Guideline

Guidelines for diagnosis and treatment of HIV/AIDS in China (2005)

Chinese Medical Association and Chinese Center for Disease Control and Prevention

Acquired immunodeficiency syndrome (AIDS), caused by the human immunodeficiency virus (HIV), has become a major public health issue in China. It not only poses formidable challenges for the health of the Chinese people, but has also influenced China’s economic development and social stability.

Tasked by the Ministry of Health, the Chinese Medical Association organized experts to develop these Guidelines for Diagnosis and Treatment of HIV/AIDS. Based on the latest national and international research developments, these guidelines adopt an evidence-based approach, taking into account the characteristics of China’s situation. Topics include epidemiology, etiology, pathogenesis, pathological changes, clinical presentation and staging, laboratory tests, diagnosis, highly active antiretroviral therapy (HAART), diagnosis and treatment of common opportunistic infections (OIs), prevention of mother-to-child transmission (PMTCT), and postexposure prophylaxis. Special attention focuses on the antiretroviral therapy.

Features of these guidelines include: 1) systematic and comprehensive coverage from basic science to the clinical, from treatment to prophylaxis; 2) evidence-based medicine that avoids recommending views and approaches yet to be proven; 3) clinically practical and innovative, building upon the consensus from Chinese experts (particularly in regard to HIV clinical staging and diagnostic criteria), epidemiology of HIV and AIDS in China and the clinical characteristics of Chinese AIDS patients; 4) recommendation of HAART regimens based on in-country drug availability.

The essence of clinical medicine is the adoption of appropriate diagnosis and treatment approaches with consideration of the specific conditions of patients and available medical resources. Given the rapid development of modern medicine and the perpetual emergence new theories, views, and diagnosis/prevention/treatment approaches, these Guidelines will be regularly revised and updated based on the latest developments in clinical medicine.

Epidemiology

From the first cases of HIV/AIDS reported in the United States in 1981 to the end of 2003, approximately 69 million cases of HIV infections have been reported globally and 27 million of them were dead. The first case of AIDS in China was reported in 1985. Since that time, it is estimated that approximately 840,000 individuals were infected by the virus by the end of 2003, including 80,000 cases of AIDS. To date, the infection has been reported in all provinces, autonomous regions, and municipalities of China and it is spreading from high-risk populations such as drug users and commercial sex workers to the general population.

Source of the infection

People living with HIV/AIDS (PLWHA) are the sole sources of HIV infection.

Routes of transmission of HIV

The virus presents predominantly in the PLWA’s blood, semen, vaginal discharge, and breast milk. HIV transmission occurs through sexual contact (including homosexual, heterosexual and bi-sexual contact), blood or blood products (such as via intravenous drug use with needle sharing or invasive medical operations) and mother-to-child (including

Correspondence to: Dr. LI Tai-sheng, Department of Infectious Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China (Tel: 86-10-65295086. Fax: 86-10-65295046. Email: litsh263.net)
prenatal, intrapartum and postpartum transmission).\textsuperscript{1} It is not transmitted through day to day contact with PLWHA, such as shaking hands, hugging, kissing for etiquette purposes, dining or drinking together; nor is it transmitted through sharing toilets, restrooms, offices, public transportation or recreational facilities.

**Vulnerable populations**

All populations are vulnerable to HIV infection. HIV infection is closely associated with behavior such that men who have sex with men, intravenous drug users (IDUs), those who have frequent sexual contact with HIV infected persons and those who frequently receive transfusions of blood or blood products (such as hemophiliacs) are at high risk of acquiring HIV.

**Case reporting**

Once a new infection is identified, the case should be immediately reported to the local CDC.

**Medical management**

Follow the principle of confidentiality, strengthen follow-up with the PLWHA, and provide medical and psychological counseling.

**Precautions**

Develop healthy sexual practices; use condoms correctly, and engage in safer sex. Refrain from drug use and needle and syringe sharing. Promote non-commercial blood donation and conduct HIV screening among blood donors. Reinforce hospital management; strictly follow disinfection procedures; control nosocomial cross infections, and prevent infections via occupational exposure. Control mother-to-child transmission. Provide medical examinations, HIV testing, and appropriate counseling services to PLWHA, other sexual partners, men who have sex with men and anyone with whom the PLWHA may share needles and syringes.\textsuperscript{2}

**Virology**

HIV is a retrovirus belonging to a group of cytopathic lentiviruses. The virus has a diameter of 100–120 nm and is spherical in shape. It is composed of an interior viral core and an outer viral envelope. The viral core contains two single strands of HIV RNA, core structural proteins and enzymes necessary for viral replication, including reverse transcriptase (RT, P51/P66), integrase (INT, P32) and protease (PI, P10). It has a coat called HIV capsid proteins (P24, P17). The exterior coat of HIV is the viral envelope, embedding two glycoproteins: gp120 (envelope glycoprotein) and gp41 (transmembrane glycoprotein).

HIV has a 9.8 kb genome, containing 3 structural genes (gag, pol, and env), 2 regulatory genes (tat—trans-activator; rev — regulator of virion protein expression) and 4 auxiliary genes (nef—negative regulatory factor; vpr — viral protein R; vpu — viral protein U; and vif — viral infectivity factor).

HIV is highly variable. Various genes have different variabilities; env has the highest variability. Major causes for HIV variation include: random variation results in a dysfunctional reverse transcriptase; host’s immunoselection pressure; gene recombination between viral DNA and host DNA; and drug selective pressure. Nonstandard and no adherence to antiretroviral therapy is a major cause for drug resistance.

HIV is classified into type HIV-1 and type HIV-2. The two viruses share a 40%—60% amino acid sequence homology. Currently, HIV-1 is globally prevalent (unless otherwise noted, HIV refers to HIV-1 in this document). HIV-1 can be further classified into different subtypes, including subtype groups M (the major group), O and N. The group M has 11 subtypes: A, B, C, D, E, F, G, H, I, J and K. In addition, multiple recombinants have been identified in recent years. HIV-2 is biologically similar to HIV-1, but features lower infectivity, slower AIDS clinical progression and milder symptoms. HIV-2 has at least 7 subtypes: A, B, C, D, E, F and G.

HIV-1 is the major epidemic strain in China. Eight subtypes have been identified in the country, including A, B (Europe and US B), B’ (Thailand B), C, D, E, F and G, in addition to different recombinants.\textsuperscript{3} A few PLWHA with HIV-2 have been reported and confirmed since 1999 in China. Timely identification and confirmation of various HIV subtypes is important for estimation of prevalence trends, diagnosis as well as development of new reagents, medicines and vaccines.
HIV enters cells via receptors on the surface of susceptible cells. Receptors include receptor type 1 (CD4, major receptor) and receptor type 2 (auxiliary receptors of CCR5 and CXCR4, etc). Based on the utilization of auxiliary receptors by HIV, HIV is classified into X4 HIV and R5 HIV. R5 usually utilizes CCR5 receptor only, while X4 often utilizes CXCR4, CCR5 and CCR3 receptors simultaneously, and sometimes utilizes CCR2b receptor.

HIV is a fragile virus and is not able to survive long outside the body. It is easily destroyed by many physical and chemical factors. Therefore, antisepsis and inactivation methods effective for HBV are also applicable for HIV. Besides, 75% alcohol can inactivate HIV, while ultraviolet or γ-ray cannot.

HIV is also very sensitive to temperature. It is more tolerant to low temperature than to high temperature. HIV in vitro will lose infectivity to T lymphocyte at 56°C for 30 minutes; this method, however, cannot completely inactivate HIV in serum. HIV can be completely inactivated at 100°C for 20 minutes.

LABORATORY TESTS

HIV laboratory tests include those for HIV antibody, quantitative plasma HIV RNA (viral load), CD4+ T lymphocyte and P24 antigen assay, etc. HIV1/2 antibody test is the “golden standard” for diagnosis of HIV infection. Viral load assays and CD4+ T lymphocyte counts are two important predictors for disease progression, response to ART and prognosis. Infants under 18 months can be diagnosed by a nucleic acid test; one needs two positive nucleic acid tests to confirm a diagnosis of HIV infection. A positive HIV antibody test after 18 months confirms HIV infection.

HIV1/2 antibody test
It is a screening (including primary screening and retest) and confirmatory test.

HIV1/2 antibody screening tests include enzyme linked immunosorbent assay (ELISA) and rapid tests (rapid test paper and gelatin particle agglutination test). ELISA is the commonly used antibody screening test. Along with the development of voluntary counseling and testing, however, rapid tests can be used. Western blot is commonly used as the HIV antibody confirmatory test.

A negative HIV1/2 antibody screening test should be reported as indicating that there is no HIV infection. On the other hand, a positive screening test does not necessarily indicate that the person is infected. Such a result should be followed by a confirmatory test. The report should therefore read “HIV antibody to be confirmed”. If the confirmatory test is positive, the result can now be reported as “positive HIV-1 (or HIV-2) antibody” meaning that the person is infected with HIV. The giving of HIV1/2 antibody results should always be accompanied by confidential counseling.

Viral load assays
Plasma viral load is generally represented by the copies of HIV RNAs per milliliter of plasma (c/ml).

Commercially available assay for viral load include reverse-transcription polymerase chain reaction (RT-PCR), nucleic acid sequence-based amplification (NASBA NucliSens) and branched DNA (bDNA) signal amplification system. Different viral load tests are compared in Table 1.

Clinical significance of viral load assay: prediction of the disease progression, indications for starting antiretroviral therapy, evaluation of treatment efficacy, guidance for change of regimen, or reference indicator for early diagnosis of acute HIV infection.

CD4+ T lymphocyte assays
CD4+ T lymphocytes are the primary target cells of HIV infection. After HIV infects a person a progressive loss of CD4+ T lymphocytes occurs resulting in an inverted ratio of CD4+/CD8+ T cells. If HAART is provided, varying degrees of increase of CD4+ T lymphocytes may be seen at different stages. The CD4+ T lymphocyte subgroup test commonly used is flow cytometry, which can directly generate an absolute value of the CD4+ T lymphocyte count. Alternatively, the absolute number of CD4+ T lymphocytes can be derived from WBC differential count. If flowcytometry is not available, absolute number of lymphocytes can be referred to. Clinical significance of CD4+ T lymphocyte count: understanding the immune status of a person who is infected, monitoring disease progression, assisting with disease staging, and when to start therapy as well as, determining clinical efficacy and the likelihood of occurrence of complications such as OIs
Table 1. Comparison of assay methods for viral load

<table>
<thead>
<tr>
<th>Technique</th>
<th>RT-PCR</th>
<th>bDNA</th>
<th>NASBA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dynamic range</td>
<td>Standard: (Amplicor 1.5)</td>
<td>bDNA Version 3.0:</td>
<td>Nuclisens HIV-1 QT:</td>
</tr>
<tr>
<td></td>
<td>400–750 000 c/ml</td>
<td>50–500 000 c/ml</td>
<td>176–3 500 000 c/ml</td>
</tr>
<tr>
<td></td>
<td>Ultrasensitive: (Ultra_Direct 1.5)</td>
<td></td>
<td>Depending on volume</td>
</tr>
<tr>
<td></td>
<td>50–75 000 c/ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtype amplified</td>
<td>Version 1.0: B only</td>
<td>A to H</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Version 1.5: B to G</td>
<td>A to G</td>
<td></td>
</tr>
<tr>
<td>Specimen volume</td>
<td>Amplicor: 0.2 ml</td>
<td>1 ml</td>
<td>EDTA, heparin</td>
</tr>
<tr>
<td></td>
<td>Ultrasensitive: 0.5 ml</td>
<td>10 µl to 2 ml</td>
<td>Plasma, whole blood, any body fluid,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PBMC, semen, tissue, etc</td>
</tr>
<tr>
<td>Tubes</td>
<td>EDTA (lavender top)</td>
<td>EDTA (lavender top)</td>
<td>EDTA, heparin</td>
</tr>
<tr>
<td>Specimen</td>
<td>Plasma</td>
<td>Plasma, PBMC, semen, tissue, etc</td>
<td>Plasma, whole blood, any body fluid,</td>
</tr>
<tr>
<td>Requirement</td>
<td>Separate plasma &lt; 6 hours and freeze prior to shipping at −20°C or −70°C</td>
<td>Separate plasma &lt; 4 hours and freeze prior to shipping at −20°C or −70°C</td>
<td>Separate serum or plasma separation &lt; 4 hours and freeze prior to shipping at −20°C or −70°C</td>
</tr>
</tbody>
</table>

and malignancies.

Intervals of CD4+ T lymphocyte count testing should be decided by clinicians based on the conditions of patients. Generally, it is recommended that asymptomatic HIV-infected patients with CD4+ T lymphocyte count > 350 × 10^6/L receive such test once per year; PLWHAs with (200–350) × 10^6/L CD4+ T lymphocyte count who are not already on ART should have a CD4 test biannually; PLWHAs on ART should have a CD4 test quarterly in the first year of treatment. Beyond one year treatment if conditions are stable, they can have the test biannually.

**PATHOGENESIS**

**HIV infection process**

*Primary infection*

HIV enters cells via receptors (receptor type 1 and receptor type 2) on the surface of susceptible cells. The envelope glycoprotein of HIV-1, gp120 binds first to receptor type 1, and then receptor type 2, inducing a conformational change in gp120 that exposes the fusion protein gp41, leading to viral fusion with the host cell membrane and HIV entry into body cells.

After its entry into human body, HIV will reach the regional lymph node within 24–48 hours; viral particles can be detected in peripheral blood in about five days. This is followed by viremia, leading to acute infection.

*HIV infection process in human CD4+ cells*

Adhesion and penetration: As stated above, after infection of human body, HIV-1 selectively adheres to the CD4 receptor type 1 of the target cell, and enters the cell under the assistance of a helper receptor, i.e., receptor type 2.

Cyclization and integration: Viral RNA is converted to cDNA under the action of reverse transcriptase which in turn is converted to a non-covalent binding double-stranded DNA under the action of DNA polymerase. Under the action of integrase, the newly formed non-covalent binding double-stranded DNA is integrated into the host cell's chromosome DNA. The integrated viral double-stranded DNA is also called a “provirus”.

Transcription and translation: When provirus is activated to undergo self transcription, viral DNA is transcribed to form RNA; some RNAs are capped to become progeny genome RNA; some other RNAs are spliced to become viral mRNAs, and translated into structural protein and nonstructural protein of virus on a cell ribosome. The synthesized viral proteins undergo saccharification and processing on endoplasmic reticulum ribosome, and are cleaved under the action of protease, resulting in proteins and enzymes of progeny virus.

Assembly, maturation and budding: Gag protein is bound and assembled with viral RNA to form nucleocapsid; the envelope of virion is obtained from the release of cytoplasmic membrane during budding, generating mature viral particles.

*Three clinical outcomes following HIV infection*

Since the immune system of human body is not able to completely clear HIV, chronic infection develops.
This is manifested clinically by one of the following outcomes: typical progression, rapid progression or long-term non-progression. Major factors which influence clinical outcomes of HIV infection include viral factors, host immune status and genetic background, etc.

Immune response to HIV infection
Immune responses to HIV include specific immune responses and nonspecific immune responses. Specific immune responses are the major responses. Specific humoral immunity: 2—12 weeks after HIV enters human body, the immune system generates a variety of specific antibodies to HIV protein, among which only the neutral antibodies have antivirus effects. Specific cellular immunity: mainly includes specific CD4+ T lymphocyte immune response and specific cytotoxic T lymphocyte (CTL) response.

As the central cells of the immune system, CD4+ T lymphocytes play an important role in the specific immune response. They excrete various cytokines, inducing B cells to generate antibody to HIV, promoting generation and maturation of specific CTLs against HIV, and activating macrophages and NK cells. CD8+ T lymphocytes are effector cells of specific cellular immunity, suppressing viral replication directly via various cytokines (such as tumor necrosis factor, interferon, etc) or by excreting cytokines.

Immunopathology
Decrease in CD4+ T lymphocyte count
When the body is infected with HIV, CD4+ T lymphocyte count will continuously decrease. The acute infection stage is characterized by a transient and rapid decrease of CD4+ T lymphocyte count within a short period of time; CD4+ T lymphocyte counts in most PLWHAs can automatically recover to the normal level or near normal level even without any specific treatment. The asymptomatic infection stage is characterized by a slow and constant decrease in CD4+ T lymphocyte counts. The number of CD4+ T lymphocytes is usually between (800—350)×10^6/L. This period varies significantly in duration (ranging from several months to more than ten years), with the average duration of about 8 years. In the symptomatic stage, CD4+ T lymphocytes again rapidly decrease; the CD4 T-lymphocyte counts in most PLWHAs go below 350 ×10^6/L; in late stage, CD4+ T lymphocyte counts in some patients even go below 200 ×10^6/L and continue to drop rapidly.

The decrease in CD4+ T lymphocyte count may be due to one or more of the following factors: CD4+ T lymphocyte destruction by the virus; reduced generation of CD4+ T lymphocytes; lymphatic tissue with holding of CD4+ T lymphocytes from peripheral blood.

CD4+ T lymphocyte dysfunction
This is manifested mainly by one or more of the following: T-helper cells 1 (Th1) switched to T-helper cells 2 (Th2); antigen presenting cell dysfunction; decrease in production of interleukin-2; and then loss of immune function to antigen reaction, resulting in susceptibility of PLWHA to various infections.

Exceptional immune activation
Another immune pathological change after HIV infection is the exceptional activation of immune system, which is manifested in the abnormal increase in proportion of CD4+ and CD8+ T lymphocytes expressing immune activation markers (CD69, CD38 and HLA-DR, etc). This proportion is positively correlated with HIV plasma viral load. In addition, along with disease progression, cell activation level is also constantly increasing. Therefore, exceptional immune activation status can not only indicate change of plasma viral load, but also predict the speed of decrease in CD4+ T lymphocytes.

Immune reconstitution
A major progress in the HIV/AIDS research arena in the recent years is the proven finding that HAART can lead to immune reconstitution in AIDS patients. Immune reconstitution in AIDS patients can be defined as the return to normal or nearly normal status of the changes in the immune system caused by HIV (and as described above) in a patient receiving HAART. Specifically: 1) the CD4+ T lymphocyte count comes back to normal; 2) CD4+ T lymphocyte function also returns to normal with the restored ability to react to memory antigen stimulation; 3) abnormal immune activation in patient recovers. As the immune system recovers, the following also happens: a decreased incidence of OIs and cancers related to HIV/AIDS, decreased
mortality rate and a decreased occurrence of late stage disease PLWHA. Nevertheless, HAART also has its own limitations in terms of HIV/AIDS immune reconstitution: 1) HAART may not result in immune reconstitution in a few AIDS patients; 2) HAART cannot reconstitute CD4+ T lymphocyte specific immune response against HIV, while CD8+ T lymphocyte specific anti-HIV capacity also decreases, meaning that patients need to be on long-term maintenance medication.

PATHOLOGICAL CHANGES

AIDS can affect many organs of the body. Categories of clinical pathological changes caused by AIDS include immune system, multisystem OIs (including protozoa, virus, bacteria and fungus) and cancers (including Kaposi’s sarcoma, malignant lymphoma and cervical cancer).

Common OIs and cancers

Pneumocystis

P. carinii principally causes pneumonia (PCP). Typically, both lungs show diffuse involvement, consolidation, increased weight and dramatic loss of alveoli air spaces. After formalin fixation, the lung tissue shows a coarse and sponge-like appearance with the alveolar cavities filled with a red-colored, cell-free and foam-like exudate. This finding is characteristic and called cancellate exudate. Alveolar epithelium proliferates into a cube shape cysts. The cysts are found in clusters in the cavity exudates. Gram and Giemsa stains help to display sporozoites, and the Giemsa stain clearly reveals the cysts. [Note that P. carinii has been renamed P. jiroveci but the eponym PCP is retained (Emerg Infect Dis 2002; 8: 891-896.)]

Toxoplasmosis

Although disseminated toxoplasmosis may involve the eyes, lungs, heart and digestive tracts, toxoplasmic encephalitis is most common. The lesion may be localized or diffuse, causing abscesses commonly in the basal ganglia or the cerebellum cortex, and even in the subarachnoid space. The uniqueness of this kind of abscess is revealed by enhanced CT imaging and is characterized by one or many cyst-like ringed lesions in gray matter. Some parts of brain have coagulative hemorrhagic necrotic lesions inside in which a small amount of toxoplasma can be found. The area of necrosis is surrounded by a cyst-forming belt that is made from congestion and vascular endothelial proliferation. The belt is heavily infiltrated by inflammatory materials, a large amount of toxoplasma tachyzoites and bradyzoite-containing pseudocysts. Tachyzoites in the brain are different from those in other tissues, which appear round or elliptical rather than crescent in shape. Sections from tissues other than the brain have tachyzoites that can be clearly observed through HE staining in which tachyzoites are 2–3 μm crescents and cysts or pseudocysts measuring 50 μm. In addition, a rise in the serum antibody titer is indicative of toxoplasma infection.

Candidiasis

Recurrent candidiasis is the most common fungal opportunistic infection in AIDS patients. For those patients with stomatic infection, the surface of their tongues shows diffuse white patches due to a layer of exudates. In some cases the exudates may appear as a thick black cover. In adults oropharyngeal candidiasis indicates that the HIV infected person has entered the stage of AIDS. Any part of the digestive tract can be involved and the esophagus is the most frequently affected. A grey pseudomembrane with irregular ulcerations may appear on the mucosal surface. The pseudomembrane consists of fibrins and necrotic materials in which a net-like pseudohyphae may be present. Disseminated candidiasis may involve many organs including the kidney (80%), brain (50%) and heart (58%), forming multiple abscesses. With histological exam C. albicans is characterized by yeast-like spores or budding spores (3–4 μm in diameter, round or oval shaped) and pseudohyphae (spores on a string).

Mycobacterium infections

AIDS patients often suffer from mycobacterium infections including Mycobacterium tuberculosis and Mycobacterium avium infections.

Tuberculosis can usually occur at any stage of HIV infection, from early to late. Extrapulmonary tuberculosis is common and is often invasive. Under the microscope, the tuberculous granuloma of AIDS patients is atypical with striking necrotic caseation. Epithelioid cells and giant cells are rare.
Tuberculosis is often exudative, with consolidation of air cavities filled with fibrin, neutrophils and histiocytes. Massive necrosis and large amounts of acid-fast bacilli are often found.

*Mycobacterium avium* infection may present in the late stages of AIDS, usually when the CD4$^+$ T lymphocyte count is less than $100 \times 10^6$/L, causing disseminated infections. Sometimes, millet-seed-like granulomas may be present on sections of the spleen, liver, lymph nodes, heart and kidneys. Under the microscope, usual structures are replaced by histiocyte clusters, which are highly swollen, strip or foam-like, and cytoplasm, which is yellow or blue stained. The nucleus is heavily dyed and giant cells are rare. Necrosis is rare or does not exist. There is no calcification or fibrosis. Acid-fast stains show swollen macrophages filled with large amounts of *Mycobacterium avium*.

**Cytomegalovirus (CMV) infection**

CMV infection in AIDS patients may cause gastrointestinal ulcerations, interstitial pneumonitis, glomerulonephritis and retinitis. CMV infections may also involve parts of the brain and spinal cord, including the spinal nerve root and cranial nerves. Autopsies show that the adrenal gland and respiratory system are most frequently involved. Under the microscope, some giant cells are present and sharp-demarcated inclusion bodies clearly appear in the nucleus and cytoplasm. The inclusion body in CMV infection is the largest among all viruses that are able to infect humans and can be present in both the nucleus and cytoplasm. The inclusion body may be: 1) a double-stain inclusion body in the nucleus, which is surrounded by a transparent halo, mimicking an owl's eye; 2) a double-stain or eosinophilic inclusion body in the cytoplasm; 3) a universally seen inclusion body in epithelial cells, endothelial cells, macrophages and smooth muscle cells. Immunohistochemistry, DNA in situ hybridization and PCR help to confirm diagnosis.

**Kaposi's sarcoma**

Kaposi's sarcoma is a common tumor of AIDS patients. Epidemic Kaposi's sarcoma and AIDS-associated Kaposi's sarcoma are different from other sarcomas: 1) male homosexuals or bisexuals are major victims, but this kind of sarcoma is also present in IDUs; 2) lesions are concentric and spread with time, involving not only the skin but visceral organs (75%). In falling frequency the following organs are involved: lung, lymph node, digestive tract, liver, urogenital tract, adrenal gland, heart and spleen. Kaposi's sarcoma in skin is a red or purple, flat spot/patch in the early stage later developing into a raised lesion which later becomes nodular. Erosion and ulceration may occur. Kaposi's sarcoma lesions are comprised of vascular spindle cells with vessel like fissures. Red blood cells can be seen in the fissures. Cells of sarcoma have characteristics of endothelial cells and smooth muscle cells. HSV-8 may be associated with occurrence of Kaposi's sarcoma.

**Pathological changes in immune system**

**HIV associated lymphadenopathy**

HIV associated lymphadenopathy falls into four categories: follicular hyperplasia without lysed follicles, follicular hyperplasia with lysed follicles, follicle degeneration and follicle depletion. Before the onset of AIDS, persistent generalized lymphadenopathy may occur. Enlarged lymph nodes are usually smaller than 3 cm, and follicular enlargement is more common before the onset of AIDS. Some AIDS patients experienced shrunken lymph nodes where lymphadenopathy manifests as follicle degeneration and depletion.

**Pathological changes in the spleen**

Spleen enlargement is common in AIDS patients. An HIV infected adult with a spleen heavier than 400 g suggests the occurrence of OIs and cancers in the spleen. The most striking change in the spleen of AIDS patients is the high depletion of lymphocytes leaving only a small amount of or even no white pulp. Splenomegaly in children is characterized by significant depletion of lymphocytes and phagocytosis of erythrocytes. About 50% of cases may present with Kaposi-like changes.

**Pathological changes in the thymus**

There are no obvious pathological changes in the thymus of adult AIDS patients, but B cell follicles may proliferate.

On the other hand, pediatric AIDS patients may experience abnormal early degeneration. HIV may impair the epithelium of the thymus causing atrophy.
and depletion of lymph tissues. Infiltration of plasma cells and, formation of multinuclear giant cells and thymus corpuscles cysts can be seen.

**Pathological changes in bone marrow**

In the early stages, three-fourths of the cases reveal bone marrow cell proliferation primarily of granulocytes and megakaryocytes. In late stages as the disease progresses, bone marrow cells decrease, and immature, ill-developed promyocytes and lymphoid cells cluster. Other changes include atypical megakaryocytes, fine net-like sclerosis, slight proliferation of blood vessels and histiocytes, and deposits of hemosiderin.

**CLINICAL PRESENTATION AND STAGING**

HIV disease progression is a long, complex process from initial infection to end stage disease. In the various stages of disease progression, there are many different clinical presentations. The Diagnostic criteria and management principles of HIV/AIDS (For trial implementation, national standard of the People’s Republic of China, GB 16000–1995) defines a staging system for HIV infection and disease which divides HIV disease progression into three stages: acute infection, asymptomatic infection and symptomatic infection including AIDS.

**Acute infection**

Acute infection usually occurs within 2—4 weeks after infection by the HIV virus. Some HIV infected persons may show clinical symptoms caused by viremia and acute damage of the immune system. Clinical symptoms are mild and improved after 1—3 weeks in most patients. Fever is the most common clinical presentation, but sore throat, night sweats, nausea, vomiting, diarrhoea, rash, arthralgia, lymphadenopathy and neurological symptoms can be present as well.

During this period, HIV-RNA and P24 antigen tests can detect HIV in the blood, while the HIV antibody can only be detected several weeks after infection. Profound reductions occur in CD4+ T lymphocyte count along with inversion of the CD4/CD8 ratio. Some patients may show mild leukopenia, thrombocytopenia or liver function abnormalities.

**Asymptomatic infection**

Following the stage of acute infection, regardless of detectible or undetectable symptoms, patients enter a stage of asymptomatic infection.

This stage generally lasts 6—8 years, with variation caused by the viral load, strain of the virus, individual immunological status, nutritional conditions, lifestyle and other factors. The high rate of HIV replication eventually makes the virus infectious, compromises the immune system, and leads to the gradual decline of the CD4+ T lymphocyte count.

**Symptomatic infection including AIDS**

Following the asymptomatic period, the CD4+ T lymphocyte count declines significantly and may go below 200 × 10^6/L. The plasma viral load (RNA) level elevates markedly. Major clinical presentations include HIV-related symptoms, OIs and cancers.

HIV-related symptoms include fever, night sweats or diarrhoea for at least one month, and weight loss at >10% body weight. Some patients may show neuropsychiatric symptoms, i.e. memory impairment, apathy, character disorder, headache, seizures and dementia. Persistent generalized lymphadenopathy may also occur, characterized by lymph nodes larger than 1.0 cm in diameter in two or more extrainguinal sites for three or more months in duration.

Common OIs and cancers in different systems are as follows (for detailed information, see section on “Diagnosis, treatment and prevention of common OIs”):

**Respiratory:** PCP, tuberculosis and recurrent bacterial/fungal pneumonia.

**Neurological:** Cryptococcal meningitis, tuberculosis meningitis, toxoplasmosis and various types of viral meningencephalitis.

**Digestive:** Candida albicans esophagitis, cytomegalovirus esophagitis, enteritis; Salmonella, Shigella flexneri, Campylobacter jejuni and Cryptosporidia enteritis.

**Oral:** Oral thrush, hairy leukoplakia, recurrent mouth ulcers and gingivitis.
Skin: Herpes zoster, molluscum contagiosum, condylomata acuminata, fungal dermatitis and onychomycosis.

Eye: Cytomegalovirus and toxoplastic retinitis.

Cancer: Malignant lymphoma and Kaposi’s sarcoma.

Note that clinical presentations and complications are diverse and vary at different stages of disease progression but are closely linked to local OIs prevalence.13

**DIAGNOSTIC CRITERIA**

The diagnosis of HIV/AIDS should be based on a comprehensive analysis of epidemiologic history (including unsafe sex, intravenous drug use, transfusion of blood or blood product, lack of HIV testing, children of HIV positive women and occupational exposure to HIV), clinical presentation and laboratory findings. HIV infection can only be confirmed by the detection of HIV in the confirmatory test. HIV RNA and P24 antigen tests are helpful for the diagnosis of HIV, especially during the “window period” of acute infection and for early diagnosis of HIV infection among newborn infants.

**Acute infection**
Diagnostic criteria: Recent epidemiologic history + clinical presentation + HIV seroconversion; or only HIV seroconversion.12,14

**Asymptomatic infection**
Diagnostic criteria: epidemiologic history + HIV seropositive; or only HIV seropositive.

**Symptomatic infection including AIDS**
1) Prolonged irregular fever (higher than 38°C) of unknown etiology (for longer than one month); 2) Chronic diarrhea, more than 3 times per day (for longer than one month); 3) Weight loss greater than 10% body weight within 6 months; 4) Recurrent oral candida infection; 5) Recurrent herpes simplex virus infection or zoster virus infection; 6) PCP; 7) Recurrent bacterial pneumonia; 8) Active tuberculosis or nontuberculous mycobacteria infection; 9) Non-superficial fungal infection; 10) Space occupying lesion in central nervous system; 11) Dementia in adolescents and adults; 12) Active CMV infection; 13) Toxoplasmosis; 14) Penicillium infection; 15) Recurrent septicemia; 16) Mucocutaneous or visceral Kaposi’s sarcoma or lymphoma.

Diagnostic criteria for AIDS: epidemiologic history + HIV seropositive + one of the above conditions; or HIV seropositive in lab test + CD4+ T lymphocyte count <200 × 10⁶/L.

**DIAGNOSIS, TREATMENT AND PREVENTION OF COMMON OIS**15

*P. jerovici* pneumonia

**Diagnosis**
1) This disease develops insidiously or subacutely, presenting as a dry cough and shortness of breath (deteriorating after physical exertion). Fever, cyanosis and even respiratory distress may occur in severe cases. 2) The lung exam may reveal very few positive signs, such as sporadic dry or wet rales. Signs are significantly disproportionate to severity of symptoms. 3) The chest X-ray shows diffuse net-nodule-like interstitial infiltration starting from the hilus, sometimes in an obscured glass-like shadow. 4) Blood-gas analysis showed hypoxemia and dramatically decreased PaO₂ in severe cases, often lower than 60 mmHg. 5) Blood levels of lactate dehydrogenase (LDH) often rises. 6) Confirmed diagnosis depends on identification of pathogen in sputum or bronchovesicular lavage in which cysts or trophozoites may be found.

**Treatment**
1) Symptomatic treatment: bed rest, supplemental oxygen, improved lung aeration, and balanced intake of water and electrolites. If a patient has obvious difficulty breathing, assisted respiration can be administered. For moderate or severe PCP patients (PaO₂ <70 mmHg or air sac-PaO₂ >35 mmHg), prescribe prednisone 40 mg bid × 5 days, then 20 mg bid × 5 days, then 20 mg/d to completion of treatment. If intravenous methylprednisolone is used, it should contain 75% of prednisone (dosage same as above). 2) Treatment of pathogen: first line regimen choice is cotrimoxazole 9—12 oral tablets/d (TMP 15 mg/kg daily, SMZ 100 mg/kg daily), 3—4 times daily. A course lasts 2—3 weeks. Cotrimoxazole injection (dosage is the same as above). 6—8 hours, IV
Table 2. Dosage, usage and main adverse reactions of anti-tuberculous drugs

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Daily regimen</th>
<th>Intermittent treatment for adult (g, 1-2 times/week)</th>
<th>Main adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adult (g)</td>
<td>Child (mg/kg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;50 kg</td>
<td>≥50 kg</td>
<td>&lt;50 kg</td>
</tr>
<tr>
<td>H</td>
<td>0.3</td>
<td>0.3</td>
<td>10-15</td>
</tr>
<tr>
<td>S</td>
<td>0.75</td>
<td>0.75</td>
<td>20-30</td>
</tr>
<tr>
<td>R</td>
<td>0.45</td>
<td>0.60</td>
<td>10-20</td>
</tr>
<tr>
<td>E</td>
<td>0.75</td>
<td>1.00</td>
<td>1.00-1.20</td>
</tr>
<tr>
<td>PAS</td>
<td>8</td>
<td>8</td>
<td>150-250</td>
</tr>
<tr>
<td>Z</td>
<td>1.5</td>
<td>1.5</td>
<td>30-40</td>
</tr>
<tr>
<td>L</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Drip. Alternative treatment: oral dapsone 100 mg, once a day combined with oral TMP 200-400 mg, 2-3 times a day for 2-3 weeks. Another treatment alternative is clindamycin 600-900 mg, IV, 6 hours, or 450 mg for orally, 6 hours combined with oral primaquine 15-30 mg, once per day for 2-3 weeks. Yet another treatment alternative is pentamidine, 3-4 mg/kg, once a day, slow IV drip (longer than 60 minutes) for 2-3 weeks.

Prophylaxis
1) Prophylaxis indication: CD4+ T lymphocyte count <200×10^6/L (adults, adolescents, pregnant women, patients on HAART). 2) Medications: first line regimen choice is cotrimoxazole: for body weight ≥60 kg, 2 tablets/d; for body weight <60 kg, 1 tablet/d. If a patient can not tolerate the medication, alternatives are dapsone and TMP. Patients receiving HAART treatment can discontinue medications for PCP prophylaxis when their CD4+ T lymphocyte count is >200×10^6/L for 6 or more months. If CD4+ T lymphocyte count relapses to <200×10^6/L, restart prophylaxis.

Tuberculosis
Diagnosis
Smear or culture positive acid fast bacillus (AFB) in sputum or bronchoscopy specimens can help diagnose pulmonary tuberculosis. Active tuberculosis can also be confirmed clinically.

Treatment
If HIV-positive patients have tuberculosis complications, they should undergo the routine treatment regimen for tuberculosis, but for a longer course of therapy. Drug interactions and incompatibility between anti-tuberculosis and antiviral medications should be considered.

Medications: isoniazid (H), amikacin (A), rifampicin (R), rifapentine (L), ethambutol (E), para aminosalicylic acid (PAS), pyrazinamide (Z) and streptomycin (S). The dosage, usage and main adverse reactions of these drugs are shown in Table 2.

Chemotherapy regimen (2 common regimens are listed below. For more information, please refer to National guidelines for treatment of tuberculosis): 1) 2HRZE/4HR: intensive therapy period: 2 months, H, R, Z, E, once per day; continuing therapy period: 4 months, H, R once per day. 2) 2H3 R3 Z3 E3/4H3 R3: intensive therapy period: 2 months, H, R, Z, E, once every other day; continuing therapy period: 4 months, H, R, once every other day. Treatment should be continued for another 7 months (total 9 months) for HIV patients with sputum positive results at 2 months.

Prophylaxis
Indication: it is not necessary to administer chemomedication prophylaxis to AIDS patients. However, the prophylaxis may be prescribed by physicians in patients with CD4+ T lymphocyte count <200×10^6/L. Regimen: 1) isoniazid + rifapentine, uninterrupted 4-6 months (for dosage, refer to the above table). 2) isoniazid, 12 months (for dosage refer to Table 2).

Mycobacterial avium infection
Diagnosis
MAC infection has similar symptoms as active tuberculosis except for a high frequency of systemic dissemination. Confirmed diagnosis: mycobacteria found in blood culture, sputum culture, biopsy of bronchi and lung, or lavage culture of bronchus sputum.

Treatment
First line regimen: clarithromycin 500 mg twice per
day or azithromycin 600 mg/d + ethambutol 15 mg · kg⁻¹ · d⁻¹. For severe patients, rifabutin (300—600 mg/d) which may be combined with amikacin (10 mg/kg IM, once per day) can be used for 6 months. Alternative treatment regimen: rifabutin (300—600 mg/d) + amikacin (10 mg/kg IM, once per day) + ciprofloxacin (750 mg each time, 2 times per day) for 6 months.

Prophylaxis
It is not necessary to administer chemomedication prophylaxis for nontuberculosis mycobacteria to AIDS patients. However, the prophylaxis may be prescribed by physicians to avoid disseminated MAC if CD4⁺ T lymphocytes <50 × 10⁶/L. Regimen: clarithromycin 500 mg twice per day or azithromycin 1200 mg/week. Prophylaxis can be discontinued once CD4⁺ T lymphocytes rise to >100 × 10⁶/L for 6 or more months.

CMV retinitis and chorioiditis

Diagnosis
Clinical manifestations include dramatic deterioration of vision. Confirmed diagnosis depends on the fundoscopic exam.

Treatment
1) Ganciclovir 10 mg · kg⁻¹ · d⁻¹, given in 2 sessions, IV drip; after 2—3 weeks, 5 mg · kg⁻¹ · d⁻¹, once a day, IV drip; continue this therapy for life. This medication may lead to leukocytopenia, thrombocytopenia and renal toxicity. For severe patients or in cases of ineffective mono-therapy, combine with foscarnet sodium 90 mg/kg, IV drip, 2 times daily. For retinitis, intraocular implanted ganciclovir can be considered.

2) Foscarnet sodium 90 mg/kg, IV drip, 2 times a day; after 2—3 weeks, 90 mg/kg, once a day, IV drip, long term maintenance. This medication may lead to renal dysfunction, nausea, and electrolyte disorder. In case of elevated creatinine clearance, adjust dosage.

Prophylaxis
For AIDS patients with CD4⁺ T lymphocyte count <50 × 10⁶/L, prophylaxis with oral ganciclovir is a must. For patients on HAART treatment with CD4⁺ T lymphocyte count >100 × 10⁶/L for at least 6 consecutive months, discontinuation of prophylaxis can be considered.

Toxoplasmosis

Diagnosis
Toxoplasmosis often occurs in AIDS patients whose CD4⁺ T lymphocyte count is <100 × 10⁶/L, manifesting as headaches, low grade fever, hypersomnolence, restlessness and lethargy due to localized or diffuse damage to the central nervous system. Key symptoms include seizure and stroke. Other symptoms include diplopia, hemianopia, blindness, ataxia, myoclonus, restlessness, personality changes, hallucinations and dizziness. Meningitis is a rare finding. Cranial CT scan shows one or more low-density sites appearing as rings or nodules when using contrast enhancement. Cranial MRI is more sensitive than CT scan, and toxoplasmosis is characterized by multiple long T1 and long T2 signals. Diagnosis may be confirmed by brain biopsy.

Treatment
First line regimen: pyrimethamine (loading dose 100 mg, oral, 2 times/d, 50—75 mg/d for subsequent maintenance) + sulfadiazine (1.0—1.5 g, oral, 4 times/d) for 3 weeks. For critical patients or patients with poor clinical or radiological responses, the therapy course may be lengthened to 6 weeks or more. For those allergic to or unable to tolerate sulfa, the following can be prescribed: clindamycin 600 mg IV, 6 hours, combined with pyrimethamine. To reduce adverse hemopoietic reactions, folinic acid 10—20 mg/d can be co-prescribed.

Prophylaxis
For AIDS patients without history of toxoplasmosis but with a CD4⁺ T count <100 × 10⁶/L and a positive IgG, a prescription of cotrimoxazole 2 single-strength tablets/d for prophylaxis purposes is indicated. For patients who have had toxoplasmosis, long term usage of pyrimethamine (25—50 mg/d) + sulfadiazine (2—4 g/d) for prophylaxis is needed. Prophylaxis can be stopped when CD4⁺ T count rises to >200 × 10⁶/L more than 3 to 6 months. For AIDS patients who are antibody negative for toxoplasma but have a CD4⁺ T count <100 × 10⁶/L, measures should be taken to avoid infection: meat
Table 3. HAART criteria for adults and adolescents with HIV/AIDS

<table>
<thead>
<tr>
<th>Clinical staging</th>
<th>CD4 cell count</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute infection</td>
<td>Irrespective of CD4 cell count</td>
<td>Consider ART</td>
</tr>
<tr>
<td>Asymptomatic infection</td>
<td>&gt;350 × 10^6/L, irrespective of plasma viral (RNA) level</td>
<td>ART temporarily not required</td>
</tr>
<tr>
<td></td>
<td>(200–350)×10^6/L</td>
<td>Regular follow-up visits</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regular follow-up visits. Start ART in case of:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1) CD4 cell count decrease &gt;30% within one year; or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2) Plasma viral (RNA) level &gt;100 000/ml; or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3) Patient urgently demands ART and promises good adherence</td>
</tr>
<tr>
<td>AIDS</td>
<td>Irrespective of CD4 cell count</td>
<td>Start ART</td>
</tr>
</tbody>
</table>

should be stored at −20°C; meat should be well cooked (higher than 60°C) in order to kill cysts in meat tissue; vegetables and fruits should be washed clean; households should not have pets.

**Fungal infection**

*Diagnosis*

Candida infection and cryptococcus neoformans infection are the more common fungal infections.

*Treatment*

1) Candida infection: For oral candida infections, the first line treatment is to apply anti-fungal agents topically and to gargle with baking soda mixed in water. If unresponsive, the following can be given: fluconazole: 50—100 mg, oral, once per day for 1—2 weeks. For esophageal candida infection: fluconazole with a priming dose of 200 mg/d, add a subsequent dose 100 mg, once per day for 1—2 weeks. For severe patients, raise the dosage of fluconazole and lengthen course of therapy. For recurrent candida infections, give fluconazole 100 mg/d as maintenance.

2) Meningitis due to *Cryptococcus neoformans*: (1) Lower intracranial pressure: The first line treatment of choice is mannitol. For very severe cases, drainage via lateral ventricle can be conducted. (2) Anti-fungal treatment: The first line medication is amphotericin B, starting at 1 mg/d, slow drip IV, 500 ml 5% glucose solution (normal saline solution is not recommended, keep away from light), for at least 6—8 hours. Dosing for the second and third days are 2 mg and 5 mg respectively (in 500 ml glucose solution). If no adverse reactions occur, dose can be increased to 10 mg on the fourth day. If free of severe adverse reactions, raise by 5 mg each day until daily amount reaches 30—40 mg (maximum dosage: 50 mg/d). Therapy course lasts for at least 3 months. Total dosage of amphotericin B is 2—4 g. Amphotericin B frequently leads to adverse reactions; therefore, close observation of the patient is necessary. Amphotericin B and 5-flucytosine (5FC) have synergistic effects. 5FC is usually given at 100 mg · kg^{-1} · d^{-1} (1.5—2.0 g, 3 times/d) and is combined with amphotericin B for at least 8—12 weeks. To use amphotericin B in conjunction with fluconazole is also acceptable: fluconazole 200 mg/d, oral or IV, for 8—12 weeks. Injection of amphotericin B if necessary: 0.5 — 1.0 mg every other day. (3) Maintenance with fluconazole after remission is recommended at 200 mg, once per day, for long term prevention of relapse.

**HAART**

*Treatment principles*

To minimize HIV replication, restore immune function, reduce fatality rate and incidence of HIV-related diseases, improve the quality of life for people living with HIV/AIDS, and contain the spread of HIV.

**Criteria for initiating HAART**

Criteria for adults and adolescents with HIV/AIDS\(^7\)

The criteria are shown in Table 3.

A total lymphocyte count of \(\leq 1200 \times 10^6\) for initiating HAART can be substituted for the CD4 count when the latter is unavailable and if HIV-related symptoms exist.

With the presence of any severe OI, treat the OI first, and start HAART after the infection is controlled.

**Criteria for infants and children with HIV/AIDS**

Taking into account the fact that HIV progresses more rapidly in infants than in older children and adults, ART is recommended for infants under 12 months, regardless of virological and immunological indicators and the development of clinical symptoms. For children over 1 year of age, treatment is...
recommended at the AIDS stage of disease progression or if CD4 T lymphocyte percentage is <15%. Treatment can be considered if CD4 T lymphocyte percentage is 15% – 20%. Treatment can be delayed if CD4 T lymphocyte percentage is 21% – 25% and changes in CD4 T lymphocyte percentage are closely monitored. Treatment can be delayed if there are no clinical symptoms and CD4 T lymphocyte percentage is >25%. Regular follow-up visits to monitor changes in clinical presentation and virologic and immunologic indicators should be conducted.

**ARVs available in China**

Globally, 24 ARVs in four classes are available: nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs) and fusion inhibitors (FIs). In China, there are currently 12 ARVs available in three classes: NRTIs, NNRTIs and PIs (Table 4).

**HAART regimens for adults and adolescents**

Based on internationally available ARV drugs, treatment regimens generally consist of a combination of three ARVs, including, two NRTIs + one NNRTI or PI, or three NRTIs. It should be noted that each regimen has its own advantages and disadvantages. Toxicity, impact of drug resistance on future treatment, practicality, feasibility, and the specific condition of each individual patient should be taken into account. Based on the availability of ARVs in China, the following regimens are recommended: Recommended first-line regimen: AZT (or d4T) + 3TC + EFV (or NVP). Alternative regimens: (1) AZT (or d4T) + 3TC + IDV; (2) ddl + d4T+ EFV (or NVP); (3) AZT + ddl + EFV (or NVP).

**HAART for special populations**

**Children with HIV/AIDS**

The preferred treatment option for children is a combination of three ARVs. Many ARVs used by adults can be used for children after the formulation is appropriately adjusted in accordance with a child's weight and body surface area.

Recommended first-line regimens for children consist of two NRTIs and EFV or NVP, the former for children aged >3 years or children who cannot swallow capsules. Alternative regimens consist of two NRTIs and one PI. LPV/RTV is the PI of choice.

**Pregnant women with HIV/AIDS**

The best time for initiating HAART in pregnant women is the same as for other adults, but there are two additional considerations. First, the treatment regimen should aim to reduce the risk of mother-to-child transmission; and second, the advantages and disadvantages of the use of ARVs must be evaluated for the pregnant women, foetuses and newborns. In general, HAART can be continued for those who started treatment before conception. If possible, AZT should be added if it was not included in the original regimen. For women who did not start HAART before pregnancy, treatment is not recommended in the first trimester.

Studies show that for pregnant women, the risk of lactic acidosis or hepatic steatosis is higher with d4T than with other NRTIs. Therefore, regimens with d4T are not recommended for HIV positive pregnant women. EFV is known for its potential teratogenicity and should not be used during the first trimester of pregnancy. PIs are usually not recommended for pregnant women due to the risk of gestational diabetes mellitus, which may lead to a large foetus, miscarriage, preterm delivery, prenatal death, and other risks.

AZT + 3TC + NVP is recommended as the first-line regimen for pregnant women.

It is important to note that data on ARV-related toxicity and side effects for pregnant women come mainly from animal models, existing cases, registered materials and clinical studies. Currently there are limited data on the pharmacokinetics and safety of ARVs for pregnant women.

**HIV/AIDS patients co-infected with tuberculosis**

Drug interactions between anti-tuberculosis drugs and ARVs can increase hepatic toxicity. If HAART has not been initiated before the diagnosis of tuberculosis, it is recommended that tuberculosis is treated first and HAART is initiated upon completion of the tuberculosis treatment. However, the delay of HAART may endanger the life of patients at the late stages of disease progression. Therefore, if the patient
### Table 4. Introduction to 12 ARVs currently available in China

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Acronym</th>
<th>Class</th>
<th>Administration and dosage</th>
<th>Major side effects and toxicity</th>
<th>ARV-interaction and considerations</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine</td>
<td>AZT</td>
<td>NRTI</td>
<td>Adults: 300 mg bid&lt;br&gt;Newborns/Infants: 2 mg/kg qid&lt;br&gt;Children: 160 mg/m² surface area bid</td>
<td>1) Bone marrow suppression, severe anemia or neutropenia&lt;br&gt;2) GI discomfort: nausea, vomiting, diarrhea, etc&lt;br&gt;3) Elevated CPK and ALT, lactic acidosis and/or hepatic steatosis</td>
<td>Do not coadminister with d4T</td>
<td>Chinese generic drugs available</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>3TC</td>
<td>NRTI</td>
<td>Adults: 150 mg bid or 300 mg qd&lt;br&gt;Newborns: 2 mg/kg bid&lt;br&gt;Children: 4 mg/kg bid</td>
<td>Few and mild. Rare headache, nausea, diarrhea, etc</td>
<td></td>
<td>Chinese generic drugs available</td>
</tr>
<tr>
<td>Didanosine</td>
<td>ddI</td>
<td>NRTI</td>
<td>Adults (tablet): weight ≥ 60 kg 200 mg bid; weight &lt; 60 kg 125 mg bid (powder): weight ≥ 60 kg 250 mg bid; weight &lt; 60 kg 176 mg bid&lt;br&gt;Newborns/Infants: 50 mg/m² surface area bid&lt;br&gt;Children: 120 mg/m² surface area bid&lt;br&gt;Take on an empty stomach</td>
<td>1) Pancreatitis&lt;br&gt;2) Peripheral neuropathy&lt;br&gt;3) GI discomfort: nausea, vomiting, diarrhea, etc&lt;br&gt;4) Lactic acidosis and/or hepatic steatosis</td>
<td>If coadministration occurs, give ddI two hours apart from IDV and RTV&lt;br&gt;Toxicity will intensify if coadministered with d4T</td>
<td>Chinese generic and imported drugs available</td>
</tr>
<tr>
<td>stavudine</td>
<td>d4T</td>
<td>NRTI</td>
<td>Adults: weight ≥ 60 kg 40 mg bid; weight &lt; 60 kg 30 mg bid; Children: 1 mg/kg bid (based on 30 kg if weight &gt; 30 kg)</td>
<td>1) Peripheral neuropathy&lt;br&gt;2) Pancreatitis&lt;br&gt;3) Lactic acidosis and/or hepatic steatosis</td>
<td>Do not coadminister with AZT</td>
<td>Chinese generic drugs available</td>
</tr>
<tr>
<td>Abacavir</td>
<td>ABC</td>
<td>NRTI</td>
<td>Adults: 300 mg bid&lt;br&gt;Newborns/Infants: not recommended</td>
<td>1) Hypersensitivity reaction. ABC should be stopped for life in case of hypersensitivity reaction</td>
<td></td>
<td>Registered</td>
</tr>
<tr>
<td>Combivir</td>
<td></td>
<td>NRTI</td>
<td>Adults: 1 tab bid&lt;br&gt;Maximum dose: 300 mg bid</td>
<td>2) Nausea, vomiting, diarrhea, etc</td>
<td>See AZT and 3TC</td>
<td>Imported drugs available</td>
</tr>
<tr>
<td>Trizivér</td>
<td></td>
<td>NRTI</td>
<td>Adults: 1 tab bid&lt;br&gt;See AZT, 3TC and ABC</td>
<td></td>
<td>See AZT, 3TC and ABC</td>
<td>Registered</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>NVP</td>
<td>NNRTI</td>
<td>Adults: 200 mg bid&lt;br&gt;Newborns/Infants: 5 mg/kg bid&lt;br&gt;Children: &lt; 8 years, 4 mg/kg bid; ≥ 8 years, 7 mg/kg bid&lt;br&gt;Caution: Only half of the dose (i.e. qd) can be administered during the lead-in period (the first 2 weeks). Then, the full dose (i.e. bid)</td>
<td>1) Rash. NVP should be stopped for life in case of severe or life threatening rash&lt;br&gt;2) Hepatic toxicity. NVP should be stopped for life in case of severe hepatitis or hepatic insufficiency</td>
<td>Decreases levels of PIs in coadministration with IDV&lt;br&gt;The dose of IDV should be increased to 1000 mg tid</td>
<td>Chinese generic drugs available</td>
</tr>
</tbody>
</table>

(To be continued)
(Continued from Table 4)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Acronym</th>
<th>Class</th>
<th>Administration and dosage</th>
<th>Major side effects and toxicity</th>
<th>ARV-interaction and considerations</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz</td>
<td>EFV</td>
<td>NNRTI</td>
<td>Is administered if no severe side effect occurs.</td>
<td>1) CNS toxicity, e.g. dizziness, headache, insomnia, abnormal CNS function, etc</td>
<td>In coadministration with IDV, the dose of IDV should be increased to 1000 mg tid</td>
<td>Imported drugs available</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adults: 600 mg qd</td>
<td>2) Rash</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children: weight 15–25 kg: 200–300 mg qd</td>
<td>3) Hepatic toxicity</td>
<td>Do not coadminister with SQV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25–40 kg: 300–400 mg qd</td>
<td>4) Hyperlipidemia and hypertriglyceridemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;40 kg: 600 mg qd</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Take at bedtime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indinavir</td>
<td>IDV</td>
<td>PI</td>
<td>Adults: 800 mg tid</td>
<td>5) Hyperbilirubinemia</td>
<td></td>
<td>Chinese generic drugs and available</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children: 500 mg/m² surface area tid</td>
<td>6) Hyperlipidemia, glucose intolerance and fat redistribution are common side effects for all PIs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Take on an empty stomach</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ritonavir</td>
<td>RTV</td>
<td>PI</td>
<td>Adults: The dose should be gradually increased to 600 mg bid</td>
<td>1) Nausea, vomit, diarrhoea, headache, etc</td>
<td>Since RTV can cause severe GI discomfort, most patients will not tolerate it. Therefore, RTV is usually used to enhance other PIs, and is used independently in rare cases</td>
<td>Registered</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>within two or more weeks. Usually: 300 mg po bid for the first and second days; 400 mg po bid from the third to fifth days; 500 po bid from the sixth to thirteenth days</td>
<td>2) Peripheral neuropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3) Elevated transaminase level and Y-OT</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4) Dyslipidemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5) Glucose intolerance, but rare diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6) Fat redistribution after long term use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lopinavir/Ritonavir (Kaletra)</td>
<td>LPVR</td>
<td>PI</td>
<td>Adults: 3 pills bid (content of each Kaletra: LPV 133.3 mg, RTV 33.3 mg)</td>
<td>1) Diarrhoea, nausea and headache</td>
<td>In coadministration with ddI, ddI should be given by mouth 1 hour before or 2 hours after Kaletra</td>
<td>Registered</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children: 7–15 kg, LPV 12 mg/kg + RTV 3 mg/kg bid; 15–40 kg, LPV 10 mg/kg + RTV 2.5 mg/kg bid</td>
<td>2) Blood lipid abnormality</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3) Raised serum transaminases</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: bid: every 12 hours, tid: every 8 hours, qid: every 6 hours.
is improving on tuberculosis treatment, HAART should be started immediately if CD4+ T lymphocyte cell count <50 x 10^6/L. If the CD4+ T lymphocyte cell count is between (50–200) x 10^6/L, HAART should be started upon the completion of intensive tuberculosis therapy.

If there is coadministration of anti-tuberculosis drugs and ARVs, the drugs of choice are AZT/3TC or d4T/3TC plus one NNRTI or ABC. If NNRTI is used, EFV is the first choice because EFV-related hepatic toxicity is milder than that of NVP. However, the dose of EFV may need to be increased to 800 mg/d. PIs are not recommended during the tuberculosis treatment due to their interaction with rifampicin.

**IDUs**

Drug abuse may affect patients’ adherence to treatment. In addition, the development of HCV may mean that patients are unable to tolerate antiretroviral therapy. Therefore, improving adherence is essential to the sustainability of HAART among IDUs.

The best time for initiating HAART among IDUs is the same as for other patients. Before starting therapy, detailed information should be provided and future adherence to treatment should be assessed so that treatment is initiated on a voluntary basis and so that efforts are made to avoid treatment failure and drug resistance.

Simplified fixed-dose combinations are the best for IDUs. An ideal regimen is d4T+3TC+NVP, but attention should be paid to NVP hepatic toxicity.

Particular emphasis should be placed on the distribution of ARVs. Ongoing monitoring of drug disbursement to patients can effectively improve adherence to treatment. The frequency of monitoring should increase after HAART is initiated. Once the patient's condition is stable, the interval between drug disbursements can be extended as appropriate. However, if the stabilized patient does not keep a regular lifestyle, ARVs should again be disbursed on a more frequent basis.

Interactions can occur between ARVs and other drugs, especially methadone. Studies indicate an increase of approximately 40% in the drug concentration of AZT when coadministered with methadone. To date, there are no proven methods to safely reduce AZT levels among this population. Therefore, efforts should be made to closely monitor AZT-related toxicity or to avoid coadministration of AZT and methadone. Methadone can decrease ddI levels by approximately 60%, which may lead to underdosing of ddI, incomplete viral suppression and development of drug resistance. In addition, some ARVs (e.g. NVP and EFV) can stimulate cytochrome P-450 to lower the plasma concentration of methadone, which may cause opioid withdrawal in some patients (usually occurring 4–8 days after initiation of therapy). Therefore, it is important to regularly assess patients who have initiated HAART so that opioid withdrawal symptoms are medically monitored and to consider changes in treatment regimen.

**Evaluation of treatment efficacy**

The effectiveness of treatment can be evaluated by virologic indicators, immunologic indicators and clinical symptoms. Virologic changes are the most important indicators.

**Virologic indicators**

HIV viral load decreases by more than 1 log in patients with 4 weeks of HAART and becomes undetectable after 3–6 months.

**Immunologic indicators**

The CD4+ T lymphocyte count increases by 30% of the pre-therapy baseline after 3 months of HAART; or, CD4+ T lymphocyte count increases by 100 x 10^6/L one year after initiating HAART.

**Clinical symptoms**

Clinical symptoms improve. The incidence of OIs and the mortality rate of HIV/AIDS are reduced significantly.

**Criteria and principles of drug substitution**

**Criteria for drug substitution**

1) Treatment failure: (1) HIV viral load decreases by less than 1 log c/ml in patient with 8 weeks of HAART or is still detectable after 6 months of HAART; (2) The reappearance of a detectable viral load after HAART has led to undetectable viral load; (3) CD4+ T lymphocyte count does not increase, returns to pre-therapy baseline or moves below pre-therapy level; (4) Patients present with recurrent OIs and/or...
HIV-related conditions during HAART.

2) ARV-related severe toxicities and side effects: i.e. bone marrow suppression, pancreatitis, severe rash, hyperlipidemia and severe hepatic dysfunction.

Principles of drug substitution

1) In case of treatment failure: (1) If drug resistance test is available, switch the drug to which resistance has developed; (2) If drug resistance test is unavailable, switch all ARVs if possible.

2) Drug substitution for ARV-related toxicities and side effects (based on currently available ARVs in China) are shown in Table 5.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Major toxicity and side effects</th>
<th>Switch to</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT</td>
<td>Bone marrow suppression, severe GI intolerance</td>
<td>d4T</td>
</tr>
<tr>
<td>d4T</td>
<td>Peripheral neuropathy, pancreatitis</td>
<td>AZT</td>
</tr>
<tr>
<td>NVP</td>
<td>Severe hepatic impairment</td>
<td>EFV</td>
</tr>
<tr>
<td></td>
<td>Severe symptoms (non-life-threatening rash)</td>
<td>EFV</td>
</tr>
<tr>
<td></td>
<td>Life-threatening rash (hyperreaction)</td>
<td>IDV</td>
</tr>
<tr>
<td>EFV</td>
<td>CNS toxicity</td>
<td>NVP</td>
</tr>
</tbody>
</table>

Adherence

Clinical research suggests that successful treatment is difficult to achieve if adherence is lower than 95%. Therefore, it is important to communicate with patients before initiating treatment and to inform them of the necessity of HAART, potential toxicities and side effects, the importance of adherence, and the need for regular follow-up visits and timely contact with medical staff in case of any discomfort. At the same time, support from patients' family members, relatives, and friends is essential to improving adherence.

PMTCT

Effective specific interventions to reduce the risk of mother-to-child transmission (MTCT) includes: obstetrical management + ARVs + non-breastfeeding, with which transmission could be reduced to less than two percent.18 Voluntary counseling and testing is necessary for all PMTCT programs.

Obstetrical management

Termination of pregnancy

HIV infected pregnant women should be provided with necessary knowledge and informed of the harm of HIV infection and of the transmitting risk during pregnancy, intrapartum and postpartum. The decision to terminate pregnancy should be made at the discretion of each individual. Prenatal counseling should be provided.

1) The operation of induced abortion should be performed as early as possible for HIV infected pregnant women who want to terminate their pregnancy so as to reduce the risk of complications.

2) Counseling should be provided for HIV infected pregnant women who want to continue pregnancy. Counseling should include information on pregnancy, prenatal and postnatal care, and preparations for breastfeeding. Necessary measures should also be taken to prevent MTCT.

Type of delivery

1) Elective cesarean section: Elective cesarean sections can reduce the rate of MTCT, but emergency cesarean sections have no obvious effect on PMTCT. In general, elective cesarean section should be performed during the 38th week of pregnancy.

2) Vaginal delivery: Episiotomy, forceps and vacuum extraction should be avoided unless strong indication for obstetric needs. In case of premature rupture of membranes, aggressive management and treatment strategies should be used to shorten the delivery process.

Antiretroviral prophylaxis

Efficiency and safety of ARV regimens on pregnant women, foetuses and newborns must be evaluated carefully.

Common treatment regimens: 1) AZT+ NVP: AZT 300 mg po bid from the 28th week of pregnancy until delivery and 300 mg po q3h from the beginning to the end of delivery. NVP 200 mg at the beginning of labor; and a repeated dose of NVP after 24 hours if there is still no delivery. In cases of elective cesarean sections, NVP 200 mg should be given two hours before operation. To newborns: NVP 2 mg/kg single dose (maximum dose 6 mg) within 72 hours of birth. 2) AZT+3TC: AZT 300 mg bid + 3TC 150 mg bid from the 36th week of pregnancy until delivery. AZT 300 mg q3h + 3TC 150 mg bid from the beginning to
the end of delivery. To mother: AZT 300 mg bid + 3TC 150 mg bid × 7 days during postpartum. To newborn: AZT 4 mg/kg bid + 3TC 2 mg/kg bid × 7 days. 3) NVP: NVP 200 mg for the mother at the beginning of labor; and a repeated dose of NVP after 24 hours if there is still no delivery. In case of elective cesarean section, NVP 200 mg should be given two hours before the operation. To newborn: NVP 2 mg/kg single dose (maximum dose 6 mg) within 72 hours of birth; and a repeated dose if vomiting within 1 hour.

**Postpartum prevention**

*Counseling on safe feeding*

HIV infected pregnant women should be counseled on the relative merits of different feeding options and informed of how to change feeding practices to minimize the risk of HIV transmission to the infant. They should also be given support to cope with psychological and social problems arising from changes in feeding practices.

*Maintain good postnatal nutrition*

Sufficient amounts of nutritious foods, vitamin supplements (e.g. iron, folic acid, zinc and other micronutrients) and high doses of vitamin A should be given to ensure adequate nutrition during the course of breastfeeding.

*Guide correct feeding techniques to help maintain healthy breast tissue*

Nipple fissures, mastitis and breast abscesses can significantly increase the risk of HIV transmission through breastfeeding.

*Feeding choices for infants born to HIV infected mothers*

1) Formula feeding: Artificial feeding is the safest feeding practice and completely prevents the transmission of HIV to the newborns, which can occur through breastfeeding.

2) Exclusive breastfeeding: Exclusive breastfeeding is safer than mixed feeding, but early weaning is very important. Exclusive breastfeeding should not be continued beyond 6 months and the weaning period should be as short as possible.

3) Other feeding choices: Breast milk can be pumped and disinfected and then used to feed the infants. The most common disinfection method is pasteurization.

**POSTEXPOSURE MANAGEMENT**

HIV-1 occupational exposure may place a healthcare worker (HCW) at risk for HIV infection and therefore requires consideration of postexposure prophylaxis (PEP).

*Assessment of infection risk*

*Evaluation of the source*

1) Low transmission risk: Low viral load level, no symptoms, or high CD4 count. 2) High transmission risk: High viral load level, end stage of HIV disease progression, primary HIV infection and low CD4 count. 3) The exposure source is unknown: Lack of information on the disease stage and HIV status of the source as well as the viral load level of the contaminated medical devices or items.

*Evaluation of exposure*

When source is body fluid or medical devices/items with body fluid or blood, the exposure should be evaluated for potential to transmit HIV based on the type of body substance involved and the route and severity of the exposure. 1) First-level exposure: contact of nonintact skin or mucous membrane, but the duration of contact are short or involve only a small area. 2) Second-level exposure: contact of nonintact skin or mucous membrane, and the duration of contact are prolonged or involve an extensive area; or a needlestick or cut to a minor degree (not by large hollow needle or deep puncture needle). 3) Third-level exposure: a severe needlestick or cut, resulting in a deep wound or with visible blood on the source.

*Principles of postexposure management*

1) Wounds and skin sites that have been in contact with blood or body fluids should be washed with soap and water. 2) Mucous membranes should be flushed with water repeatedly. 3) Expressing contaminated blood from the lesion by gently squeezing the wound. 4) The use of 75% alcohol or 0.5% iodophor and bandage for wound care.

**Postexposure prophylaxis**

*Recommended PEP regimens*

Basic regimens: AZT+3TC, recommended; ddl+d4T; d4T+3TC. Expanded regimens: AZT+3TC+IDV,
**Table 6. Indications for PEP**

<table>
<thead>
<tr>
<th>Degree of exposure</th>
<th>VL level of the source</th>
<th>PEP</th>
<th>PEP regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-level</td>
<td>Low risk</td>
<td>Not recommended</td>
<td>Basic regimen</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>Recommended</td>
<td>Basic regimen</td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>Recommended</td>
<td>Basic regimen</td>
</tr>
<tr>
<td>Second-level</td>
<td>Low risk</td>
<td>Recommended</td>
<td>Expanded regimen</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>Recommended</td>
<td>Basic regimen</td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>Recommended</td>
<td>Expanded regimen</td>
</tr>
<tr>
<td>Third-level</td>
<td>Low risk</td>
<td>Recommended</td>
<td>Expanded regimen</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>Recommended</td>
<td>Expanded regimen</td>
</tr>
<tr>
<td></td>
<td>Unknown</td>
<td>Recommended</td>
<td>Basic regimen</td>
</tr>
</tbody>
</table>

recommended; Basic regimen + EFV (resistance to PI is known); Basic regimen + ABC.

**Timing of PEP initiation and recommended duration**
PEP should be initiated as soon as possible. If possible, PEP should be started within 2 hours after an exposure and no later than 24 hours. However, even exceeds 24 hours, there is believed benefit from PEP for humans. PEP should be administered for 4 weeks, if tolerated.

**Indications for PEP**
Indications for PEP are shown in Table 6.

**Postexposure counseling and monitoring**

**Postexposure counseling**
Medical institutions should provide HIV-exposed HCWs counseling and regular follow-up. These exposed HCWs should be advised to do HIV antibody test regularly and to seek medical evaluation for any acute illness that occurs during the follow-up period. And HCWs who choose to take PEP should also be provided information about the side effects of the drugs, measures to minimize these effects, and the methods of clinical monitoring for toxicity during the follow-up period.

**Postexposure testing**
HIV-antibody testing should be performed at baseline and repeated at 4 weeks, 8 weeks, 12 weeks and 6 months postexposure for monitoring seroconversion. If available, HIV p24 antigen enzyme immunoassay or polymerase chain reaction for HIV RNA assays could be used in establishing HIV infection.

**Exposure report**
Details of the occupational exposures should be reported every 6 months by medical institutions to the provincial CDC and the summarized date should be reported to the central CDC.

**Managements to prevent occupational exposure**
Healthcare facilities must provide personal protective equipment and HCWs must use personal protective equipment when performing procedures for which it is reasonably anticipated that exposure to blood might occur. Personal protective equipment consists of gloves for possible hand contact with blood, and impervious gowns and face/eye shields when splashes, spray, or spatter of blood or other potentially infectious material may be generated.

Healthcare facilities should consider implementing other strategies demonstrated to be effective in reducing blood exposures such as double gloving for high risk surgical/obstetrical procedures, blunted suture needles, and self sheathing needles.

Healthcare facilities must provide certain engineering controls proven to reduce exposure to risk, such as leakproof secondary containers for transporting blood and impervious needle disposal containers.

**Acknowledgements:** We thank the following institutions and experts for their tremendous support and consultation: WHO country and regional offices, and Division Treatment and Care, National Centre for AIDS/STD Control and Prevention, Chinese CDC, particularly Dr. Connie Osborne (WHO, China), Dr. CHEN Hong (WHO, China), Dr. Michel Tailhaedes (WPRO, Philippines), and Jennifer Pan (Division Treatment and Care, National Centre for AIDS/STD Control and Prevention, Chinese CDC) and Jessica Haberer (Division Treatment and Care, National Centre for AIDS/STD Control and Prevention, Chinese CDC).

**Members of editorial team:** WANG Ai-xia, WANG Fu-sheng, WANG Qing-yue, WANG Jian, FENG Tie-jian, LU Hong-zhou, SUN Hong-qing, SUN Yong-tao, YE Han-hui, LI Tai-sheng, LI Xing-wang, LIU Zheng-yin, XING Yu-lan, HE Yun, WANG Ning, WU Hao, WU Nan-ping, ZHANG Fu-jie, ZHOU
REFERENCES


(Received June 16, 2006)