Serology testing for syphilis in pregnancy: is it still relevant?

In Focus

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Until the emergence of HIV and other more spectacular viral diseases, syphilis has probably been referred to more than any other infectious disease throughout history – in theatre, literature and politics. During the 19th century, aside from being a notorious disease transmitted sexually, it was the diverse clinical and pathological forms of syphilis which led to much of this mystique and fear.

The main consequences of syphilis are the long-term effects of dementia or damage to the cardiovascular and central nervous systems or transmission to the fetus during pregnancy. Prior to the introduction of the Wassermann complement fixation test in 1906, there was no laboratory confirmation for the diagnosis of syphilis and the manifestations of many other diseases – for example most inflammatory diseases of the eye, a number of psychiatric conditions and congenital malformations – were incorrectly attributed to syphilis.

After the 1940s, a variety of penicillin-based clinical treatments in pregnancy were shown to effectively prevent neonatal transmission of syphilis. Consequently, this disease began to decline. The success of penicillin also reflected a decline in the number of cases of syphilis in the general community.

Antenatal testing

One of the most tragic consequences of syphilis is congenital syphilis. Congenital syphilis is the result of transplacental passage of *Treponema pallidum* from an infected mother. This occurs when a mother is infected or becomes infected during pregnancy. As with other intrauterine infections, there is a widespread spectrum of disease ranging from intrauterine death to mild effects. Because of this wide spectrum, it has been estimated that many infections go unnoticed. However, some specific pathological and radiological signs are unique to this infection.

Serological screening for syphilis during pregnancy is advocated because the effective prevention of congenital syphilis depends on the diagnosis and treatment of the disease in a pregnant woman. Unlike other causes of intrauterine infection such as rubella and cytomegalovirus, syphilis does not have to be acquired during the pregnancy. Serology should be carried out as part of antenatal screening, preferably at the first prenatal visit.

Maternal treatment in preventing congenital syphilis has an overall success rate of >98%. Most failures of maternal treatment in preventing congenital syphilis occur if the mother is in the secondary stage, the most infectious stage of the disease. Success rates of maternal treatment also vary with the gestational age at which treatment is initiated. Most successful outcomes occur when the disease is diagnosed and treated early in the course of the disease, as the success rate in preventing congenital infection may be as low as 90% after 26 weeks. This emphasises the need to test at the first antenatal visit.

Apart from management of the pregnant woman with syphilis, information regarding the disease status of partners must also be obtained. Contact tracing and testing of the partners of women diagnosed with syphilis in pregnancy is important in order to prevent re-infection during the pregnancy. The CDC recommends that these women should also be tested for HIV.

Recently, the testing strategies for syphilis screening in pregnancy have changed largely due to the development of automated enzyme immunoassays using recombinant antigens of *T. pallidum*. Prenatal screening using Reagin serological tests is still feasible and affordable in most undeveloped countries. One issue, however, is that some of these non-treponemal Reagin tests are prone to giving false-positive results in pregnancy. Consequently, all positive results must be confirmed with treponemal-specific tests. Conversely, if treponemal-specific tests are used for screening, a Reagin test (usually RPR) is required to determine the stage of the disease and as a base line for monitoring treatment. Once the mother has been treated during pregnancy, sequential titres using RPR or other Reagin assays should be performed to monitor the response to treatment. Although not common in Australia, serological testing and interpretation of results is complicated in women who have been infected with HIV. This may be further complicated in intravenous drug-users whose serum can give false-positive Reagin tests.

Testing of the newborn

Congenital syphilis is largely a preventable disease. However, it continues to be an important public health problem both in developed and developing countries. Even with treatment during pregnancy, CDC recommendations are that all infants born to women who have positive serological tests during pregnancy should be examined thoroughly for evidence of infection, including microscopic examination of placenta or umbilical cord using a specific fluorescent staining.
Serological evidence of congenital infection in the past could only be established by following the decline of maternal antibody or persistence of antibody in the neonate during the first 6 months of life. This has a number of disadvantages, in that the actual decline in the Reagin will depend on the gestational age of the baby and the titre of Reagin in the mother’s serum at delivery. The development of specific IgM assays, including the IgM FTA, has made the serological diagnosis of syphilis more convenient and practical. Overall, decisions on treatment will result after examination of clinical, laboratory and radiographic evidence of congenital syphilis.

The argument for continued screening

During the 1990s, some experts were suggesting that syphilis would soon be eradicated from Western society. In the USA, syphilis testing was mandatory before marriage licences could be obtained in several States, but over the years this requirement lost support and, as of 2008, Mississippi was the only State in USA still requiring couples to take a blood test for syphilis before marriage. Following these decades of decline, in 2000 overall rates of syphilis began rising throughout the developed world, especially in sexually active homosexual men. An increase in the rates of infectious syphilis in south-eastern Sydney between 1999 and 2004 was reported 5 and continues to the present time (Table 1) 6.

Various factors have been blamed on the resurgence of syphilis in this century, including ‘safe sex fatigue’ and the evidence that decline in safe sex behaviour has occurred since antiretrovirals were introduced in 1990s. In some cases, journalists have blamed the internet for the increase in the sexually transmitted disease due to the rise in the number of net-based networks of infected men seeking partners for unprotected sex.

The Australian national notifications of congenital syphilis rose in 2001 (Table 2) 7, possibly reflecting a spillover into heterosexuals and bisexual males. This figure does not, however, reflect the number of infections diagnosed and treated in pregnancy. In Australia, syphilis screening during pregnancy is reimbursed by Medicare in a series of items. In 2006/07 the cost of reimbursement of these antenatal screening items was more than $9.6m. Antenatal syphilis screening is not itemised separately but is grouped with various combinations of other screening tests, including hepatitis C, hepatitis B and rubella. Thus it is not possible to determine how many syphilis tests were carried out during pregnancy in Australia to estimate a cost benefit analysis.

The resurgence of syphilis infections and the knowledge that congenital syphilis, a devastating disease, can be prevented by antenatal treatment leaves no doubt that testing for syphilis in pregnancy is still relevant. One risk is that, in many people’s minds, the disease does not tend to be associated with patients in higher socioeconomic groups and, to avoid offending these patients, syphilis testing is not included in the request for an antenatal serological screen. There are a number of well documented instances where this has had disastrous consequences. This mindset is also reflected in the changes that were made to the Medicare item for antenatal serological screening – previously it was mandatory to include syphilis testing, but the item was changed so that now syphilis screening in pregnancy has become optional.

References

Peter Robertson supervises the SESAMS Area Serology Laboratory, which is also a State reference laboratory for HIV diagnosis, as well as having an active role in teaching and research. Recently, his main research interest has been in the development and evaluation of an antibody assay for diagnosis of invasive Meningococcal disease (MDM) and for evaluating responses to N meningitidis serogroup C vaccine. He has twice been invited to deliver lectures on serological diagnosis at the National Institute of Health in Maryland USA and has been author of more than 50 publications in refereed journals. One of his most important achievements was using IgA antibody to identify Bordetella pertussis as a major cause of chronic cough in adults, a study he published in 1987. This study prompted developed countries to alter vaccination strategies in an attempt to eliminate this debilitating disease in adults.

Table 1. Infectious syphilis in south-eastern Sydney 2001-2007 6.

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<thead>
<tr>
<th>Year</th>
<th>Patients with infectious syphilis: as a % of population and broken down by gender</th>
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<tbody>
<tr>
<td>2001</td>
<td>0.46% (61.4% male)</td>
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<tr>
<td>2002</td>
<td>0.68 (73.6% male)</td>
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<tr>
<td>2003</td>
<td>1.44 (73.2% male)</td>
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<tr>
<td>2004</td>
<td>1.60 (81.7% male)</td>
</tr>
<tr>
<td>2005</td>
<td>1.39 (83.7% male)</td>
</tr>
<tr>
<td>2006</td>
<td>1.95 (84.8% male)</td>
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<tr>
<td>2007</td>
<td>1.95 (86.1% male)</td>
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Table 2. Notifications of congenital syphilis 7.

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<thead>
<tr>
<th>Year and no. notifications</th>
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<tbody>
<tr>
<td>1998</td>
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<tr>
<td>1999</td>
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<td>2001</td>
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<td>2002</td>
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