—from the institutional level to the community and home, as shown in Figure 1.[6] A peer support group's ability to make these linkages, exchange information and offer emotional and moral support has been found to be essential all over the world.

To enter a care continuum, a diagnosis must be made in a way that promotes and encourages further care-seeking and support.

Figure 1
THE HIV/AIDS CONTINUUM OF CARE



© *Eric van Praag/Daniel Tarantola*
HIV/AIDS and Sexually Transmitted Diseases/WHO

CLINICAL GUIDELINES

The clinical spectrum of HIV infection differs from region to region.[7,8] In resource-constrained countries, mycobacterium tuberculosis is a frequent complication of HIV infection. Penicillium marneffi infection is only seen in AIDS patients in certain parts of Southeast Asia. Pneumocystis carinii pneumonia (PCP), cytomegalovirus (CMV), retinitis and mycobacterium avium complex (MAC) infection are opportunistic infections often found in industrialized countries. Because of these differences in clinical presentation—and because of resource-constrained health systems' limited ability to diagnose opportunistic diseases—the clinical approach to PLHA's medical problems differs in various parts of the world.

Health workers frequently have no choice but to use a syndromic approach in settings where the diagnostic infrastructure is underdeveloped and referrals for diagnostic work-ups would be difficult or impossible. In recognition of the need to deliver at least a minimum of health care in settings with severe diagnostic and therapeutic limitations, WHO in the early 1990s produced guidelines to care for people with clinically defined AIDS, based on different diagnostic and therapeutic capacity.[9] The main problems covered in the guidelines are weight loss, fever, diarrhea,

pulmonary symptoms, neurological disorders and oral and skin disorders and pain. The guidelines are intended to be adapted to the disease presentation, disease stage, health infrastructure and resources available. In many countries, national guidelines have been established using the WHO guidelines as a template. But their use has varied widely; very few have been evaluated and recent developments in prevention and treatment of opportunistic infections have not been included. In addition, ARV therapy had not yet been fully developed when the guidelines were produced, and therefore was not mentioned. Separate guidance modules on the clinical, organizational, laboratory, regulatory and ethical aspects of ARV treatment have recently been developed by WHO and UNAIDS. An updated clinical guide on the safe and effective use of ARVs (with particular reference to resource-constrained settings) was published in September 2000 by WHO, the International AIDS Society (IAS) and UNAIDS.[10]

WHO has also produced a guide on treatment options for HIV/AIDS in its Model Prescription Information series, and UNAIDS has published a guide on the adaptation of clinical guidelines for care for PLHA. This chapter and the guides mentioned should encourage updates of currently available national guidelines. (See Recommended Reading for accessing these guides.)

Table 1

List of Clinical Conditions by Clinical Stage

Clinical Stage 1

1. Asymptomatic infection.
2. Persistent generalized lymphadenopathy.
3. Acute retroviral infection.

Performance scale 1: Asymptomatic, normal activity.

Clinical Stage 2

4. Unintentional weight loss < 10% of body weight.
5. Minor mucocutaneous manifestations (seborrheic dermatitis, prurigo, fungal nail infections, oropharyngeal ulcerations, angular cheilitis, etc.).
6. Herpes zoster within the previous five years.
7. Recurrent upper respiratory tract infections (such as bacterial sinusitis).

And/or performance scale 2: Symptomatic, but nearly fully ambulatory.

Clinical Stage 3

8. Unintentional weight loss > 10% of body weight.
9. Chronic diarrhea > one month.
10. Prolonged fever (intermittent or constant) > one month.
11. Oral candidiasis (erythematous or pseudomembranous).
12. Oral hairy leukoplakia.
13. Pulmonary TB (typical or atypical) within the previous year.
14. Severe bacterial infections (such as pneumonia, pyomyositis).
15. Vulvovaginal candidiasis, chronic (> one month) or poorly responsive to therapy.

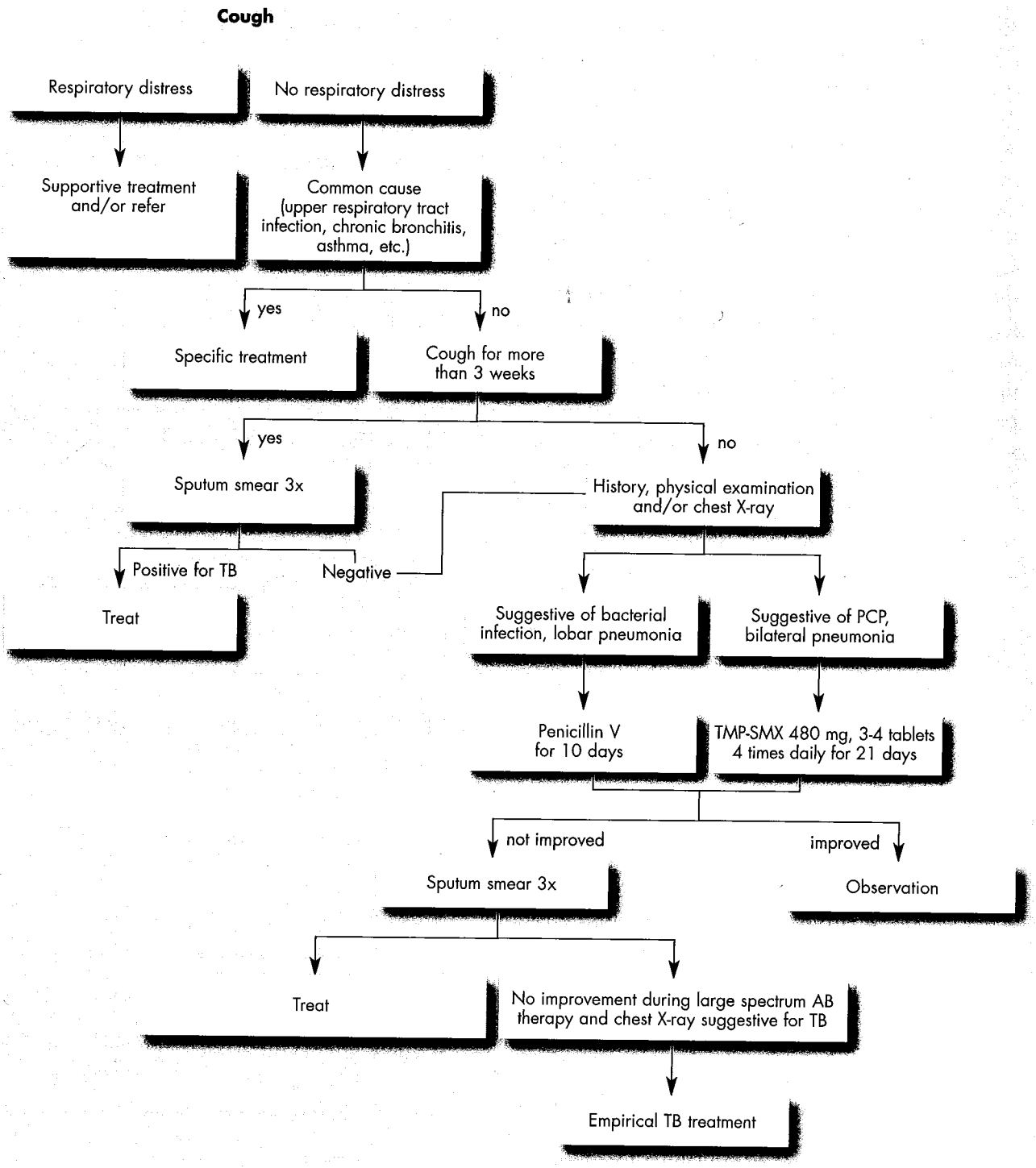
And/or performance scale 3: In bed < 50% of normal daytime, but > normal, during previous month.

Clinical Stage 4

16. HIV wasting syndrome.
17. *Pneumocystis carinii* pneumonia.
18. Toxoplasmosis of the brain.
19. Cryptosporidiosis with diarrhea > one month.
20. Isosporidiosis with diarrhea > one month.
21. Cryptococcosis, extrapulmonary.
22. Cytomegalovirus disease of an organ other than liver, spleen or lymph node.
23. Herpes simplex virus infection, mucocutaneous (> one month) or visceral (any duration).
24. Progressive multi-focal leukoencephalopathy.
25. Any disseminated endemic mycosis (histoplasmosis, coccidioidomycosis, etc.).
26. Candidiasis of the oesophagus, trachea, bronchi, or lungs.
27. Atypical mycobacteriosis, disseminated.
28. Non-typhoid salmonella septicaemia.
29. Extrapulmonary TB.
30. Lymphoma.
31. Kaposi's sarcoma.
32. HIV encephalopathy.

And/or performance scale 4: In bed > 50% of normal daytime during previous month.

Figure 2


Cough
Respiratory distress
No respiratory distress
Supportive treatment and/or refer
Common cause (upper respiratory tract infection, chronic bronchitis, asthma, etc.)
yes
no
Specific treatment
Cough for more than 3 weeks
yes
no
Sputum smear 3x
History, physical examination and/or chest X-ray
Positive for TB
Negative
Treat
Suggestive of bacterial infection, lobar pneumonia
Suggestive of PCP, bilateral pneumonia
Penicillin V for 10 days
TMP-SMX 480 mg, 3-4 tablets 4 times daily for 21 days
not improved
improved
Sputum smear 3x
Observation
Treat
No improvement during large spectrum AB therapy and chest X-ray suggestive for TB
Empirical TB treatment

MANAGEMENT OF HIV-RELATED PROBLEMS

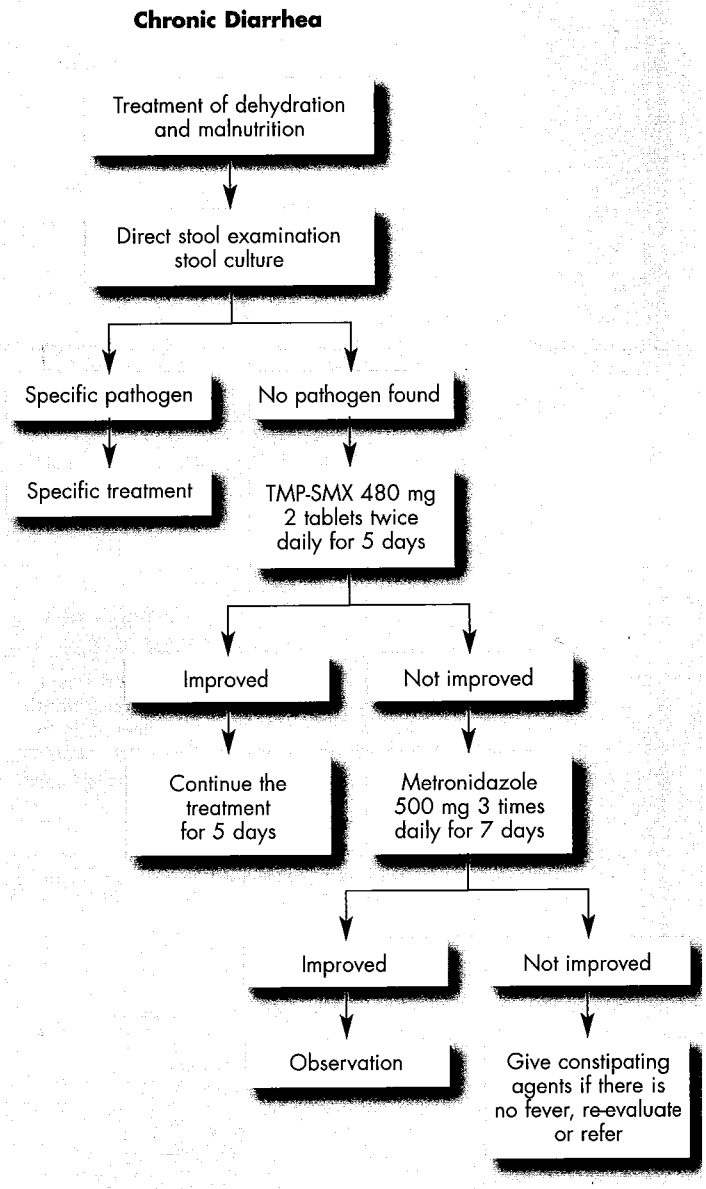
Managing the health problems of a person infected with HIV depends largely on his/her degree of immune deficiency. In the early stages of infection, patient complaints will often be unrelated to the infection itself. In advanced stages, however, opportunistic infections or cancers are to be expected. Therefore, algorithmic flow charts for the diagnosis and treatment of PLHA health problems differ according to the stages of disease. Ideally, CD4 lymphocyte counts should be measured to determine a patient's degree of immune deficiency, but this is often impossible in resource-constrained settings. To classify patients in different stages of disease in settings where CD4 lymphocyte counts are not available, a clinical classification system has been proposed by WHO (Table 1).[11]

Chronic diarrhea

Dehydration and weight loss can cause fast decline of the general condition. Before starting diagnostic procedures, a health care worker should determine whether a patient needs oral or parenteral rehydration. Recommendations about hygiene and nutrition should be given and potassium supplements considered.

Figure 3 provides an example of an algorithm for the management of chronic diarrhea (more than three loose stools per day for at least 30 days).

Figure 3



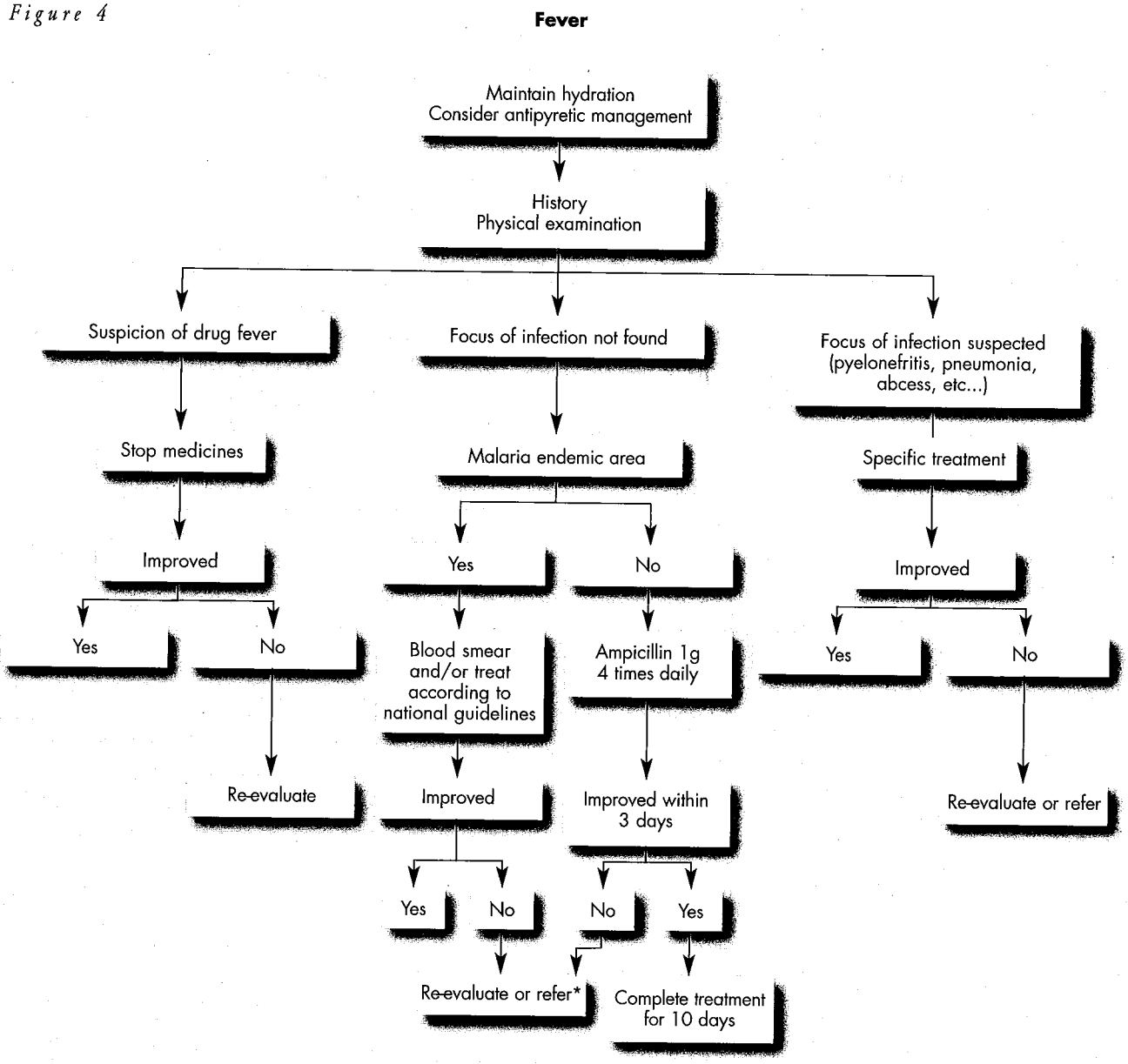
Fever

If the following clinical symptoms/signs are present, the patient should be referred immediately to a reference health facility: altered consciousness, convulsions, neck stiffness, shock and severe dyspnea. If these alarm symptoms/signs are not present, the following algorithm is proposed (Figure 4).

Cough

In the absence of respiratory distress, clinical management of a patient with HIV infection and cough can generally be done in a peripheral health center (Figure 2).

Figure 4

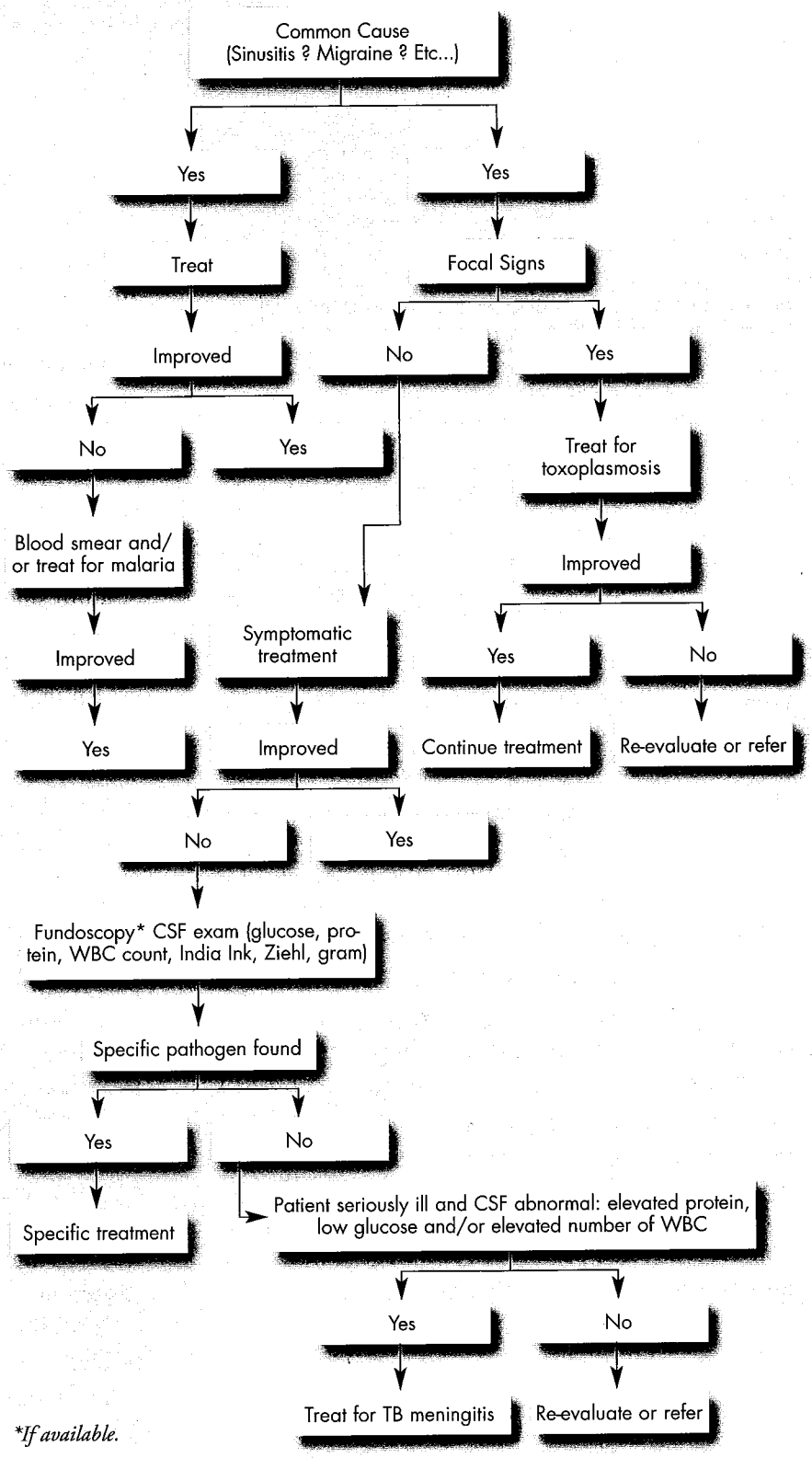


**Consider opportunistic infections, certainly if clinical signs/history are suggestive of immune deficiency (sputum smear, chest X-ray, fundoscopy, CSF examination...)*

Headache

Headache is generally due to a common cause such as stress or sinusitis in HIV-infected people with good immune systems. The work-up of headache in a person with severe immune deficiency—certainly in the presence of other symptoms and signs (including a neurological deficit)—is much more complicated and may require referral to a reference center (Figure 5).

Figure 5 **Headache**



**If available.*

HIV-related skin diseases

Dermatological abnormalities are very often observed in people infected with HIV. Table 2 describes the treatment of some of these skin lesions.

PROPHYLAXES FOR OPPORTUNISTIC INFECTIONS

Two studies in Abidjan, Côte d'Ivoire, showed cotrimoxazole significantly reduced both hospitalizations and mortality from opportunistic infections. (In a study among TB patients, mortality was decreased by nearly 50 percent). Whether large-scale administration of cotrimoxazole in resource-constrained settings will be feasible and beneficial remains to be studied. Use of this drug should be watched to determine whether it leads to increased bacterial resistance.

(For information on TB prophylaxis, see the following section).

Pneumococcal vaccination did not protect against pneumococcal infections in a clinical trial in Uganda.

Table 2

Herpes zoster	Local lesion care/if available: acyclovir 10 mg/kg three times daily for seven days.
Herpes simplex	Local lesion care/if available: acyclovir 5 mg/kg three times daily for seven days.
Molluscum contagiosum	Prick each lesion with a needle and touch with phenol.
Condyloma acuminatum	Treat with podophyllin 20% solution, once or twice weekly until cleared.
Furunculosis, impetigo, pyoderma or folliculitis	Local lesion care/treat with penicillin for 10 days.
Hidradenitis suppurativa	Local lesion care/treat with tetracycline 500 mg twice daily for six weeks.
Pyomyositis	Surgical drainage and antibiotics.
Dermatophytosis	Treat with topical broad-spectrum antifungal.
Kaposi's sarcoma	Cryotherapy, intralesional therapy, surgical excision, radiotherapy, chemotherapy.
Drug eruptions	Withdraw drug/local lesion care.
Prurigo	Topical calamine lotion.
Seborrhoeic dermatosis or generalized erythroderma	Topical 1% hydrocortisone.
Psoriasis	Coal tar in salicylate ointment twice daily.
Scabies	Topical benzylbenzoate lotion 25% or ivermectin.

TB/HIV Dual Infections

An HIV-infected person is 10 times more likely to develop TB than an uninfected person. In resource-constrained countries, more than 30 percent of people infected with HIV will develop TB, and it can occur at any point in the course of the infection. The clinical presentation of TB depends on the degree of immune deficiency. In patients in an early stage of HIV infection, TB presents in a manner similar to that in non-HIV-infected persons. In late-stage disease, disseminated TB is more common.

TB Diagnosis

The highest priority for TB control is the diagnosis of sputum smear-positive pulmonary TB cases. Clinically, this diagnosis should be suspected in the presence of the following symptoms:

- Cough more than three weeks
- Sputum production
- Weight loss

Ideally, patients with symptoms suggestive of pulmonary TB should submit three sputum samples for microscopy: one on-the-spot sample, a second early-morning sample and a third on-the-spot sample. No chest X-ray pattern is absolutely typical for pulmonary TB.

Sputum smear-negative pulmonary TB

Such a diagnosis should be considered in a patient who continues to cough despite treatment with broad-spectrum antibiotics, and who has repeatedly negative sputum smears.

Extrapulmonary and disseminated TB

An increased incidence of extrapulmonary and disseminated TB is seen in PLHA. Diagnosis is made on clinical grounds or based on the result of a bacteriological or histological examination (such as a lymph node aspiration and a Ziehl coloration of the smear).

TB Treatment

Several treatment regimens can be followed for TB patients with and without HIV infection (Table 3). The regimen recommended depends on the patient treatment category. There is a standard code for TB treatment regimens. Each anti-TB drug has an abbreviation (shown in Table 3). A regimen consists of two phases. The number before the phase is the duration of that phase in months, and a number in subscript after a letter is the number of doses of that drug per week. If there is no number in subscript after a letter, treatment with that drug is daily.

TB/HIV co-infected patients should never be treated with thiacetazone because they are at higher risk of severe, sometimes fatal, allergic reactions (Steven Johnson syndrome). Hypersensitivity reactions

Table 3
Recommended TB Treatment Regimens

TB treatment category	TB treatment regimens	
	Initial phase	Continuation phase
■ New smear-positive PTB	2 HRZE(S)	6 HE
■ Seriously ill, extra-pulmonary or	2 HRZE(S)	4 HR
Smear-negative PTB	2 HRZE(S)	4 H_3R_3
Smear-positive PTB		
■ Relapse	2 HRZES/1 HRZE	5 $H_3R_3E_3$
■ Treatment failure	2 HRZES/1HRZE	5 HRE
■ Return after default		
Not seriously ill, extra-pulmonary	2 HRZ or 2 $H_3R_3Z_3$	6 HE
TB or smear-negative PTB	2 HRZ or 2 $H_3R_3Z_3$	2 HR/4H
Extrapulmonary TB	2 HRZ or 2 $H_3R_3Z_3$	2 H_3R_3/4H
Chronic case (still sputum-positive after supervised re-treatment)	Refer to specialist center if second-line drugs available	

PTB: pulmonary TB, H= Isoniazid, R= Rifampicin, E= Ethambutol, Z= Pyrazinamide, S= Streptomycin

may occur with all anti-TB drugs and are particularly frequent in people infected with HIV. Patients with severe drug reactions should be referred to specialized TB centers.

In regions of high HIV-prevalence in resource-constrained countries—where needles and syringes are often inadequately sterilized—oral ethambutol should replace streptomycin injections.

Adherence to anti-TB treatment

Strict adherence to anti-TB treatment is essential to avoid the development of multiple drug-resistant TB. Ways to improve adherence:

1. Short course chemotherapy. By using more effective anti-TB drugs, TB treatment can be reduced to six months (see Table 3).
2. Direct observed therapy, short course (DOTS). Such treatment should be given as close to the patient's home as possible. A member of the health staff in a peripheral health facility, a trained local community member or a family member should supervise the therapy.
3. Treatment counseling by health care workers. Health care workers should explain how to take anti-TB drugs, their potential side effects and when patients must return for follow-up.
4. There should always be an adequate supply of anti-TB drugs in the health facility and patients should have easy access to them.

Monitoring TB treatment

TB patients should be monitored the same way, whether they are or are not infected with HIV. Recording the treatment results of sputum smear-positive pulmonary TB patients is vital to monitor patient cure rates and the effectiveness of the National TB Control Program.

Mortality of TB patients infected with HIV will be higher than mortality of non-HIV-infected TB patients: 20 percent of the TB/HIV co-infected patients will generally die within one year after starting TB treatment. This excess mortality is due partly to the TB itself, and partly to other HIV-related problems. Early mortality is often due to TB, while later deaths usually result from other HIV-associated causes.

HIV Testing in TB Patients

It is impossible to diagnose HIV infection in a TB patient solely on the basis of clinical symptoms. HIV infection may be suggested by certain symptoms—such as severe weight loss, chronic diarrhea, persistent fever despite effective anti-TB treatment, a history of herpes zoster, a chronic papular pruritic eruption, oral

Table 4

Drugs of the Essential Drug List for HIV/AIDS Treatment in Resource-Constrained Settings

Acyclovir
Albendazole
Amphotericin B
Ampicillin or benzylpenicillin
Anti-TB drugs
Aspirin
Calamine Lotion
Calcium folinate
Ceftriaxone
Ciprofloxacin
Chloramphenicol (or other broad spectrum antibiotic)
Chlorpromazine
Clindamycin
Codeine phosphate
Cotrimoxazole
Daraprim
Dapsone
Diazepam
Flucytosine
Gentian Violet
Hydrocortisone cream
Ketoconazole
Metronidazole
Morphine
Multivitamins
Nystatin
Paracetamol
Pentamidine
Primaquine
Pyrimethamine
Sulfadiazine
Sulfadoxine/pyrimethamine
Trimethoprim

candidiasis, a persistent painful genital ulceration, anemia, leucopenia or thrombocytopenia. But a diagnosis of HIV infection can only be made and announced to a patient based on the result of an HIV test. Therefore, health care workers involved in TB care must be trained in HIV counseling (see Chapter 23). TB treatment centers in regions of high HIV prevalence may require additional staff to cope with the increased workload.

Prevention of TB

Early diagnosis and treatment of sputum smear-positive TB patients and good adherence to TB treatment are the best ways to prevent the further spread of TB. By diagnosing TB early, patients can be treated in an outpatient setting. This avoids transmission in hospital wards. Ideally, wards where TB patients are treated should have large windows, sputum collection rooms, and microbiology laboratories. Doors should be kept closed and windows open.

Patients should be instructed to keep their mouths covered with their hands when coughing and to use sputum pots with lids. Patients with sputum smear-positive TB ideally should wear face masks when they are moved from one part of a hospital to another. But masks generally do not provide health care workers with effective protection against inhaling other people's infectious droplets. The exception is during a cough-inducing procedure, such as a bronchoscopy. If possible, sputum-positive TB patients should be admitted in a special room/ward separate from other patients, and patients should be admitted to a TB ward only after a diagnosis of TB has been confirmed.

TB Prophylaxis in HIV-Infected People

Studies indicate that isoniazid (IHG) for six to nine months or rifampicin and pyrazinamide for three months can reduce the incidence of TB in PLHA when a positive skin test indicates they are already infected with mycobaterium TB.[12] This prophylaxis, however, has not been studied sufficiently to show reduced mortality, and it remains unknown how long its protective effect will last. Before starting TB

Table 5

Minimum Requirements to Introduce Antiretrovirals (ARVs)

- Health care workers must have sufficient knowledge about ARV drugs. Patients should receive appropriate counseling. Advantages and disadvantages of ARV drugs should be discussed.
- Patients should be willing to adhere to the treatment regimen.
- ARVs should be stored in optimal conditions and distributed by trained staff.
- ARV treatment should be sustainable.
- It should be possible to diagnose and treat concomitant illnesses.
- There should be capacity to provide prophylaxis for opportunistic infections.
- A minimum of laboratory monitoring should be possible, including routine hematological and biochemical tests to detect side effects of drugs. CD4+ lymphocyte counts and viral load measurements are needed to decide whether to start ARV treatment in asymptomatic patients.

prophylaxis, it should be certain that the patient has no active TB. Therefore, an extensive clinical history and examination including a chest x-ray should be performed.

WHO and UNAIDS recommend that preventive therapy for TB should be included in the health care package of PLHA whenever possible.[2]

BCG Vaccination and HIV Infection

There have been some reports of disseminated Bacille Calmette Guerin (BCG) infection after BCG vaccination of HIV-infected children. In the majority of cases, however, BCG immunization has been shown to be safe. The advantages of BCG vaccination outweigh the possible disadvantages in countries where there is a high prevalence of TB. WHO therefore continues to recommend BCG vaccination of all children in these countries, except for children with symptoms of HIV/AIDS.

IMPROVING ACCESS TO ESSENTIAL DRUGS

Drugs are needed primarily for infectious complications that are easily diagnosable and treatable (at low cost), particularly those that may occur during relatively early stages of HIV infection—such as other sexually transmitted diseases (STDs), salmonella septicemia, bacterial pneumonia and TB. For some of these infections (TB and STDs), access to treatment—at low or no cost—is important to avoid their further spread. Symptomatic treatment should be available to treat diarrhea, fever and pain. UNAIDS and the WHO Action Program on Essential Drugs and Vaccines recently established a list of essential drugs for HIV/AIDS (Table 4). (See Chapter 4 for more information on managing essential drugs for HIV/AIDS patients.)

IMPROVING ACCESS TO ANTIRETROVIRAL DRUGS (ARVS)

Providing optimal ARV therapy to all persons for whom such treatment may be beneficial should be the goal. But in resource-constrained settings there are many obstacles to achieving this. Minimum requirements to introduce ARV drugs are shown in Table 5.

ARVs are increasingly used in resource-constrained countries and certainly in medium-income countries, such as those in South America. The issue is therefore how to use these ARV drugs in the most efficient and safest manner. Guidelines have been developed by WHO in collaboration with IAS and UNAIDS (see Recommended Reading). Countries with limited resources should establish a list of priorities for the use of ARV drugs. An example is given in Table 7.

What Should *Not* Be Done with ARV Treatment

- Start therapy in someone whose HIV diagnosis has not been confirmed.
- Begin when long-term provision cannot reasonably be guaranteed.
- Start in a patient not motivated to follow such treatment, or in a person who is unaware of his/her seropositivity.

Table 6

Licensed Antiretroviral Drugs and Commonly Used Regimens for Initiating Treatment

Nucleoside Analogue Reverse Transcriptase Inhibitors (NRTI)	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)
Zidovudine (ZDV)	Nevirapine
Didanosine (ddI)	Delavirdine
Zalcitabine (ddC)	Efavirenz
Lamivudine (3TC)	
Stavudine (d4T)	
Abacavir (ABC)	
	Protease Inhibitors (PI)
	Indinavir
	Ritonavir
	Saquinavir
	Nelfinavir
	Commonly Used Regimens for Initiating Treatment
	1 PI + 2NRTI (e.g., indinavir + ZDV + 3TC)
	1NNRTI + 2 NRTI (e.g., nevirapine + d4T + ddI)

- Prescribe ARV monotherapy, except for the prevention of perinatal HIV transmission and post-exposure prophylaxis (PEP).
- Start without laboratory monitoring. In resource-constrained settings, anemia with hemoglobin levels seven to eight grams per deciliter is relatively frequent. These patients may be particularly at risk for severe anemia during zidovudine and cotrimoxazole treatment. Chronic hepatitis caused by hepatitis B and C infections is also very common in resource-constrained countries; ARV drugs are all potentially hepatotoxic and should be prescribed with caution to these patients. If these drugs are given, liver function should be monitored. In cases of renal insufficiency, dosage of certain ARV drugs such as stavudine and indinavir should be modified.
- Start without providing adequate information about how and when to take the drugs, potential side effects, interactions with other drugs, when to stop the drugs, etc.
- Provide treatment without the capacity to diagnose, treat or prevent opportunistic infections.
- Provide treatment unless patient's other needs, such as sufficient nutritional support, adequate home care, etc. can be met.
- Continue treatment despite serious side effects or possible irreversible damage.
- Strict adherence to treatment cannot be assured, since this is essential to avoid the development of resistance.

How to Improve Adherence to ARV Treatment

Treatment decisions should be made jointly by the patient and the clinician after careful discussion of:

- Advantages and disadvantages of ARV treatment
- Different treatment options
- Possible adverse reactions
- Cost of treatment
- Need for a long-term emotional and financial commitment

Choice of an ARV treatment regimen should take into account the lifestyle of the patient:

- Patients may accept a twice-daily, but not a three-times-daily, treatment regimen.
- Patients who eat at irregular time intervals may have problems adhering to certain ARV treatment regimens.

Once an ARV treatment regimen has been chosen, the following should be explained very carefully:

- How and when the drugs should be taken: Written information should be given the patient or a family member if they can read. Clearly illustrated materials should be given illiterate patients.
- Potential adverse reactions of such treatment and what to do about them.
- How and where the patient can get information about possible treatment problems.
- When the patient should return for follow-up visits, blood tests and other monitoring.
- Who will help the patient adhere to the treatment regimen—partner, another family member, a friend, a nurse.
- Where to get psychosocial support.

Patients should be able to consult regularly with a trained counselor to discuss all aspects of adherence. Communication skills of the doctor/counselor are very important. There should be a reliable, long-term and regular supply of ARV drugs that patients can easily access.

ARVs to Prevent Transmission of HIV

Studies with macaques provide compelling evidence that ARV therapy can prevent acquisition of HIV. Animals provided ARVs before or after exposure can be protected from infection. [13,14] A single retrospective study suggests that ARVs can prevent acquisition of HIV after needlestick exposure.[15] (See Chapter 21 for more information on HIV transmission in health care settings.)

The use of ARVs to prevent mother-to-child transmission (MTCT) of HIV emphasizes the power of biological prevention strategies. (See Chapters 18 and 19 for more information on ARV therapy to reduce MTCT of HIV.)

Recent work in Uganda[16] and Zambia[17] demonstrates that HIV concentration in blood—and by extension, genital secretions—determines the efficiency of sexual transmission in discordant couples.

Table 7

Suggested Priority to be Accorded to ARV Treatment According to Disease Stage

Disease stage (WHO stage 1-4)	
1. Acute HIV illness	No ARV drugs
Asymptomatic phase	No ARV drugs
2. Early symptomatic phase	No ARV drugs
3. Symptomatic phase, non-AIDS	ARV drugs*
4. AIDS	ARV drugs
5. Terminal AIDS	No ARV drugs

**It is strongly recommended that CD4 lymphocyte and, if available, viral load results should determine when ARV treatments are used. Where budgets are limited, it is probably best not to begin treatment too early, to assure continuation of this therapy once it has been started. A maximum beneficial impact on the quality of life of patients is expected in patients with CD4 lymphocyte counts < 200/mm³ and/or a viral load > 30.000-100.000 copies/ml plasma. With a small budget it is probably better to delay ARV treatment in TB patients because the TB treatment itself is complicated, and rifampicin cannot be given in association with certain ARV drugs (protease inhibitors). Ideally, tritherapy should always be considered because bitherapy will rapidly lead to drug resistance.*

These observations and extensive work with macaques[13] suggest that ARV therapy can be used to reduce transmission of HIV. Such therapy could be used to prevent transmission from an infected person to his/her uninfected partner, or to prevent HIV acquisition through pre- or post-exposure ARV prophylaxis.

But there have been no studies of ARV sexual prophylaxis in humans, largely because of the difficulty in developing research strategies capable of proving the benefit of prophylaxis.[18] Research that demonstrates the feasibility of prophylaxis does not prove that such prophylaxis works.

Table 8
Clinical Markers of Perinatally Acquired HIV

Strongly suggestive of HIV
Pneumocystis carinii pneumonitis
Non-suppurative parotitis
Esophageal candidiasis
Kaposi's sarcoma (rare)
Multi-dermatomal herpes zoster
Hyperglobulinaemia without obvious cause
Suggestive of HIV
Failure to thrive
Chronic diarrhea
Nephrotic syndrome
Persistent oral thrush
Cardiomyopathy
Frequent, slowly responsive bacterial infections
Immune thrombocytopenia
Extapulmonary TB
Non-cavitary pulmonary TB
Suggestive of HIV in the context of known maternal infection
Extensive lymphadenopathy
Hepatosplenomegaly
Development delay
Drug eruptions
Finger clubbing
Generalized dermatitis
Prematurity

HIV INFECTION IN CHILDREN

Diagnosis and Management of HIV Infection in Infants

It is difficult to detect HIV infection in infants because they passively acquire HIV antibodies from their mothers. Maternal antibodies may last as long as 18 months, but uninfected children usually revert to a negative status before age nine to 10 months. A single negative HIV antibody test result can be considered diagnostic of absence of infection.

In better-equipped settings, diagnosis is made by HIV DNA PCR testing. This should be performed before the infant is 48 hours old, at age one to two months, and at age three to six months. HIV infection is diagnosed by two positive HIV virologic tests, performed on separate blood samples. In the absence of biological markers, clinical markers of perinatally acquired HIV infection should be used, as shown in Table 8.

Monitoring Pediatric HIV Infection

Ideally, CD4 lymphocyte counts should be done. CD4 lymphocyte counts in healthy infants who are not infected with HIV are considerably higher than in uninfected adults, and slowly decline to adult levels by age six. Therefore, levels of CD4 lymphocyte counts in HIV-infected children are higher than in adults with the same stage of disease. When there is no access to CD4 lymphocyte counts or viral load during regular clinical check-ups, weight, growth and development should be monitored to determine whether treatments are effective.

Management of Opportunistic Infections

Frequent opportunistic infections in children include candida, tuberculosis (TB) and pneumocystis carinii pneumonia. In resource-constrained settings, pneumocystis carinii pneumonia seems to occur more frequently, and TB less frequently, in infected children than adults. Cryptococcal meningitis and cerebral toxoplasmosis also are less common in children than in adults. Children infected with HIV often present with recurrent ordinary bacterial infections.[19]

The United Nations Children's Fund (UNICEF) approach to Integrated Management of Childhood Illnesses (IMCI) provides a framework for managing common diseases and malnutrition. This approach could also be used as a basis for the treatment of infected children. WHO has also produced algorithms specifically for the management of medical problems of pediatric HIV/AIDS patients. Adequate nutritional support is essential, and vitamin A supplementation may be useful for children with persistent diarrhea.

Prophylaxis Against Opportunistic Infections

Primary prophylaxis with cotrimoxazole has been proposed for all infants born to HIV-infected women from four weeks of age until their infection status is established. Cotrimoxazole prophylaxis may decrease pneumococcal and other bacterial infections, but may increase the risk of selecting resistant organisms. So far, however, the efficacy and cost-effectiveness of this strategy has not been evaluated in HIV-infected children in resource-constrained settings.

Vaccinations

Inactivated polio vaccine should be preferred over oral polio vaccine. Where the risk of measles is high—especially during hospital admission—measles vaccine should be given at six and nine months. In children with known symptomatic HIV infection, BCG and yellow fever vaccination are contraindicated. Otherwise, no changes in immunization schedules are indicated for children born to mothers who are suspected or known to be infected with HIV.[19]

HIV Infection in Women

Women are particularly vulnerable to HIV infection due to physiological, socioeconomic and (often) cultural factors. The vast majority of infected women are of reproductive age, and are at particular risk of stigmatization, abandonment by their partner/family or becoming victims of violence. One important response to discrimination has been the formation of self-help groups. Women infected with HIV generally have access to fewer resources than do men; increasing their economic independence is an important step toward enabling women to reduce infection risks for themselves and their families. Small credits and skills development can help them achieve independence. Legal assistance may be needed to protect the inheritance rights of widows.

Gynecological Problems

Gynecological symptoms may be the first sign of HIV infection in women. These include recurrent or persistent vaginal candidiasis, recurrent or persistent herpes simplex tubo-ovarian, genital ulcerations, genital ulcerations caused by ulcus Ducrey, syphilis, pelvic inflammatory disease (PID) (especially tubo-ovarian abscesses) and cervical dysplasia caused by human papillomavirus infection. Women infected with HIV are approximately 10 times more likely to develop cervical cancer than those not infected, and should be screened regularly for cervical abnormalities. In addition, infected women often suffer from infertility caused by other STDs. Women in late-stage disease frequently present with oligomenorrhoea or amenorrhoea.

HIV Infection in Pregnancy

In making reproductive decisions, HIV-infected women should be provided with information and counseled about their pregnancy options. Contraceptive counseling should be offered to those who do not desire pregnancy. Condoms should be used, since the efficacy of hormonal contraceptives may be reduced by drugs such as rifampicin or protease inhibitors. Intrauterine contraceptive devices are

not recommended because they are associated with an increased risk of PID, and also may cause endometriosis, increased menstrual bleeding and micro-abrasions on the penis (which may increase the risk of HIV transmission to an unprotected partner). The use of female condoms could be proposed if the sexual partner is not willing to use a male condom. Although there is in vitro evidence that some spermicidal agents act against HIV, their efficacy in vivo has not been established. Recent studies indicate that nonoxynol-9 may actually increase the risk of HIV acquisition, and is not recommended for prevention of HIV in women.

Where legally accepted, prenatal and safe abortion services should be available by referral. Pregnancy among HIV-infected women does not appear to increase maternal morbidity or mortality, but the following adverse pregnancy outcomes have been reported in women infected with HIV, particularly in women with advanced HIV disease: increased risk of fetal loss, intrauterine growth retardation, pre-term birth and low birth weight.

Many infected women refuse contraceptives for a variety of reasons: They have no access to them; they are unable to tell their partner they are HIV-infected (risk of violence, risk of abandonment); they are expected to become pregnant; or they want to become pregnant. With greater availability of ARV drugs, more infected women will probably consider becoming pregnant. If a partner is HIV-seronegative, artificial insemination could be proposed. (See Chapter 18 for antenatal intrapartum and postnatal management.)

HEALTH SECTOR REFORM AND HIV/AIDS

In many resource-constrained settings, health care is changing: Reforms are being introduced to improve the quality and effectiveness of services delivered—often by transferring responsibility for planning and management of services and budgets to the district level. Health sector reform may also reduce the accountability and affordability of HIV/AIDS health services in the public sector. Privatization of health care is increasing, while cost constraints are limiting public sector services.

What does this mean for HIV/AIDS care? Most PLHA will have no choice but to continue to seek care through the public sector. But cost-sharing schemes may inadvertently disclose serostatus and, for those with few resources, further limit access to care. As the number of people seeking care is rapidly increasing, there is urgent need for decentralized services to cope with growing demand. The challenge remains to integrate HIV/AIDS comprehensive care into district and local services and ensure access to care across a continuum—from hospital to community to home. For the moment, too many patients are treated in large hospitals. Overcrowding in these health facilities means both PLHA and those with other diseases do not receive adequate care. Decentralization of care, with the involvement of district management teams knowledgeable about HIV/AIDS and guidelines for referral between services, will be needed (see Figure 1).

FUTURE CHALLENGES

Progress in the treatment of people infected with HIV has been made mainly in industrialized countries. The challenge now is to look at ways to introduce new treatment regimens into resource-constrained settings. A minimum package of HIV care should include simple diagnostic facilities and counseling, accurate information about HIV/AIDS, psychosocial support, symptomatic treatment, treatment for easily diagnosable and treatable conditions such as salmonella septicemia, bacterial pneumonia, TB, STDs and oral candidiasis, as well as palliative care.

There has been very little research into the biomedical and socioeconomic aspects of care and support for people infected with HIV in resource-constrained settings. Very few studies have evaluated the quality of care and the efficacy of clinical algorithms. A number of trials are underway to evaluate the efficacy of prophylaxes against opportunistic infections and the effect of ARV therapy in preventing perinatal transmission. Operational research is now needed to evaluate whether certain successful interventions can be implemented on a larger scale, outside research settings.

RELEVANT CHAPTERS

Chapter 3 *Responding to the Socioeconomic Impact of HIV/AIDS*

Chapter 4 *Improving Access to Drugs for People Living with HIV/AIDS*

Chapter 18 *Reducing the Risk of Mother-to-Child Transmission of HIV During Pregnancy and Delivery*

Chapter 19 *Mother-to-Child Transmission of HIV Through Breastfeeding: Strategies for Prevention*

Chapter 21 *Transmission of HIV in Health Care Settings*

Chapter 23 *Counseling, Testing and Psychosocial Support*

REFERENCES

1. Harrington M, Carpenter CCJ. Hit HIV-1 hard, but only when necessary. *Lancet* 2000;355:2147-2152.
2. Carpenter CCJ, Copper DA, Fischl MA, et al. Antiretroviral therapy in adults. Updated recommendations of the International AIDS Society-USA Panel. *JAMA* 2000;283:381-390.
3. Centers for Disease Control and Prevention, Atlanta, Georgia. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. *MMWR* 1998;47(RR-4).
4. United Kingdom NGO AIDS Consortium Working Group on Access to Treatment for HIV in Developing Countries. Access to treatment for HIV in developing countries; statement from international seminar on access to treatment for HIV in developing countries, London, June 5-6, 1998. *Lancet* 1998;352:1379-1380.
5. Wood E, Braitstein P, Montaner JSG, et al. Extent to which low-level use of antiretroviral treatment could curb the AIDS epidemic in sub-Saharan Africa. *Lancet* 2000;355:2095-2100.
6. Osborne CM, van Praag E, Jackson H. Models of care for patients with HIV/AIDS. *AIDS* 1997;11(suppl B):S135-S141.
7. Lucas SB, Hounnou A, Peacock C, et al. The mortality and pathology of HIV infection in a West African city. *AIDS* 1993;7:1569-1579.
8. Gilks CF, Brindle RJ, Otieno LS, et al. Life-threatening bacteraemia in HIV-1 seropositive adults admitted to hospital in Nairobi, Kenya. *Lancet* 1990;336:545-549.
9. World Health Organization/Global Programme on AIDS. *Guidelines for the Clinical Management of HIV Infection in Adults.* Geneva: WHO/GPA, June 1991.
10. Joint United Nations Programme on HIV/AIDS. *Developing HIV/AIDS Treatment Guidelines.* Geneva: UNAIDS, 1999.
11. World Health Organization. Acquired immunodeficiency syndrome (AIDS). Interim proposal for a WHO staging system for HIV infection and disease. *Wkly Epidem Rec* 1990;65:221-228.
12. Centers for Disease Control and Prevention. Prevention and treatment of TB among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. *MMWR* 1998;47(RR-20).

13. Black, RJ. Animal studies of prophylaxis. *Am J Med* 1997;102:39-44.

14. Tsai CC, Emau P, Follis KE, et al. Effectiveness of postinoculation (R)-9-(2-phosphonylmethoxypropyl) adenine treatment for prevention of persistent simian immunodeficiency virus (SIV) infection depends critically on timing of initiation and duration of treatment. *J Virol* 1998;72(5):4265-4273.

15. Cardo DM, Culver DH, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *N Engl J Med* 1997;337:1485-1490.

16. Quinn TC, Wawer MJ et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med* 2000;342(13):921-929.

17. Fideli US, et al. Virologic and immunologic determinants of heterosexual transmission of human immunodeficiency virus type 1 (HIV-1) in Africa. (In press).

18. Cohen MS, et al. The global prevention of HIV. In M.A. Sande and P.A. Volberding, eds. *The Medical Management of AIDS.* Sixth edition. Philadelphia: W.B. Saunders, 1999.

19. Marum LH, Tindeybwa D, Gibb D. Care of children with HIV infection and AIDS in Africa. *AIDS* 1997;11(suppl B):S125-S134.

RECOMMENDED READING

Gilks C, Floyd K, Haran D, et al, eds. *Sexual Health and Health Care: Care and Support for People with HIV/AIDS in Resource-Poor Settings.* London: United Kingdom Department for International Development, 1998.

Harries AD, Maher D. TB/HIV: *A Clinical Manual.* (WHO/TB/gb.200). Geneva: WHO, 1996.

Joint United Nations Programme on HIV/AIDS. *HIV-Related Opportunistic Diseases.* Geneva: UNAIDS, October 1998.

Joint United Nations Programme on HIV/AIDS. *Access to Drugs.* Geneva: UNAIDS, October 1998.

Joint United Nations Programme on HIV/AIDS. *Developing HIV/AIDS Treatment Guidelines.* Geneva: UNAIDS, 1999.

Laga M, De Cock KM, Kaleeba N, et al, eds. *AIDS in Africa.* Second edition. *AIDS* 1997;11(suppl 1):S1-S169.

Mahler D, Chaulet P, Spinaci S, Harries A. Treatment of tuberculosis: guidelines for national programmes. Geneva: World Health Organization, 1997.

van Praag E, Fernyak S, Martin Katz A. *The Implications of Antiretroviral Treatments.* Informal consultation. (WHO/ASO/97.2). World Health Organization. WHO, 1997.

World Health Organization/Global Programme on AIDS. Guidelines for the clinical management of HIV infection in adults. Geneva: WHO/GPA, June 1991.

World Health Organization/Global Programme on AIDS. Guidelines for the clinical management of HIV infection in children. Geneva: WHO/GPA, April 1993.

World Health Organization/Global Tuberculosis Programme/Office of the United Nations High Commissioner for Refugees. *Tuberculosis Control in Refugee Situations: An Inter-Agency Field Manual.* Geneva: WHO, January 1997.

World Health Organization. *Standard Treatments and Essential Drugs for HIV-Related Conditions. Access to HIV-Related Drugs.* Geneva: WHO, December 1997.

World Health Organization /Joint United Nations Programme on HIV/AIDS. *Guidance Modules on Antiretroviral Treatments.* (WHO/ASO/98.1). Geneva: WHO, January 1998.

World Health Organization. *WHO Model Prescribing Information. Drugs Used in HIV-related Infections.* (WHO/DMP.DSI/99.2). Geneva: WHO, February 1999.

World Health Organization/International AIDS Society/Joint United Nations Programme on HIV/AIDS. *Safe and Effective Use of Antiretroviral Treatments in Adults with Particular Reference to Resource Limited Settings.* (WHO/ASI.2000.04). Geneva: WHO, April 2000.

World Health Organization. Fact sheet on HIV/AIDS for Nurses and midwives. Geneva: WHO, 2000.