Perinatal and infant HIV infection: Screening to minimise risk

Infants and young children are uniquely vulnerable to infection with the human immunodeficiency virus (HIV) which causes the acquired immune deficiency syndrome (AIDS), and chance alone determines their fate when born to HIV-infected mothers. Hundreds of thousands of children throughout the world are newly infected with HIV each year and many of these infections could be prevented. Antenatal screening for maternal HIV infection is the foundation for reducing the risk of perinatal and infant infection. All pregnant women in the UK are now offered screening for HIV infection during antenatal care. Understanding how screening programmes are developed and assessed allows nurses and midwives to help parents appreciate the risks and benefits of screening for them as individuals and for their children.

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Keywords

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Key points

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1. Screening is an essential component of public health services designed to reduce the risk of disease or disability and improve the health of the population.
2. Nurses, midwives and other healthcare professionals need to be aware of the risks and benefits of screening in order to provide parents with relevant information to help them make informed choices.
3. Appraisal criteria are used to assess the viability, effectiveness and appropriateness of antenatal screening programmes designed to protect infants from human immunodeficiency virus (HIV) infection.
4. The benefits to mothers and infants of antenatal screening appear to outweigh potential harm.

Prevention

Programmes for preventing ill health or disability are a core feature of the work of the United Kingdom (UK) National Health Service (NHS) and are often referred to as primary, secondary and tertiary prevention. Primary prevention programmes focus on helping people avoid disease or injury, e.g. smoking cessation to decrease the risk of lung cancer, wearing car seat belts to reduce risk of injury in a road traffic accident. Secondary prevention measures are aimed at identifying and treating asymptomatic people who have risk factors or undiagnosed early disease, e.g. hypertension, diabetes. Tertiary prevention activities involve treatment and care to help people with established disease, injury or disability halt further progression of their condition, reduce disease-related complications and return to their maximum level of health.

Screening is the most common activity associated with secondary prevention and, although it cannot be a guarantee of diagnosis and cure, it does provide an opportunity to reduce the risk of contracting a disease or suffering its complications.

Screening can be defined as:

'A public health service in which members of a defined population, who do not necessarily perceive they are at risk of, or are already affected by, a disease or its complications, are asked a question or offered a test to identify those individuals who are more likely to be helped than harmed by further tests or treatment to reduce the risk of disease or its complications'[1].

Screening programmes

Screening programmes monitored by the UK National Screening Committee (NSC) are well established and integrated into comprehensive control programmes, developed and implemented by UK Health Departments for health problems based on different stages of the life cycle, i.e. antenatal, child, men, women and the older person[1]. Screening programmes encompass the screening test, the diagnostic test and any treatment or action that follows on from these[2].

Testing and screening

Screening programmes employ tests that are designed to detect a condition, e.g. an infection or disease, in seemingly healthy persons who could benefit from a therapeutic intervention. A variety of tests can be used depending on the condition being investigated, e.g., physical examination, X-rays, mammography, hearing tests, electrocardiogram, ultrasound scans, and a wide range of serological tests. The efficacy of any test used in a screening programme must be assessed against specific criteria i.e. its effectiveness, safety, acceptability and costs[3]. Effectiveness is assessed by determining the test's sensitivity, specificity and predictive value.

1. The condition sought should be an important health problem.
2. The epidemiology, natural history of the condition, including development from latent to symptomatic disease, should be adequately understood and there should be reliable markers of disease stage.
3. A quick, simple, safe, effective and validated screening test to detect HIV infection must be available.
4. The test must be acceptable to the population.
5. Informed consent must be given by those offered the screening test
6. There should be good quality evidence that the proposed screening programme and the associated interventions/prophylaxis are effective in reducing the incidence of maternally transmitted HIV infection, and infant morbidity and/or mortality.
7. There must be an accepted treatment for mothers and infants detected with the infection and adequate facilities and resources for confirmatory diagnosis and treatment.
8. The financial costs of the screening programme must be justified in relation to the expected health benefits obtained.
9. The likelihood of physical or psychological harm to those screened should be less than the likelihood of benefit
10. Quality assurance, monitoring and audit procedures must be designed into the programme.

TABLE 1 Assessment criteria: Antenatal screening for HIV infection[1,3,4]

Sensitivity, specificity and predictive value

No test is 100% accurate in detecting those persons with the condition being investigated. Occasionally the test will miss identifying a person with the condition, i.e. a false-negative result, and sometimes the test will incorrectly identify a person as having the condition when, in fact, they do not have the condition i.e. a false-positive result. The ability of a test to correctly identify those with the condition – a true-positive result – is referred to as the test sensitivity. The ability of a test to detect those without the condition – a true-negative result – is known as the test specificity. A good screening test will be one with a high degree of sensitivity and specificity. A positive predictive value is the probability of a patient with positive test results who is correctly diagnosed as actually having the condition, while the negative predictive value is the probability of those with a negative test not having the condition.

Benefit vs. harm

For screening to be beneficial the quality of life of the person or their family should be improved as a result of some change that results from the screening programme[2]. Good quality screening programmes provide opportunities for early detection and treatment of many serious diseases and disabilities and benefit populations. However, when individuals consent to screening they need to be aware not only of the potential benefits of being screened, but also of the limitations and potential adverse effects of screening and subsequent interventions. The greatest concern is the possibility that a false-negative result will occur and result in diagnostic delay and subsequent treatment. Conversely a false-positive test result may lead to subsequent potentially harmful diagnostic or treatment interventions. False-negative results are inherent in any screening programme that does not have 100% sensitivity. To enhance benefit and minimise the potential for harm, screening programmes need to be carefully considered and systematically developed. In the UK, screening programmes are only developed on advice to government by the NSC. Appraisal criteria are used by NSC to inform their advice regarding initiating, continuing or stopping screening programmes[3].

Appraisal criteria

Criteria for appraising proposed and current screening programmes were originally developed in the late 1960s[4] and have since been further elaborated[1,3]. These criteria need to be met before screening for a condition is initiated. In this article, these criteria have been somewhat abbreviated (**TABLE 1**) but they demonstrate how nurses, midwives and other healthcare professionals can use them to review the viability, effectiveness and appropriateness of the screening programmes they or their patients or clients are involved in. The complete appraisal criteria developed by the UK NSC can be downloaded from their website[1]. Antenatal screening for maternal HIV infection provides a good example of how screening appraisal criteria can be used to assess any screening programme.

Assessing antenatal screening for maternal HIV infection

1. The condition sought should be an important health problem

At the end of 2006, an estimated 17.7 million women somewhere in the world were living with and dying from HIV infection[5,6]. Over 2 million women become newly infected each year and, as more and more women become infected, the risk of perinatal and infant HIV infection accelerates as a direct consequence of maternal infection. Throughout the world, over 2.3 million children are living with HIV/AIDS and each day, more than 1500 children become infected with HIV and another 1000 die as a result of AIDS (**TABLE 2**)[5-7]. HIV disease has established itself as one of the greatest threats to global public health in our time and its abysmal impact on maternal and child health is appalling. Since the beginning of the UK epidemic, 1,264 infants have become infected with HIV as a result of being born to an HIV-infected mother[8].

2. The natural history of the condition should be adequately understood and there should be reliable markers of disease stage

The aetiology, means of viral transmission and pathogenesis of HIV disease in adults and children are well understood

2006 global HIV and AIDS estimates Children (<15 years)	
• Children living with HIV	2.3 million (1.7-3.5 million)
• New HIV infections in 2006	530,000 (420,000-670,000)
• Deaths due to AIDS in 2006	380,000 (290,000-500,000)

TABLE 2 Data on HIV infection and mortality due to AIDS from UNAIDS.

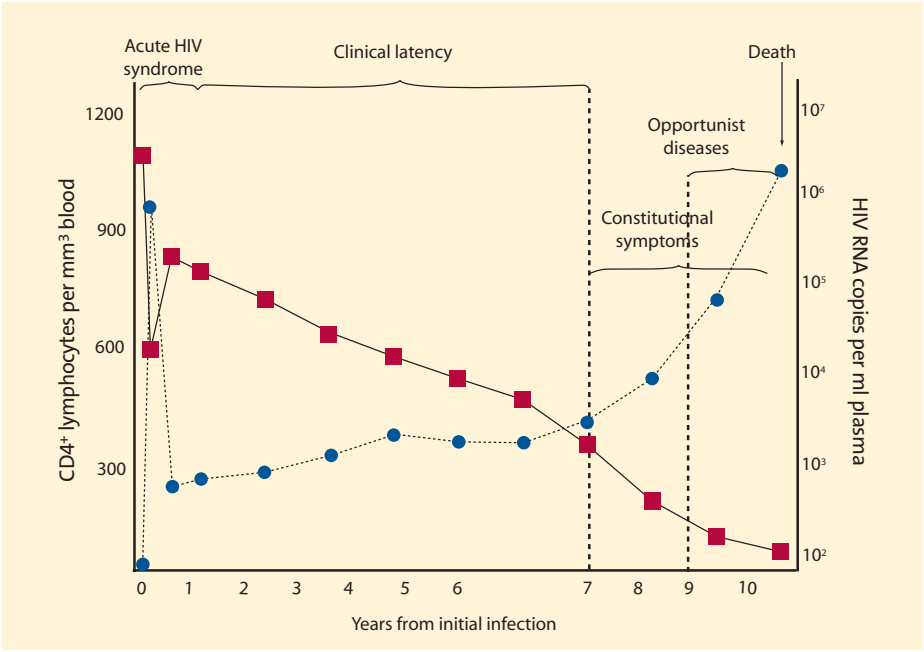

FIGURE 1 The clinical course of HIV infection and disease in relation to the CD4+ T-lymphocyte cell count ■ and the viral load ●. (From: **Pratt R.J. et al.** Tuberculosis: A Foundation for Nursing and Healthcare Practice. 2005. London: Hodder-Arnold).

(**FIGURE 1**)[9,10]. Following primary infection, individuals progress into an asymptomatic stage that is in turn followed by symptomatic illness and end-stage disease, i.e. AIDS.

The natural history of HIV disease has been likened to a train journey, beginning with infection and terminating at a station called AIDS[10]. Two serological markers can monitor a passenger's progress on this journey – the level of peripherally circulating CD4+ T-lymphocytes ('helper' cells) and the plasma level of viral RNA (viral load). In this analogy (**FIGURE 2**), the CD4+ count (the sleepers on the rail track) measure the amount of immune system damage sustained, i.e., where they are on that journey from infection to AIDS. The lower the count, the closer they are to their final destination. The viral load measures the rate of viral replication and level of virus in the blood and signifies how fast infected persons are travelling towards that destination, i.e., the higher the viral load, the more rapidly they are progressing to AIDS[11].

3. A quick, simple, safe, effective and validated screening test must be available

Serological tests for HIV infection have been widely used throughout the world since 1984/5. They detect antibody to HIV, a confirmed positive result indicating infection. These tests have an extraordinary high degree of specificity (99.7%) and sensitivity (99.9%) and a positive predictive value, that have been well validated[12].

4. The test must be acceptable to the population

HIV infection is not perceived as a relevant issue for many clients and their partners attending for antenatal care. For others, the socio-cultural implications of being tested, or even worse, testing positive, may be overpowering. Stigma, discrimination and rejection are sadly sometimes an outcome of being tested. Consequently, an HIV test may not be acceptable to all women in antenatal care. However, a randomised controlled trial examining the uptake and acceptability of antenatal HIV testing concluded that HIV testing is acceptable to most clients[13]. Another study of 'opt out' testing (in which an HIV test is considered routine and is performed unless the patient declines) in non-pregnant women found that uptake of testing increased from 35% to 65% and that HIV testing was acceptable to women[14]. This study also highlighted the value of staff education and of using a specialist midwife to lead the antenatal screening programme. Factors associated with an increased uptake of antenatal testing have been reviewed elsewhere[12,15].

5. Informed consent must be given by those offered the screening test

The HIV antibody test, like all screening tests, requires the informed consent of the client. 'Informed' means that the reasons why the test is being recommended are carefully explained to each client in language they can understand, along with a discussion of the potential advantages and disadvantages of testing, both for the client, her family and her new baby. Additional information relating to the actual test is discussed, as are issues surrounding confidentiality. It is also useful to explain the client's rights to take time to consider her decision, to seek further advice before reaching this decision, and to refuse testing. This discussion, and the response to it, must be documented in the client's case notes.

6. There should be good evidence that the screening programme and associated interventions/prophylaxis effectively reduce infant HIV infection

Mother-to-child-transmission (MTCT) of HIV can occur during pregnancy, but most children become infected from their mothers during or shortly after delivery. There is good quality evidence to show that antiretroviral treatment of infected mothers, or at least a short course of

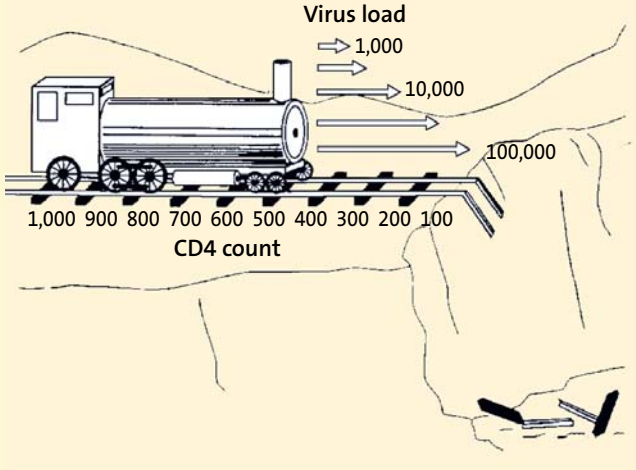

FIGURE 2 Train analogy relating HIV progression to viral load and CD4 count. (From: **Coffin J.M.** HIV viral dynamics. *AIDS* 1996; **10**(suppl. 3): S75-S84. Reprinted by permission of Lippincott, Williams & Wilkins.

antiretroviral prophylaxis will significantly reduce the risk of infants becoming infected. Other important evidence-based interventions to minimise the risk of MTCT of HIV include avoiding breastfeeding when and where it is safe and affordable to do so, and caesarean section delivery. These measures and the supporting evidence of effectiveness have been previously described in more detail in a previous issue of this journal[9] and elsewhere[10]. There is no doubt that the identification of HIV infection in pregnant women during antenatal care facilitates impressive opportunities for providing them with clinically effective interventions that will dramatically reduce their risk of transmitting HIV infection to their newborn infant.

7. Accepted treatment for mothers and infants must be available

Since the early 1990s, effective antiretroviral therapy for HIV disease has been available. This has had a dramatic and beneficial impact on the lives of HIV-infected persons, reducing viral load, increasing peripheral blood $CD4^+$ T-lymphocyte counts, delaying the onset of AIDS and improving quality of life. A variety of antiretroviral drugs is now available, able to interfere with different stages of viral replication, and combinations of different antiretroviral drugs are used in treatment regimens. As antiretroviral therapy is a complex and rapidly evolving specialism, treatment guidelines from the British HIV Association in the UK are regularly updated and available to the public and healthcare professionals on the internet[16]. Additionally, the NHS provides high quality technical facilities for confirming positive test results and an unparalleled quality of treatment and care for all those with HIV disease, including mothers and their children.

8. The costs of the screening programme must be justifiable

In the UK, universal antenatal HIV testing has been assessed as meeting the cost effectiveness criteria applied to other screening programmes and this has been shown for the country as a whole, as well as for most individual health authorities[17]. Identifying pregnant women during antenatal care who are infected with HIV disease allows early access to effective antiretroviral therapy which will significantly delay the onset of serious health problems and frequent periods of expensive inpatient care. Measures taken to minimise the risk of maternal transmission of HIV to infants will have obvious economic and humanitarian benefits.

9. Benefit must be greater than harm

The screening test is usually performed on blood taken from pregnant women for other antenatal screening tests e.g. syphilis, hepatitis B infection, rubella. In the UK, it is highly unlikely that any woman would be physically harmed as a result of venesection, however in resource poor countries there is always the risk of infection from the use of contaminated needles.

In any screening test, there is a risk of a false-positive or false-negative result, but as the HIV test has a validated degree of sensitivity and specificity of over 99.6%, this risk is minimal in properly conducted, quality assured testing programmes. The risk of a false-positive result can be further minimised by using a second test to confirm the result.

There is a risk of psychological unease in being tested for a condition as serious as HIV infection, and in waiting for the results. For women who have a confirmed positive test result, important harms may ensue e.g. rejection, abandonment, abuse, partner violence and physical assault from others. Notification of a positive result can also lead to emotional and psychological distress, such as anxiety, depression and suicide. These potential harms may be minimised by providing counselling support to newly diagnosed women and their partners.

The greatest benefit ensuing from antenatal HIV screening is the opportunity to provide information that will allow pregnant women and their partners to make choices about treatment and access measures to reduce the risk of infection to their baby. Ultimately, each woman needs to consider the balance between the benefits and potential harm to herself and her baby within the context of her own particular family, social, religious and occupational situations.

10. Quality assurance, monitoring and audit procedures must be designed into the programme

Antenatal screening standards in the NHS have been established to ensure that the achievement of the national objective of identifying maternal HIV infection and reducing to an absolute minimum the number of children born with HIV infection, is achieved. Health authorities are required to monitor and audit their antenatal screening programmes and document relevant data. A minimum core of information needs to be collected including the number of women:

- who booked for antenatal care
- who were offered an HIV test
- who decided to accept/decline a test
- who were found to be infected
- who accepted interventions to reduce MTCT transmission as well as which interventions were accepted[17].

Conclusion

Each year, children are born to mothers with unrecognised HIV infection and risk becoming infected. This can largely be avoided by detecting maternal infection during antenatal care and employing a variety of proven interventions to minimise the risk to babies of maternally transmitted HIV infection[9,10,12].

Offering and encouraging antenatal screening for HIV infection to all pregnant women ('universal offer') is at the core of the UK national strategy to ensure that maternal transmission of this deadly virus does not continue to consign some of their children to a lifetime dominated by HIV disease.

Screening offers the opportunity to reduce risk of contracting a disease but this benefit needs to be weighed against possible harms. Assessing screening programmes using established appraisal criteria provides insight into the balance of benefit and harm[1]. Using these criteria to examine antenatal HIV screening suggests that the benefits of screening appear to outweigh harms[12] and that screening offers the best and only chance of reducing risk and protecting babies from HIV infection.

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