

# HIV Manual

**Special Preventive Programme**  
**Public Health Services Branch**  
Centre for Health Protection  
Department of Health  
Government of the HKSAR



**衛生署**  
Department of Health

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*This Manual is a compilation, by Special Preventive Programme, of selected local Guidelines and Recommendations promulgated by the Scientific Committee on AIDS and Committee on Promoting Acceptance of People Living with HIV/AIDS of the Hong Kong Advisory Council on AIDS and the Scientific Working Group on Viral Hepatitis Prevention between 2001 and 2005*

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***Section One***

***HIV Management and Clinical  
Guidelines***

## **Chapter One**

### **Recommended Framework for the Delivery of HIV Clinical Care in Hong Kong**

**Scientific Committee on AIDS  
co-sponsored by the Hong Kong Advisory Council on AIDS  
and  
the Centre for Health Protection,  
Department of Health**

**January 2005**

## **Recommended Framework for the Delivery of HIV Clinical Care in Hong Kong**

### **Purpose**

1. This paper sets out the recommended goal, principles and standards of a practical model for delivering HIV clinical care in the Hong Kong setting. These core components are knitted to form a framework for effective HIV care. The objective of constructing the framework is, based on the progress made in the last two decades, to recommend the minimum components of an HIV clinical care system that is locally relevant, with a view to make further improvement.

### **Background**

2. As from the 1980s, Hong Kong has been providing clinical care to People Living With HIV and AIDS (PLWHA). The Special Medical Service of the Queen Elizabeth Hospital (QEH) and the Special Preventive Programme of the Department of Health (DH)<sup>1</sup> are the two designated units providing specialist care to PLWHA. At QEH, inpatient and ambulatory care are integrated at service level. At DH, the service is outpatient based. Since 2001, the Infectious Disease (ID) unit of Princess Margaret Hospital (PMH) has joined the Kowloon Bay Integrated Treatment Center (KBITC) of DH in the delivery of HIV clinical care. (Annex I)

3. HIV clinical care has undergone revolutionary changes in recent years as a result of scientific advancement in HIV medicine, changing epidemiology and the expectations of PLWHA and the community. In the course of summarizing the local experiences, the Scientific Committee on AIDS<sup>2</sup> proposes a framework for the HIV clinical care model that is relevant to the Hong Kong setting. (Annex II)

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<sup>1</sup> Special Preventive Programme is incorporated within the Public Health Services Branch of the Centre for Health Protection (CHP) of the Department of Health, effective from 1 June 2004.

<sup>2</sup> A Working Group on HIV clinical care was formed by the Scientific Committee on AIDS in November 2003 to review the subject and draft the recommendations in this paper. The Working Group comprised the following members – Dr ST Lai, Dr Patrick Li and Dr KH Wong, and was supported by Dr Michael Chan of the Committee Secretariat, and Dr SS Lee of the Council Secretariat.



## Rationales

4. While HIV respects no country barrier, the dimensions and diversity of its societal impacts vary from one place to another. The development of clinical care models must naturally tie in with other factors – epidemiology, advances in medical sciences, local strategy and the existing health infrastructure. Their characteristics provide the rationales for establishing the goal and the principles in this recommendation.

5. Over the years, the HIV prevalence in Hong Kong has remained at a low level of <0.1% in the general population. The Advisory Council on AIDS has put forward the goal of “maintaining Hong Kong as a low HIV prevalence area” in its proposed strategy for 2002 to 2006.<sup>3</sup> A focused approach aiming at the provision of clinical management to as many HIV positive individuals as possible would serve the dual purpose of effective clinical care and public health control.

6. On the other hand, advances in medical sciences have led to the use of highly active antiretroviral therapy (HAART) as an effective means of restoring health in patients living with the infection. In Hong Kong, antiretroviral drugs were first introduced in 1987. HAART has become generally available in the public service ever since 1997. Essential laboratory investigations including CD4 and viral load determinations are regularly used in disease monitoring. A body of expertise has steadily grown, despite the small critical mass.

7. Finally, in the delivery of HIV care, a robust health care system is crucial. There is in place a coordinated and comprehensive health infrastructure for managing patients with chronic illnesses, plus a public health programme on disease control. HIV management can be effectively integrated with the existing infrastructure.

## Goal and Principles of HIV Clinical Care

8. Naturally, the aim of any form of clinical care is to restore optimum health in affected individuals. This applies to PLWHA, who should be able to lead a healthy life. There is the need to establish a overarching public health goal to guide the development of effective delivery of HIV care. It is, therefore, proposed to establish the goal of minimizing morbidity arising from HIV/AIDS in Hong Kong.

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<sup>3</sup> Hong Kong Advisory Council on AIDS. *Recommended HIV/AIDS strategies for Hong Kong 2002 to 2006*. Hong Kong: ACA, 2002.

9. Six principles are proposed to exemplify the public health goal:
- (a) HIV medicine shall be developed as expertise area for promoting the delivery of specialist care to PLWHA.
  - (b) A multidisciplinary professional team, working in line with international standards, shall lead the coordination and governance of HIV care.
  - (c) Easy access to quality clinical care and services in all settings is ensured.
  - (d) Continuum of prevention and care shall be observed, with the integration of clinical care with public health control of the infection.
  - (e) Community involvement should be promoted through the encouragement of participation and the mobilisation of community resources.
  - (f) HIV patient's confidentiality and privacy must be upheld.
10. These principles should not be interpreted in isolation but rather treated as the common pillars in support of the development of core service components, for achieving the aim of effective delivery of HIV care. The observance of the principles requires that the clinical care model be integrated with the health care infrastructure. For each principle a number of standards are recommended. (Annex III)

### **Principle One: Practice of HIV Medicine**

11. HIV medicine is fast becoming a medical specialty of its own. As the cornerstone of HIV care, the standards of HIV medicine are reflected by (a) the practice of specialist physicians, (b) provision of antiretroviral treatment, and (c) provision for sustainable expertise development.
12. For effective delivery of clinical care, *clinician(s) with a special interest in HIV medicine* should lead and oversee the HIV service. The clinician should preferably be an infectious disease (ID) physician but could also be a general internist, or specialist physician in any branch of internal medicine.
13. Through the work of an HIV physician and his/her team, HIV patients shall have *access to HAART* when clinically indicated. The decision is supported by CD4 enumeration and viral load determination, coupled with access to resistance testing, which are fast becoming the standards in laboratory monitoring. Antiretroviral therapy

forms the core of the clinical consultation for controlling the course of the diseases, which must be paralleled by prophylaxis against opportunistic infections, and treatment of complications as they arise.

14. To ensure that a sustainable system is in place, *training* in HIV medicine must be developed. This can be undertaken in conjunction with specialist training in Hong Kong.

### **Principle Two: A Multidisciplinary Professional Team**

15. A multidisciplinary team approach in the clinical management of HIV/AIDS should be adopted. Psychological, social and physical care is part and parcel of the overall management of HIV patient. HIV physician, nurse, medical social worker form the *core members of the team*. They are supported by nutritionist, clinical psychologist and pharmacist. The inputs of other disciplines would also be desirable, for example, psychiatrist, dermatology-venereologist, occupational therapist and physiotherapist. (Principle Three). The participation of public health professionals provides a dimension that links treatment with HIV prevention, a concept enshrined also in Principle Three.

16. The service system should allow the *development of professional expertise* in the care and management of HIV infection. A doctor practising HIV medicine should commit to continuing professional development. A nurse acts as the case manager and is professionally competent in overseeing drug adherence, counselling patient, planning nursing care and coordinating services for each patient. *Capacity building* is an essential part of the care model. Members of the multidisciplinary team should undergo both theoretical and in-service training and participate in continuing education so as to keep abreast of advances in management of HIV infection. Participation in *research* is important for generating locally important new knowledge and evaluating and improving the local service model.

17. A governance framework shall be developed to ensure the delivery of quality service, against a set of established standards. Governance here refers therefore to clinical as much as administrative governance of the team-based organization of HIV services.

**Principle Three: Prevention and Care Continuum**

18. The provision of clinical care to HIV patients contribute to the overall control of the infection in a public health context. HIV care services provide a window of opportunity to focus prevention on those living with the infection, highlighting the principle of *prevention and care continuum*.

19. In realising the principle, the following standards are proposed: (a) incorporation of risk reduction counseling for PLWHA, (b) access to STI (sexually transmitted infection) diagnosis and treatment, (c) provision and/or access to partner counseling and referral, (d) prevention of mother-to-child HIV transmission, and (e) the operation of antiretroviral adherence programme both for enhancing clinical effectiveness and to minimize the emergence of mutants. In practice, an HIV clinical service plays an active role in the public health surveillance of HIV/AIDS.

**Principle Four: Access to Care**

20. HIV patients should have access to care in order to achieve optimal health outcomes as are expected from current medical knowledge and technology. This standard is gauged by the patient's access to (a) designated HIV services, (b) range of other clinical and (c) support services, and by such access in different settings.

21. HIV patients should, as for other patients with a chronic condition, have equal access to services provided by other *clinical specialties* if medical complications arise, as well as *palliative care* for the terminally ill. The former includes psychiatric, ophthalmologic, surgical, obstetric/gynecological and other clinical consultations as the condition may require. All services must be affordable, as in the case of other chronic illnesses.

22. In the development of the care system, working partnership should be developed to enable effective and efficient referral. Health care professionals under different specialties should be involved in the care of HIV patients. To ensure *continuity of care*, relevant medical information should be readily available to the clinician providing care to the patient during hospitalization and out-patient visits. Effective communication between HIV clinician and laboratory personnel must be established to enable prompt actions to be initiated in case of needs.

23. VCT (voluntary counseling and testing) offers the best contact point for the

diagnosis and management of HIV infection. Access to care shall however not be limited to that provided by designated HIV service. Quality care shall be accessible in other settings including the prison, and irrespective of the risk factors associated with the infection. In the latter situation, drug users, men having sex with men (MSM) and commercial sex workers should have access to care no different from that for other individuals with the same clinical condition.

### **Principle Five: Community Involvement**

24. Involvement of the community enhances the effectiveness of the care model on one hand, and contributes to the role of promoting acceptance of PLWHA on the other.

25. Community involvement can take many forms. In the Hong Kong setting, medical social workers and/or specialty nurses play the coordinating role in the mobilization of community resources. This could range from conducting support groups to the involvement of community based organizations to support care delivery. The role of the private sector would need to be enhanced to broaden community participation.

### **Principle Six: Confidentiality and Privacy**

26. Medical information of PLWHA, like that for other clinical conditions, should be kept in strict confidence. The disclosure of one's HIV status is generally not required, and must be treated on a need-to-know basis in the health care setting.

27. Infection control refers to protective measures in the health care setting for preventing and controlling the spread of infections. In the case of HIV, standard precaution should be practiced, which is adequate both for protecting the carers and other patients. HIV patients should be treated no differently from other patients. Stigmatization arising from infection control practices should be avoided.

### **Issues of Concern and for Future Consideration**

28. The rationales in para 4 to 7 set out not only the foundations for the principles, but also spell out the limitations inherent in the proposed models, which

are, respectively, the HIV epidemiology, applications of medical sciences, and the current health infrastructure, as are explained in the following paragraphs.

29. The current framework was developed at a time when the HIV prevalence was low. It is assumed that currently most, if not all, of the diagnosed cases are offered treatment and care in accordance with the established principles. These principles should be upheld in the event that the HIV rate rises. The delivery model may however need to be adjusted appropriately.

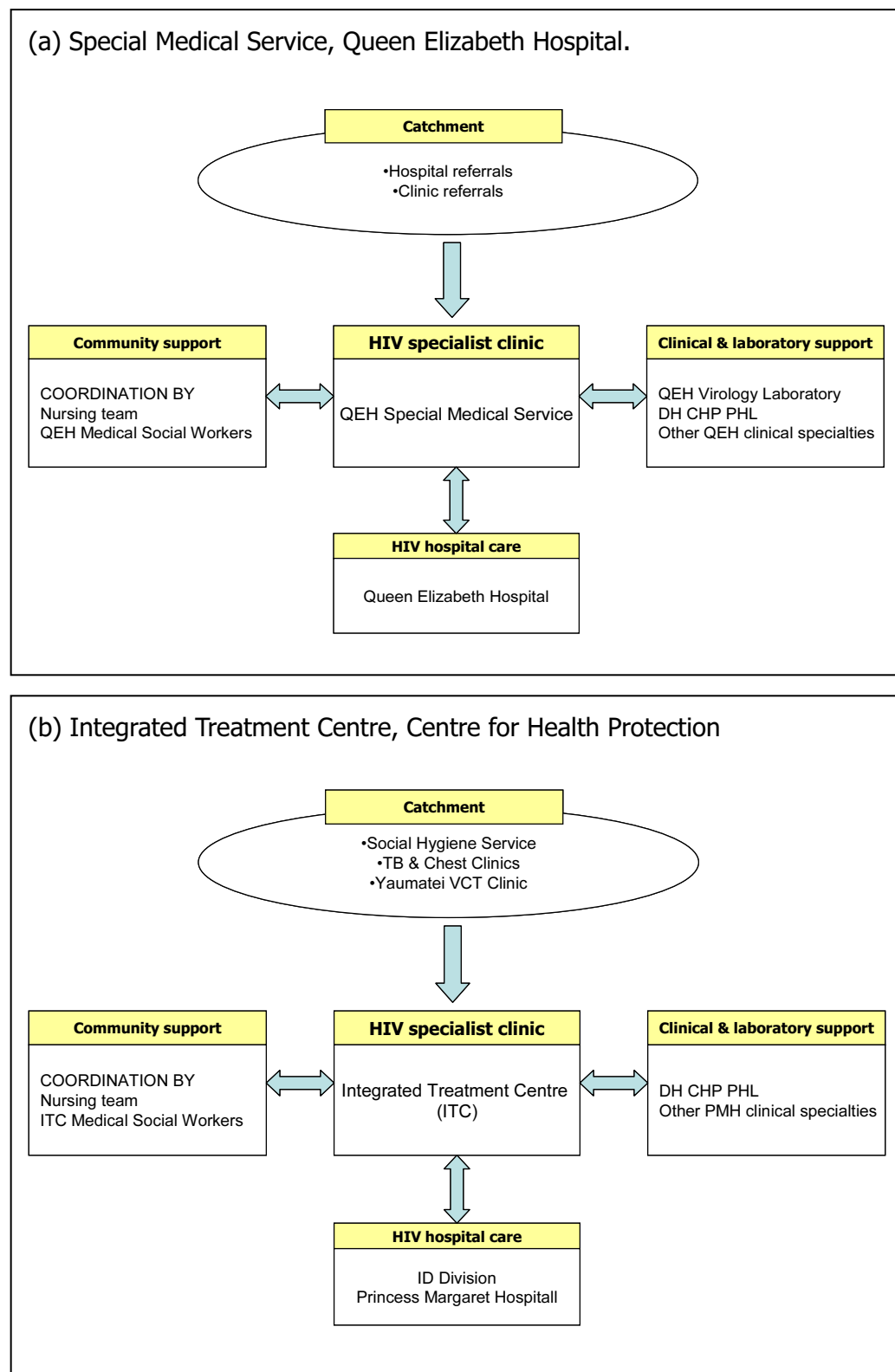
30. State-of-art HIV treatment is provided to PLWHA. This refers to treatment options that have been proven to be effective, using an evidence-based approach. In the absence of effective clinical trials system, the access to treatment does not extend to experimental therapy.

31. Currently, HIV care is delivered almost exclusively through the public service (Hospital Authority and Department of Health). Treatment is heavily subsidized under the current mode of health care financing in the public service. While there is the advantage of realizing the prevention and care continuum, and hence the recommendation of a public health goal, the framework has not YET included the option of providing for similar care systems in the private sector, nor has considered the impacts of any alteration in the health care infrastructure in due course.

32. Finally, the framework has been developed with the care of adult patients in mind, though the principles shall equally apply to paediatric patients. The emphases may however vary, with stronger focus on integrated care, and less on the public health role in the reduction of risk behaviours associated with HIV spread.

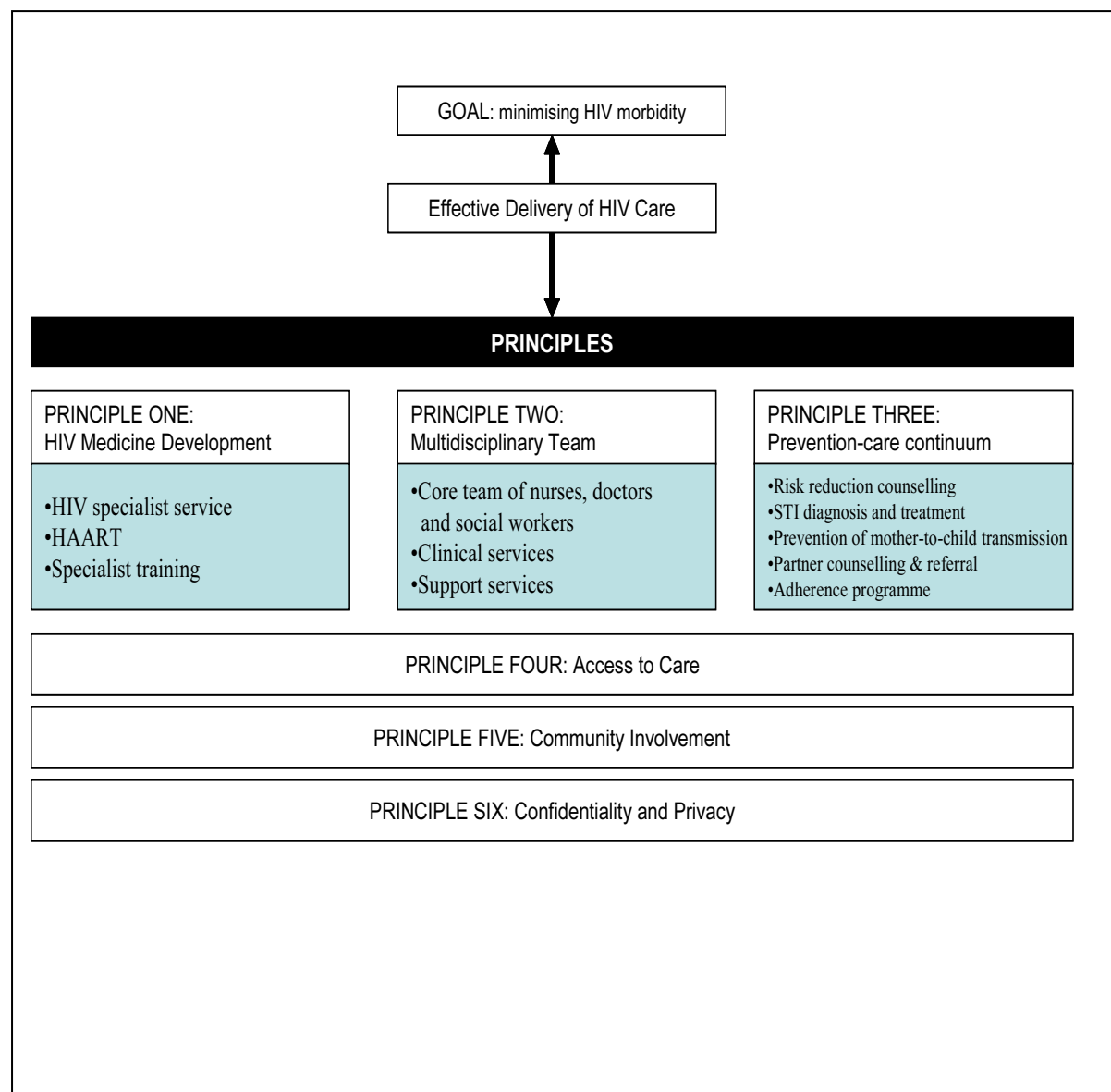
*Scientific Committee on AIDS*

## Annex I. Layout of HIV services in Hong Kong



\*Catchment refers to the main sources of referrals, which includes but is not limited to those in the box.

## Annex II. A flow diagram to represent the recommended framework for the delivery of HIV care in Hong Kong





**Annex III: Checklist on the development of standards in clinical HIV care**

- ☒ Protocols on clinical management that have been established in accordance with international and/or local guidelines
- ☒ An audit or equivalent mechanism, for example, chart review, to ensure the adherence to standards recommended in protocols
- ☒ An evaluation framework for monitoring output and outcome of the service
- ☒ Preventive intervention as a component of the service or through referral to the appropriate public health service
- ☒ Pursuance of quality standards in Infection control practice
- ☒ An information system to support service development and evaluation
- ☒ Training as an integral component for enhancing expertise development in medicine, nursing and other health care disciplines
- ☒ Linkage, where appropriate, to community-based care
- ☒ Participation in research

## **Chapter Two**

### **Recommended Principles of Antiretroviral Therapy in HIV Disease**

**Scientific Committee on AIDS  
of Hong Kong Advisory Council on AIDS**

**January 2005**

**Recommended Principles of Antiretroviral Therapy in HIV Disease****Preamble**

In 1996, protease inhibitor became available in Hong Kong. Added to conventional nucleoside therapy, it provided potency and subsequently durability in the treatment of HIV infection. In line with experience abroad, mortality of HIV infected patients has decreased since then.

In 1996 and 1998, the Scientific Committee on AIDS (SCA) published its consensus statements on antiretroviral therapy, providing guidance to the local use of antiretrovirals.

With the rapid advancement of HIV medicine, certain principles of antiretroviral use have evolved. Hence, the SCA sees the need to define such principles for the local medical practitioners, having examined the availability of antiretroviral treatment, ancillary professional support, laboratory services as well as expertise in HIV disease management. Comments were also sought from the medical profession.

As such, the SCA views these principles as attainable and should be adhered to for the maximal benefit of patients. They effectively serve as the basis of the local standard of care.

## Recommended principles

### **I. Highly active antiretroviral therapy (HAART) with potent and durable viral suppression to undetectable levels is the preferred therapy under most clinical circumstances.**

1. For practical purposes, HAART may be defined as therapy which is potent enough to suppress HIV viraemia to undetectable levels, as measured by the most sensitive assay available, and which is durable in its virologic effect. Operationally defined as such, HAART implies the need of viral load for monitoring of efficacy.<sup>1</sup> Failure of full virologic suppression or rebound from undetectability calls for immediate review of the regimen.

2. HAART conventionally includes three or more drugs from at least two classes. Currently, there are three classes of antiretrovirals available in Hong Kong, the nucleoside reverse transcriptase inhibitor (including the nucleotide, tenofovir disoproxil fumarate), non-nucleoside reverse transcriptase inhibitor, and protease inhibitor.

3. However, as long as there is full and durable suppression of viral load, any regimen should be regarded as HAART. On the other hand, known suboptimal regimens, e.g. monotherapy, double nucleoside, or certain triple nucleoside combinations are not HAART and are contraindicated in HIV disease.

4. The goal of potent and durable viral suppression is paramount whether the treatment is the initial or subsequent regimens. A failing regimen generally requires at least two, and preferably three new drugs without cross resistance in a subsequent regimen to achieve this goal. Thus, adding or substituting only one new medication is contraindicated.

5. In certain circumstances it is difficult to concoct a regimen to achieve full viral suppression. These include multiple drug resistance, intolerance and multiple allergy to therapy. Nevertheless, limited viral suppression may still confer clinical benefit to the patient.<sup>2</sup> This phenomenon extends to prophylaxis against

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<sup>1</sup> Mellors J, Munoz A, Giorgi J, et al. Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. *Ann Intern Med* 1997;126:946-54.

<sup>2</sup> Deeks SG, Barbour JD, Grant RM, Martin JN. Duration and predictors of CD4 T-cell gains in patients who continue combination therapy despite detectable plasma viremia *AIDS* 2002;16:201-7.

mother-to-child transmission where incomplete viral suppression by monotherapy reduces risk, although the goal of treatment should still be full suppression. In the case of post-exposure prophylaxis, viral suppression is not a factor, and use of lesser drug regimens, e.g. double nucleosides, may be reasonable.

**II. The initiation of antiretroviral therapy is a carefully meditated decision following a thorough medical evaluation and informed discussion with the patient.**

6. Most authorities agree that symptomatic HIV infection, including AIDS-defining conditions and category 'B' symptoms warrant antiretroviral treatment.<sup>1</sup> In primary HIV infection, there are also theoretical advantages of immediate treatment which are being evaluated in clinical trials.

7. In chronic, asymptomatic HIV infection, a low CD4 count below 200/ul is a widely accepted threshold for initiation of treatment.<sup>2,3,4</sup> Nevertheless, in those with higher CD4 counts, the decision to initiate treatment should be a composite evaluation of the following factors:

- The level and trend of CD4 count – A marginal and falling CD4 count favours treatment
- The level of viral load – a high level in company with a marginal CD4 count favours treatment.

8. In all events, the patient's willingness to initiate and adhere to treatment is important.<sup>5</sup> This should be based on his full comprehension of the rationale of treatment and its requirements. Specifically, he should understand

- the need of strict adherence and regular medical followup,
- the adverse effects and immune reconstitution associated with treatment, their implications and management, and

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<sup>1</sup> Scientific Committee of the Advisory Council on AIDS. Classification system for HIV Infection and surveillance case definition for AIDS in adolescents and adults in Hong Kong (Available at <http://www.aids.gov.hk>. Accessed Nov 28, 2003)

<sup>2</sup> US Department of Health and Human Services. Guidelines for the use of antiretroviral agents in HIV-1 infected adolescents and adults. Oct 29, 2004. (Available at [http://www.aidsinfo.nih.gov/guidelines/adult/AA\\_111003.pdf](http://www.aidsinfo.nih.gov/guidelines/adult/AA_111003.pdf). Accessed Jan 10, 2005)

<sup>3</sup> The EACS Euroguidelines Group. European guidelines for the clinical management and treatment of HIV-infected adults in Europe. *AIDS* 2003;17(suppl):S3-26

<sup>4</sup> British HIV Association (BHIVA) guidelines for the treatment of HIV-infected adults with antiretroviral therapy. *HIV Med* 2003;4(S1):1-41

<sup>5</sup> Wood E, Hogg RS, Yip B, et al. Effect of medication adherence on survival of HIV-infected adults who start highly active antiretroviral therapy when the CD4+ cell count is 0.200 to 0.350 X 10<sup>9</sup> cells/L. *Ann Intern Med* 2003;139:810-6

- the antiretroviral options available to him.

**III. The design of a regimen should take into consideration factors related to the patient as well as the virus, with long term disease control as a major goal.**

9. As the availability of antiretrovirals expands, the number of possible combinations multiplies, many of which qualify as HAART because of its virologic potency and durability as shown in clinical trials. However, all regimens do not perform equally for a patient. Furthermore, antiretroviral therapy is long term and potentially carries serious adverse effects. It is therefore imperative that a regimen be individualised, after assessment of the following:

- possibility of unfavourable drug interactions,
- host factors that may hinder adherence, e.g. irregular working hours, depression, gastrointestinal disturbance, etc,
- viral factors that will suggest resistance, e.g. acquisition of HIV from a partner on treatment, and
- underlying risk factors or disease that will predispose to adverse effects of treatment, e.g. cardiovascular risk factors, metabolic syndrome, diarrhoea, etc.

10. The regimen itself is then optimised in frequency of administration, convenience and pill burden, before it is recommended to the patient.

11. This process is done to facilitate the design of a regimen and not to exclude certain patients from treatment. Assessment should be repeated during subsequent followup, with a view to timely adjustment to achieve long term control of disease.

**IV. The offer of antiretroviral therapy is not dependent on predicted adherence. Anticipated difficulties in adhering to a regimen are proactively and empathically managed by appropriate selection of antiretrovirals, intensive counselling and disease monitoring, and correction of factors contributing to non-adherence.**

12. There can be no overstating the importance of adherence in the successful use of HAART.<sup>6</sup> Certain lifestyle factors are conventionally believed to be associated with non-adherence, most notable of which are substance use and commercial sex

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<sup>6</sup> Press N, Tyndall MW, Wood E, Hogg RS, Montaner JS. Virologic and immunologic response, clinical progression, and highly active antiretroviral therapy adherence. *J Acquir Immune Defic Syndr* 2002;31 Suppl 3:S112-7.

work. However, data supporting such associations are conflicting and their predictability of nonadherence is crude.<sup>7,8</sup> To the contrary, it has been repeatedly shown that doctors' prediction of adherence is poor.<sup>9</sup>

13. Recommendation for antiretroviral therapy should therefore be based solely on medical considerations. Although patient assessment includes that of factors contributing to nonadherence, the objective is to proactively correct these factors before and during antiretroviral use.<sup>10</sup> Depending on circumstances, it may be appropriate to intensify monitoring of adherence<sup>11</sup> and disease, and institute preventive measures against adverse effects. Antiretroviral should be selected in ways conducive to long term adherence which is to be actively monitored in all subsequent clinical encounters. Regardless, it is unacceptable to withhold treatment or prescribe suboptimal therapy because of expected noncompliance.<sup>12</sup>

**V. Highly active antiretroviral treatment is but one of a whole array of medical therapies of HIV disease, the other components being effective infection prophylaxis, nutritional therapy, and immunisation.**

14. The success of HAART overshadows other interventions in HIV disease that have shown proven clinical benefit. These include but are not limited to correction of anaemia, appropriate prophylaxis against opportunistic infections, nutritional therapy, and certain behavioural modifications that avoid contact with pathogens.<sup>13</sup> Although treatment of latent tuberculosis probably does not prolong survival, the reduction in morbidity also justifies its use in HIV infected patients.<sup>14</sup> Where appropriate, all these measures should be combined with HAART.

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<sup>7</sup> Mocroft A, Madge S, Johnson AM, et al. A comparison of exposure groups in the EuroSIDA study: starting highly active antiretroviral therapy (HAART), response to HAART, and survival. *J Acquir Immune Defic Syndr* 1999;22:369-78.

<sup>8</sup> Palepu A, Tyndall M, Yip B, O'Shaughnessy MV, Hogg RS, Montaner JS. Impaired virologic response to highly active antiretroviral therapy associated with ongoing injection drug use. *J Acquir Immune Defic Syndr* 2003;32:522-6.

<sup>9</sup> Gross R, Bilker WB, Friedman HM, Coyne JC, Strom BL. Provider inaccuracy in assessing adherence and outcomes with newly initiated antiretroviral therapy. *AIDS* 2002;16:1835-7.

<sup>10</sup> Fong OW, Ho CF, Fung LY, et al. Determinants of adherence to highly active antiretroviral therapy (HAART) in Chinese HIV/AIDS patients. *HIV Med* 2003;4:133-8.

<sup>11</sup> Ho CF, Fong OW, Wong KH. Patient self-report as a marker of adherence to antiretroviral therapy. *Clin Infect Dis* 2002;34:1534-5.

<sup>12</sup> Tchetgen E, Kaplan EH, Friedland GH. Public health consequences of screening patients for adherence to highly active antiretroviral therapy. *J Acquir Immune Defic Syndr* 2001;26:118-29.

<sup>13</sup> US PHS, IDSA. Guidelines for Preventing Opportunistic Infections Among HIV-Infected Persons – 2002. *MMWR* 2002;51(RR08):1-46.

<sup>14</sup> Scientific Committee on AIDS, Hong Kong Advisory Council on AIDS. Recommendations on the treatment of latent TB infection in HIV-positive persons in Hong Kong: Advisory Council on AIDS. 2002 (Available at <http://www.aids.gov.hk>. Accessed Nov 28, 2003).

15. Immunisation is available against infections that share similar routes of infection, e.g. hepatitis B, and against infections that may opportunistically infect HIV-positive patients, e.g. pneumococcus. They should be considered in HIV infected patients.

**VI. Novel antiretroviral therapy should be used only in a clinical trial setting where the patient understands the rationale and design of the trial, his potential gains from enrolment, possible adverse effects, and his right to withdraw at any point of time.**

16. The rapid advancement of HIV medicine has witnessed unexpected drug interactions<sup>15</sup> and reversal of recommendations.<sup>16,17</sup> The lesson of caution is thus obvious in the use of novel combinations and novel drugs. A properly conducted clinical trial setting is most appropriate should such therapy be contemplated.

17. Use of novel agents or novel use of available agents is based on potential gains over established therapy. This situation is exemplified by the occurrence in some patients of multiple drug resistance where there is no standard salvage therapy. In a clinical trial setting, the overriding principle is that a patient should only enrol after fully understanding its implications – especially the potential benefits to the patient and potential adverse effects with new treatment. Such studies should be administered according to the Declaration of Helsinki<sup>18</sup> and after proper evaluation of their ethical implications. Mechanisms of data monitoring and its regular review should be in place, detailed records should be kept, and informed consent be properly obtained. Should new relevant data or opinions emerge in the course of a study, they should be made known to the patients as soon as possible, even if this encourages them to withdraw from the study.

**VII. HIV infection is not only a multi-organ disease but beset with enormous social implications. It can be successfully managed only by a multispecialty and multidisciplinary approach, with sensitivity and empathy.**

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<sup>15</sup> US FDA. 2003 Safety Alerts for Drugs, Biologics, Medical Devices, and Dietary Supplements, Viread. (Available at <http://www.fda.gov/medwatch/SAFETY/2003/safety03.htm#viread>. Accessed Nov 28, 2003).

<sup>16</sup> Harrington M, Carpenter CC. Hit HIV-1 hard, but only when necessary. *Lancet* 2000;355:2147-52.

<sup>17</sup> Kaplan JE, Hanson DL, Cohn DL, et al. When to begin highly active antiretroviral therapy? Evidence supporting initiation of therapy at CD4+ lymphocyte counts <350 cells/microL. *Clin Infect Dis* 2003;37:951-8.

<sup>18</sup> World Medical Association. Declaration of Helsinki. (Available at <http://www.wma.net/e/policy/b3.htm>. Accessed Nov 28, 2003).



18. HIV infection transcends organ systems and requires management by a multispecialty effort. Experts in antiretroviral therapy should collaborate with specialists of other disciplines, including ophthalmologists, surgeons, neurologists, psychiatrists, gynaecologists, dermatologists, paediatricians and primary care internists. Assistance of other professionals like medical social workers, counsellors, nutritionists and occupational therapists is also essential to a holistic, client-centred approach.

19. Intangible barriers to effective treatment exist in our society in the form of social marginalisation, although attempts are ongoing to eradicate all forms of discrimination against HIV-infected patients.<sup>19</sup> Until then, the physician should be sensitive to such dynamics and be empathic in rendering care. Issues such as confidentiality, unprejudiced medical management, equitable access to care, and partner notification are particularly relevant.

**VIII. Long term antiretroviral therapy should be prescribed only by physicians competent in the management of HIV disease, and in settings organised for optimal care.**

20. The complexity of antiretroviral treatment, the lifelong commitment of patients to such therapy, and the unforgiving nature of drug resistance mandate prescription only by competent physicians. Currently, the high cost of medications practically limits prescription privileges to physicians of designated HIV clinics in Hong Kong. However, as availability improves and cost decreases, there is a risk of inappropriate use and emergence of resistance, in a scenario reminiscent of antibiotics.

21. The SCA supports attempts to define qualities of practitioners required for appropriate prescription of antiretrovirals for the long term management of HIV disease. Such attempts should take into account the knowledge base of the physician, his experience and record of care of HIV patients, and evidence of continuing medical education.

22. It is also important that antiretrovirals be used in a setting where there is adequate laboratory support, especially in regard to the measurements of viral load and CD4 count, and testing of drug resistance. The indications for the latter are

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<sup>19</sup> Committee on Promoting Acceptance of People Living with HIV/AIDS, Hong Kong Advisory Council on AIDS. Setting the agenda of promoting acceptance of people living with HIV/AIDS in Hong Kong - a strategy paper, 2001. (Available at <http://www.aids.gov.hk>. Accessed Nov 28, 2003).

evolving and reference should be made to the best available evidence. There should also be access to consultations with other medical specialties and assistance by other professionals required for optimal care.

23. Short-term antiretroviral use is indicated in post-exposure prophylaxis and occasionally in prevention against mother-to-child transmission, sometimes on an urgent basis. Nevertheless, appropriate prescribing is still important in these circumstances. Therefore, the prescribing physician should either be qualified in antiretroviral use, or have access to expert advice. A peer-reviewed protocol should be available in settings where such use of antiretrovirals is conceivable, e.g. the Accident and Emergency Dept.

**IX. While experience of antiretroviral use in overseas countries provides useful guidance, it is desirable that a local, systematized surveillance system be in place for monitoring of efficacy and unexpected adverse effects.**

24. Most pre-licensure data on antiretrovirals were obtained in developed countries from studies on ethnic groups other than Chinese. Experience has shown that ethnicity may play a role in the incidence and pattern of adverse effects,<sup>20,21</sup> as well as the very immunologic profile.<sup>22</sup> Local viral factors such as primary resistance may also be relevant. In addition, postmarketing surveillance has uncovered adverse effects never encountered before licensure.<sup>23</sup>

25. It is thus a matter of principle that surveillance for adverse effects and antiviral efficacy be carried out despite drug licensure locally or abroad. It is also desirable that such collection of data be done in a systematic manner.

*Scientific Committee on AIDS*

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<sup>20</sup> Ho TY, Wong KH, Chan KCW, Lee SS. High incidence of nevirapine-associated rash in HIV-infected Chinese. *AIDS* 1998;12:2082-83.

<sup>21</sup> Wong KH, Chan KCW, Lee SS. Sex differences in nevirapine rash. *Clin Infect Dis* 2001;33:2096-2097.

<sup>22</sup> Kam KM, Wong KH, Li PCK, Lee SS, Leung WL, Kwok MY. Proposed CD4+ T-cell criteria for staging human immunodeficiency virus-infected Chinese adults. *Clin Immun Immunopath* 1998;89:11-22.

<sup>23</sup> Ho TTY, Chan KCW, Wong KH, Lee SS. Abnormal fat distribution and use of protease inhibitors. *Lancet* 1998;351:1736-7

**Chapter Three**

**Recommended principles on the application of the  
HIV antibody rapid test in Hong Kong**

**December 2003**

**Scientific Committee on AIDS  
of the Hong Kong Advisory Council on AIDS**

## **Recommended principles on the application of the HIV antibody rapid test in Hong Kong**

### **Background**

1. HIV antibody testing is an important part of the clinical and public health management of HIV infection. It forms a crucial step prior to the initiation of HIV counselling, medical care, disease surveillance and prevention. The Conventional HIV antibody testing is a two step procedure. Normally, the first step is a screening ELISA assay followed by a confirmatory test with Western Blot. At least 95% of patients become serologically HIV antibody positive within 3 months after infected by the virus.

2. In November 2002, Oraquick Rapid HIV-1 Antibody Test for the diagnosis of HIV infection was approved by the US Food and Drug Administration (FDA). The availability of this rapid test may signify a revolution of our current system of HIV counselling and testing provision and subsequent referral and care.

### **Purpose**

3. This paper summarizes the essential background, pros and cons of the rapid test and its applicability at different settings and serves as a reference for health care workers and community workers in the prevention and care of HIV/AIDS.

### **Definition & Performances**

4. Definition: A rapid test is a easy-to perform, point-of-care investigation for detecting antibody to HIV the result of which is provided at the same setting of the consultation. The test result is normally available within 30 minutes. Oraquick test is the first FDA approved rapid test falling into this category.

5. Performances: The sensitivity of Oraquick is 99.6% and the specificity is 100%. The performances of the test are reproducible in tested specimens from other geographic areas in the world. Compared with other licensed EIA tests, Oraquick has the same capabilities of detecting seroconversion changes.

**Advantages of the Rapid Test**

6. The advantages of the rapid test are multiple:-
- (a) The test is a single step procedure.
  - (b) The test can be offered at the point-of-care setting. This significantly reduces the turnaround time to only 45 minutes.
  - (c) The test offers the opportunity to perform more testing, especially in underserved populations like urgent care settings, emergency rooms, and new venues outside of healthcare setting.
  - (d) The test provides rapid answers on the clients' HIV status before initiating HAART in case of post exposure prophylaxis and HIV pregnant mother who presents late during delivery.
  - (e) The new test ensures that results are promptly obtained by the clients. In US, about 30% of HIV infected people tested by the conventional HIV test did not return for their results. These people did not receive proper care and counselling.
  - (f) The test is technically simple to perform. Oraquick is one of the Clinical Laboratory Improvement Amendments (CLIA) waived tests. In the US, CLIA-waived tests can be performed and interpreted in a physician office or other settings without going through certified laboratory

**Limitations of the Rapid Test**

7. The rapid test has the following limitations:-
- (a) The accuracy of the test in terms of specificity, sensitivity and predictive values in individual local setting has not been determined. It is extremely important for studies on the feasibility and acceptability of the test to be conducted in local setting.
  - (b) The rapid test is still a screening test that requires confirmation.
  - (c) Different form of counselling and support services are required as clients may not be prepared for the rapid results, especially in settings like bars and other venues where there is a great influence of drugs and alcohol.
  - (d) The advantage of replacing conventional test with rapid test in HIV testing services is not known such as in settings where a low defaulter rate is achieved with conventional HIV test.<sup>1</sup>
  - (e) The low prevalence of HIV infection at our locality may increase the chance of false positivity of the test.

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<sup>1</sup> Special Preventive Programme and Social Hygiene Service are settings where there is a low defaulter rate

- (f) The cost of implementing the HIV rapid test into the health care programme may be considerable.

### **Applications in Hong Kong**

8. Rapid test may complement the conventional HIV testing in the following areas.
- (a) Antenatal clinics when HIV infected mother presents late and therefore antenatal care and screening is impossible, e.g. in labour ward. Rapid test HIV antibody can support decision to start antiretroviral therapy in order to prevent mother to child transmission.
  - (b) Hospitals or clinics settings where a high risk of acute needle-stick injury is anticipated. Rapid test can be offered both to the source and victim so as to clarify the need for post exposure prophylaxis with antiretroviral therapy at the point-of-care
  - (c) Out-reach setting where conventional HIV testing may not reach certain high risk practising peers like the drug addicts, sex workers and homosexuals.
  - (d) Conventional HIV care setting where there is a high defaulter rate. The availability of the rapid testing at the point-of- care will reduce the defaulter rate and prevent further spread of the disease.

### **Requisites for performing the Oraquick Rapid test**

9. The following requisites are suggested before performing the rapid test
- (a) All operators must be familiar with standard infection control practice in health care setting.<sup>2</sup>Universal Precautions for Prevention of Blood-borne pathogens in health-care setting
  - (b) For the best performance of the test, a standardized protocol should be developed and followed in each service. Operators should be clearly informed and instructed.
  - (c) The test should be performed in the normal office lighting, and allow adequate time for the test process and interpretation.
  - (d) Clients enrolled for the test should understand the implications of the test results.
  - (e) Pretest counselling is an essential component of the rapid test and must be offered to all clients receiving the test
  - (f) After a rapid test positive result has been validated by confirmatory testing, an effective treatment, clinical care and referral should be provided to the client.

*Scientific Committee on AIDS*

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<sup>2</sup> Guideline of Universal Precautions for Prevention of Blood-borne pathogens in health-care setting

**Chapter Four**

**Reprint of *HIV Infection and the Health Care Workers  
Recommended Guidelines ACA, 1994***

**Advisory Council on AIDS**

**December 2003**

**Reprint of *HIV Infection and the Health Care Workers - Recommended Guidelines ACA, 1994*****(1) BACKGROUND****1.1**

AIDS (Acquired Immunodeficiency Syndrome) is caused by a retrovirus named HIV, the human immunodeficiency virus. The syndrome, characterised by development of complications like opportunistic infections or tumours, was first described in 1981 in the USA. The human race is now hard hit by the pandemic. An estimated total of 15 million people worldwide have already been infected so far.

**1.2**

HIV is transmitted largely through three routes: (a) sexual contact with an HIV-infected person, (b) exposure to contaminated blood and needles, and (c) perinatally from an infected mother to her baby. Worldwide over three-quarters of the infection have been contracted through sex, and largely heterosexual contacts.

**1.3**

HIV infection has been reported to occur in health care settings by exposure to contaminated blood through cutaneous injuries or mucous membranes. The estimated risk of contracting the virus after such injuries or exposure to infected blood is 0.4%.

**1.4**

The chance of HIV transmission from an infected health care worker to his / her client is much lower. The CDC (Centre for Diseases Control) in Atlanta has reported that six patients of an HIV-positive dentist in Florida were infected since 1990. There is still controversy as to how the transmission has occurred but this is the only case documented so far. In other 'look-back' studies of over 15000 clients of 32 HIV infected health care workers, including dentists and surgeons, none was found to have caught the virus.

**1.5**

Taken the extremely low risk of HIV transmission in the health care setting, universal precaution in handling blood and other body fluids was generally advocated as the most effective measure in further minimising the chance of infection. HIV has been isolated from blood, semen, saliva, tears, urine, vaginal secretion, cerebrospinal fluid,



synovial fluid, breast milk and amniotic fluid of infected individuals. However only blood, blood products, semen, vaginal secretion and breast milk have been linked to HIV transmission.

## **(2) GENERAL PRINCIPLES**

### **2.1**

The most effective means of preventing HIV transmission in health care setting is through adherence to universal precautions, thereby decreasing the risk of direct exposure to blood and/or body fluids.

### **2.2**

Voluntary instead of mandatory HIV testing is the best way of encouraging people (including health care workers) at risk of infection to seek counselling and appropriate treatment.

### **2.3**

Health care workers should consider receiving counselling and HIV antibody testing if they have reason to suspect that they have been infected.

### **2.4**

Health care workers are generally not required to disclose their HIV status to their patients or employers. Disclosure, if any, should be made on a need-to-know basis and with consent of the worker. Maintaining confidentiality is one way to prevent interference with individual privacy. It is also essential in encouraging the health care workers (either infected or at risk of infection) to receive proper counselling and management.

### **2.5**

Currently there is no justification for restricting practice of health care workers on the basis of the HIV status alone. Restriction or modification, if any, should be determined on a case-by-case basis.

## **(3) GUIDELINES**

### **3.1**

#### *Enforcement of Infection control*

The best way of preventing blood-borne diseases is to treat all blood (and certain body fluids) as potentially infectious. Universal precautionary measures should be adopted when handling blood, amniotic fluid, pericardial fluid, pleural fluid,

peritoneal fluid, synovial fluid, cerebrospinal fluid, semen and vaginal secretion. The risk of HIV transmission from faeces, saliva, nasal secretion, sputum, sweat, tears, urine and vomitus without overt blood staining is extremely low, and good simple hygienic measures should be sufficient.

Sound infection control practice with appropriate quality assurance should be implemented at all levels, taking into consideration factors unique to individual setting.

***(a) Infection control committee***

Rapid advancement in medicine and technology has meant that it is essential to keep updated on issues relating to infection control practice. Infection control committee should efficiently serve the functions of developing, promulgating and updating infection control policies in each institution and for each clinical specialty.

***(b) Written infection control guidelines***

Written infection control guidelines on universal blood/body fluid precaution should be developed and periodically updated in all health care settings – by infection control committees or equivalents for institutions/government departments and by professional bodies for health care professionals in private and solo practice.

***(c) Infection Control training***

The subject of infection control should be made an integral part of undergraduate, pre-registration or pre-employment training for all health care workers who may come into contact with blood/body fluids. Similarly regular courses tailored to the infection control needs of individual specialties, should be organised by professional bodies, universities/polytechnics as well as relevant government departments. It should be made known that those who fail to use appropriate infection control techniques to protect patients may be subject to charges of professional misconduct by the relevant governing body.

***3.2 HIV Counselling & related services for health care workers***

Information and counselling should be made easily available for health care workers who may have been exposed to HIV through risk behaviour, exposure to contaminated blood/blood products or occupational accidents. The importance of voluntary, confidential and anonymous counselling and HIV testing should be underlined.

### ***3.3 Rights & responsibilities of HIV infected health care worker***

#### ***3.3.1 Confidentiality***

In general, health care workers are not required to disclose their HIV status to their employers or clients. HIV infection and AIDS are not notifiable diseases by law in Hong Kong, and reporting is on a voluntary basis. There are, however, occasions where the HIV status has to be made known on a need-to-know basis, and this will normally be with the consent of the infected worker. For example, doctors or specialists involved in evaluating an infected health care worker may need to know his HIV status. In exceptional circumstances, breach of confidentiality may be warranted, for instance when an HIV infected health care worker refuses to observe the restrictions and patients have been put at risk.

#### ***3.3.2 Right to work***

The status and rights of an HIV infected health care worker as an employee should be safeguarded. If work restriction is required, employers should make arrangement for alternative work, with provision for retraining and redeployment.

#### ***3.3.3 Ethical issues***

An HIV infected health care worker should seek appropriate counselling and to act upon it when given. It is unethical if one fails to do so as patients are put at risk. The attending doctor of an HIV-infected health care worker should seek the advice of the expert panel formed by the Director of Health on the areas of management and possible need for job modification. The doctor who has counselled an HIV infected colleague on job modification and who is aware that the advice is not being followed and patients are put at risk, has a duty to inform the Medical/Dental Council for appropriate action.

#### ***3.3.4 Source of advice***

Referral to the expert panel should be made by the health care worker's attending physician. Formed by the Director of Health, the panel shall decide on whether job modification, limitation or restriction is warranted. A case-by-case evaluation would be undertaken considering multiple factors that can influence risk and work performance.

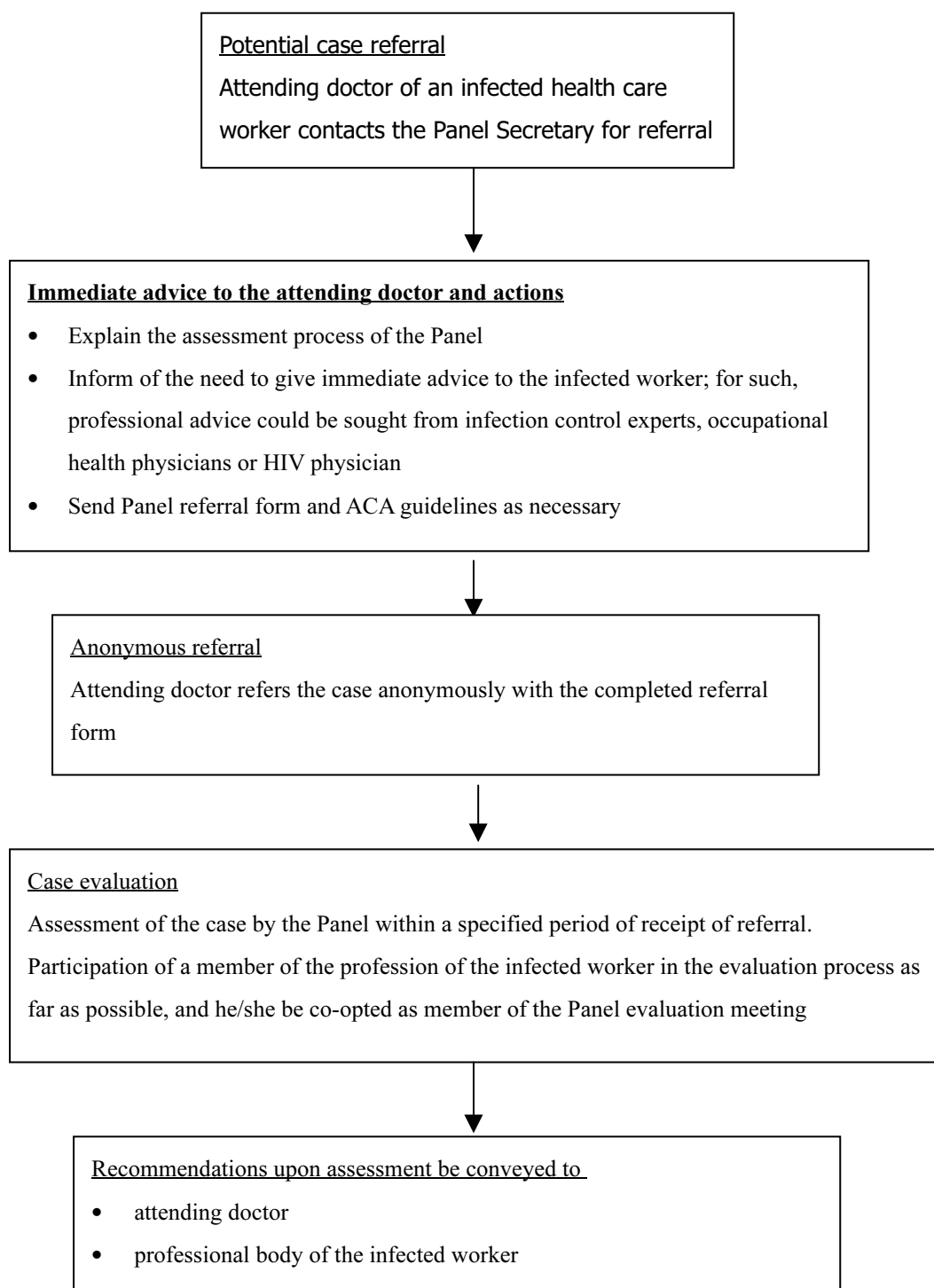
### ***3.4 Responding to the public***

The issue of HIV transmission in health care setting has caused much public concern despite the minimal risk incurred. Focusing on health care setting in fact deflects the society from proper attention to the major transmission routes through sex and drug

abuse. The health care profession has the duty of constantly reassuring the public, and to educate the clients on how HIV can and cannot be contracted. More importantly, the public looks on the health care profession as an example of how AIDS should be dealt with. By adhering to the guidelines for prevention of HIV infection in the health care setting, public fear can be allayed.

*Hong Kong Advisory Council on AIDS*

## Appendix

**Proposed workflow of Expert Panel on HIV Infection of Health Care Workers  
(2004-2006)**

**Chapter Five**

**Recommendations on the Treatment of Latent TB infection  
in HIV Positive Persons in Hong Kong**

**Scientific Committee on AIDS  
of  
Hong Kong Advisory Council on AIDS**

**January 2002**

## **Recommendations on the Treatment of Latent TB infection in HIV-positive Persons in Hong Kong**

### **BACKGROUND**

1. Tuberculosis (TB) is an important complication of human immunodeficiency virus (HIV) infection. In the United states, the Centers for Disease Control and Prevention (CDC) has classified TB as an AIDS-defining illness for surveillance purpose.<sup>1</sup> In Hong Kong, the Scientific Committee on AIDS proposed to include extrapulmonary TB as an AIDS-defining condition, while pulmonary TB is included only if one's CD4 count is below 200/ul.<sup>2</sup> This decision was made to take into consideration the low HIV rate and the endemicity of TB in the Hong Kong setting.

2. The prevention of TB in HIV infected individuals shall be achieved through the prevention of exposure to infectious TB in the first place. If infection has or has likely taken place, "preventive" treatment may be indicated. Preventive treatment using isoniazid (INH) monotherapy had been recommended by the American Thoracic Society (ATS) as early as in the 1960's.<sup>3</sup> In the recent guidelines by ATS, the term "treatment of latent TB infection (LTBI)" is preferred to "preventive therapy" or "chemoprophylaxis".<sup>4</sup> In as early as 1990, the United States CDC recommended INH for 12 months for treatment of LTBI in all HIV-infected persons with a positive tuberculin skin test (TST) as well as those who had recently been exposed to infectious TB.<sup>5</sup>

3. The applicability of such recommendations to Hong Kong was initially questioned because of a number of concerns: different TB epidemiology, higher prevalence of INH resistance, and wide coverage with BCG vaccination confounding interpretation of TST results. In subsequent years, 7 randomized controlled trials in

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<sup>1</sup> CDC. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR* 1992;41:No. RR-17.

<sup>2</sup> Scientific Committee on AIDS. *Classification system for HIV infection and surveillance case definition for AIDS in adolescents and adults in Hong Kong*. Hong Kong: Advisory Council on AIDS, 1995.

<sup>3</sup> American Thoracic Society. Preventive treatment in tuberculosis: a statement by the Committee on Therapy. *Am Rev Respir Dis* 1965;91:297-8.

<sup>4</sup> American Thoracic Society. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Respir Crit Care Med* 2000;161:S221-47.

<sup>5</sup> CDC. The use of preventive therapy for tuberculosis infection in the United States: recommendations of the Advisory Committee for Elimination of Tuberculosis. *MMWR* 1990;39:RR-8.

the United States, Haiti and some Sub-Saharan African countries have evaluated different regimens for the treatment of LTBI in HIV-positive individuals.<sup>6,7,8,9,10,11,12</sup> These studies provided support to the regimens and their effectiveness in groups of subjects who would benefit from the strategy.

4. In February 1998, World Health Organisation (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) issued a policy statement indicating that *there can ... no longer be any doubt that treatment of PPD+ (and HIV infected) individuals living in a setting with a high prevalence of TB with INH will reduce the risk of developing active TB in the short term to around 40%, and INH preventive treatment should be part of the package of care for people living with HIV/AIDS.*<sup>13</sup>

5. Taking reference from the research findings and national/international strategies, the following recommendations are formulated by the Scientific Committee on AIDS to facilitate the development of protocols in the management of LTBI in Hong Kong. The likely benefits of the recommendations are the reduction of morbidity and possibly mortality related to TB in HIV infected persons, secondary transmission to others, and probable HIV progression aggravated by TB. The algorithm of the proposed management is in Appendix I.

## GUIDING PRINCIPLES

6. To prevent the development of TB in HIV seropositive individuals, measures for the prevention of exposure to infectious sources should be emphasised.

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<sup>6</sup> Pape JW, Jean SS, Ho JL. Effect of isoniazid prophylaxis on incidence of active tuberculosis and progression of HIV infection. *Lancet* 1993;342:268-72.

<sup>7</sup> Hawken MP, Meme HK, Elliot LC, et al. Isoniazid preventive therapy for tuberculosis in HIV-I-infected adults: results of a randomized controlled trial. *AIDS* 1997;11:875-82.

<sup>8</sup> Gordin FM, Matts JP, Miller C, et al. A controlled trial of isoniazid in persons with anergy and human immunodeficiency virus infection who are at high risk for tuberculosis. *N Engl J Med* 1997;337:315-20.

<sup>9</sup> Whalen CC, Johnson JL, Okwera A, et al. A trial of three regimens to prevent tuberculosis in Ugandan adults infected with the human immunodeficiency virus. *N Engl J Med* 1997;337:801-8.

<sup>10</sup> Mwinga A, Hosp M, Godfrey-Faussett P, et al. Twice weekly tuberculosis preventive therapy in HIV infection in Zambia. *AIDS* 1998;12:2447-57.

<sup>11</sup> Halsey NA, Coberly JS, Desormeaux J, et al. Rifampin and pyrazinamide vs isoniazid for prevention of tuberculosis in HIV-1 infected persons: an international randomized trial. *Lancet* 1998;351:786-92.

<sup>12</sup> Gordin FM, Chaisson RE, Matts JP, et al. An international, randomized trial of rifampin and pyrazinamide versus isoniazid for prevention of tuberculosis in HIV-infected persons. *JAMA* 2000;283:1445-50.

<sup>13</sup> WHO Global Tuberculosis Programme, UNAIDS. *Policy statement on preventive therapy against tuberculosis in people living with HIV*. Geneva: UNAIDS, 1998. WHO/TB/98.255.



7. HIV-associated tuberculosis is an opportunistic infection, the development of which decreases markedly once the CD4 count is over 100 cells/ml.<sup>1</sup> Highly active antiretroviral therapy (HAART) is effective in substantially reducing the risk of developing TB.<sup>2</sup>
8. INH preventive treatment (IPT) is the standard therapy for LTBI in the vast majority of individuals dually infected by TB and HIV. The high prevalence of primary INH resistance is however noted, the implications of which should be monitored over time.
9. The effectiveness of treatment for LTBI depends on its proper diagnosis, which is in turn reliant on the correct interpretation of the TST. A cutoff value of 5 mm as recommended by ATS<sup>4</sup> is appropriate for considering the initiation of treatment in HIV infected persons in the local setting.
10. Regimens for LTBI treatment are not only inadequate for active TB but would foster the development of resistance. Before treatment of LTBI is begun, active disease should be ruled out. It is necessary also to monitor for the development of TB symptoms during LTBI treatment.
11. In an HIV-infected person diagnosed with LTBI, a course of treatment with INH for 12 months is recommended.

## INITIAL EVALUATION

12. For persons newly diagnosed as having HIV infection, TST should be done as part of the initial evaluation. If the result is negative and the individual is at significant risk for exposure to MTB, annual repeat testing should be considered although the reliability of the TST might diminish as the CD4+ T-lymphocyte count declines. For persons whose immune function has improved because of HAART, repeat TSTs may also be considered. Testing with anergy panel is no longer appropriate as no benefit is demonstrated with treatment for LTBI in those who are TST negative or anergic.<sup>3</sup>

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<sup>1</sup> Pozniak A. HIV-associated tuberculosis in the era of HAART. *Int J Tuberc Lung Dis* 2000;4(11):993-994.

<sup>2</sup> Jones JL, Hanson D, Dworkin MS, et al. HIV-associated tuberculosis in the era of highly active antiretroviral therapy. *Int J Tuberc Lung Dis* 2000;4:1026-31.

<sup>3</sup> CDC. Anergy skin testing and preventive therapy for HIV-infected persons: revised recommendations. *MMWR* 1997;46:RR-15.

13. A proper diagnosis of LTBI is crucial in guiding its subsequent management. This is in turn reliant on the correct interpretation of the TST. It must be cautioned that recent conversion to TST positivity in an HIV infected individual may represent a boosted phenomenon, new TB infection, or improvement of cell mediated immune function. Active TB should be ruled out in all circumstances.

14. The cutoff value for the TST depends on the purpose of testing and the population tested. In the general population in Hong Kong including primary school children, a cutoff value of 10 mm has been used after testing with 2 units of PPD-RT23.<sup>4</sup> In relation to the purpose of deciding whether or not to give treatment for LTBI in HIV infected individuals, a lower cutoff value of 5 mm as recommended by ATS<sup>4</sup> is more appropriate in the local setting.

## COMMENCEMENT OF LTBI TREATMENT

### Standard regimen

15. In an HIV-infected person diagnosed with LTBI, INH at a dose of 5mg/kg daily (maximum 300 mg daily) for 12 months is recommended. The maximal beneficial effect of LTBI treatment is usually achieved by 9 month, and minimal additional benefit is gained by extending therapy beyond 12 months<sup>4</sup>. Though these figures were elicited in HIV-negative individual, they are likely to be applicable in HIV-positive persons.

16. The main indication for LTBI treatment is a positive TST, which is defined as an induration of 5 mm or greater. Before initiating treatment, active TB must first be ruled out.<sup>5</sup> This is done by both a chest radiograph examination and noting relevant symptoms and/or signs. Sputum smears and cultures for AFB should be considered if there is any clinical suspicion. There must also be:

- (a) Low suspicion of infection with INH or multi-drug resistant TB.
- (b) No contraindication to INH.

17. The contraindications to treatment of LTBI with INH are:

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<sup>4</sup> Chest Service of the Department of Health, Hong Kong. *Annual Report*. Hong Kong: Department of Health, 1999.

<sup>5</sup> CDC. 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus. *MMWR* 1999;48:RR-10.

- (a) Previous treatment of TB or treatment of LTBI. However, repeat treatment may be considered for those who have recently been close contacts of infectious TB patients.
- (b) Previous adverse reactions to INH.

18. Compliance is essential for treatment of LTBI to work. Proper counselling before starting treatment is essential. Rationale of treatment for LTBI, its limitations, possible side effects, and the need for good compliance are to be discussed. Available information suggests that directly observed treatment (DOT) is associated with higher rates of treatment completion compared to self-administered treatment, and is, under certain circumstances, more cost-effective.<sup>6</sup>

### **Alternative regimens**

19. Treatment of LTBI with drugs other than INH should be considered in circumstances where infection with INH resistant TB is suspected, where there is contraindication to the use of INH, or when prolonged therapy is not desirable. Regimens using rifampicin (RIF) and/or pyrazinamide (PZA) with or without INH have been evaluated in comparison with INH monotherapy against TB in HIV positive individuals<sup>9-12</sup>. These regimens have the advantages of being of comparatively shorter duration. The use of RIF 600mg and PZA 20mg/kg daily for two months is one such alternative regimen, the efficacy of which is equivalent to 12 months of INH 300 mg daily<sup>12</sup>. Liver toxicity is a concern and intensive monitoring is recommended.<sup>7</sup> The other disadvantages are increased cost and pill burden. Moreover, potential drug-drug interactions between RIF and a PI or an NNRTI should first be addressed and dosage adjusted. Rifabutin (RFB) may need to be considered in place of RIF to minimize drug interaction although, as treatment for LTBI, it has never been evaluated.

20. The generally accepted dosage when RIF or RFB is combined with some PI and NNRTI is as in Appendix II.<sup>8</sup>

21. Other authorities have advocated the treatment of HIV infected individuals

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<sup>6</sup> Sepkowitz KA. AIDS, tuberculosis, and the health care worker. *Clin Infect Dis* 1995;20:232-42.

<sup>7</sup> CDC. Update: Fatal and severe liver injuries associated with rifampicin and pyrazinamide for latent tuberculosis infection, and revisions in American Thoracic Society / CDC recommendations – United States, 2001. *MMWR* 2001;50:733-5.

<sup>8</sup> CDC. Notice to Readers: Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-Infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors *MMWR* 2000;49:185-89

who're close contacts of active TB. The best regimen for the treatment of LTBI in those who are close contacts of infectious MDR-TB has not been established. Some authorities recommend PZA+ethambutol or PZA+quinolone (levofloxacin or ofloxacin) for 12 months<sup>4</sup>. Consultation with experts is advisable.

## MONITORING TREATMENT

22. During treatment, the client should be evaluated for adverse effects or development of active TB. INH is associated with a relatively high incidence of peripheral neuropathy in HIV-infected persons. Concomitant pyridoxine is advisable. INH-induced hepatitis is more prone to occur in the older age groups. It is important to watch out for signs and symptoms of hepatitis, and to monitor with liver function tests when clinical suspicion of hepatitis arises.

23. Currently there are no data supporting the regular use of continuous or repeated courses of INH for treatment of LTBI in HIV-infected persons. Neither is the treatment of LTBI indicated after treatment of active TB. TST after a course of treatment for LTBI is unnecessary.

24. It must be noted that the efficacy of treatment for LTBI is never 100%. Exogenous re-infection is also a genuine possibility with passage of time, especially in high prevalence areas like Hong Kong. The clinician is advised to maintain a high index of suspicion of TB when the clinical presentation is compatible, regardless of whether treatment for LTBI has been given.

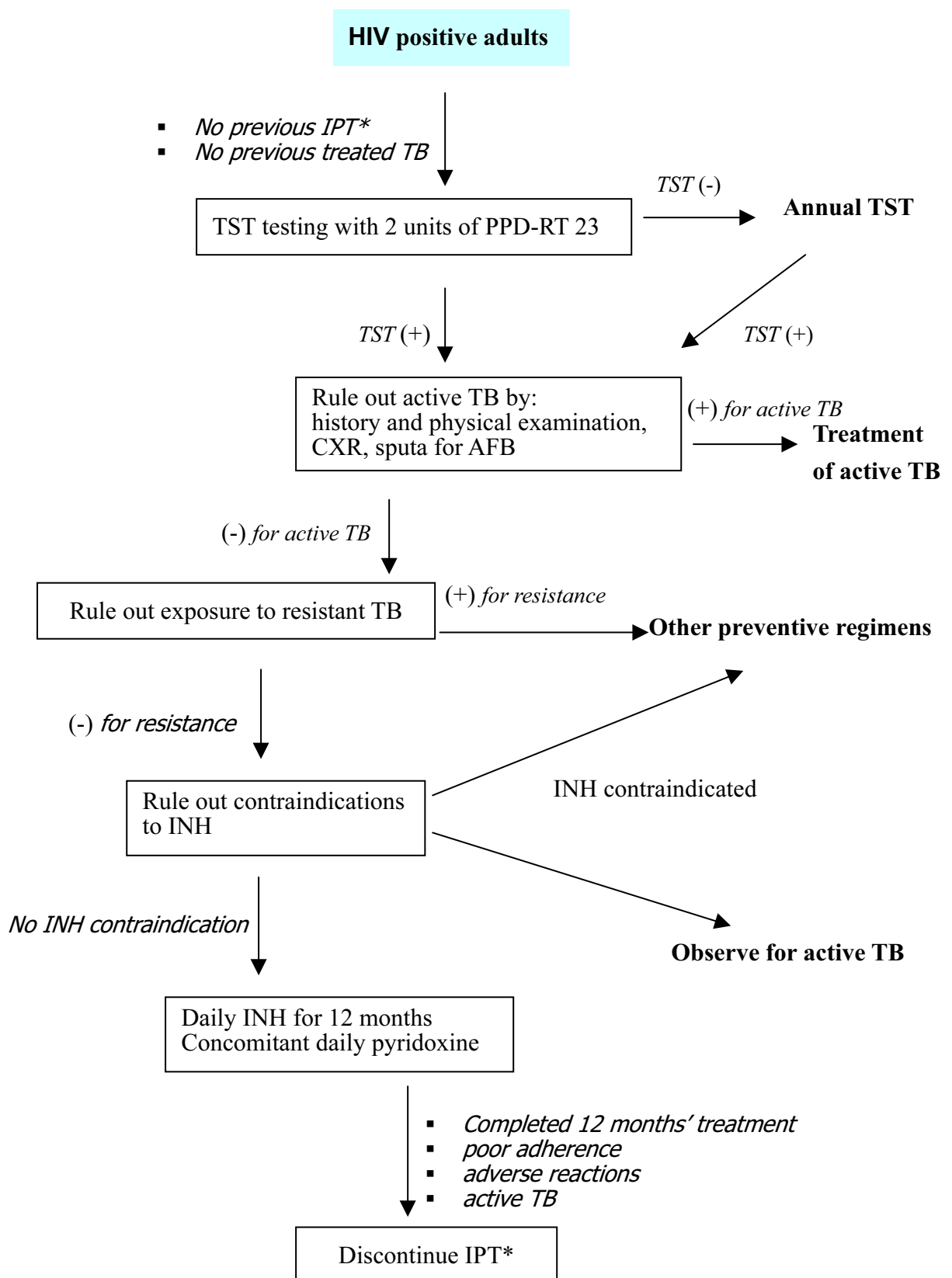
## OTHER CONSIDERATIONS

25. TB in HIV is an increasing health problem. The prevention of HIV-related TB depends on the ability to control TB as much as the control of HIV infection. HIV-associated tuberculosis is an opportunistic infection, the development of which decreases markedly once the CD4 count is over 100 cells/ml.<sup>14</sup> Highly active antiretroviral therapy (HAART) is effective in substantially reducing the risk of developing TB.<sup>15</sup> The provision of HAART therefore forms one important arm of the management of the dual infection of TB and HIV.

26. Some other areas are worth noting. There are the uncertain roles of repeat

courses or continuous treatment of LTBI in high prevalence areas, and the impacts on the prevalence of INH resistance when INH monotherapy for LTBI is widely prescribed without direct observation. The treatment of LTBI in paediatric HIV-infected patients who have been BCG vaccinated is another area which has not been adequately studied. Generation of local data on the treatment of LTBI among the HIV-infected is desirable to evaluate the approach relevant for the local setting. Continuous review of the literature will also be required for updating and/or revision of the recommendations in this document.

*Scientific Committee on AIDS*

Appendix I: Algorithm on the Treatment of LTBI in HIV infection

\* IPT: INH preventive treatment

**Appendix II. Dosage adjustment for LTBI treatment for concomitant antiretroviral therapy**

**Table 1. Dosage adjustment of Rifampicin (RIF) in combination with common antiretroviral regimens (daily dosage in mg)**

	NVP 200 bid	EFV 600 qd	RTV/SQV combination 400/400 bid	RTV 600 bid
<b>RIF</b>	<b>600 qd +</b>	<b>600 qd +</b>	<b>600 qd +</b>	<b>600 qd +</b>

**Table 2. Dosage adjustment of Rifabutin (RFB) in combination with common antiretroviral regimens (daily dosage in mg unless otherwise specified))**

	NVP 200 bid	EFV 600 qd	SGC-SQV 1200 tid	APV 1200 bid	IDV 1000 q8h, or 1200 q8h	NFV 750 tid, or 1000 tid, or 1250 bid	RTV 600 bid
<b>RFB qd</b>	<b>300 qd +</b>	<b>450 qd +</b>	<b>300 qd +</b>	<b>150 qd +</b>	<b>150 qd +</b>	<b>150 qd +</b>	<b>Daily RFB contra- indicated; 150 mg biw - tiw +</b>

ABBREVIATIONS: APV – amprenavir; EFV – efavirenz; IDV – indinavir; NFV – nelfinavir; NVP – nevirapine; RTV – ritonavir; SQV – saquinavir; SGC-SQV – soft gel capsule saquinavir.

**Chapter Six**

**Recommendations on the Management of HIV Infection  
in Infants and Children**

**Scientific Committee on AIDS  
of  
Hong Kong Advisory Council on AIDS**

**first published July 2001, revised January 2002**



## **Recommendations on the Management of HIV Infection in Infants and Children**

### **INTRODUCTION**

1. In Hong Kong, the number of known infections in children has remained small. A majority of the infected children in the mid- and late- nineteen eighties were haemophiliacs or recipients of contaminated blood. Mother-to-child transmission is now the single most important mode of HIV infection in children in Hong Kong. Worldwide, it accounts for over 90% of all paediatric HIV infections.

2. Early identification of human immunodeficiency virus (HIV)-infected pregnant women prior to delivery could effectively reduce perinatal transmission of the infection. However, treatment of HIV-infected women will not completely eliminate all mother-to-child infections. The proportion of infections occurring *in utero* is estimated to be approximately 25% to 40% among children who are not breast-fed. (1) Mathematical modelling suggests that much of this *in utero* transmission occurs relatively late in gestation. (2) The absolute risk for *in utero* transmission is estimated to be 5% or 6%, and for intrapartum transmission, approximately 13% to 18%. Therefore, a small number of infants may still be infected before the diagnosis of the mother. Another reason of perinatal infection is that not all HIV-infected pregnant women may be diagnosed and can receive therapy in time.

3. Advances in HIV treatment are changing the landscape of HIV/AIDS in the clinical setting. Prior to effective viral suppressive therapy, a majority of the infected infants developed marked immunosuppression and AIDS-defining conditions by approximately seven years of age. *Pneumocystis carinii* pneumonia (PCP), HIV encephalopathy, developmental delay, failure to thrive and recurrent bacterial infections were commonly observed problems. Today, children receiving antiretroviral agents often have different clinical and pharmacokinetic profiles, and have slightly different side effects as compared to adults.

4. The current set of recommendations is developed by the Scientific Committee on AIDS (SCA)\* to suggest a standard approach in the management of infants and children perinatally exposed and/or infected with HIV, based on scientific evidence and a review of international experience and recommendations. (3,4,5). However, since HIV

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\* Dr Susan Chiu of the Department of Paediatrics, The University of Hong Kong assisted in the preparation of the recommendations, in association with the clinical team of the Integrated Treatment Centre, Department of Health, Hong Kong. This publication supercedes the previous version dated July 2001.

research in children usually lags behind that in adults, some recommendations have been extrapolated from adult data. A local perspective is nevertheless adopted in the preparation of the document. This document supersedes the *SCA Guidelines on Management of HIV infection Children* published in 1995.

## PRINCIPLES

5. The guiding principles in the following recommendations are:
  - (a) HIV-exposed or infected children should be evaluated as soon as possible after birth for the diagnosis of HIV infection.
  - (b) Postnatal antiretroviral treatment should be completed according to the perinatal prophylaxis regimen chosen for the mother.
  - (c) Prophylaxis against PCP should normally be commenced at 6 weeks of age for an infant born to an HIV-infected mother.
  - (d) Early treatment of HIV-infected infants regardless of clinical and immunologic parameters is the preferred approach for achieving viral suppression. Other options exist and shall be considered in clinical context and in consideration of issues relating to adherence.
  - (e) Childhood immunisation is an important part of the clinical management for HIV infected children, the practice of which is similar to that for healthy infants and children with slight adjustment.
  - (f) Highly Active Antiretroviral Therapy (HAART) is the standard in management of HIV-infected children, if antiretroviral therapy is indicated.
  - (g) A multispecialty, multidisciplinary approach involving the following expertise is needed for the comprehensive care of HIV-infected children: paediatric infectious disease, paediatric neurology, paediatric cardiology, nursing, social work, psychology, nutrition, and pharmacology. Life-long continuous care is recommended.
  - (h) Recommendations for therapy and management will have to be updated frequently as the management of HIV infection in infants, children and adolescents is rapidly evolving and becoming increasingly complex.
  - (i) A mechanism shall be in place to enhance the local knowledge-base in HIV management in children, and the exposure (infection or otherwise) of children to antiretroviral treatment.

**DIAGNOSIS OF HIV INFECTION IN CHILDREN**

6. Diagnosis of HIV infection in perinatally exposed children can be made by the culture of peripheral blood mononuclear cells (PBMC) or HIV DNA polymerase chain reaction (PCR). International literature has recommended DNA PCR as the virologic method for early diagnosis of HIV infection in infants. The test, if available, should be performed within the first 48 hours of life. This method has very good sensitivity and specificity for detecting the presence of the virus within PBMCs. The sensitivity of the HIV DNA PCR has been studied: 38% of infected infants were positive within 48 hours of life, 93% were positive by 14 days of age, and 96% were positive by 4 weeks of age. Infants with 2 positive results can be determined to be infected.(6) Infants with negative tests during the first 6 weeks of life should be re-tested between 1 to 2 months of age, and again between 4 to 6 months of life. (4) Initially there was concern that prophylactic antiretroviral treatment of the infant might interfere with the early diagnosis of HIV infection. However, to date, zidovudine (ZDV) has not been shown to decrease the sensitivity and predictive values of virologic assays. (4,7)

7. Currently, both HIV culture and HIV DNA PCR are not available as routine diagnostic tests. In clinical practice, HIV RNA PCR assay is recommended as the alternative for diagnostic purpose in Hong Kong. The latter assay is available in clinical laboratories and can be used to test for plasma virus. There has been concern about potential false-positive results near the assay's limit of detection. (8,9,10) In all circumstances, clinical correlation and the advice of virologist should be sought in the interpretation of the results.

8. A child born to an HIV-infected mother is considered uninfected if

- (a) there is no clinical evidence of HIV infection, and
- (b) in the absence of breastfeeding , 2 or more virologic determinations (culture or PCR) are persistently negative, both of which are performed at 1 month of age or older, and one of which is performed at 4 months of age or older, or
- (c) 2 negative HIV antibody tests at least 1 month apart, performed at greater than 6 months of age.(6)

**CARE OF INFANT BORN TO AN HIV-INFECTED MOTHER**Antiretroviral therapy

9. All infants born to HIV-infected women who have been started on the ACTG 076 prophylaxis regimen should receive a 6-week course of oral ZDV. ZDV is also recommended for the infant born to an HIV-infected woman who has received no antiretroviral therapy during pregnancy or delivery.(11) Alternatives include the use of nevirapine or ZDV/ lamivudine (3TC) combination or ZDV/nevirapine combination. If the mother is not diagnosed until labour and has received an alternative antiretroviral prophylaxis regimen, the infant should receive the same antiretroviral agent according to the regimen. Breastfeeding by their HIV-infected mothers is contraindicated in Hong Kong since there are safe alternatives to breast milk. (refer to the Scientific Committee on AIDS *Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission* published in April 2001) (12)

Laboratory monitoring

10. Complete blood picture (CBP) and differential count should be performed on the newborn as a baseline evaluation before administration of ZDV. Anaemia is the primary short-term complication of the 6-week ZDV regimen in the neonate. Repeat measurement of haemoglobin is required during and after the completion of the regimen. Infants who have anaemia at birth or who are premature warrant more intensive monitoring.

11. CD4+ lymphocyte count and percentage should be monitored at 1 and 3 months of age and then continued at 3-month-interval until HIV infection in the infant can be ruled out.

12. Quantitative immunoglobulins should be measured when the infant is 4 to 6 months of age.

Prophylaxis for *Pneumocystis carinii* pneumonia (PCP)

13. PCP used to be the most common AIDS presenting illness in children before the days of effective antiretroviral therapy. It occurs most often between 3 and 6 months of age when many HIV-exposed infants have not yet been identified as being infected. In 1995, CDC revised the recommendation for PCP prophylaxis in HIV-exposed infants. (13) (Table 1) All infants born to HIV-infected women should begin prophylaxis at 6

weeks of age, following completion of the ZDV prophylaxis regimen, regardless of CD4+ lymphocyte counts or percentage. The drug regimens are shown in Table 2.

## **CARE OF THE HIV-INFECTED INFANT OR CHILDREN**

14. The following recommendations apply to all newly diagnosed HIV infected children. Once HIV infection is established in a child, the following initial steps should be taken:

### Complete and detailed medical history and physical examination

15. Depending on the individual situation, baseline assessment of the child and family may be done in the inpatient setting. This approach has several advantages: more time can be spent during the initial encounter between the family and the medical team; the family can familiarise themselves with the medical team and the hospital; doctors and nurses can observe the social dynamics of the family; and the initiation of antiretroviral drugs can be supervised and monitored.

16. Attention should be paid to clinical symptoms commonly seen in HIV infection, e.g., failure to thrive, developmental delay, lymphadenopathy, hepatomegaly, splenomegaly, candidiasis. The clinical categorisation of paediatric HIV infection is detailed in Table 3. If the child is the first member of the family diagnosed with HIV infection, both parents and other siblings should also be counselled and evaluated for HIV infection.

### Baseline and follow-up investigations

17. The main investigations are T cell subset enumeration and viral load measurement. Other investigations are also included in this section.

#### *(a) T-cell subsets*

Absolute CD4+ lymphocyte number and percentage are surrogate markers of disease progression in HIV infection and should be monitored. Profound decrease in CD4+ lymphocyte counts in the first year of life signifies rapid progression of HIV disease and indicates the immediate need for highly active antiretroviral therapy (HAART). The immunological classification system for HIV infection in children is in Table 4.

(b) *HIV virus load*

Quantification of free virus in plasma can be performed using HIV RNA assays. The dynamics of HIV RNA burden observed in infants is very different from that of adults. Perinatally infected infants exhibit primary HIV viraemia in the first month of life when they have a relatively immature system. They exhibit an extremely high plasma virus load, commonly greater than  $10^6$  copies/ml plasma by HIV RNA PCR. Over time the virus load tends to fall. In general, elevated HIV RNA viral load after the first month of life correlates with rapid disease progression, although some children with high HIV RNA levels in the first year do not progress as rapidly. (14,15,) Due to considerable inpatient biologic variability in HIV RNA levels, only changes greater than 0.7 log in HIV RNA viral load in children under 2 years and those greater than 0.5 log in children older than 2 years should be considered significant.

(c) *Other laboratory investigations*

Baseline assessment includes CBP with differentials, liver and renal function tests, amylase, lipid, lipase levels, lactate dehydrogenase and quantitative immunoglobulins. Baseline antibody titres should be considered for *toxoplasma*, cytomegalovirus (CMV), Epstein-Barr virus, varicella-zoster virus, herpes simplex virus (HSV) and hepatitis viruses. Initial titres drawn at the neonatal period would reflect the immune status of the mother. Repeat testing should be done at 12 months of age and then annually if they are negative. The results provide information about these children's exposure and susceptibility to specific infection. For example, CMV negative HIV infected children should receive CMV negative blood in the case of transfusion and if unavailable, leukofiltered blood should be used if possible. For older children, functional antibodies against common antigens could be assessed. This is usually achieved by measuring their immune status after routine immunisation, e.g. IgG against measles and tetanus. Since primary CMV infection in the first months of life has been associated with an increase in HIV replication, urine culture for CMV may also be obtained in the first 6 months of age.

(d) *Other evaluations*

- i) Chest X-ray – A baseline chest X-ray (CXR) should be obtained and then annually even in asymptomatic children. This test identifies mediastinal enlargement, lung lesions, lymphoid interstitial pneumonitis (LIP) and cardiomegaly. Patients with chronic lung changes should also have oxygen saturation measured at every visit.

- ii) Cardiac assessment – HIV cardiomyopathy starts early in life. When patients are examined by ECG or during autopsy, cardiac abnormalities are detected more often than expected from physical examination. A study on HIV-infected children using ECG has shown that subclinical cardiac abnormalities are common, which may be persistent and often progressive. (16) A baseline and annual cardiac assessment that includes at least a CXR and an ECG is recommended.
- iii) Visual screening - Children who can cooperate with the examiner should have an annual ophthalmology examination. Children with immune category 3 (table 4) should preferably be examined by an ophthalmologist every 6 months, especially if they are seropositive for toxoplasmosis or CMV.
- iv) Neurodevelopmental assessment - For older children, as well as young infants with neurologic deficits, imaging of the brain (MRI or CT) should be performed at baseline for evaluation of possible brain atrophy. Older children are referred for a baseline neurodevelopmental assessment by a neurologist. Infants can be referred after 6 months of age if there are no neurologic symptoms, and earlier if they are symptomatic.
- v) Psychosocial assessment - The diagnosis of HIV infection in a child is very devastating for a family. Since the care of an HIV-infected child is a chronic issue, clinicians should aim to establish a long-term relationship with the patient and the family. The establishment of trust and rapport greatly improves adherence to medical treatment. The family should be assessed by the medical social worker to address the needs for social service or financial support. Members of the family should be offered referral to the clinical psychologist as appropriate.

### Antiretroviral Therapy

18. The goals of antiretroviral therapy include:

- (a) *Life prolongation*
- (b) *Prevention of disease progression*
- (c) *Maintenance or improvement of quality of life.*

19. Based on our current understanding of the viral dynamics and disease pathogenesis, the best way to achieve these goals is to suppress HIV replication to very low levels

indefinitely. Since drug resistance and virologic failure may be inevitable if viral replication persists in the face of therapy, the immediate goal of therapy should be complete viral suppression. With the implementation of universal testing of pregnant women for HIV infection, most HIV infants can be diagnosed in the first month of life. With the commitment of child carers to adherence to long-term therapy, early treatment of these recently infected infants offers the best chance for complete viral suppression. Initiating therapy very early in primary infection may also prevent the spread of HIV to long-lived reservoirs like memory CD4+ T lymphocytes.

20. Since the selection for resistant virus by non-adherence may be worse than ongoing replication of untreated wild type virus, the caregivers need to have a good understanding of the importance of adherence before initiating therapy. It is usually a struggle to administer medications to young children and it is not uncommon that they spit out unpalatable medications. Caregivers should be advised to contact the clinicians immediately if the child repeatedly vomits the antiretroviral drugs. It must be emphasised that the effectiveness of an antiretroviral regimen is directly related to adherence.

21. The following are the recommended principles in the use of antiretroviral treatment in infants and children, and the rationale involved.

*(a) Early treatment of all infants under 12 months of age recently diagnosed of HIV infection is recommended.*

Although only limited data are available on the effectiveness of early combination antiretroviral therapy in children, studies on primary infection in adults have demonstrated that early aggressive treatment might preserve immune function, decrease viral seeding, lower the viral set point. Recent data from a multicentre observational cohort study suggest that infected children exposed to ZDV during pregnancy or birth had more rapid disease progression if effective multidrug therapy was not initiated.(17) These studies lend support to the early treatment of HIV infected infants

*(b) All HIV infected children with clinical symptoms of HIV infection (clinical categories A, B or C) or evidence of immune suppression (immune categories 2 or 3) (Table 3 and 4) should be treated, regardless of age or virus load. (18)*

It is recommended that all immunologic and clinical symptomatic HIV-infected children be treated as soon as possible.(4)

*(c) Antiretroviral therapy should be initiated in infected children aged  $\geq 1$  year regardless of age or symptom status.*



One option (the preferred approach) is to initiate therapy in all HIV-infected children, regardless of age or symptom status. Such an approach would ensure treatment of infected children as early as possible in the course of disease with the highest chance of intervening before immunologic deterioration.

- (d) *Although early initiation of antiretroviral therapy is favoured, there are situations when deferment of treatment can be considered.*

In asymptomatic children aged  $\geq 1$  year with normal immune status and a low viral load in whom the risk for clinical disease progression is considered low, and when other factors including the issues of drug safety and concern for adherence due to unreliable caregivers, postponing treatment may be justified. When treatment is deferred, antiretroviral therapy should be initiated when i) HIV RNA levels increase significantly ( $> 0.7$  log in children under 2 years and  $> 0.5$  log in children over 2 years), ii) CD4<sup>+</sup> decline into category 2, iii) development of HIV related symptoms, iv) HIV RNA  $> 10^5$  copies/ml in any child or v) in children older than 30 months who have HIV RNA levels  $> 10^4$  copies/ml.

- (e) *The regimen should be effective in achieving a sustained viral suppression and the side effects should be tolerable.*

Antiretrovirals will need to be administered for many years, if not life-long. The choice of initial therapy needs to take several issues into consideration. Potential limitations in subsequent treatment options due to cross-resistance should it occur would also need to be taken into consideration.

- (f) *Highly Active Antiretroviral Therapy (HAART) is indicated*

When antiretroviral treatment is indicated, the highly active anti-retroviral therapy (HAART) should be prescribed. The recommended regimen includes 2 nucleoside reverse transcriptase inhibitors (NRTIs) and 1 protease inhibitor (PI). The rationale for the choice is to attain maximal suppression of virus replication. This approach has been successful in children with reduction of HIV RNA to undetectable levels. (19,20,21) While waiting for more clinical trials of antiretroviral drugs on children, some information regarding the efficacy of these drugs can be extrapolated from trials involving adults. The absence of clinical trials addressing paediatric-specific manifestations of HIV infection does not preclude the use of any approved antiretroviral drug in children. All antiretroviral drugs approved for treatment of HIV infection may be used for children when indicated — irrespective of labelling notations. The characteristics of antiretroviral drugs are listed in Table 5, 6 and 7.

For clinicians and patients who prefer to spare the use of protease inhibitors, an

option is to initiate therapy with 2 NRTIs with a non-analogue nucleotide reverse transcriptase inhibitor (NNRTI), e.g., nevirapine.

### Prophylaxis for PCP

22. The recommendations are covered earlier (paragraph 13).

### Prevention of other opportunistic infections

23. Caregivers play a role in preventing opportunistic infections in the infants. Caregivers should be advised to avoid consumption of raw or undercooked meat, seafood or poultry, unpasteurised milk products as well as food prepared under doubtful hygiene conditions to decrease the risk of enteric infection. They should also be advised of the potential risks of infection from pets, e.g. cats that can transmit *toxoplasma* and *bartonella*, and turtles and reptiles that can transmit *salmonella*. Exposure to young farm animals should also be avoided to reduce the risk of cryptosporidiosis. On the other hand, HIV infected children should not drink or swim in lake or river water to reduce the risk of *Cryptosporidium* or *Giardia* infection. Practice of good handwashing and personal hygiene should be emphasised.

## **IMMUNISATION**

### Active immunisation

24. HIV-exposed and infected infants and children should receive standard paediatric immunisations with a few exceptions. Inactivated polio vaccine (IPV) should be given instead of the live oral polio vaccine (OPV). OPV-1 routinely given to all local newborns confers marginal benefit nowadays as compared to the situation in the sixties. Given its potential hazard to the HIV infected babies and their households, it is recommended that the first dose of OPV-1 routinely administered after birth prior discharge be omitted in babies born to HIV infected mothers (irrespective of whether the baby is infected). For infected children, IPV should continue to be used in the subsequent polio vaccination according to the schedule as for the normal children. If the child is ultimately found not to be infected, yet lives in a household with an immunocompromised person, polio vaccination should be continued with IPV.

25. Measles-mumps-rubella (MMR) vaccination is recommended for HIV-infected

children who are not severely immunocompromised (CDC immune category 3)(22). This is due to the concern of possible dissemination of live attenuated vaccine viruses. Varicella vaccine should be considered in HIV-infected children with a CD4 T-lymphocyte percentage of  $\geq 25\%$ . Eligible children should receive 2 doses 3 months apart. (23). Influenza vaccine should be given seasonally and repeated annually for children who are at least 6 months of age and are infected (24,25,26) with HIV. Hepatitis A is prevalent in Hong Kong, with over 90% of adults above 40 years of age seropositive. There is no data to suggest that hepatitis A causes increased morbidity in HIV-infected individuals. Hepatitis A vaccination should therefore be considered on an individual basis (27).

26. HIV-infected children are at increased risk for infection by encapsulated organisms. Although a recent study found that less than a third of children with HIV had a detectable antibody response 6 weeks following vaccination, HIV-infected children should be immunised with the currently available 23-valent polysaccharide vaccine at 2 years of age with a booster dose 3-5 years after the first dose. When more information is available regarding the applicability of the currently licensed heptavalent conjugate pneumococcal vaccine in Hong Kong, immunisation with the conjugate pneumococcal vaccine should be considered. Conjugate *Haemophilus influenzae* type b vaccine should also be given according to schedule starting at 2 months of age.

27. Concern has been raised about the occurrence of disseminated BCG infection in HIV-infected infants immunised with BCG. However, in countries where the prevalence of tuberculosis is high, the World Health Organization recommends that BCG vaccination for infants at birth should be a standard practice and this applies to asymptomatic HIV infected infants on a risk-benefit basis (28). BCG is therefore recommended to all infants born to HIV-infected mothers in Hong Kong. Summary of the recommended immunisation programme for the local children with HIV infection is shown in table 9.

### Passive immunisation

#### *Immune Globulin Intravenous (IGIV) Therapy*

28. Double-blind, placebo-controlled trials have demonstrated that intravenous immune globulin reduces serious and minor bacterial infections and hospitalisations in HIV- infected children with early or advanced disease (29,30,31). IGIV at a dose of 400 mg/kg given every 4 weeks is recommended for HIV-infected children with the following:

- a) hypogammaglobulinaemia (IgG <250 mg/dL);
- b) recurrent, serious, bacterial infections (defined as 2 or more serious bacterial infections such as bacteraemia, meningitis, or pneumonia during a 1-year period), although IGIV may not provide additional benefit to children who are receiving daily trimethoprim-sulfamethoxazole (TMP-SMX); or
- c) failure to form antibodies to common antigens (eg., tetanus, measles, polio).

However, it should be noted that IGIV therapy inhibits response to MMR and pneumococcal vaccines.

29. Since HIV infected children do not have a reliable immune response to vaccination, therefore, for those children who are exposed to measles, varicella or zoster should receive IG prophylaxis and tetanus immune globulin should be administered to an HIV-infected child with a tetanus-prone wound regardless of immunisation status (27). However, children who have received IGIV or VZIG within 2 weeks of exposure do not require additional passive immunisation. The recommendations are summarised in table 10.

### Nutrition

30. Breastfeeding by an HIV-infected mother carries a 16% excess risk of HIV infection for the infant and should be avoided. Wasting syndrome is a significant problem in HIV infected children, accounting for 17% of the reported AIDS-defining condition in the US in 1994. HIV-infected children require high-energy, high-protein, nutrient-dense diets. Depending on the child's ambulatory and clinical status, energy needs range from 75% to 150% of the recommended daily allowance (RDA) and protein needs should be between 100% and 150% of the RDA to support the immune system and avoid muscle wasting. (32) For early intervention, all infants and children diagnosed of HIV infection should receive a baseline nutritional assessment within 3 months of diagnosis with follow-up every 1 to 6 months depending on the child's status.

### **CARE OF ANTIRETROVIRAL EXPOSED, UNINFECTED CHILDREN**

31. There are theoretical concerns of potential carcinogenicity of the nucleoside

analogue antiretroviral drugs used in children postnatally and/or in utero exposure of ZDV or other antiretroviral agents. NRTIs may inhibit DNA polymerase gamma, a specific mitochondrial enzyme that controls mitochondrial DNA replication. In vitro, the NRTIs have demonstrated significant mitochondrial toxicity, with the eventual development of myopathy. ZDV use during pregnancy has also been associated with the development of mitochondrial toxicity among newborns. The concern for this and other yet unknown potential adverse effects have led clinicians to propose that children with antiretroviral exposure should be followed up into adulthood.(33) Long-term follow-up should include annual physical examination; and for older adolescent females, gynaecologic evaluation with pap smears has been proposed by some experts. A mechanism to evaluate antiretroviral exposed children in Hong Kong should be considered.

*Scientific Committee on AIDS*

## Appendix

**Table 1. Recommendations for PCP Prophylaxis and CD4+ Lymphocyte Monitoring for HIV-Exposed Infants and HIV-infected Children by Age and HIV Infection Status**

Adapted from: CDC. 1995 revised guidelines for prophylaxis against PCP for children infected with or perinatally exposed to HIV. *MMWR* 1995;44:RR-4

<b>Age and HIV Infection Status</b>	<b>PCP Prophylaxis</b>	<b>CD4+ Monitoring</b>
Birth to 4-6 wk, HIV-exposed	None	1 m of age
4-6 wk to 4m, HIV-exposed	Prophylaxis	3 m of age
4-12 m, HIV-infected or indeterminate	Prophylaxis	6,9 and 12 m of age
HIV infection reasonably excluded	None	None
1-2 y, HIV-infected	Prophylaxis if CD4+ count < 750 cells/ $\mu$ L in first 12m or <500 cells/ $\mu$ L at 12-24m, or CD4+ percentage < 15%	Every 3-4 m
2-5y, HIV-infected	Prophylaxis if CD4+ count < 500 cells/ $\mu$ L or CD4+ percentage < 15%	Every 3-4m
6-12y, HIV-infected	Prophylaxis if CD4+ count <200 cells/ $\mu$ L or CD4+ percentage < 15%	Every 3-4 m
Any age, HIV-infected, prior PCP	Prophylaxis till adulthood and lifelong prophylaxis should refer to latest recommendation for adults with HIV infection	Every 3-4 m

**Table 2. Drug Regimens for PCP Prophylaxis for Children**

Adapted from: CDC. 1995 revised guidelines for prophylaxis against PCP for children infected with or perinatally exposed to HIV. *MMWR* 1995;44:RR-4

<b>Recommended regimen</b>
TMP-SMX*, 150 mg/m <sup>2</sup> /d (or 5 mg/kg/d) of trimethoprim with 750 mg/m <sup>2</sup> /d (or 25 mg/kg/d) of sulfamethoxazole, divided BD PO, 3x/week on consecutive days
<b>Acceptable alternative TMP-SMX dosage schedules</b>
150 mg/m <sup>2</sup> /d of trimethoprim with 750 mg/m <sup>2</sup> /d of sulfamethoxazole QD PO, 3x/week on consecutive days
150 mg/m <sup>2</sup> /d of trimethoprim with 750 mg/m <sup>2</sup> /d of sulfamethoxazole, divided BD PO 7 days/week
150 mg/m <sup>2</sup> /d of trimethoprim with 750 mg/m <sup>2</sup> /d of sulfamethoxazole, divided BD PO, 3x/week on alternate days
<b>Alternative regimens when therapy with TMP-SMX is not tolerated*</b>
Dapsone, 2mg/kg (not to exceed 100 mg), QD PO
Aerosolised pentamidine (for children ≥ 5y), 300 mg via Respirgard II inhaler, once a month
If neither dapsone nor aerosolized pentamidine is tolerated, some clinicians administer 4 mg/kg of pentamidine intravenously every 2 or 4 weeks

♣ TMP-SMX indicates trimethoprim-sulfamethoxazole

\* There is no official recommendation on children with G6PD deficiency

**Table 3. Revised HIV Paediatric Classification System: Clinical Categories**

Adapted and modified from:

- CDC. 1994 revised classification system for HIV in children less than 13 years of age. MMWR1994;43:RR-12
- Scientific Committee on AIDS. Guidelines on management of HIV infection in children. (revised edition) Hong Kong: Advisory Council on AIDS, 1995.
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. [www.hivatis.org](http://www.hivatis.org)

<b>Category N: Not Symptomatic</b>
Children who have no signs or symptoms arising from HIV infection or who have only ONE of the conditions listed in Category A
<b>Category A: Mildly Symptomatic</b>
Children with $\geq 2$ of the conditions listed below but none of the conditions listed in Categories B and C.
* Lymphadenopathy ( $>0.5$ cm at $> 2$ site, bilateral =1 site)
* Hepatomegaly
* Splenomegaly
* Dermatitis
* Parotitis
* Recurrent or persistent upper respiratory tract infection, sinusitis or otitis media
<b>Category B: Moderately Symptomatic</b>
Children who have symptomatic conditions other than those listed for Category A or C that are attributed to HIV infection. Examples of conditions in clinical Category B include, but are not limited to:
* Anaemia ( $<8$ g/dL), neutropaenia ( $<1000/\text{mm}^3$ ), or thrombocytopaenia ( $< 100,000/\text{mm}^3$ ) persisting for $\geq 30$ days
* Bacterial meningitis, pneumonia, or sepsis (single episode)
* Candidiasis, oropharyngeal (thrush) persisting $>2$ months in children $> 6$ months of age
* Cardiomyopathy
* Cytomegalovirus infection, with onset before 1 month of age
* Diarrhoea, recurrent or chronic
* Hepatitis
* Herpes simplex virus (HSV) stomatitis, recurrent ( $>2$ episodes within 1 year)
* HSV bronchitis, pneumonitis, or oesophagitis with onset before 1 month of age
* Herpes zoster (shingles) involving $\geq 2$ distinct episodes or more than 1 dermatome
* Leiomyosarcoma
* Lymphoid interstitial pneumonia (LIP) or pulmonary lymphoid hyperplasia complex
* Nephropathy
* Nocardiosis
* Persisting fever (lasting $>1$ month)
* Toxoplasmosis, onset before 1 month of age
* Varicella, disseminated



Category C: Severely Symptomatic
These are AIDS-defining conditions:
* Serious bacterial infections, multiple or recurrent (i.e., any combination of $\geq 2$ culture-confirmed infections within a 2-year period) of the following types: septicaemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity (excluding otitis media, superficial skin or mucosal abscesses, and in-dwelling catheter-related infections).
* Candidiasis, oesophageal or pulmonary (bronchi, trachea, lungs)
* Coccidioidomycosis, disseminated (at site other than or in addition to lungs or cervical or hilar lymph nodes)
* Cryptococcosis, extrapulmonary
* Cryptosporidiosis or isosporiasis with diarrhoea persisting $> 1$ month
* Cytomegalovirus disease with onset of symptoms at age $> 1$ month (at a site other than liver, spleen or lymph nodes)
* Encephalopathy ( $\geq$ one of the following progressive findings present for $\geq 2$ months in the absence of a concurrent illness other than HIV that could explain the findings): <ul style="list-style-type: none"> <li>a) failure to attain or loss of developmental milestones or loss of intellectual ability, verified by standard development scale or neuropsychological test;</li> <li>b) impaired brain growth or acquired microcephaly demonstrated by head circumference measurements or brain atrophy demonstrated by computerised tomography or magnetic resonance imaging (serial imaging is required for children <math>&lt; 2</math> years of age);</li> <li>c) acquired symmetric motor deficit manifested by <math>\geq 2</math> of the following: paresis, pathologic reflexes, ataxia, or gait disturbance</li> </ul>
* Infection with HSV causing a mucocutaneous ulcer that persists for $> 1$ month; or bronchitis, pneumonitis, or oesophagitis for any duration in a child $> 1$ month of age
* Histoplasmosis, disseminated (at a site other than or in addition to lungs or cervical or hilar lymph nodes)
* Kaposi's sarcoma
* Lymphoma, primary, in brain
* Lymphoma, small, noncleaved cell (Burkitt) or immunoblastic or large cell lymphoma of B-cell or unknown immunologic phenotype
* <i>Mycobacterium tuberculosis</i> , disseminated or extrapulmonary; if pulmonary or cervical, patients need to be in immune category 3
* <i>Mycobacterium</i> , other species or unidentified species, disseminated (at a site other than or in addition to lungs, skin, or cervical or hilar lymph node)
* <i>Mycobacterium avium</i> complex or <i>Mycobacterium kansasii</i> , disseminated (at site other or in addition to lungs or cervical or hilar lymph nodes)
* <i>Pneumocystitis carinii</i> pneumonia
* Progressive multifocal leukoencephalopathy
* <i>Salmonella</i> (nontyphoid) septicaemia, recurrent
* Toxoplasmosis of the brain with onset at $> 1$ month of age
* Wasting syndrome in the absence of a concurrent illness other than HIV infection that could explain the following findings: <ul style="list-style-type: none"> <li>a) persistent weight loss <math>&gt; 10\%</math> of baseline, or</li> <li>b) downward crossing of at least one of the following percentile lines on the weight-for-age chart (e.g., 95<sup>th</sup>, 75<sup>th</sup>, 50<sup>th</sup>, 25<sup>th</sup>, 5<sup>th</sup>) in a child <math>\geq 1</math> year of age, or</li> <li>c) <math>&lt; 5^{\text{th}}</math> percentile on weight-for-age chart on 2 consecutive measurements, <math>\geq 30</math> days apart) plus 1) chronic diarrhea (at least 2 loose stools/day for <math>\geq 30</math> days) or, 2) documented fever (for <math>\geq 30</math> days, intermittent or constant)</li> </ul>
* Penicilliosis, disseminated

**Table 4. 1994 Revised Pediatric HIV Classification System: Immunologic Categories Based on Age-specific CD4+ Lymphocyte Count and Percentage**

Adapted from:

- CDC. 1994 revised classification system for HIV in children less than 13 years of age. MMWR1994;43:RR-12
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. [www.hivatis.org](http://www.hivatis.org)

	Age of Child		
Immune Category	≤ 12 months	1-5 years	6-12 years
	Cell/mm <sup>3</sup> (%)	Cell/mm <sup>3</sup> (%)	Cell/mm <sup>3</sup> (%)
Category 1: No suppression	≥ 1500 (≥ 25)	≥ 1000 (≥25)	≥ 500 (≥ 25)
Category 2: Moderate suppression	750-1499 (15-24)	500-999 (15-24)	200-499 (15-24)
Category 3: Severe suppression	<750 (<15)	<500 (<15)	<200 (<15)

**Table 5. Characteristics of Nucleoside Analogue Reverse Transcriptase Inhibitors**

Adapted from:

- Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV infected adults and adolescents. USA: Department of Health & Human Services and the Henry J Kaiser Family Foundation; February 7, 2001. [www.hivatis.org](http://www.hivatis.org)
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. [www.hivatis.org](http://www.hivatis.org)

Generic Name	Zidovudine (ZDV/AZT)	Didanosine (ddI)	Zalcitabine (ddC)	Stavudine (d4T)	Lamivudine (3TC)	Abacavir (ABC)
Trade name	Retrovir	Videx	Hivid	Zerit	Epivir	Ziagen
Preparation	100mg capsules 300 mg tablets 10 mg/ml IV solution 10 mg/ml oral solution	25, 50, 100, 150, 200 mg chewable tablets 100, 167, 250 mg sachets Delayed-release capsules: VIDEX EC-125, 250, 400 mg	0.375, 0.75 mg tablets	15,20,30,40 mg capsules 1mg/ml oral solution	150 mg tablets 10 mg/ml oral solution	300 mg tablets 20 mg/ml oral solution
Dose	<i>During labour and delivery:</i> Continuous IV infusion 2 mg/kg first hour, then 1 mg/kg until delivery  <i>Neonatal:</i> 2 mg/kg Q6h  <i>Paediatric:</i> 90-180 mg/m <sup>2</sup> TDS or QID  <i>Adult:</i> 200 mg TDS or 300 mg BD	<i>Neonatal (&lt;90 days):</i> 50 mg/m <sup>2</sup> q12h  <i>Paediatric:</i> 90-150 mg/m <sup>2</sup> q12h  <b>Adolescent/</b>  <i>Adult:</i> ≥60 kg, 200 mg BD; < 60 kg 125 mg BD; VIDEX EC: ≥60 kg: 400 mg qd; <60 kg: 250 mg qd	<i>Neonatal:</i> unknown  <i>Paediatric:</i> 0.005 to 0.01 mg/kg TDS  <i>Adult:</i> 0.75 mg TDS	<i>Neonatal:</i> unknown  <i>Paediatric:</i> 1 mg/kg BD  <i>Adolescent/Adult:</i> < 60 kg, 30 mg BD; ≥60 mg, 40 mg BD	<i>Neonatal (&lt;30 days):</i> (under study) 2 mg/kg BD  <i>Paediatric:</i> 4 mg/kg BD  <i>Adolescent/Adult:</i> < 50 kg, 2mg/kg BD; ≥ 50 kg, 150 mg BD	<i>Neonatal:</i> not approved for infants <3m. Infants 1-3m of age, 8 mg/kg BD under study  <i>Paediatric/</i>  <i>Adolescent:</i> 8 mg/kg BD, max 300 mg BD
Food Effect	No regard to meals	Take 1 h before or 1 h after meal	No regard to meals	No regard to meals	No regard to meals	No regard to meals
Toxic Effects	Anaemia, neutropaenia, headache.  Less frequently: myopathy, myositis, hepatitis	Gastro-intestinal upset. Less frequently: peripheral neuropathy, electrolyte disturbances, hyperuricaemia. Rarely: pancreatitis hepatitis, retinal de-pigmentation	Headache, fatigue. Rarely peripheral neuropathy, pancreatitis hepatitis, skin rashes, oral and oesophageal ulcers, anaemia, neutropaenia	Headache, gastro-intestinal upset, skin rashes. Less frequently: peripheral neuropathy, pancreatitis, hepatitis, lactic acidosis and severe hepatomegaly with steatosis, including fatal cases reported	Headache, fatigue, gastro-intestinal upset, skin rashes. Less frequently: peripheral neuropathy, pancreatitis, hepatitis, neutropaenia, lactic acidosis and severe hepatomegaly with steatosis, including fatal cases reported	Nausea, vomiting, headache, fever, rash, anorexia, fatigue. Rarely potentially fatal hypersensitivity reaction, with fever, malaise, nausea, vomiting, diarrhoea and abdominal pain. Many have lymphadenopathy, mucous membrane ulceration or rash. lactic acidosis and severe hepatomegaly with steatosis, including fatal cases reported

Adolescents should be dosed according to the Tanner Stage instead of chronologic age. Adolescents with Tanner Stage I and II should be dosed according to the paediatric age group while those with Tanner stage III and IV should use adult dosing. Careful monitoring of response and adverse effects is needed during this time of growth and change

**Table 6. Characteristics of Non-nucleoside Reverse Transcriptase Inhibitors:**

Adapted from:

- Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV infected adults and adolescents. USA: Department of Health & Human Services and the Henry J Kaiser Family Foundation; February 7, 2001. [www.hivatis.org](http://www.hivatis.org)
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. [www.hivatis.org](http://www.hivatis.org)

Generic Name	Nevirapine	Delavirdine	Efavirenz
Trade Name	Viramune	Rescriptor	Stocrin
Preparation	200 mg tablets 10mg/ml liquid	100 mg tablets 200 mg tablets	50mg, 100 mg, 200 mg capsules
Dose	<i>Neonatal through 2 months</i> (under ACTG P365): 5 mg/kg qd or 120 mg/m <sup>2</sup> qd for 14 days, then 120 mg/m <sup>2</sup> q12h for 14 days, then 200 mg/m <sup>2</sup> q12h. <i>Paediatric:</i> 120-200 mg/m <sup>2</sup> q12h Start at 120 mg/m <sup>2</sup> (maximum 200 mg) qd for the first 2 weeks and increase to BD full dose <i>Adolescent/Adult:</i> 200 mg q12h (initiate at half dose for the first 14 d)	<i>Neonatal and Paediatric:</i> unknown <i>Adolescent/Adult:</i> 400 mg TDS or 600 mg BD (investigational)	<i>Neonatal:</i> unknown <i>Paediatric:</i> (no data on appropriate dosage under 3 yrs of age) 10- <15 kg: 200 mg qhs; 15- <20 mg: 250 mg qhs; 20- <25 kg: 300 mg qhs; 25- <32.5 kg: 350 mg qhs; 32.5- <40 kg: 400 mg qhs; ≥ 40 kg: 600 mg qhs <i>Adolescent:</i> 600 mg qhs
Food Effect	Can be given with food	Can be taken with food	Can be taken with or without food, avoid high fat meal with drug
Toxic Effects	Skin rash, (some severe, and life threatening), fever, headache, gastrointestinal. Rarely hepatitis, very rarely liver failure and granulocytopenia	Skin rash, headache, fatigue, gastro-intestinal disturbances	Rash, CNS involvement (somnolence, insomnia, abnormal dreams, confusion, impaired concentration, agitation, hallucinations), elevated aminotransferase

Adolescents should be dosed according to the Tanner Stage instead of chronologic age. Adolescents with Tanner Stage I and II should be dosed according to the paediatric age group while those with Tanner stage III and IV should use adult dosing. Careful monitoring of response and adverse effects is needed during this time of growth and change

**Table 7. Characteristics of Protease Inhibitors:**Adapted from:

- Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV infected adults and adolescents. USA: Department of Health & Human Services and the Henry J Kaiser Family Foundation; February 7, 2001. [www.hivatis.org](http://www.hivatis.org)
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. [www.hivatis.org](http://www.hivatis.org)

Generic Name	Nelfinavir	Indinavir	Ritonavir	Saquinavir	Amprenavir	Lopinavir/ Ritonavir
Trade Name	Viracept	Crixivan	Norvir	Invirase[hard gel], Fortovase [soft gel]	Agenerase	Kaletra
Preparation	50mg/scoop powder 250 mg tablets	200 mg, 400 mg capsules	80 mg/ml liquid 100 mg capsules	200 mg capsule Saquinavir hard gel capsule is not recommended except in combination with ritonavir	15 mg/ml liquid 50 mg, 150 mg capsules	80mg lopinavir and 20 mg ritonavir/ml capsules: 133.3 mg lopinavir/33.3 mg ritonavir
Dose	<i>Neonatal</i> (no data, under PACTG 353): 40 mg/kg BD <i>Paediatric</i> : 20-30 mg/kg TDS but many experts give a higher dose: 45 mg/kg/dose q8h to a maximum of 2 gm/dose (exceeding the adult dose of 1.25 gm BD) <i>Adolescent/Adult</i> : 750 mg TDS or 1.25 gm BD	<i>Neonatal</i> : dose unknown, should not be given to neonates (hyperbilirubinaemia) <i>Paediatric</i> (under study): 500mg/m <sup>2</sup> q8h. Patients with small body surface areas may require lower doses (300-400mg/m <sup>2</sup> q8h) <i>Adolescent/Adult</i> : 800 mg q8h	<i>Neonatal</i> : dose unknown <i>Paediatric</i> : 350-450 mg/m <sup>2</sup> BD, start at 250 mg/m <sup>2</sup> q 12h and increase stepwise over 5 days <i>Adolescent/Adult</i> : 600 mg BD, start at 300 mg BD and increase to full dose over 5 days	<i>Neonatal</i> : dose unknown <i>Paediatric</i> : under study: 50 mg/kg q8h as single PI; 33 mg/kg q8h as therapy with nelfinavir <i>Adolescent/Adult</i> : 1200 mg TDS or 1600 mg BD	<i>Paediatric</i> : <u>Liquid formulation</u> : 4-12 and 13-16 yrs (if <50 kg): 22.5 mg/kg Bid or 17 mg/kg TDS (maximum daily dose 1800 mg) <u>Capsules</u> : 4-12 and 13-16 yrs (if <50 kg): 20 mg/kg BD or 15 mg/kg TDS (maximum daily dose 2400 mg) <i>Adult</i> : 1200 mg BD	<i>Neonatal</i> : no data on children < 6 m <i>Paediatric</i> : <u>Not receiving nevirapine or efavirenz</u> : 7-<15 kg: 12 mg/kg lopinavir/3 mg/kg ritonavir BD with food 15-40 kg: 10 mg/kg lopinavir/2.5 mg/kg ritonavir BID with food >40 kg: 400 mg lopinavir/100 mg ritonavir (3 capsules or 5 ml) BD with food OR 230 mg/m <sup>2</sup> /57.5 mg/m <sup>2</sup> ritonavir BD with food up to maximum of 400 mg lopinavir/100 mg ritonavir <i>Adult/Adolescent</i> : 400 mg lopinavir/100mg ritonavir <u>On concomitant ritonavir or efavirenz or PI experienced</u> : 7-<15 kg: 13 mg/kg lopinavir/3.25 mg/kg ritonavir BD with food

						15-50 kg: 11mg/kg lopinavir/2.75 mg/kg ritonavir BD with food > 50 kg: 533 mg lopinavir/133 mg ritonavir (4 capsules or 6.5 ml) BD with food OR 300 mg/m <sup>2</sup> lopinavir/75 mg/m <sup>2</sup> ritonavir BD with food up to a maximum of 533 mg lopinavir/133 mg ritonavir Adult/Adolescent: 533 mg lopinavir/133 mg ritonavir BD with food
<b>Food Effect</b>	Administer with meal or light snack	Empty stomach 1 hr before or 2 hrs after a meal (or taken with a light meal)	Food increases absorption	Administer within 2 hours of a full meal to increase absorption. Grapefruit juice increases absorption	Can be given with or without food	Administer with food. High fat meal increases absorption, especially for liquid preparation
<b>Toxic Effects</b>	Diarrhoea, abdominal pain, fatigue, rash. Rarely: hyperglycaemia and diabetes	GI disturbances, headache, asymptomatic hyperbilirubinaemia. Less frequently: nephrolithiasis spontaneous bleeding episodes in haemophiliacs, hyperglycaemia, diabetes	GI disturbances, circumoral paraesthesia, hepatitis. Rarely: spontaneous bleeding episodes in haemophiliacs pancreatitis, increased triglycerides, cholesterol, hyperglycaemia, diabetes	GI disturbances. Rarely: spontaneous bleeding episodes in haemophiliacs, hyperglycaemia, diabetes	GI disturbances, rash, paraesthesia, Stevens-Johnson syndrome (1%), depression or mood disorder (15%), hyperglycaemia, hypertriglyceridaemia, hypercholesterolaemia	Diarrhoea, headache, asthenia, nausea and vomiting, increased in blood lipids, rash. Rarely: spontaneous bleeding episodes in haemophiliacs, pancreatitis, hyperglycaemia, ketoacidosis, diabetes, hepatitis

Adolescents should be dosed according to the Tanner Stage instead of chronologic age. Adolescents with Tanner Stage I and II should be dosed according to the paediatric age group while those with Tanner stage III and IV should use adult dosing. Careful monitoring of response and adverse effects is needed during this time of growth and change

**Table 8. Combinations of Antiretroviral drugs for Use in Paediatric Settings**Adapted from:

- Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the use of antiretroviral agents in HIV infected adults and adolescents. USA: Department of Health & Human Services and the Henry J Kaiser Family Foundation; February 7, 2001. [www.hivatis.org](http://www.hivatis.org)
- Working Group on Antiretroviral Therapy and Medical Management of HIV Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatrics HIV Infection. USA: National Pediatric and Family HIV Resource Center and Health Resources and Services Administration; August 8, 2001. [www.hivatis.org](http://www.hivatis.org)

Frequently used initial combination therapies in paediatrics:

Zidovudine + lamivudine + nelfinavir or ritonavir  
 Stavudine + didanosine + nelfinavir or ritonavir  
 Stavudine + lamivudine + nelfinavir or ritonavir  
 Zidovudine + lamivudine + nevirapine  
 Stavudine + lamivudine + nevirapine  
 Stavudine + didanosine + nevirapine  
 Efavirenz + 2NRTI  
 Efavirenz + nelfinavir + 1 NRTI  
 Nelfinavir + nevirapine + zidovudine + lamivudine  
 Nelfinavir + efavirenz + zidovudine + lamivudine

Regimens to be avoided due to overlapping toxicity or antagonistic antiviral effect:

Zidovudine + stavudine  
 Didanosine + zalcitabine  
 Stavudine + zalcitabine  
 Zalcitabine + lamivudine  
 Monotherapy

Currently licensed antiretroviral preparations in the USA for treatment of HIV infection. (All except for Delavirdine, Amprenavir and Lopinavir/ritonavir are registered in Hong Kong and these three drugs can be obtained by special arrangement).

NRTI	NNRTI	PI
Zidovudine (ZDV or AZT)*	Nevirapine*	Ritonavir*
Zalcitabine (ddC)*	Efavirenz	Indinavir
Lamivudine (3TC)*		Saquinavir
Stavudine (d4T)*		Amprenavir*
Abacavir (ABC)*		Lopinavir/Ritonavir*

NRTIs: Nucleoside analogue reverse transcriptase inhibitors

NNRTIs: Non-nucleoside analogue reverse transcriptase inhibitors

PIs: protease inhibitors

\* paediatric formulations commercially available

**Table 9. Suggested programme of immunisation for HIV infected children (Hong Kong SAR)**  
**[programme for normal children for reference]**

AGE	IMMUNISATION RECOMMENDED	
	Normal Children	HIV Infected Children
Newborn*	B.C.G. Vaccine	B.C.G. Vaccine
	Hepatitis B Vaccine - First Dose	Hepatitis B Vaccine - First Dose
	OPV-1	
1 month	Hepatitis B Vaccine - Second Dose	Hepatitis B Vaccine - Second Dose
2-4 months	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - First Dose	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - First Dose
	Trivalent OPV- First Dose	IPV- First Dose
		Hib-first dose at 2 months and second dose at 4 months of age
3-5 months	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Second Dose	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Second Dose
	Hepatitis B Vaccine - Third Dose	Hepatitis B Vaccine - Third Dose
4-6 months	DPT Vaccine (Diphtheria, Pertussis & Tetanus) – Third Dose	DPT Vaccine (Diphtheria, Pertussis & Tetanus) – Third Dose
	Trivalent OPV - Second Dose	IPV - Second Dose
		Hib-third dose at 6 months
		Influenza vaccine at 6 months and then annually
1 year	MMR Vaccine (Measles, Mumps & Rubella) - First Dose	MMR Vaccine (Measles, Mumps & Rubella) - First Dose [see text]
1½ years	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Booster Dose	DPT Vaccine (Diphtheria, Pertussis & Tetanus) - Booster Dose
	Trivalent OPV - Booster Dose	IPV - Booster Dose
2 years		Polysaccharide Pneumococcal vaccine-first dose
Primary 1	DT Vaccine (Diphtheria & Tetanus) - Booster Dose	DT Vaccine (Diphtheria & Tetanus) - Booster Dose
	Trivalent OPV - Booster Dose	IPV - Booster Dose
	MMR Vaccine (Measles, Mumps & Rubella) - booster Dose	MMR Vaccine (Measles, Mumps & Rubella) - booster Dose [see text]
		Polysaccharide Pneumococcal vaccine-booster dose
Primary 6	DT Vaccine (Diphtheria & Tetanus) - Booster Dose	DT Vaccine (Diphtheria & Tetanus) - Booster Dose
	Trivalent OPV- Booster Dose	IPV- Booster Dose

*\*NB. OPV-1 should be omitted for those children born from HIV infected mothers irrespective of whether those babies are truly infected or not. Hepatitis A and Varicella vaccine are not included but should be considered on individual basis (see text)*



**Table 10. Passive Immunisation in HIV Infected Children Regardless of Immunisation Status**

Possible Exposure	Passive Immunotherapy	Dosage
Measles	Immune globulin (IG)	0.5 ml/kg IM (maximum 15 ml) for HIV symptomatic child 0.25 ml/kg IM for HIV positive but asymptomatic child
Tetanus-prone wound	Human tetanus immune globulin (TIG)	250U IM
Varicella-zoster virus	Varicella-zoster immune globulin (VZIG)	VZIG 125U/10 kg IM (maximum 625U) Varitect 5-25IU/kg IV
Hepatitis B	Hepatitis B IG (HBIG)	0.5 ml IM (perinatal) 0.06 ml/kg IM (postexposure)

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**Chapter Seven**

**Recommended Clinical Guidelines on the  
Prevention of Perinatal HIV Transmission**

**Scientific Committee of the  
Advisory Council on AIDS, Hong Kong**

*April 2001*

## **Recommended Clinical Guidelines on the Prevention of Perinatal HIV Transmission**

### **Preamble**

In 1994, interim findings from the landmark study Pediatric AIDS Clinical Trials Group (PACTG) 076 indicated that the use of zidovudine (ZDV) significantly reduced the mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV). This was followed by other studies that either elucidated the risk factors associated with transmission or evaluated alternative interventions to prevent MTCT. It is imperative that these scientific findings be translated into standard clinical practice if their full potential in public health can be realised.

These guidelines are developed under the auspices of the Scientific Committee on AIDS (SCA). They are intended to suggest preferable approaches toward the prevention of HIV by mother-to-child-transmission (MTCT) based on synthesis of scientific evidence. Application of these guidelines, however, should be flexible, in order to accommodate the wide-ranging circumstances whereby the clinical problem may present itself.

### **The principles**

- I. Universal testing of HIV antibody should be performed for antenatal women in Hong Kong.
- II. The prevention of mother-to-child transmission of HIV involves the administration of antiretroviral prophylaxis.
- III. Clinical management should include that for the maternal HIV infection.
- IV. The mode of delivery and its management should be considered on the grounds of obstetric indications as well as HIV status
- V. Paediatric management should be offered to reduce the risk of MTCT of HIV.
- VI. Coordinated efforts should be made to strengthen our knowledge base regarding MTCT of HIV in Hong Kong.

**Recommendations and Rationales****I. Universal testing of HIV antibody should be performed for antenatal women in Hong Kong.**

In Hong Kong, about half the mothers of perinatally exposed children were diagnosed of HIV infection only after delivery (surveillance data of the AIDS Unit, Department of Health). The fact that effective treatment is available to help prevent an incurable infection argues strongly for testing all antenatal mothers for HIV. Before its recommendation on universal HIV antibody testing, the SCA has evaluated the seroprevalence of HIV in antenatal clients and the potential impact on health care resources, in accordance with guidelines of UNAIDS<sup>1</sup>. A pilot study of universal testing in a local hospital also demonstrated a high level of acceptance (97.5%) in antenatal mothers<sup>2</sup>.

Since HIV testing is a clinical procedure with potentially serious social and medical implications, informed consent and pre- and post-test counselling should be provided. The SCA reckons that the standards of testing should not be compromised by universal testing, and the right of refusal to be tested should be respected.

**II. The prevention of mother-to-child transmission of HIV involves the administration of antiretroviral prophylaxis.**

Antiretroviral regimen for prophylaxis against MTCT of HIV is effective. It should be administered in the event of a diagnosis of HIV infection in an antenatal mother continuing her pregnancy. PACTG 076<sup>3 4</sup>, a randomised controlled trial of the standard regimen below, has demonstrated a 66% reduction of MTCT in women with CD4 count above 200/ul, from 23% to 8%. The efficacy of this regimen was corroborated by PACTG 185<sup>5</sup> with women of advanced disease and prior ZDV therapy. However, there is evidence that efficacy is reduced if both the antepartum and postpartum components are

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<sup>1</sup> UNAIDS. Prevention of HIV transmission from mother to child. Strategic Options. UNAIDS Best Practice Collection 1999

<sup>2</sup> Tse HY, Lai FK, Wong J, et al. Screening of human immunodeficiency virus infection in pregnant women. XVIIth Asian and Oceanic Congress of Obstetrics and Gynaecology July 9-14 2000, Singapore (Abs FPMISC 03)

<sup>3</sup> Connor EM, Sperling RS, Gelder RD, et al. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. Reduction of maternal-infant transmission of human immunodeficiency type 1 with zidovudine treatment. *N Engl J Med* 1994;331:1173-80

<sup>4</sup> Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment, and the risk of human immunodeficiency virus type 1 from mother to infant. Pediatric AIDS Clinical Trials Group Protocol 076. *N Engl J Med* 1996;335:1621-9

<sup>5</sup> Stiehm ER, Lambert JS, Mofenson LM, et al. Efficacy of zidovudine and hyperimmune HIV immunoglobulin for reducing perinatal HIV transmission from HIV-infected women with advanced disease: results of Pediatric AIDS Clinical Trials Group Protocol 185. *J Infect Dis* 1999;179:567-75



shortened<sup>6</sup>. Alternative regimens have also been evaluated and found to be useful (see appendix II). Nevertheless, it is unlikely that they are superior to the standard ZDV regimen, pending a direct comparison trial.

**II.A The standard regimen comprises the use of zidovudine (ZDV) beginning as early as 14 weeks of pregnancy, continuing through labour by intravenous administration, and followed by treatment of the newborn for 6 weeks.**

**II.B Alternative antiretroviral prophylaxis should be administered in special circumstances where the standard regimen is considered not practicable.**

**II.C When maternal HIV infection is not diagnosed until labour, the options of antiretroviral prophylaxis are:**

- (i) standard regimen of ZDV abbreviated to intrapartum and postpartum components only;**
- (ii) nevirapine (NVP) one dose to mother and one dose to newborn at 48-72h;**
- (iii) ZDV/3TC intrapartum, and to newborn for 7 days, and;**
- (iv) abbreviated ZDV + nevirapine**

Details of these options are in appendix I and II. It is noted that the ZDV/3TC regimen, i.e. option (iii), is modified in non-breast feeding women by the deletion of the maternal postpartum component. The use of abbreviated ZDV combined with nevirapine, i.e. option (iv), is based on theoretical considerations. This regimen may yield better protection in those mothers who have viruses resistant to either ZDV or NVP, but may also result in more toxicity.

The choice depends on the considerations of compliance, potential toxicity, likelihood of resistant viruses, and the availability of drugs. Studies on the relative efficacy of these regimens are not available.

***II.D In infants born to HIV-infected mothers who have not taken antiretroviral therapy, the recommended regimen is 6 weeks of ZDV as soon as possible.***

The regimen is a 076 regimen abbreviated to the postpartum component only (see appendix I and II). The rationale of this abbreviated regimen is based on the results of an observational study<sup>7</sup>. It is noted that therapy given at 3 days or later after birth is unlikely

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<sup>6</sup> Lalléman M, Jourdain G, Le Coeur S, et al. A trial of shortened zidovudine regimens to prevent mother-to-child transmission of human immunodeficiency virus type 1. *N Engl J Med* 2000;343:982-91

<sup>7</sup> Wade NA, Birkhead GS, Warren BL, et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *N Engl J Med* 1998;339:1409-14

to be useful. The use of additional drugs in this situation has not been studied. Besides the balance between additional efficacy and toxicity is unknown.

### **III. Clinical management should include that for the maternal HIV infection**

**III.A A pregnant woman who is HIV positive shall receive the same standards of care established for HIV-infected nonpregnant patients. To best balance between benefits and risks to the foetus, mother and newborn, management should be assisted by a physician specialising in HIV medicine.**

Evidence is accumulating that optimal control of maternal HIV disease is beneficial to reducing MTCT as both the magnitude of viral load and CD4 count are related to transmission<sup>8 9 10</sup>. The major standards of care<sup>11</sup> in HIV disease are:

- (i) prophylaxis against opportunistic infections based on history and CD4 count, and
- (ii) antiretroviral treatment as determined by viral load, CD4 count and clinical history.

Regular CD4 cell enumeration and viral load testing are indicated as in non-pregnant patients. A viral load result near term is preferable to help determine the mode of delivery. Modern day management of HIV infection is complex and consultation with specialists should be sought.

**III.B A woman who is diagnosed HIV positive in the course of pregnancy should be counselled on the long term care plan, informed of the efficacy of prophylaxis against MTCT, and evaluated for antiretroviral treatment.**

It is important to distinguish drugs used for maternal HIV disease from those for prophylaxis against MTCT, as their indications are different. In cases where HAART is not indicated for maternal HIV infection, standard ZDV regimen is recommended for prophylaxis against MTCT, as explained above.

If medical therapy of maternal HIV disease is also indicated, the best regimen for both

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<sup>8</sup> McGowan JP, Crand M, Wiznia AA, et al. Combination antiretroviral therapy in human immunodeficiency virus-infected pregnant women. *Obstet Gynecol* 1999;94(5):641-6

<sup>9</sup> Saffer N, Roongpisuthipong A, Siriwasin W, et al. Maternal virus load and perinatal human immunodeficiency virus type 1 subtype E transmission, Thailand. *J Infect Dis* 1999;179:590-9

<sup>10</sup> Mofenson LM, Lambert JS, Stiehm ER, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. *N Engl J Med* 1999;341:385-93

<sup>11</sup> Scientific Committee of the Advisory Council on AIDS. Consensus statement on principles of antiretroviral therapy for HIV infection in Hong Kong. Mar 1998 Hong Kong

mother and foetus is one that has the greatest antiretroviral potency, minimal teratogenicity and toxicity, and maximal efficacy against MTCT. ZDV should be incorporated in the HAART regimen unless contraindicated. Apart from the usual parameters in non-pregnant patients, the choice of other components of a HAART regimen should also be based on potential toxicity to mother and foetus, altered pharmacokinetics in pregnancy, and compliance. However, if there is intolerance to ZDV, then the nevirapine regimen may be substituted (see appendix II).

While the use of ZDV in pregnancy is probably safe<sup>12</sup>, data on other antiretrovirals are sparse. At any rate, toxicity including teratogenicity to the foetus would be greatest in the first trimester. It is therefore acceptable that treatment be postponed until 10 -12 weeks of gestation. The potential adverse effect on disease progression and MTCT of HIV should be made known to the mother.

**III.C In mothers who become pregnant while receiving antiretroviral therapy, evaluation should be made of the treatment regarding antiretroviral potency, potential toxicity to the mother and foetus, and prophylactic efficacy against MTCT. The rationales of alteration or continuation of therapy should be fully explained to the mother to facilitate decision.**

For these clients, reevaluation of the antiretroviral regimen is required to maximise control of HIV disease, minimise teratogenicity and provide prophylaxis against MTCT. As one consideration might compromise another, the mother's wishes are important, and full explanation should be given of the rationales of continuing or altering the regimen.

If the current regimen does not contain ZDV, it should be added or substituted even if the mother has had prior experience with the drug. If there is intolerance to ZDV, the nevirapine regimen may be used for prophylaxis against MTCT (see appendix II).

At any rate, the toxicity including teratogenicity to the foetus would be greatest in the first trimester. Some mothers may choose to interrupt treatment in the first 10 – 12 weeks of gestation. The potential adverse effect on disease progression and MTCT of HIV should be made known to the mother.

**IV. The mode of delivery and its management should be considered on the grounds of obstetric indications as well as HIV status**

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<sup>12</sup> Culanne M, Fowler M, Lee SS, et al. Lack of long-term effects of in utero exposure to zidovudine among uninfected children born to HIV-infected women. JAMA 1999;281:151-7

The finding that elective caesarean section before rupture of membranes confers additional protection against MTCT should be taken into consideration, along with other factors, in the decision on the mode of delivery. The wish of the mother should be respected.

Studies have validated the independent protection from MTCT conferred by elective cesarean section<sup>13 14</sup>. However, it cannot be overemphasised that the operation carries obstetric risks of its own. The efficacy of elective caesarean section in reducing MTCT should only be one of many factors in the final decision on the mode of delivery. Examples of those factors relating to HIV disease include the use of antiretroviral prophylaxis, the viral load near term, and expected compliance with the postpartum component of ZDV prophylaxis<sup>15</sup>.

Prolonged rupture of membranes (especially if more than 4 hours), invasive foetal monitoring, and instrumental vaginal delivery should be avoided to reduce MTCT.

#### **V. Paediatric management should be offered to reduce the risk of MTCT of HIV.**

The paediatrician should be involved early and before delivery in each case of HIV exposed pregnancy. Apart from continuing the prophylactic regimen against transmission of HIV, the paediatrician shall look for possible congenital defects or other consequences as a result of exposure to antiretrovirals.

The most common adverse effect of ZDV in the newborn is anaemia. As data on teratogenicity are rare, the paediatrician should also be on the lookout for unexpected congenital abnormalities.

The mother shall be advised against breastfeeding. It has been estimated that the added risk of transmission by breastfeeding was 16.7%<sup>16</sup>. In Hong Kong, the benefits of breastfeeding are outweighed by the risk of HIV transmission it carries.

For management of paediatric HIV infection, please refer to guidelines on this subject by

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<sup>13</sup> The International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1: a meta-analysis of 15 prospective cohort studies. *N Engl J Med.* 1999;340:977-87

<sup>14</sup> The European Mode of Delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. *Lancet* 1999;353:1035-39

<sup>15</sup> Stringer JSA, Rouse DJ, Goldenberg RL, et al. Prophylactic cesarean delivery for the prevention of perinatal human immunodeficiency virus transmission. The case for restraint. *JAMA* 1999;281:1946-49

<sup>16</sup> Nduati R, Grace J, Mbori-Ngacha D, et al. Effect of breastfeeding and formula feeding on transmission of HIV-1: a randomized clinical trial. *JAMA* 2000;283:1167-74

the SCA<sup>17</sup>.

## **VI. Coordinated efforts should be made to strengthen our knowledge base regarding MTCT of HIV in Hong Kong.**

The science of treating and preventing HIV infection is evolving. In Hong Kong, a coordinated effort is needed to track the local epidemiology of HIV infection in women, use of prophylactic measures against perinatal transmission, and outcome of such treatment. This knowledge base will be useful in formulating strategies toward preventing this disease in children.

### **Implementation strategies**

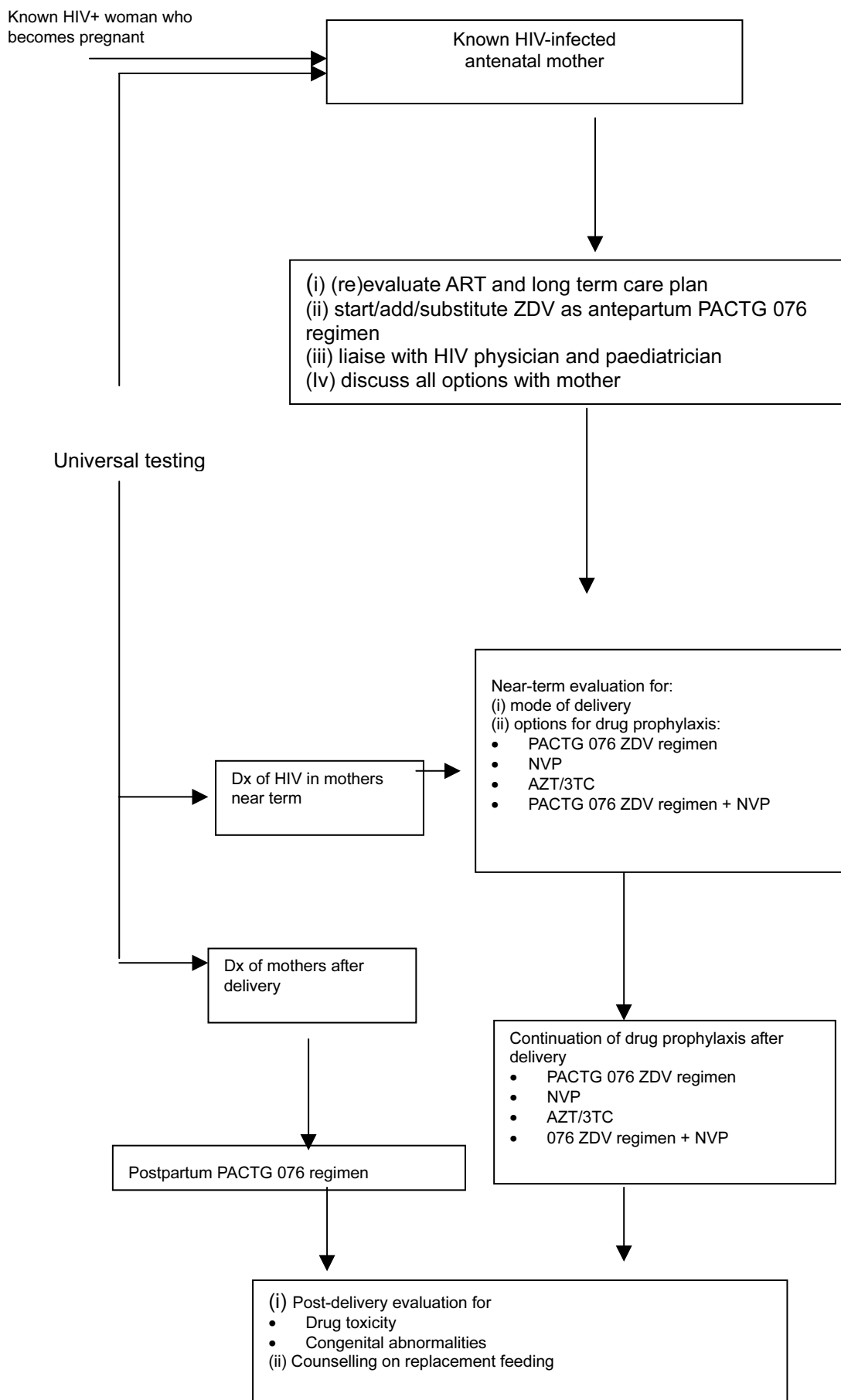
In realising the objective of achieving prevention of MTCT, it is proposed to:

- (a) promote the adoption of the principles in the health care settings in both the private and public service in Hong Kong,
- (b) encourage the development of protocols relevant to individual service, based on the recommended principles,
- (c) enhance the understanding of the health care profession and the community about the importance of preventing MTCT,
- (d) establish a sustainable system and build capacity in the health care services involved in the prevention of MTCT, and
- (e) evaluate and monitor the progress of implementation of universal antenatal testing.

*Scientific Committee on AIDS*

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<sup>17</sup> Scientific Committee of the Advisory Council on AIDS. Guidelines on management of HIV infection in children. Revised edition 1995 Hong Kong

**Appendix I. Management algorithm to prevent perinatal HIV transmission**

## Appendix II. Antiretroviral prophylaxis against MTCT of HIV

Regimen	dosing	Evidence of efficacy (reference study)	Remarks
Standard 076 ZDV regimen	<i>Antepartum</i> - ZDV 300 mg bid (or 200 mg tds) initiated at or after 14 wk <i>Intrapartum</i> - IV ZDV at loading dose of 2 mg/kg in hr, followed by 1 mg/kg till delivery <i>Postpartum</i> - ZDV syrup at 2 mg/kg q6h to newborn begun at 8-12 h for 6 wk (IV ZDV at 2 mg/kg q6h in those who could not tolerate oral intake; ZDV at 1.5 mg/kg IV or po q12h in preterm infants of <34 wk for the first 2 wk may be considered <sup>i</sup> )	Transmission rate was 7.6%; Placebo group was 22.6% (PACTG 076 <sup>3 4</sup> )	No breastfeeding
AZT/3TC	3-part regimen: (ZDV 300 mg + 3TC 150 mg) bid from 36 wk to labour; (ZDV 300 mg + 3TC 150 mg) q3h during labour; (ZDV 4mg/kg + 3TC 2mg/kg) bid to newborn and (ZDV 300 mg + 3TC 150 mg) bid to mother for 7 d Modified 2-part regimen (in non breastfeeding women): <i>Intrapartum</i> - (ZDV 300mg-600 mg po + 3TC 150 mg) as loading dose, then ZDV 300 mg q3h + 3TC 150 mg q12h; <i>Postpartum</i> - (ZDV 4mg/kg + 3TC 2mg/kg) q12h to newborn for 7d	At 6 wk, transmission was 8.6% (3-part regimen), and 10.8% (without prenatal component); Placebo group was 17.2% (PETRA <sup>ii</sup> )	Breastfeeding; Intrapartum ZDV alone was ineffective;
Nevirapine	NVP 200 mg at the onset of labour; NVP 2 mg/kg to newborn at 48-72h	Transmission rate was 13.1% at 14-16 wk Comparison arm (ZDV intrapartum and to newborn for 7 d) was 25.1% (HIVNET-012 <sup>iii</sup> )	Breastfeeding in 95% Rapid emergence of resistance in mother <sup>iv</sup>
Abbreviated ZDV 076 regimens	ZDV 076 regimen begun prenatally, intrapartum or in newborns	Transmission rates were 6.1% (prenatal), 10% (intrapartum) and 9.3% if ZDV initiated within 48h in newborn; Transmission rate without ZDV was 26.6% (observational study in New York State <sup>7</sup> )	No breastfeeding
ZDV + nevirapine	<i>Intrapartum</i> - IV ZDV at loading dose of 2 mg/kg in hr, followed by 1 mg/kg till delivery + NVP 200 mg at the onset of labour; <i>Postpartum</i> - ZDV syrup at 2 mg/kg q6h to newborn begun at 8-12 h for 6 wk + NVP 2 mg/kg to newborn at 48-72h	Unknown; based on extrapolation from existing data	

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- i USPHS. Recommendations for the use of antiretroviral drugs in pregnant women infected with HIV-1 for maternal health and for reducing perinatal HIV-1 transmission in the United States. <http://www.hivatis.org>. Feb 25 2000
  - ii Saba J, and the PETRA Trial Study Team. Interim analysis of early efficacy of three short courses of ZDV/3TC combination regimens to prevent mother-to-child transmission of HIV. The PETRA Trial. <http://www.retroconference.org>. 6<sup>th</sup> Conference on Retroviruses and Opportunistic Infections, Chicago. Jan/Feb 1999 (Symposium S8)
  - iii Guay LA, Musoke P, Fleming T, et al. Intrapartum and neonatal single dose nevirapine compared with zidovudine for prevention of mother to child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomized trial. *Lancet* 1999;354:795-80
  - iv Becker-Pergola G, Guay L, Mmiro F, et al. Selection of the K103N nevirapine resistance mutation in Ugandan women receiving NVP prophylaxis to prevent HIV-1 vertical transmission (HIVNET-006). 7<sup>th</sup> Conference on Retroviruses and Opportunistic Infections, San Francisco. Jan/Feb 2000 (Abstract 658)



## ***Section Two***

### ***Ethical Principles***

## **Chapter Eight**

### **Recommended Ethical Principles on Partner Counselling and Referral for HIV Infected Individuals in Hong Kong**

**November 2004**

**Committee on Promoting Acceptance of  
People Living with HIV/AIDS (CPA)  
of the Hong Kong Advisory Council on AIDS**

## **Recommended Ethical Principles on Partner Counselling and Referral for HIV Infected Individuals in Hong Kong**

### **Introduction**

1. The spectrum of public health activities in which current and past partners of individuals with HIV infection are notified, counselled about their exposure and offered appropriate referrals have been described by different authorities as *contact tracing*, *partner notification* and *partner counselling*. The U.S. Centres for Disease Control and Prevention introduced the term *Partner Counselling and Referral Services (PCRS)*<sup>1</sup> to describe the nature of activities for working with the sex and needle-sharing partners of HIV infected persons. In this recommendation, the term PCRS is used to cover all activities with similar functions but in a local context. Specifically, “partners” refers to people who have had sex, shared injection equipment with a HIV infected person since the time of one’s HIV infection.

2. The goals of PCRS are to firstly, prevent HIV transmission to people who may be exposed either sexually or through needle sharing and secondly, improve care and support for the already infected partners. Specific objectives are 1) to inform partners who have had significant HIV exposure; 2) to provide appropriate information to partners that will assist them to evaluate their risk and to decide whether to go for an HIV test or not; 3) to provide access to HIV counselling and testing, HIV treatment and other supporting services when necessary; and 4) to alert partners of any possible secondary transmission to other partners and their children.

3. PCRS is recommended by overseas authorities as one component of a comprehensive HIV prevention programme. The advance of highly active antiretroviral therapy (HAART), on the one hand, has dramatically decreased the morbidity and mortality of HIV infection, on the other hand has also prolonged the period during which HIV transmission can possibly occur. A local study has revealed that one quarter of the HIV infected patients did not disclose their serostatus to their spouse or co-inhabiting partners<sup>2</sup>. In Hong Kong, specific HIV treatment is available at the public clinical services. It is expected that, by promoting early diagnosis, appropriately conducted PCRS

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1 US Department of Health and Human Services. HIV Partner Counseling and Referral Services Guidance. Atlanta: Centre for Disease Control and Prevention; 1998.

2 Lau JTF, Tsui HY & Li CK et al. Needs assessment and social environment of people living with HIV/AIDS in Hong Kong. AIDS Care 2003;15(5):669-706

would maximize the benefits from appropriate treatment to infected individuals, and strengthen the control of HIV infection.

4. The Committee of Promotion of Acceptance of People Living with HIV/AIDS of the Hong Kong Advisory Council on AIDS concurs with the aforementioned benefits of appropriately conducted PCRS, and hence sets out the following ethical principles. It aims to provide health professionals with an ethical framework for considerations when conducting PCRS for HIV infected persons.

**Principle ONE: PCRS should be conducted by health professionals who are taking care of HIV infected patients. Appropriately conducted PCRS is beneficial to HIV infected individuals, their partners and the community.**

5. Disclosure is one of the most significant factors affecting the quality of life of HIV positive persons<sup>3</sup>. Through the counselling process, the issue of disclosure is addressed, while information and counselling on risk behaviours as well as encouragement, support and choices to inform their partners are provided.

6. Not only do the partners who test positive benefit from early diagnosis and treatment, PCRS also addresses the rights of individuals to be informed of their exposure to HIV. It serves as a channel for risk communication and raising awareness of HIV infection among the notified partners who might then take up preventive actions<sup>4</sup>. As for the community, successfully conducted PCRS is a critical measure to control HIV infection from the source of an infection, i.e., people with HIV infection.

7. However, it should be noted that PCRS carries potential risks. Relationship conflict, psychological stresses, domestic violence, breakdown of the trusting relationship between health care providers and patients are the quoted examples of such. On the extremes, patients may refrain from HIV testing and other services when they consider that their autonomy is threatened.<sup>1</sup>

8. Above all, the benefits of PCRS should outweigh its risks when *appropriately conducted*. Health professionals should therefore assess and minimize the risks of PCRS

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3 Jones RH, Candlin CN & Yu KK. Culture, communication and the quality of life of people living with HIV/AIDS in Hong Kong. Hong Kong: City University of Hong Kong; 2000.

4 Hoxworth T, Spencer NE & Peterman TA et al. Changes in Partnerships and HIV risk behaviours after partner notification. Sexually Transmitted Diseases 2003; 30(1);83-8

to their best, and attempt to conduct PCRS for every HIV infected patient. The process should be documented properly.

**Principle TWO: Approaches to provide PCRS is diversified with different pros and cons. Health professionals should work with the patient to decide on the most appropriate approach.**

9. A brief description of PCRS methods and their respective pros and cons are provided in Appendix I.

10. There is no single method that stands out to be superior to the others. The approach, or approaches adopted is an individualized and joint decision made by the patient and the attending health professionals, who should support and work with the patients throughout the counselling and referral process. Together, they should choose and formulate the most appropriate method or combination of methods, at the appropriate time and context to ultimately notify the partners and minimize potential negative consequences.

**Principle THREE: The conduct of PCRS should always comply with local law and professional codes.**

11. In Hong Kong, there is currently no HIV-specific legislation or administrative means on the control of HIV transmission. PCRS, as a public health tool to control HIV spread should always comply with existing law in its execution. The ethical dogma of beneficence, nonmaleficence, autonomy, justice, and confidentiality should be upheld and established guidelines followed all the times.

12. Guidelines on the disclosure of medical information to third parties and handling of serious contagious/infectious diseases, sections III.A.1.4 and III.G.29 of the Professional Code and Conduct established by The Hong Kong Medical Council (Appendix II and III), and under the Privacy Ordinance (excerpts in Appendix IV) should be referred to when appropriate.

13. Health professionals should understand that exceptional circumstances occur should the risk of HIV transmission to partners justifies a duty to inform, even though they are being bound by the rule of confidentiality and autonomy.

**Principle FOUR: PCRS protocol should be developed by individual health service taking care of HIV infected patients. In case of doubt when handling difficult cases, advice from relevant authority should be sought.**

14. Establishment of protocol facilitates the conduct of PCRS by frontline health professionals. Health services should develop their own set of protocol relevant to their unique setting, taking reference from local and overseas recommendations and experiences. Health professionals should, if necessary, seek advice from relevant professional authorities or ethical committees on case-by-case basis.

*Committee on Promoting Acceptance  
of People Living with HIV/AIDS*

## Appendix I

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### PCRS Methods

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- (a) **Source referral (Patient referral, client referral or self referral):** HIV positive people are encouraged to counsel partners concerning their possible exposure to HIV by themselves. This is usually the most socially accepted method but could be less effective than other means.
- (b) **Provider referral:** HIV positive people give the name(s) of the partners to a health care provider who then counsels the partner(s) directly. The health care providers do not disclose the name of the source person, but only provide the information that the partner is likely to have been exposed to HIV infection. This method demands more resources, requires patient cooperation to locate the partners and an informed consent needs to be obtained whenever possible. It is more effective than source referral and immediate counselling and support can be provided to the partners. Confidentiality very often is the area for concern for both patients and the health care workers.
- (c) **Conditional referral (Contract referral):** health care providers of the source client obtain names of the partners, but allow the source client a period of time to counsel the partners him/herself. If partners are not counselled and tested within this time period at certain designated sites, the health care providers will contact and counsel the partners, without naming the source client concerned.
- (d) **Dual referral:** the partners are informed by the HIV infected patient in the presence of the health care providers, who can render immediate counselling and referrals when needed.

These methods are recommended to be used in combination and have to be culturally accepted.

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Source of information:

US Department of Health and Human Services. HIV Partner Counseling and Referral Services Guidance. Atlanta: Centres for Disease Control and Prevention;1998.

UNAIDS and WHO. Opening up the HIV/AIDS epidemic. Guidance on encouraging beneficial disclosure, ethical partner counselling and appropriate use of HIV case-reporting. Geneva: UNAIDS; 2000.

**Appendix II****Guidelines on disclosure of medical information to third parties. Professional Code and Conduct. Hong Kong Medical Council****III.A.1.4. Disclosure of medical information to third parties**

1.4.1. A doctor should obtain consent from a patient before disclosure of medical information to a third party not involved in the medical referral.

1.4.2. In exceptional circumstances medical information about a patient may be disclosed to a third party without the patient's consent. Examples are: (i) where disclosure in the public interest or in the interests of an individual is justified because the failure to disclose the appropriate information would expose the patient, or someone else, to a risk of death or serious harm; (ii) when required by law to do so.

1.4.3. However, before making such a disclosure a doctor must weigh carefully the arguments for and against disclosure and be prepared to justify the decision. If in doubt, it would be wise to discuss the matter with an experienced colleague or to seek help from a medical defence society, a professional association or an ethics committee.

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Source of information:

Medical Council of Hong Kong. Professional Code and Conduct for the guidance of registered medical practitioners. 2000. Available at <http://www.mchk.org.hk/draft.htm> . Accessed 14 February 2004.



**Appendix III****Guidelines on handling of serious contagious/infectious diseases. Professional Code and Conduct. Hong Kong Medical Council****III.G.29. Serious contagious/infectious diseases**

29.1 All patients, including those with serious contagious/infectious diseases, are entitled to timely and appropriate investigations and treatment. A patient should not be denied of care even if his own actions and lifestyle may have contributed to the disease condition.

29.2 In any given case when it appears that others - spouses, those close to the patient, other doctors and health care workers - may be at risk if not informed that a patient has a serious infection, the doctor should discuss the situation fully and completely with the patient laying particular stress, in the case of other medical or allied health staff, on the need for them to know the situation so that they may, if required, be able to treat and support the patient. In the case of spouses, or other partners, similar considerations will apply, and the doctor should endeavour here also to obtain the patient's permission for the disclosure of the facts to those at risk.

29.3 Difficulties may clearly arise if the patient, after full discussion and consideration, refuses to consent to disclosure. If mutual trust between doctor and patient has been established such a case will, hopefully, be rare. In this case, it is covered by the general ethical standards of the profession and should be respected. Should permission be refused, however, the doctor will have to decide how to proceed, in the knowledge that the decision reached, may have to be justified subsequently. Should it appear that the welfare of other health workers may be properly considered to be endangered, the Council would not consider it to be unethical if those who might be at risk of infection, whilst treating the patient, were to be informed of the risk to themselves. They in their turn would, of course, be bound by the general rules of confidentiality.

29.4 In the exceptional circumstances of spouses or other partners being at risk, the need to disclose the position to them might be more pressing, but here again the doctor should urgently seek the patient's consent to disclosure. If this is refused, the doctor may, given the circumstances of the case, consider it a duty to inform the spouse or other partner.

29.5 Doctors involved in the diagnosis and treatment of HIV infection or AIDS must endeavour to ensure that all allied health and ancillary staff, e.g. in laboratories, fully understand their obligations to maintain confidentiality at all times.

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Source of information:

Medical Council of Hong Kong. Professional Code and Conduct for the guidance of registered medical practitioners. 2000. Available at <http://www.mchk.org.hk/draft.htm>. Accessed 14 February 2004.

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**Appendix IV**

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**Personal Data (Privacy) Ordinance (excerpts)****Scope of Coverage**

The Ordinance covers any data relating directly or indirectly to a living individual (data subject), from which it is practicable to ascertain the identity of the individual and which are in a form in which access or processing is practicable. It applies to any person (data user) that controls the collection, holding, processing or use of personal data.

**Data Protection Principles**

**Principle 1** -- Purpose and manner of collection. This provides for the lawful and fair collection of personal data and sets out the information a data user must give to a data subject when collecting personal data from that subject.

**Principle 2** -- Accuracy and duration of retention. This provides that personal data should be accurate, up-to-date and kept no longer than necessary.

**Principle 3** -- Use of personal data. This provides that unless the data subject gives consent otherwise personal data should be used for the purposes for which they were collected or a directly related purpose.

**Principle 4** -- Security of personal data. This requires appropriate security measures to be applied to personal data (including data in a form in which access to or processing of the data is not practicable).

**Principle 5** -- Information to be generally available. This provides for openness by data users about the kinds of personal data they hold and the main purposes for which personal data are used.

**Principle 6** -- Access to personal data. This provides for data subjects to have rights of access to and correction of their personal data.

**Part VIII - EXEMPTIONS****59. Health**

Personal data relating to the physical or mental health of the data subject are exempt from the provisions of either or both of-

(a) data protection principle 6 and section 18(1)(b);

(b) data protection principle 3, in any case in which the application of those provisions to the data would be likely to cause serious harm to the physical or mental health of-

- i. the data subject; or
- ii. any other individual

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Source of information:

Chapter 486. Personal Data (Privacy) Ordinance. Office of the Privacy Commissioner for Personal Data. Hong Kong. Available at <http://www.pco.org.hk/english/ordinance/ordglance.html>. Accessed 14 February 2004.

**Chapter Nine**

**Recommended Ethical Principles Regarding the Use of Assisted  
Reproduction in HIV Infected Individuals**

**April 2004**

**Committee on Promoting Acceptance of  
People Living with HIV/AIDS (CPA)**

**of the Hong Kong Advisory Council on AIDS**

## **Recommended Ethical Principles Regarding the Use of Assisted Reproduction in HIV Infected Individuals**

### **Background**

1. The desire of HIV positive individuals to procreate has become increasingly witnessed in the HAART era when the morbidity and mortality of HIV infection have been dramatically reduced. To acknowledge their procreative rights, assisted reproductive therapy(a) has been in use for HIV positive patients overseas to prevent HIV transmission to the HIV negative partners and their offspring. None of the 3000 women and 400 children undergoing the procedures worldwide has been tested HIV positive so far. Albeit appearing a safe procedure, the possible risks of infecting the partners and the offspring associated could not be eliminated.
2. The birth of the first baby conceived by assisted reproductive technology in Hong Kong took place in 1986. Since then, Queen Mary Hospital, Prince of Wales Hospital, Kwong Wah Hospital and some private practitioners have been offering assisted reproduction to their clients. Although there has been no documented case of its use in HIV positive patients locally, requests of such were noted recently. In view of the possible demand in the future, the committee put forward the following recommended ethical principles to be observed regarding the use of assisted reproduction in HIV infected individuals in Hong Kong.

### **Ethical Principles Regarding the Use of Assisted Reproduction in HIV Infected Individuals**

3. **HIV infected individuals should enjoy equal right to access assisted reproductive treatment in Hong Kong as to those who are HIV negative.** Although there is a lack of local experience in using assisted reproduction in HIV infected individuals in Hong Kong, this should not constitute a reason for declining such request given that it is technically feasible. People with HIV/AIDS are protected under the *Disability Discrimination Ordinance*.<sup>1</sup> According to its section 26, it is unlawful to refuse to provide a person with

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(a) Assisted reproductive therapy is defined as all treatments or procedures that include the in vitro handling of human oocytes and sperm or embryos for the purpose of establishing a pregnancy. Retrieved from <http://www.who.int/reproductive-health/infertility/report.pdf> on 13 May 2003

1 Disability Discrimination Ordinance. Ord. No 86 of 1995. Hong Kong

disability (i.e., *a person with HIV/AIDS*) with services of any profession (i.e., *assisted reproductive treatment*), unless the provision of such services would impose unjustifiable hardship on the service providers.

4. When seeking advice on their reproductive options, **HIV infected individuals should be given comprehensive information and appropriate counselling on their reproductive options** (refers to Appendix 1) **and the pros and cons on each of the options** (refers to Appendix 2). A multidisciplinary team, consisting of HIV physicians, assisted reproduction specialists, nurse counsellors and medical social workers should be equipped with such knowledge. They should adopt a **supporting attitude** by providing appropriate and unprejudiced information and medical assistance when necessary. The common goal is to minimize the possible risks of procreation and the use of assisted reproduction, and maximize the well-being of the child and the couples<sup>2</sup>.
5. To evaluate possible clients for assisted reproduction, **the same principles under the *Code of Practice on Reproductive Technology & Embryo Research* should be applied irrespective of their HIV status** (refers to Appendix 3), and in particular, the *welfare of the child* will be of paramount importance. The latest ethical guidelines set out by overseas authorities should be referred to. (Examples of such are attached in Appendix 4). A set of criteria and recommendations recently published by overseas authorities for the use of assisted reproduction among HIV infected men and women should also be taken as a reference (refers to Appendix 5).
6. **The final decisions as to procreate or not and which reproductive options to opt for should be made by the couples themselves** after counseling. The decisions made should be free from coercion of any kind from any health care providers.

## **Conclusion**

7. To conclude, HIV infection per se should not be an exclusion criteria for access to assisted reproduction. The HIV positive individuals should enjoy equal access to such service and be evaluated using the same principles as applied to the uninfected people. Health care workers should preferably be equipped with

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2 Ethics Committee of the American Society for Reproductive Medicine. Human immunodeficiency virus and infertility treatment. *Fertil Steril* 2002;77:218-222 Retrieved from <http://www.asrm.org/Media/Ethics/hivethics.pdf> on 13 May 2003

knowledge to provide appropriate information and counselling in a non-discriminatory manner. The dogma in medical ethics, namely autonomy, beneficence, nonmalefeasance and justice should be considered at all times and the final decisions concerning the procreative choices should always be made by the patients and be respected by the health care providers.

*Committee on Promoting Acceptance of  
People Living with HIV/AIDS*

## Appendix 1

### Summary of Reproductive Options for HIV Infected Individuals

The basic concern for HIV infected individuals to procreate is to prevent HIV infection of the uninfected partners and the offspring. The following table summarizes the reproductive options for HIV Infected Individuals.

#### Reproductive Options for HIV Infected Individuals

status Reproductive options		HIV discordant couples		both are HIV positive
		HIV positive men	HIV positive women*	
Unprotected intercourse^		✓	✓	✓/?
Artificial insemination using	Washed sperms	✓	✓	
	Donors' sperms	✓		
Adoption		✓	✓	

\* PMTCT (using antiretrovirals &/ C- Section, avoiding breastfeeding) should be employed

^ The chances of the female and the male being infected during an unprotected vaginal intercourse are estimated to be 0.05 to 0.15% and 0.03% to 0.09% respectively

To wash semen free from HIV, three basic methods are currently being used. Sperm washing separates the cells from seminal fluid by repeated cycles of centrifugation. Swim up method further separates the sperms, which are motile, from other cells by adding an overlying medium to the cell pellets. Only the sperms would be able to swim up and be collected in the medium. The third technique employed density gradient columns and centrifugation to obtain isolated sperms. Sperm samples are then tested for viral particles using immunofluorescence, HIV RNA and HIV DNA PCR. Only HIV negative sperms are used for insemination.

Combinations of the above methods have often been used overseas; and experience so far has shown a 0.9%-6% chance of obtaining a positive PCR test. More than 3000 intrauterine inseminations on about 1200 HIV negative women have been performed in Italy, Spain, German, United Kingdom and some centres in the United States resulting in almost 400 children being born. About 300 cycles of intracytoplasmic insemination (ICIS) and in-vitro fertilization (IVF) have also been performed giving birth to 50 children. None of these women or children has been found HIV positive.<sup>3</sup> The only single documented case of HIV transmission during assisted reproduction in 1990 in the United States was presumed to be due to inadequate washing.<sup>4</sup>

3 Bendikson KA, Anderson D, Hornstein MD. Fertility options for HIV patients. Curr Opin Obstet Gynaecol. 2002;14(5):453-7

4 Centres for Disease Control and Prevention. HIV -1 infection and artificial insemination with processed semen. MMWR 1990;39:249,255-6

Insemination with HIV negative donors' sperms and adoption are the only risk-free methods to ensure giving birth to a HIV negative child but the genetic relationship to either or both parents are removed.

The use of assisted reproductive treatment in HIV positive women avoids HIV transmission to the male partners but not the offspring. There is no report on the use of assisted reproduction in HIV positive women to-date. Only one review paper documented its use in some centres in France for HIV infected women, especially those with subfertility.<sup>5</sup>

The options are all applicable to couples which both the man and woman are HIV positive. The use of reproductive technologies avoids unprotected sex and hence HIV superinfection. There is a possible risk of the infant to become orphaned prematurely and no optimal guideline is currently available.

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5 Englert Y, Van Vooren JP, Place I, Liesard C, Lauruelle C and Delbaere A. ART in HIV-infected couples, has the time come for a change of attitude? *Hum Repro* 2001;16(7):1309-15



## **Appendix 2**

### **Risks and Benefits of Assisted Reproduction in HIV Infected Individuals**

**Possible risks** involved in using assisted reproduction in HIV infected individuals include

- (a) HIV infection of the children,
- (b) early orphanage of the children,
- (c) HIV infection of the uninfected partners,
- (d) HIV infection of the staff,
- (e) contamination of other embryos in the laboratory, and
- (f) the risk of assisted reproductive reproduction itself.

Risks (a), (b) and (c) were often the main deterrents in the past but the outlook has been changing because of (i) the advance of HAART in decreasing the morbidity and mortality associated with HIV infections, (ii) the improvement in prevention of mother to child transmission, and (iii) the apparent success of using assisted reproduction in HIV infected individuals as described above. These risks have been much reduced but not removed.

Local experience in the use of HAART in HIV infection and prevention of MTCT is accumulating and encouraging. Currently about 1000 patients are regularly receiving treatment at one of the two HIV specialist services, where HAART is prescribed according to clinical indications. All six babies born to HIV positive women during the first year of implementation of the Universal Antenatal HIV Antibody Testing Programme have been tested negative so far. Despite of the lack of local experience in using assisted reproduction in HIV infected individuals, the technologies and techniques required are apparently available.

At present, there is no evidence to suggest risks (d) and (e) justify as reasons to withhold treatment when specific infection control guidelines and universal precautions are straightly followed.<sup>6</sup> For risk (f), most studies have shown a negligible or only a slight excess risk of major and minor birth defects in babies conceived by assisted reproduction. However, the associations of assisted reproduction with increased risks of major birth defects, low birth weights and congenital abnormalities have been reported<sup>7</sup>.

**Possible benefits** of using assisted reproduction in HIV infected individuals include

- (a) an apparent lower chance of HIV infection in the uninfected partners and the children compared to unprotected intercourse,

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6 American Fertility Society. Guidelines for human embryology and endrology laboratories. Fertil Steril 1992;58(supp):S1-6

7 Gosden R, Trasler J & Faddy M. Rare congenital disorders, imprinted genes, and assisted reproductive technology. Lancet 2003; 361: 1975-77

- (b) promotion of protected intercourse<sup>8</sup>,
- (c) psychological benefit of the couples<sup>9</sup>.
- (d) meeting the needs of HIV positive patients in an appropriate and non-discriminatory manner.

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8 Semprini AE, Fiore S & Pardi G. Reproductive counselling for HIV discordant couples. *Lancet* 1997;349:1401-2

9 Kass NE. Policy, ethics, and reproductive choice: pregnancy and childbearing among HIV-infected women. *Asta Paediatr* 1994;400(supp):95-8

## Appendix 3

**Assessment of Clients for Reproductive Technology Treatment in Hong Kong <sup>10</sup>**

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Clients should be offered fair and unprejudiced assessment. Client's medical condition should be fully assessed to determine the most appropriate treatment option.

In assessing clients' suitability for reproductive technology treatment, the welfare of the child is of paramount importance. The assessment should take into account the clients' physical, mental and social well-being, including the following factors –

- (a) their commitment to having and bringing up a child or children;
  - (b) their ability to provide a stable and supportive environment for any child born as a result of treatment;
  - (c) their medical histories and the medical histories of their families;
  - (d) their ages and likely future ability to look after or provide for a child's needs;
  - (e) their ability to meet the needs of any child or children who may be born as a result of treatment, including the implications of any possible multiple births or disability;
  - (f) any risk of harm to the child or children who may be born, including the risk of inherited disorders, problems during pregnancy and of neglect or abuse.
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*Code of Practice on Reproductive Technology & Embryo Research, Council on Human  
Reproductive Technology, December 2002*

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<sup>10</sup> Para 4.3, Code of Practice on Reproductive Technology & Embryo Research, Council on Human Reproductive Technology, December 2002

## Appendix 4

**Latest ethical guidelines on the use of assisted reproduction in HIV infected individuals by ACOG and ASRM**

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- 1 **2001 The Committee on Ethics of American College of Obstetrics and Gynaecology (ACOG)** commented that ‘offering ART to HIV patients is consistent with balancing respect for autonomy with fetal beneficence. There is also precedent for offering ART to individuals with other chronic and potentially lethal diseases. With the emerging consensus that ART may be offered to some couples with HIV, practitioners who have knowledge and expertise in this field should be ethically obliged to provide care to them.’<sup>11</sup>
  - 2 **2001 Ethics Committee of American Society of Reproductive Medicine (ASRM, formerly The American Fertility Society)** suggested that ‘individuals are not acting unethically in proceeding with reproduction if they have taken all reasonable precautions to prevent disease transmission and are prepared to love and support the child, regardless of the child’s medical condition. Likewise, health care workers are not acting unethically if they have taken all reasonable precautions to limit the risk of transmitting HIV to offspring or to an uninfected partner. Patients should be referred to a tertiary centre with the facilities that can provide the most effective evaluation, treatment and follow up, or alternatively, advised to look at options and consider donor sperm, adoption or not having a child.’<sup>12</sup>
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11 American College of Obstetricians and Gynaecologists. The Committee on Ethics of the American College of Obstetricians and Gynaecologists. Human immunodeficiency virus infection: physicians’ responsibilities. Committee Opinion NO, 255. April 2001.

12 Ethics Committee of the American Society for Reproductive Medicine. Human immunodeficiency virus and infertility treatment. *Fertil Steril* 2002;77:218-222 Retrieved from <http://www.asrm.org/Media/Ethics/hivethics.pdf> on 13 May 2003

## Appendix 5

**Criteria and Recommendations for the Use of Assisted Reproductive Technologies among HIV Infected Men and Women <sup>13</sup>**

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- Disclosure of serostatus between partners
- Preconception counselling
- Informed consent (risks, benefits, and alternatives must be explained and documented)
- Absence of opportunistic infections or prophylaxis
- CD4 cell count >350 cells/mm<sup>3</sup> and HIV RNA level <50,000 copies/ml
- Patients receiving HAART:
  - HIV RNA level <400 copies/ml
  - Regimen without teratogenic drugs
  - Adequate tolerance to the regimen
  - Antiretroviral therapy for at least 1 year with appropriate follow up (stable viral load and CD4 cell count)
- Semen samples analyzed for HIV by PCR before insemination (only negative samples should be used)
- Close follow-up and appropriate therapy during pregnancy and after birth
- Intrapartum zidovudine chemoprophylaxis
- Follow up of the child (strongly recommended)
- HIV infected women
  - normal results of Pap's smear or at most low grade squamous intraepithelial lesion with confirmed colposcopy and appropriate follow up
- HIV hepatitis C virus coinfecting women
  - hepatology consultation, stable liver enzymes for >1 year and no evidence of liver cirrhosis

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Al-Khan A, Colon J, Palta V & Bardeguet A. Assisted Reproductive Technology for Men and Women Infected with Human Immunodeficiency Virus Type 1. *Clinical Infectious Diseases* 2003; 36 : 197

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13 Al-Khan A, Colon J, Palta V & Bardeguet A. Assisted Reproductive Technology for Men and Women Infected with Human Immunodeficiency Virus Type 1. *Clin Infect Dis* 2003;36:197

## ***Section Three***

### ***Infection Control***

## **Chapter Ten**

### **Recommendations on Infection Control Practice for HIV Transmission in Health Care Settings**

**Scientific Committee on AIDS  
co-sponsored by the Hong Kong Advisory Council on AIDS  
and  
the Centre for Health Protection,  
Department of Health**

**January 2005**

## **Recommendations on Infection Control Practice for HIV Transmission in Health Care Settings**

### **Background**

1. Human Immunodeficiency Virus (HIV), the cause of Acquired Immune Deficiency syndrome (AIDS), is transmitted through sexual contacts, exposure to infected blood or blood components, needle stick injury, and perinatally from an infected mother to neonate. Transmission of HIV from infected patients to health care workers (HCW) has been documented after parenteral or mucous membrane exposure to blood. The risk of transmission from an infected HCW to patients is very low; estimated to be less than 0.5%.<sup>1</sup> Albeit the minimal risk, the transmission of HIV in health care setting is often a cause of anxiety. HCW should be familiar with precautionary measures to further minimize the potential risk of HIV transmission in health care settings.

### **Definition and Scope**

2. Standard precaution (SP) is the core concept for the prevention of HIV transmission in all health care settings. SP is defined as a set of precautionary measures including good hand hygiene practices and use of protective barriers during routine patient care carried out by health care workers (HCW).<sup>2</sup> SP encompasses precautions in the handling of blood, all body fluids, secretions and excretions; and avoidance of contamination of non-intact skin and mucous membrane. In this connection, HCW is defined as any person whose activities involve contact with patients or with blood or other body fluids from patients in a health care setting.<sup>3</sup>

3. The setting of infection control for the prevention of HIV can be a) in-patient, b) ambulatory care setting like out-patient clinics and Accident and Emergency Departments, c) Special settings like the dental clinics, surgical theatres. The principles of SP can be adapted for use in community settings like schools, elderly homes and other care institutions. The recommendations highlighted here are intended primarily for use in health care settings, including both in-patient and out patient settings.

4. The scope of infection control for HIV prevention is vast in health care settings. Apart from SP, there are the following dimensions: environmental infection control



practices, consideration of work restrictions, occupational safety and health advice, post exposure management of exposed HCW and immunizations against vaccine-preventable diseases and community application of infection control practices.

5. The recommendations highlighted relate specifically to HIV infection. HCW are advised to treat this as general principles on the prevention of HIV in health care settings. Specific protocols shall be developed as appropriate. Local and international infection control guidelines should be consulted for specific details. This guideline replaces the one on “Prevention of Transmission of HIV in Health Care Settings” edited by the Scientific Committee of Advisory Council on AIDS in 1995.

### **Principles**

6. The recommendations on infection control for the prevention of HIV in health care settings are based on the following principles:

- (a) In the context of infection control, HIV is treated as a bloodborne pathogen. The recommended practices therefore apply to HIV as much as they apply to the control of other bloodborne infections in health care settings.
- (b) SP is the core practice recommended for HCW in all settings in relation to the prevention of bloodborne infections including HIV and tuberculosis.
- (c) HCW who are at risk of contracting HIV should receive occupational advice on case by case basis.
- (d) Risk assessment is the most vital tool in the management of HCW after exposure to HIV. The provision of post exposure prophylaxis, including antiretroviral therapy, should follow thorough risk assessment and counseling tailored to the need of the injured.
- (e) A surveillance system should be in place to monitor the potential risk of HIV transmission in health care settings. This would involve primarily the reporting of needle stick injury.
- (f) Training and education of HCW on infection control practices are of paramount importance. This should be started well before HCW enter their clinical practice, and should include an effective governance system for promoting the compliance of HCW.
- (g) For infection control of transmission of tuberculosis associated with HIV in health care settings, transmission based precaution in addition to standard

precaution should be applied.

### **Overview and Specificities of Standard Precaution**

7. SP is the result of a synthesis of Universal Precautions (UP) and Body Substance Isolation (BSI) into a single set of precautionary measures in health care settings. This is a consensus among infection control experts of Hospital Infection Control Practices Advisory Committee (HICPAC), US CDC.

8. UP, as originally defined by US CDC in 1985, applied only to blood and body fluids that have been implicated in the transmission of blood borne infections (semen and vaginal secretions), body fluids with an unknown risk of HIV transmission (amniotic, cerebrospinal, pericardial, peritoneal, pleural and synovial fluids) and to body fluids that contaminated with blood. However, it did not apply to faeces, nasal secretions, sputum, sweat, urine or vomitus which were later included under the recommendations of Body Substance Isolation. In the early 1990s, some countries like Australia adopted a broader definition of UP and applied the latter to all blood and body substances considered to be potentially infectious. These two guidelines were united in 1994 in order to avoid confusion. Today, most patients with conditions that require disease specific precautions are now all covered under SP.

9. The specific recommendations of SP in this document are adapted from the US guidelines on hospital and health care personnel infection control practice.<sup>2, 4</sup> These precautions, under category 1B, are practices strongly recommended for all hospitals by HICPAC, US CDC. The recommendations must be augmented by hospital administrative policies especially in education and adherence to precautions, environmental infection control, occupational health and post-exposure management of exposure.

10. SP covers the following practices:

#### **(a) Handwashing**

Hands must be washed before and after patient contact. Hands must be washed immediately after touching blood, body fluids and removal of gloves. Plain soap and water are used for routine handwashing.

*(b) Protective barriers*

Disposable gloves must be worn when there is a direct contact or possibility of contact with blood, body fluids, mucous membrane and non-intact skin of all patients. Gloves should preferably be changed after patient contact and before administering care to another patient. Gloves must be changed whenever they are torn and when a needle-stick or other injury occurs and when they are visibly dirty with blood.

Mask, eye protection or face shield, and gown must be worn as appropriate during procedures and patient care activity that may result in splashing of blood and body fluids.

*(c) Sharps handling*

Precautions should be taken to prevent injuries caused by needles, scalpels and other sharp instruments. Used needles should not be recapped and if recapping of needles is unavoidable, a “scoop” technique or a needle- recapping device should be used. All used sharps should be placed in a puncture-resistant sharps box which should be located in the area where it is used. The sharps box should not be overfilled. Sharps boxes that have been used should be placed in red plastic bags and disposed of as medical waste.

Good work practices should also be adopted in the operation rooms to prevent sharps injury. Some of these should include using instruments, rather than fingers, to grasp needles, retract tissue, and load or unload needles and scalpels; to give verbal announcements when passing sharps; to avoid hand-hand passage of sharp instruments by using a basin or neutral zone; to use alternative cutting methods such as blunt electrocautery and laser devices when appropriate and to use round-tipped scalpel blades instead of sharp-tipped blades.<sup>5</sup>

The use of new technology and devices to prevent needle stick injury should be adopted whenever possible. This includes the needleless system, the retractable lancet and the close blood collecting system.

*(d) Patient-care equipment handling*

Patient-care equipment soiled with blood, body fluids, secretions, and excretions should be handled in a manner that prevents skin and mucous membrane

exposures.

Reusable equipment should not be used for the care of another patient until it has been properly cleaned and reprocessed. Single-use items should be properly discarded.

Used linen soiled with blood, body fluids, secretions, and excretions should be handled in a manner that prevents skin and mucous membrane exposure.

(e) Patient placement

Patient who contaminates the environment should be placed in a private room. If a private room is not available, infection control officer should be consulted regarding placing the patient in alternative area.

### **Environmental IC Procedures**

11. The environment is a potential source of health-care-associated bloodborne infections. Decontamination of the environment and equipment is an essential infection control practice in every setting. This fundamentally consists of disinfection, sterilization and handling of medical wastes.

12. All contaminated equipment should be disinfected according to established disinfectant policy formulated by local hospitals (Queen Mary Hospital. Infection Control Manual, November 1999). Reference shall be made to the guidelines published by US CDC, HICPAC. <sup>6</sup>

13. Heating is an effective mean of disinfection. HIV is inactivated by moist heat at 60°C in 30 minutes. Chemical disinfectant like sodium hypochlorite (household bleach), 2% glutaraldehyde and ortho-phthalaldehyde (OPA) can be used in the disinfection of contaminated article.

14. Environment spilled with blood and body fluids should be cleaned immediately. Disposable absorbent material held in gloves should be used. The infected site should be cleansed with 10,000 ppm hypochlorite solution. Ordinary environmental surface such as wall, floor and other surface have not been associated with transmission of HIV. Common housekeeping procedures are adequate for cleaning environmental surface.

15. Medical wastes should be handled according to established policy of the institution. Articles contaminated with infected material should be appropriately discarded, bagged and labeled before sent for decontamination and processing. They should be sent for incineration or disposed in special landfill as recommended by Environmental Protection Department guideline.<sup>7</sup>

### **Work Restriction and Occupational Health Advice**

16. Work restriction is an important concept not only from the point of view of management of hospital infection outbreak and alert contact tracing but also in preventing further transmission of infection through granting leave to infected HCW or deployment to low risk work areas. Work restriction protocol should be developed in health institution. The protocol should include work-exclusion policies, designation of personnel who have authority to relieve duties, responsibility of infected staff in early reporting of conditions and list of potentially transmissible infectious disease.

17. Currently, general work restrictions of HCW infected with HIV are not recommended. However, HCW infected with these conditions should be restricted from exposure-prone invasive procedures.<sup>8</sup>

18. Specific recommendations for HIV infected HCW have been formulated by the Hong Kong Advisory Council on AIDS (ACA). (ACA. HIV Infection and the Health Care Workers – Recommended Guidelines, 1994, December 2003). The general principles include:

- (a) adherence to standard precautions
- (b) promotion of voluntary HIV testing in case of risk exposure
- (c) referral to Expert Panel for advice on work restriction on a case-by case basis
- (d) confidentiality and disclosure on need-to know basis

19. Immunization against preventable infection is an essential component of occupational safety practices in infectious disease. Hepatitis B vaccination with post-vaccination serological testing is recommended for all susceptible HCW.<sup>9</sup> Vaccine should be provided to HCW before blood exposure. Immunization against other bloodborne infections like Hepatitis C and HIV is currently not available.

20. Occupational safety and health advice should be constantly promoted in HCW.

These occupational health advice include those on occupational risks of the infectious disease, patient care practices, isolation precautions, post exposure management, counseling and vaccination. HCW should be educated on occupational safety and this can be achieved through training.

### **Post Exposure Management**

21. Post exposure management refers to practices to minimize health risk whenever HCW have been exposed to occupational hazards. The occurrence of accidental bloodborne exposure is not uncommon but is less hazardous under strict adherence to standard infection control practice. Most accidental exposure happened in health care settings but exposure in community setting may occur.

22. The main emphases of post exposure management are risk assessment and counseling of exposed HCW. Each and every case should be evaluated by its own circumstances especially as regards to the provision of post-exposure prophylaxis (PEP). HIV PEP should be recommended to HCW who has high risk of contracting the infection after occupational exposure to HIV.

23. The Scientific Committee on AIDS and Scientific Working Group on Viral Hepatitis Prevention had issued its recommendations on the management and post exposure prophylaxis of needlestick injury or mucosal contact to HBV, HCV and HIV. (Scientific Committee on AIDS, Hong Kong Advisory Council of AIDS. Recommendations on the Management and Postexposure prophylaxis of Needlestick Injury or Mucosal Contact to HBV, HCV and HIV. March, 2003) This is in line with the guideline published by CDC. <sup>9</sup> The guiding principles are:

- (a) an integrated approach should be taken by considering collectively the most important bloodborne infections, i.e. HBV, HCV and HIV
- (b) risk assessment is the basis for the prescription of post-exposure prophylaxis
- (c) scientific evidence, international developments and local perspectives should be taken into consideration when recommending practice

### **IC in Special Settings**

24. SP comprising barrier protection, handwashing and sharps disposal should be routinely practised by HCW in special settings such as surgical and other invasive intervention settings. The main aim is to avoid cross infection from HIV infected blood, blood contaminated fluids and other body substances that potentially transmit the HIV virus. Protocols should be established through the incorporation of SP and the development of standards pertinent to the requirements of such settings. Transmission-based precaution would need to be introduced whenever appropriate.

25. In the handling of dead bodies, apart from the minimal practice of SP, adopted precautions may also be disease-specific, in line with recommendations to achieve transmission-based precautions. For the specifics and details of the prevention of HIV transmission in these specific health care settings, one should consult the relevant local and international guidelines and references.<sup>5, 10-15</sup>

## **Supporting the Implementation of Precautionary Measures**

### **Surveillance**

26. Surveillance is the most important initial step in infection control. A surveillance system should be in place in a health care setting to encourage reporting and documentation of occupational exposure to HIV especially through needle-stick injury. The collected data should be analyzed and disseminated in such a way that it will enhance evaluation of the effectiveness of the HIV infection control programme in health care settings. The development of measurable outcome indicators for HCW safety programmes is recommended.<sup>16</sup>

### **Training and education**

27. Training and education for HCW is the cornerstone of all effective infection control programme. Training on infection control precautionary measures should be provided to all staff at all levels. HIV/AIDS education should be focused on mode of HIV transmission, use of standard precautions to prevent HIV infections, issues of stigma and discrimination, human rights and obligations. Besides, training programme should address the expressed anxiety of HCW about getting infected and support them to comply with the best practices of infection control. Training programmes are best carried out by infection control committees set up in the particular setting.

**Auditing**

28. An effective governance system for auditing the compliance with SP by HCW is indispensable in maintaining the standards of infection control practice in health care settings. This can be achieved by regularly monitoring clinical practices of HCW through a customized, comprehensible check-list. The infection control committee should hold regular meetings to assess the extents of compliance and the reasons for not complying. While the attitude of such auditing exercise should be non-judgemental, HCW who do not practise according to the recommendations of SP should not be penalized but encouraged to adhere to the precautionary measures.

*Scientific Committee on AIDS*



**Annex 1****Community Application of IC Practices -  
Infection Control in Community Setting With Potential Exposure to Bloodborne Pathogens****Infection control in school / workplace**

The recommended principles of infection control for health care settings generally apply. For bloodborne pathogens including HIV and hepatitis, disregarding the status of the individual, standard precautions should be adopted. For specific infectious diseases which are air-borne, spread by droplet and contact; transmission based precautions should be practised.

All staff and pupils in schools should be familiar with these precautionary measures. In case of the prevention of bloodborne diseases in schools, pupils should be taught about the prevention methods and transmission routes of HIV, hepatitis B and C. Knowledge about sexually transmitted diseases and proper use of condoms should also be introduced. Specific details of precautionary measures and prevention advice should be referred to the Guidelines on the Prevention of Blood-Borne Diseases in Schools (Department of Health and Education Department, 2001). Handwashing and gloving when administering first-aid are practices that should be followed.

**Infection control in social service**

Infection control in social service settings where there is provision of personal care like elderly home is gaining importance recently. With the expansion of the elderly population, there is a shift of patients with chronic conditions from hospital to home care in the community. Infection control practices in this kind of setting are not well structured.

In the prevention of bloodborne infections, barrier precautions with the use of gowns, gloves and masks in the care of patients under SP should be practised. If the patient is suspected to be suffering from other infectious diseases that have specific transmission pattern, transmission based precaution in addition to SP should be applied. Specific details of infection control in social service settings can be found in General Guidelines on Working with People with HIV/AIDS (Social Welfare Department, 2004) and

guideline published by US CDC; Infection Control in Home Care.<sup>17</sup>

### **Infection control relating to injection drug use in community setting**

Needle sharing among injection drug users (IDU) is an important route of HIV transmission. Infection control targeting risk behaviours of IDU should be promoted in community settings.

IDU should be encouraged to stop sharing of drug equipment, to use sterile needles and syringes and to use bleach to disinfect needles and syringes that will be reused.<sup>18, 19</sup> Disposal of injection equipment should be handled with precautions to avoid sharps exposure. HIV testing shall be promoted in IDU both for supporting effective clinical care and public health control of the infection.

### **HIV infection control in correctional facilities**

HIV infection control in correctional facilities has been receiving due attention recently. The reasons are two fold: (a) the practice of risk behaviours related to HIV transmission like coerced sexual activity, injection drug use is cause for concern; and (b) HIV transmission has been shown to occur in correctional setting overseas. Standard precautions should be implemented as first line defense against occupational transmission of HIV.<sup>18</sup> Guideline has been drawn up by the Correctional Services Department in this regard.

HIV counseling and testing of inmates are recommended by CDC.<sup>20, 21</sup> There should be protocol in maintaining confidentiality and results disclosure. Infected inmates with HIV infection should be referred to appropriate medical care for follow up.

**Annex 2****List of local Hong Kong guidelines used in this recommendation:**

Queen Mary Hospital. Infection Control Manual, November 1999.

Advisory Council of AIDS of Hong Kong. HIV Infection and the Health Care Workers – Recommended Guidelines, December 2003.

Scientific Working Group on Viral Hepatitis Prevention, Department of Health, Hong Kong. Recommendations on Hepatitis B Vaccination Regimens in Hong Kong. March 2004.

Scientific Committee on AIDS and Scientific Working Group on Viral Hepatitis Prevention, Hong Kong. Recommendations on the Management and Postexposure prophylaxis of Needlestick Injury or Mucosal Contact to HBV, HCV and HIV. March, 2003

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Department of Health, Hospital Authority, Food and Environmental Hygiene Department, Hong Kong. Precautions for handling and disposal of dead bodies. January 2002 (4<sup>th</sup> edition).

Department of Health and Education Department. Guidelines on the Prevention of Blood-Borne Diseases in Schools. [http://: www. aids.gov.hk](http://www.aids.gov.hk).

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14. Simonds RJ, Holmberg SD, Hurwitz RL, et al. Transmission of human immunodeficiency virus type 1 from a seronegative organ and tissue donor. *N Engl J Med* 1992; 326:726-32.
15. US CDC. Guidelines for Preventing Transmission of Human Immunodeficiency Virus Through Transplantation of Human Tissue and Organs. *MMWR*, 1994/43(rr-8); 1-17.
16. Gold J, Tomkins M, Melling P, Bates N. Guidance Notes on Health Care Worker Safety from other Blood Borne Infections. Health, Nutrition and Population (HNP) Discussion Paper, May 2004.
17. US CDC Infection Control in Home Care; *MMWR* 2001; Vol 7, No 2, p 1- 10.
18. US CDC Update: Reducing HIV Transmission in Intravenous-Drug Users Not in Drug Treatment – United States; *MMWR* 1990/39(31); 529,536-538.
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20. US Department of Justice, Issues and Practices 1996-1997 Update: HIV/AIDS, STDs, and TB in Correctional Facilities, July 1999, p xiv – xv.
21. US CDC HIV Prevention in the US Correctional System, 1992/41(22); 389-391,397.

## **Chapter Eleven**

### **Recommendations on the Management and Postexposure Prophylaxis of Needlestick Injury or Mucosal Contact to HBV, HCV and HIV**

**Scientific Committee on AIDS  
Scientific Working Group on Viral Hepatitis Prevention  
March 2003**

## **Recommendations on the Management and Postexposure Prophylaxis of Needlestick Injury or Mucosal Contact to HBV, HCV and HIV**

### **Background**

1. Due to its work nature, health care workers (HCW) are exposed to a variety of occupational hazards. Of these, the transmission of blood-borne infections is a major concern that has received much attention. Adherence to standard infection control practices and avoidance of exposure to blood or body fluids is the best way of preventing blood-borne infections in health care setting. However, accidental exposure still happens from time to time and poses risk to the HCW. Postexposure management comes into play when such incidents occur. Rarely, significant exposure with risk of contracting blood-borne infections may occur in community settings.
2. The Scientific Committee of the Hong Kong Advisory Council on AIDS (SCA) and the Scientific Working Group on Viral Hepatitis Prevention (SWGVP) of the Department of Health recognise the importance of occupational exposure in health care setting. On the prevention side, *Prevention of transmission of HIV in health care settings – guidelines and practices* was published by the SCA in 1992, and revised in 1995. Also, the *Procedures for management of needlestick injury or mucosal contact with blood or body fluids – recommended guidelines for HIV and hepatitis prevention* was first formulated by SCA and SWGVHP in 1992. The latter guidelines were revised in 1995 to incorporate hepatitis C, and further in 1997 to update on the postexposure management of HIV.
3. In the recent years, new findings and practices on the management of occupational exposure to HIV, especially on postexposure prophylaxis (PEP), have been published. The US Centers for Disease Control and Prevention (CDC) released the updated guidelines on management of occupational exposures to hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) in June 2001. Against these backgrounds, the SCA and SWGVHP jointly embark on a revision of the guidelines of 1997.

### **Guiding principles**

4. This set of revised guidelines is recommended according to the following guiding principles:
  - (a) An integrated approach is taken by considering collectively the most important blood-borne infections to date, i.e. HBV, HCV and HIV .
  - (b) Risk assessment and counseling constitute the main emphasis of postexposure management, which lead to the specific option for PEP. As such, a case-by-case evaluation is crucial.
  - (c) Recommended practice has been put forth, based on evidence and scientific grounds where available and relevant; international developments and recommendations, as well as local perspectives have been taken into consideration.

### **Blood-borne infections and the transmission risk in health care setting**

5. HBV infection is endemic in Hong Kong. About half of the adult population above 40 years of age have been infected with hepatitis B. About 8% of the population are carriers. Up to 25% of the carriers may eventually die of chronic liver diseases, principally hepatocellular carcinoma (HCC) and cirrhosis.<sup>1</sup> The estimated risk of contracting hepatitis B through needlestick injury involving HBV infected blood ranges from 2% to 40%.<sup>2</sup>
6. Between 70 to 80% of people infected with HCV results in chronicity. A significant proportion of chronic HCV infection has resulted in chronic hepatitis, cirrhosis and HCC in 10-30 years of time.<sup>3</sup> Prevalence of anti-HCV positivity in new blood donors was 0.035-0.099% in the last decade<sup>4</sup> and it was estimated that some 0.2-0.3% of the population have been infected with hepatitis C. The estimated risk of contracting hepatitis C through needlestick injury involving HCV infected blood is 3-10%.<sup>2</sup>
7. HIV causes AIDS (acquired immune deficiency syndrome), which is characterized by

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<sup>1</sup> Chu CM. Natural history of chronic hepatitis B virus infection in adults with emphasis on the occurrence of cirrhosis and hepatocellular carcinoma. *J Gastroenterol Hepatol.* 2000;15(Suppl):E25-30.

<sup>2</sup> Gerberding JL. Management of occupational exposures to blood-borne viruses. *N Engl J Med* 1995; 332:444-51

<sup>3</sup> Yatsuhashi H, Yano M. Natural history of chronic hepatitis C. *J Gastroenterol Hepatol.* 2000;15(Suppl):E111-6.

<sup>4</sup> Department of Health. Surveillance of viral hepatitis in Hong Kong – 2000 update report. 2001



the development of opportunistic infections or tumors. HIV infection has been reported to occur in health care settings through exposure to contaminated blood from percutaneous injuries or mucosal contacts. The estimated risk of contracting the virus after needlestick injuries with exposure to infected blood is below 0.4%.<sup>2</sup> The risk after mucosal contact is even lower. In Hong Kong, the HIV prevalence has been estimated to be <0.1% in the adult population.

8. The prevention of HBV, HCV and HIV transmission in health care setting depends on the practice of infection control measures based on the principle of universal precaution. The details of infection control practice, however, falls outside the scope of this document. Postexposure management involves provision of first aid, reporting, risk assessment, counselling and additional procedures specific to individual pathogens implicated. (Annex I) It is important that health care workers responsible for postexposure management should familiarize themselves with the principles and procedures involved.

### **First Aid**

9. First aid is of importance after exposure to blood or body fluids. In case of needlestick injury, the wound should be washed immediately and thoroughly with soap and water. The wound should then be disinfected and dressed. For mucosal contact, e.g. spillage into the eyes, the exposed part should be washed immediately and liberally with running water. The exposed person should seek medical advice for proper wound care and postexposure management.

### **Reporting**

10. The institution should ensure that a mechanism is in place to facilitate reporting and management of post occupational exposure.

### **Management of accidental exposure to HBV**

11. The management of an incident of accidental exposure to HBV involves proper risk assessment, counselling tailored to the needs of individual client, and the prescription of postexposure prophylaxis as appropriate. As a rule, for the best protection, all health care staff with potential risk of exposure to blood and body fluids are advised

to receive hepatitis B vaccination as soon as possible for their own safety.

12. The efficacy of hepatitis B immunoglobulin (HBIG) and HBV vaccine for postexposure protection in occupational exposure can be referenced from the scene in perinatal transmission. HBIG could lower the carrier rate of infants born to HBsAg positive mothers from 92% to 54% at 1 year.<sup>5</sup> Multiple doses of HBIG is 70-75% effective in preventing perinatal transmission.<sup>6</sup> The efficacy of protection could be increased to 85-95% by adding a standard HBV vaccination regimen to HBIG.<sup>7,8</sup>
13. The need for HBIG administration and HBV vaccination depends on the exposure, and HBV status of the source and the exposed. (Annex II) Individuals who lack HBsAg and have not previously developed satisfactory immune response to the virus may be susceptible. They could be offered HBIG for immediate protection of significant exposure to HBV. An individualised approach founded on risk assessment is recommended for the management of a health care worker with unknown response to hepatitis B vaccination, one who has been exposed to an unknown source or a source with unknown hepatitis status. In such circumstances, the HBV status of the source and/or the exposed should be determined where appropriate. The exposed person may be managed as in the case of an injury involving an HBsAg positive source person if the HBV status of the latter cannot be ascertained.

### **Management of accidental exposure to HCV**

14. To ascertain whether HCV infection has occurred from the exposure, health care personnel exposed to HCV should have blood taken as a baseline soon after exposure and again 6 months later for HCV antibody testing. The US CDC also recommends alanine aminotransferase testing for client exposed to known HCV-infected source.<sup>9</sup>

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<sup>5</sup> Beasley RP, Hwang LY, Lee GC, et al. Efficacy of hepatitis B immune globulin for prevention of perinatal transmission of the hepatitis B virus carrier state: final report of a randomized double-blind, placebo-controlled trial. *Hepatology* 1983;3:135-41.

<sup>6</sup> CDC. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the US through universal childhood vaccination: recommendation of the Immunization Practices Advisory Committee (ACIP). *MMWR* 1991;40(no. RR-13) 1-25.

<sup>7</sup> Beasley RP, Hwang LY, Lee GC, et al. Prevention of perinatally transmitted hepatitis B virus infection with hepatitis B immune globulin and hepatitis B vaccine. *Lancet* 1983;2:1099-1102.

<sup>8</sup> Wong VCW, Ip HMH, Reesink HW, et al. Prevention of the HBsAg carrier state in newborn infants of mothers who are chronic carriers of HBsAg and HBeAg by administration of hepatitis B vaccine and hepatitis immunoglobulin: double-blind randomized placebo-controlled study. *Lancet* 1984;1:921-6.

<sup>9</sup> US CDC. Updated US Public health service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. *MMWR* 2001; 50(RR-11): 1-52.

15. Currently, there is no effective vaccine or chemoprophylactic agent for preventing HCV infection after accidental occupational exposure. Limited data indicate that anti-HCV therapy, such as interferon  $\alpha$ , might be beneficial when started early in the course of HCV infection, but no guidelines exist for guiding the administration of therapy during the acute phase of infection.<sup>10</sup>

### **Management of accidental exposure to HIV**

16. Assessment of source patient for risk of HIV infection, if possible, should be made. Counselling and HIV testing with consent should be offered where appropriate. If the source patient is HIV antibody positive, suspected to be positive or is of unknown status, the exposed person should be encouraged to have blood taken for HIV antibody as a baseline. Counselling and consent are again important in this situation.
17. Assessment of potential risk of HIV infection from the exposure is of paramount importance in deciding on the need for chemoprophylaxis. The risk depends on the setting, type and severity of exposure, type and amount of fluid/tissue exposed/transferred, HIV status of source, and susceptibility of the injured. It has been shown that some factors of the accident itself were associated with a higher potential of seroconversion after percutaneous exposure to HIV-infected blood: (a) injury with a device visibly contaminated with the patient's blood, (b) a procedure that involved a needle directly placed in a vein or artery, (c) deep injury, and (d) exposure to source patients with AIDS or high plasma viral burden.<sup>11</sup>
18. Though the disease stage of a known HIV-infected source impacts on the risk of transmission, it is not uncommon that HIV status of the source is unknown. In such case, the likelihood of HIV infection in the source could be assessed by clues such as (a) HIV-related illnesses, e.g. *Pneumocystis carinii* pneumonia, oral thrush, (b) HIV-related risk behaviors, e.g. unprotected sex, multiple sex partners, needle-sharing for drug injection, and (c) HIV prevalence of the community group which the source belongs to.
19. Antiretroviral prophylaxis should be offered to the injured if the exposure is assessed to constitute significant risk of HIV infection. (Annex III) Pros and cons of

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<sup>10</sup> US CDC. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. MMWR 1998;47(RR19):1-39.

<sup>11</sup> Cardo DM, Culver DH, Ciesielski CA et al. A case-control study of HIV seroconversion in health-care workers after percutaneous exposure. N Engl J Med 1997; 337: 1485-90

antiretroviral chemoprophylaxis should be adequately explained. Prophylaxis should be initiated as soon as possible, preferably within 1-2 hours postexposure, after the decision is made; however, delayed initiation may still be indicated on a case-by-case consideration. Even though zidovudine is the only drug with proven efficacy for postexposure chemoprophylaxis, combination antiretroviral prophylaxis is recommended based on their observed benefits in other clinical situations as well as scientific researches.

20. A basic two-drug regimen of AZT/3TC can be considered if high risk factors are not present. Otherwise, the addition of a protease inhibitor (PI), e.g. indinavir, nelfinavir, is indicated. The use of nevirapine to spare PI has caused severe morbidity and even deaths, which is thus contraindicated in PEP.<sup>12</sup> Usage of efavirenz for PEP has not been well studied.
21. The optimal duration of PEP is unknown but a complete course is normally 4 weeks. Many HCWs who took PEP experienced one or more symptoms and a substantial proportion could not complete the course.<sup>13</sup> Pretreatment counseling on all potential side effects might improve the compliance of PEP.
22. The exposed person should be followed up for at least 6 months and be asked to report signs/symptoms of acute HIV seroconversion. Blood taking should be performed soon after injury, at 3-6 months after exposure and when there is suggestion of seroconversion. Individuals started on chemoprophylaxis should also be monitored for drug toxicity and tolerance.
23. Strict confidentiality of the HIV status of source patient and injured person must be observed.

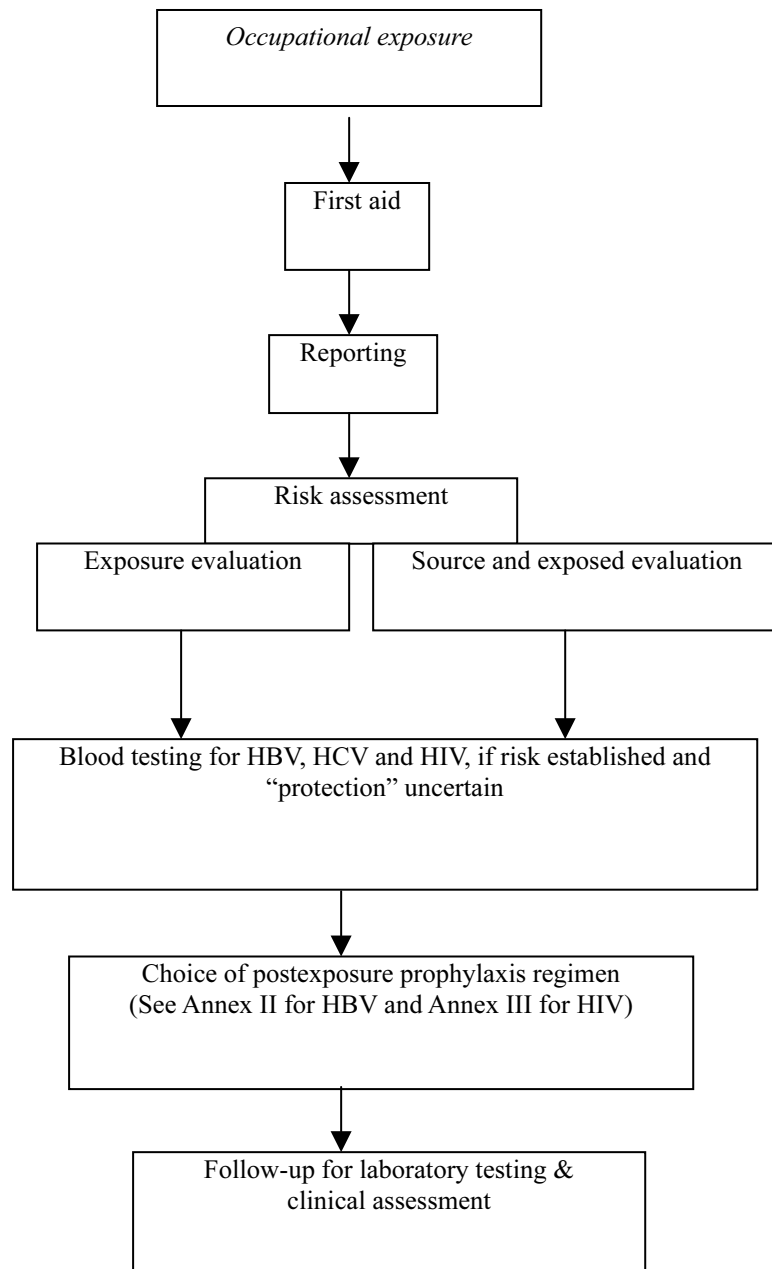
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<sup>12</sup> US CDC. Serious adverse events attributed to nevirapine regimens for postexposure prophylaxis after HIV exposures – Worldwide, 1997-2000. MMWR 2001; 49: 1153-56

<sup>13</sup> Parin JM, Murphy M, Anderson J et al. Tolerability and side-effects of post-exposure prophylaxis for HIV infection. Lancet 2000; 355: 722-23

**Annex I****Flow chart for the management of occupational exposure to  
HBV, HCV and HIV**

**Annex II****Postexposure prophylaxis against HBV infection**

	POSTEXPOSURE PROPHYLAXIS				
	Previously Vaccinated			Unvaccinated	
	<i>Known Responders</i>	<i>Known Hypo/Non-responders</i>	<i>Unknown Response</i>	<i>HBsAg -ve AND anti-HBs -ve<sup>†</sup></i>	<i>HBsAg +ve OR anti-HBs +ve</i>
<b>I. SOURCE KNOWN</b>					
(a) HBsAg + ve	Nil	HBIG within 24 hours repeat after 1 month	Dependent on anti-HBs* status of exposed person	HBIG + HB Vac	Nil
(b) HBsAg – ve	Nil	Nil	Nil	HB Vac	Nil
(c) HBsAg unknown	Nil	Dependent on source HBsAg status	Dependent on anti-HBs* status of exposed person	HBIG + HB Vac, or HB Vac; depending on source HBsAg status	Nil
<b>II. SOURCE UNKNOWN</b>	Nil	as in I(a)	as in I(a)	as in I(a)	Nil

**N.B.**

1. Blood should be taken from the source and the exposed person whenever possible and indicated, particularly if the latter has not received hepatitis B vaccination before.
2. Where indicated, one dose of HBIG (dosage as recommended by the manufacturer) should be given within 24 hours of exposure, and preferably within 7 days. Attention is drawn to the need of blood taking before administering HBIG.
3. Hepatitis B vaccination (HB Vac) may be offered for (a) health care workers (HCW) who have not received HBV vaccination before, and (b) HCW who are hypo-/non-responder to one previous course of HBV vaccine. HB Vac is given IM into the deltoid at a dose of 10ug (B-Hepavac II) or 20ug (Engerix-B). The second and the third doses are to be given one and six months afterwards.
4. HBIG and HBV vaccine can be given together but at different sites. If HBIG has been given, the first dose of vaccine can be delayed for up to 1 week after exposure, pending results of serological test. If HB Vac is given, the second dose of HBIG can be omitted if the HCW is not a known hypo-/non-responder.

\*For a previously vaccinated person with unknown response, he/she should be tested for anti-HBs

- no treatment is required if anti-HBs is positive
- HBIG ± HBV vaccine can be offered if anti-HBs is negative

**Annex III****Postexposure prophylaxis against HIV**

<b>Regimen</b>	<b>Dosage</b>	<b>*Indications</b>
Expanded regimen	<ul style="list-style-type: none"><li>• Zidovudine (200mg tid/300mg bid) + lamivudine (150mg bid) + indinavir (800mg q8h)/nelfinavir (750mg tid/1250mg bid)</li></ul>	<ul style="list-style-type: none"><li>• Substantiated risk of HIV infection from an exposure with presence of high risk factors</li></ul>
Basic regimen	<ul style="list-style-type: none"><li>• Zidovudine (200mg tid/300mg bid) + lamivudine (150mg bid)</li></ul>	<ul style="list-style-type: none"><li>• substantiated risk of HIV infection from an exposure without high risk factors</li></ul>
No PEP	<ul style="list-style-type: none"><li>• no antiretroviral drugs</li></ul>	<ul style="list-style-type: none"><li>• risk not substantiated or patient declined PEP</li></ul>

\*dependent on risk assessment regarding the setting, type and severity of exposure, type and amount of fluid/tissue exposed/transferred, HIV status of source, and susceptibility of the injured