

Universal antenatal human immunodeficiency virus testing in Hong Kong: consensus statement

香港人類免疫缺陷病毒的產前普及測試：結論綜述

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 Following the recommendations of the Advisory Council on AIDS, Hong Kong, the Hospital Authority announced plans to introduce universal antenatal screening for human immunodeficiency virus infection and hence, a consensus conference was held to discuss strategies for implementing such screening in Hong Kong. This paper reports the discussions of the consensus conference. The consensus meeting group consisted of 15 clinicians and scientists from Hong Kong, Macau, and Thailand. Seven commonly asked questions concerning mother-to-child transmission of human immunodeficiency virus were selected for discussion by the participating panellists. Information on the laboratory diagnosis of human immunodeficiency virus infection and the efficacy of preventive measures in reducing mother-to-child transmission of human immunodeficiency virus were reviewed. Data from local studies was also presented and discussed. The timing, potential problems, and cost issues involved in testing all pregnant women in Hong Kong for human immunodeficiency virus were then considered.

Key words:

*Disease transmission, vertical;
 HIV infections;
 Hong Kong;
 Mass screening;
 Prenatal diagnosis*

關鍵詞：

疾病傳播，垂直的；
 HIV 感染；
 香港；
 大型檢查；
 產前診斷

HKMJ 2001;7:421-7

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根據香港愛滋病顧問局的建議，醫院管理局宣佈了引入人類免疫缺陷病毒感染的產前測試之計劃，並召開會議討論有關於香港執行這項計劃的策略。本文報告了這會議的討論結果。會議由15名來自香港、澳門和泰國的臨床醫生和科學家組成。與會者對有關人類免疫缺陷病毒母嬰傳播的七個常見問題進行了分組討論，並對人類免疫缺陷病毒在實驗室中診斷的資料，及減少這種病毒母嬰傳播的預防措施的成效進行了回顧，同時也報告和討論了各地的研究資料。最後，對全港孕婦的人類免疫缺陷病毒測試的推行時間、潛在問題、以及費用方面進行了探討。

Introduction

Human immunodeficiency virus (HIV) is the cause of acquired immunodeficiency syndrome (AIDS). It is now known that there are three main routes of HIV transmission: sexual activity; exposure to contaminated blood, commonly referring to the sharing of needles by intravenous drug users; and mother-to-child transmission (MTCT). While behavioural intervention is the main strategy to minimise HIV infection through sexual activity and needle-sharing, medical advances have contributed to the reduction in MTCT of the infection.

The landmark study PACTG 076, showed that antepartum, intrapartum, and postnatal zidovudine (AZT) treatment could effectively reduce the MTCT rate of HIV by two thirds.¹ This led to various studies on the

Table. Clinical trials of antiretroviral agents for the prevention of mother-to-child transmission of human

Study	Regimen	Antepartum		
		14-28 weeks	29-36 weeks	> 36 weeks
PACTG 076 ¹	ZDV [†]			
Thai ¹⁹	ZDV			
Cote d'Ivoire ¹⁸	ZDV			
DITRAME ¹⁷	ZDV			
Wade ²⁴	ZDV			
	ZDV			
	ZDV			
Global Strategies ²¹	ZDV + 3TC [‡]			
	ZDV + 3TC			
	ZDV + 3TC			
PETRA Arm A ²³	ZDV + 3TC			
PETRA Arm B ²³	ZDV + 3TC			
PETRA Arm C ²³	ZDV + 3TC			
Blanche ²⁰	ZDV + 3TC			
	ZDV			
HIVNET ²²	ZDV or NVP [§]			

* Shaded area indicates period of treatment with antiretroviral agents

[†] ZDV zidovudine

[‡] 3TC lamivudine

[§] NVP nevirapine

optimum duration of AZT treatment and trials of other antiretroviral agents. Antiretroviral regimens investigated and their efficacy are summarised in the Table. This research interest also led to the establishment of recommendations for universal antenatal HIV screening in the US in 1995,² and in the UK in 1998.³ More recently, the US Public Health Service has revised these recommendations, strongly recommending universal HIV testing for all pregnant women.⁴

In Hong Kong, HIV infection is still relatively uncommon in women, with a cumulative total of 265 cases (17.2% of the total of 1542) reported at the end of 2000.⁵ In an unlinked anonymous screening program conducted by the Department of Health, the prevalence of HIV infection among pregnant mothers was 0.03%. A similar rate of 0.06% was reported in a study involving over 5000 pregnant women in Kwong Wah Hospital.⁶ According to the annual report of the Hospital Authority (HA), there were 59 250 deliveries in Hong Kong in 1997 and 52 977 in 1998.⁷ Henceforth, this provides an estimate of between 15 to 30 HIV-positive pregnancies in Hong Kong each year. Assuming the rate of MTCT of HIV is 20%, approximately three to six babies would be born annually with the virus, if no intervention were instituted.

In Hong Kong, HIV testing is currently offered sparingly to pregnant mothers who are considered by obstetricians to be at risk. Available data indicates that the opportunity for prevention of MTCT of HIV was frequently missed by such a strategy. Of 28 babies born to HIV-positive mothers between 1993 to

2000, the HIV status of the mother was unknown in 50% of cases (Department of Health, unpublished data, 2001). The fact that effective treatment is available for prevention of an incurable disease argues strongly for a revision of existing practice. In late 2000, the Hong Kong Advisory Council on AIDS proposed the adoption of a new strategy involving universal testing of all pregnant women on a voluntary basis.

Process of consensus

The consensus meeting on Universal Antenatal HIV Testing: Translating Science into Public Health Policy was held on 21 April 2001, as the third current topic in infectious diseases organised by the Centre of Infection, the University of Hong Kong. A panel of experts from the fields of obstetrics, paediatrics, public health, and virology was provided with the latest scientific papers^{1-5,8-19} and participants were invited to speak on and discuss various aspects of the topic.

After the formal presentation, a panel discussion was held with briefing notes (addressing seven questions) distributed to all meeting attendees. All attendees participated actively in the discussion, which was focused on elaboration of the feasibility, cost-effectiveness, and operational details of universal antenatal HIV testing in Hong Kong.

Finally, conclusions were drawn on the basis of current scientific information and the views expressed by the panel and other participants.

immunodeficiency virus*

Intrapartum	Postpartum		Relative efficacy (% reduction in transmission)
	1 week	2-6 weeks	
	Infant		67.5
			50.3
			43.8
	Mother		34.5
	Infant		77.0
	Infant		62.4
	Infant <48 hrs		65.0
	Infant >72 hrs		30.8
	Infant		47.1
	Infant		44.5
	Infant		47.7
	Mother and infant		52.0
	Mother and infant		40.0
			0
	Infant		2.6
	Infant		6.5
	Infant		
			Transmission rate 25.1% (ZDV) vs 13.1% (NVP)

Questions and discussion

Do we have a robust test to reliably determine the human immunodeficiency virus infection status of the mother and the baby?

In adults, the most effective and common way to determine whether a person is suffering from HIV infection is through detection of HIV antibodies. Hong Kong follows testing guidelines and procedures agreed internationally. The HIV enzyme-linked immunosorbent assay (ELISA) is generally used as a screening test and is available at the Government Virus Unit of the Department of Health, and some HA hospitals and private laboratories. The Government Virus Unit also provides confirmatory testing using the Western blot technique. Most of the commercially available ELISA kits have a sensitivity and specificity greater than 99%. Due to the impact of a diagnosis of HIV infection, however, testing for HIV antibodies is *only* reported as positive when a repeatedly reactive ELISA test is confirmed by a more specific assay, such as the Western blot technique.

In neonates and infants younger than 1 year old, transfer and persistence of maternal antibodies complicates the diagnosis of HIV infection. Other techniques for the diagnosis of HIV infection include p24 antigen detection, isolation of HIV by culture, and the polymerase chain reaction (PCR). Studies have shown that PCR is by far the most sensitive and timely method for diagnosing HIV infection. The US Center for Disease Control and Prevention recommended in 1998 that diagnostic testing should be

performed at the following ages: 48 hours, between 1 and 2 months, and between 4 and 6 months.⁴ A positive PCR test should be confirmed by a repeat virologic test on a second specimen. Although HIV DNA PCR was initially reported as the preferred virologic method, subsequent studies have shown that HIV RNA amplification is more sensitive than DNA PCR for early diagnosis of perinatal infection in infants exposed to HIV. Extracellular HIV RNA appears soon after infection and the viral load is much higher than the detection limit of quantitative HIV RNA. Quantitative HIV RNA is available in Hong Kong and is used currently to diagnose paediatric cases.

Is there evidence that knowledge of the human immunodeficiency virus status would be beneficial to the mother and the baby?

Early diagnosis of HIV infection has a number of benefits. Firstly, it allows counselling and assessment before the disease manifests at an advanced stage as AIDS. With the advent of highly active antiretroviral therapy, there is increasing evidence that the prognosis in terms of quality of life and survival can be improved by timely treatment. Secondly, knowledge of HIV status allows the mother to make informed choices about the management of her pregnancy. Thirdly, it provides an opportunity for prevention of MTCT of HIV infection.

Several studies have shown that good obstetric care combined with antiretroviral prophylaxis can reduce the risk of perinatal HIV infection by about two thirds.^{1,17-23} The US has seen a dramatic reduction

in the MTCT of HIV, following the launch of a programme in 1995 consisting of routine counselling and voluntary testing of pregnant women for HIV, and offering antiretroviral prophylaxis to infected women during pregnancy and delivery, and for the infant after birth. To maximise MTCT prevention efforts, women must be identified with HIV infection early in pregnancy to allow prompt initiation of antiretroviral prophylaxis. Studies of antiretroviral prophylaxis regimens¹⁷⁻²⁴ support selection of the PACTG 076 study regimen, which commenced AZT therapy at 14 weeks of gestation, and achieved a 67.5% to 77.1% relative reduction in the risk of HIV transmission (Table).^{1,24} Besides offering chemoprophylaxis, the mother could also be counselled regarding methods of delivery and baby feeding. The risk of MTCT attributable to breastfeeding is estimated at between 7% and 22%.^{25,26} In one study, delivery by Caesarean section and avoidance of breastfeeding were shown to reduce the rate of MTCT from 25% to less than 5%.¹⁵ Finally, for babies known to be born to an HIV-infected mother, appropriate assessment and evaluation can be arranged to allow early diagnosis of paediatric HIV infection and initiation of prophylaxis to prevent life-threatening *Pneumocystis carinii* pneumonia.

Is the provision of universal antenatal human immunodeficiency virus testing an acceptable strategy for the pregnant women?

Before any new antenatal screening test is introduced, the opinions of pregnant women should be considered. This is particularly true for HIV testing. Studies conducted overseas showed that women were generally in favour of a test offer and were more concerned about having an unhealthy baby. Routine testing rather than a selective protocol was preferred by many as it eliminated the stigma of agreeing to testing.

A study conducted at Kwong Wah Hospital in 1999, saw 5597 pregnant women offered the screening test, with 97.5% of the women accepting the offer.⁶ A further study conducted at Tsan Yuk Hospital, concerned the acceptance and attitude towards universal antenatal HIV antibody screening (Li CFI, unpublished data, 2001). Seventy-two percent of pregnant women (n=537) agreed that the test should be offered, and 54% indicated they would accept the test if offered. Acceptance was correlated positively with perceived risk of infection. In this particular study, it was also documented that more than 80% of women felt there was inadequate information available in Hong Kong on antenatal HIV infection.

Do we have the health infrastructure to implement universal antenatal human immunodeficiency virus testing in Hong Kong?

There are between 50 000 and 60 000 births every year in Hong Kong. Almost all births occur in hospitals and more than 90% of pregnant women now receive antenatal care. As part of routine antenatal care, pregnant women are currently counselled and screened for various conditions, including syphilis, rubella, hepatitis B status, and thalassaemia. Thus, it would be more feasible to introduce universal antenatal HIV testing as part of the antenatal screening programme, rather than as a separate test. Provision of key information on HIV infection and MTCT would also be required before and after testing.

Currently, various units in HA hospitals and the Department of Health are designated for and are experienced in providing care for patients who are HIV-positive or have AIDS. As there are relatively few HIV-positive mothers, they can be referred to these pre-existing units to continue their care. Nonetheless, there must be a territory-wide monitoring system to follow up all HIV-infected mothers to document their management and outcome. Babies delivered, whether infected or not, should also be monitored by this territory-wide system.

What is the additional cost involved in the implementation of universal antenatal testing? Are we justified in introducing the programme with respect to the costing implications?

In the US, the costs of universal HIV screening are considered to be low, and the benefits high. Assuming that the marginal cost of adding an ELISA test to the existing prenatal panel of tests is HK\$24 per woman, and the prevalence of HIV in pregnant women is 2 per 10 000, then the cost of routine prenatal testing per HIV-positive woman identified would be HK\$120 000.¹⁵ Similarly, universal screening with pre-test discussion was estimated to be cost-effective in the UK, particularly in London where the prevalence of HIV infection among pregnant women was 0.19%. Elsewhere in the UK, where the infection is less prevalent (0.02%), a universal screening program was deemed cost-effective only if the uptake was above 90%.¹³

There is a lack of good local data on the cost-effectiveness of the test. Nonetheless, no local data on the cost-effectiveness of universal antenatal syphilis and rubella screening tests were available before implementation of such screening in Hong Kong. Perhaps the question should be whether the cost of the

screening programme is affordable and reasonable. The laboratory cost for screening all pregnant women for HIV was estimated to be HK\$1.6 million annually. Assuming a prevalence of 3 cases in 5000 and an uptake of 90%, the laboratory cost per HIV-positive woman identified would be HK\$59 000. Compared with the cost of universal screening of blood (HK\$430 000) to prevent one transmission of HIV via blood transfusion,²⁷ the cost of universal, voluntary antenatal HIV screening seems reasonable.

***Is this the right time to introduce the programme?
Are we too early, or are we late and why?***

In the US, universal HIV testing of pregnant women commenced in 1995, shortly after the publication of the PACTG 076 study. Recently, the recommendations were updated, emphasising that universal HIV testing with patient notification be a routine component of prenatal care.^{4,15} In the UK, an intercollegiate working party for enhancing voluntary confidential HIV testing during pregnancy was convened and the programme implemented in 1998.³ According to the Department of Health (UK), the target is to increase uptake of antenatal HIV testing to 90%, and identification of HIV-infected pregnant women to 80% nationally by the end of 2002, offering this latter group advice and treatment during antenatal care. It is anticipated that these targets will result in an 80% reduction in the number of children with HIV acquired from an infected mother during pregnancy, birth, or through breastfeeding.³

Routine HIV testing during pregnancy is being implemented in many other European countries. A consensus statement from a pan-European group has recommended that every pregnant woman should, as of right, have access to HIV testing and information; and that provision of testing without undue obstacles should be mandatory for health care providers.²⁸ France and The Netherlands have further stated that the offer of maternal HIV testing by health professionals is a mandatory requirement.²⁹

In Thailand, a universal voluntary HIV counselling and testing programme has been in place for some years, with great support from the general public as well as from the government. In Macau, an unlinked, anonymous sero-surveillance programme was introduced in 1997. Since last year, HIV testing has been offered routinely to all mothers receiving antenatal care in Macau.

It is, therefore, definitely not too early to introduce such a programme in Hong Kong. It should not be

implemented hastily, however. Operational details should be determined. Definite targets should also be set in order to monitor the uptake, progress, and effectiveness of the programme implemented.

Are there disadvantages associated with a universal testing system? Is there a role for an alternative mechanism?

One alternative to universal testing is selective testing of those who are identified as high risk for HIV. Selective testing may stigmatise women, however, and is liable to miss many of those infected. In the UK, it has performed poorly.³⁰ If the uptake rate of a universal programme in Hong Kong were low, however, a large proportion of HIV-positive women would still remain undiagnosed. In order to ensure a high uptake, an 'opt-out' strategy where patients actively decline the test is preferable.

Finally, one must remember that being given a diagnosis of HIV infection during pregnancy is a tremendously stressful experience. Support and counselling should be available on an urgent basis. In a low prevalence population, the false positive rate of even a highly sensitive and specific test would still be substantial. The false positive rate using a single test on one sample in a local study was 0.24%, which is higher than the true positive rate of 0.06%. However, this false positive rate was calculated on the basis of a single ELISA test. If the standard currently adopted by the Government Virology Unit of the Department of Health is followed—that is, testing for HIV antibodies is only reported as positive when a repeatedly reactive ELISA test is confirmed by the Western blot technique—then all false-positive reporting of the diagnosis would be eliminated.

Conclusion

The HIV prevalence in pregnant mothers in Hong Kong is estimated to be 0.03% to 0.06%, which is relatively low compared with other countries. The number of women diagnosed as HIV-positive, however, is increasing. As MTCT is a route for the transmission of HIV, the number of children with HIV can also be expected to increase.

Research conducted since 1994 indicates that MTCT can be reduced by a number of interventions.^{1,17-23} These include termination of pregnancy, early antepartum and intrapartum administration of antiretroviral agents to HIV-positive mothers and to babies postnatally, delivery by caesarean section, good obstetric care, and avoidance of breastfeeding.

The success of these measures, however, hinges on the very first step of identifying HIV-positive mothers. Voluntary universal HIV testing as part of routine antenatal care has been shown to be effective in identifying HIV-infected pregnant women and in reducing MTCT of HIV. This strategy applies to both high and low prevalence populations, and is effective in developed as well as resource-poor countries. For Hong Kong, as the costs of screening are low and the effectiveness apparently high, such screening appears cost-effective, and a formal cost-effectiveness study does not appear necessary.

While the implementation of universal, voluntary antenatal HIV testing is well founded scientifically, these principles cannot be translated into practice without addressing the essential features of an effective programme. First of all, the operational details should be determined and the rationale made known to the community. A vigorous evaluation and monitoring system for the entire programme should be put in place. Additional costs required to implement such a system must be identified, and the resources and structure necessary assembled before the screening is introduced. Secondly, health care professionals involved need to be provided with appropriate training in the care of HIV-positive pregnant women, their babies, and family. Thirdly, clinical protocols must be established based on an 'opt-out' approach, where patients must actively decline screening, in order to ensure a high uptake. Fourthly, testing should be made on a voluntary basis after providing patients with appropriate information. Finally, patient confidentiality should be protected.

Considering the broader perspective, working targets are needed and the programme should be regularly evaluated. Antenatal HIV screening as a means of prevention of MTCT of HIV is a perfect example of how health objectives should be established and priorities considered in context, so as to ensure effective use of resources. For success, support from the community and the government will be required. From the data gathered locally to date, it seems that there is widespread acceptance among pregnant women of universal HIV testing as part of antenatal care. It is also clear that more information on MTCT of HIV needs to be provided to the public.

The Hong Kong Advisory Council on AIDS recently recommended that universal antenatal screening be adopted in Hong Kong and the government has reaffirmed its support of this policy.¹⁶ It is now time for the medical community to respond to these initiatives.

Acknowledgement

The consensus meeting was sponsored by Abbott Laboratories Ltd, Hong Kong.

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