Serological diagnosis of syphilis in pregnancy

Experiences at King Edward VIII Hospital, Durban

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Summary

Three different serological screening tests for syphilis were performed at the 'booking' visit of 500 antenatal patients at the King Edward VIII Hospital, Durban. The prevalence of active syphilis was 7,4%. The rapid plasma reagent test not only had a high biological false-positive rate at 11,8%, but also failed to detect 18,9% of the 37 patients diagnosed as having syphilis by means of the IgM-specific fluorescent treponemal antibody absorption (FTA-ABS) test. The *Treponema pallidum* haemagglutination (TPHA) test had a similarly high biological false-positive rate of 15,8%, but did not miss any of the 37 cases of active syphilis. The TPHA test is therefore advocated for screening patients for syphilis.

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In developing countries syphilis remains an important cause of perinatal deaths, with perinatal mortality rates of as high as 8/1 000 total births among unbooked patients.[1] In a perinatal mortality study carried out by Ross *et al.*[2] at King Edward VIII Hospital, Durban, the perinatal mortality due to congenital syphilis was 3,2/1 000 (72% stillborn infants and 28% early neonatal deaths). Accurate diagnosis and early and effective treatment are therefore essential in order to reduce the high perinatal mortality rate.

The diagnosis of syphilis depends on obtaining a history of contacts, finding the typical lesions of the different stages of disease, and serological testing. The clinical features of primary syphilis are uncommon in pregnancy because the lesions (primary chancre) may be mild or undetectable, or occur on the cervix.[3] The lesions seen most commonly in secondary syphilis in pregnancy are condylomata lata. Constitutional symptoms are usually slight and are often unrecognized. The diagnosis of syphilis in pregnancy is therefore mainly based on the results of serological testing or on the presence of syphilitic infection in the newborn infant.

The serological methods used to diagnose syphilis vary in their sensitivity in detecting *Treponema pallidum*. In an unpublished study performed in Durban by I. Hoosen (personal communication, 1979), unsatisfactory results were obtained with both the rapid plasma reagent (RPR) and the *T. pallidum* haemagglutination (TPHA) tests in antenatal screening for syphilis. Of 200 patients screened, 63 had a positive fluorescent treponemal antibody absorption (FTA-ABS) test. Eighteen of these had IgM-type antibodies, suggesting active infection. If we accept the FTA-ABS test as the standard by which the serological diagnosis of syphilis is made, then 11,8% of the results of the RPR test were false-positive, and 5 of 18 cases of active syphilis were missed. The TPHA test also missed 5 cases of active syphilis.

The present study was conducted in order to: (*i*) evaluate and compare the serological tests available for the diagnosis of syphilis; (*ii*) establish the prevalence of syphilis; (*iii*) establish the incidence of congenital syphilis in babies whose mothers had been treated for syphilis; and (*iv*) propose ways and means of improving the serological diagnosis of syphilis at King Edward VIII Hospital.

Patients and methods

The 500 patients attending the antenatal clinic of King Edward VIII Hospital underwent the following serological tests at their first antenatal 'booking' visit: the RPR, TPHA and FTA-ABS tests. The FTA-ABS test was taken as the standard by which the diagnosis of syphilis was made. All serological testing was performed by a senior technician and the results were obtained within a week. The diagnosis of syphilis was made only if the FTA-ABS test was positive. Patients in whom the diagnosis of syphilis was established were referred to the venereal disease clinic for treatment and follow-up. An FTA-ABS test was performed on all newborn infants whose mothers had positive serological test results for syphilis. Both IgG- and IgM-specific FTA-ABS studies were performed on cord blood.

Treatment

Mothers: Treatment consisted of 2 doses of 2 400 000 IU benzathine penicillin (Penilente) given 7 days apart.

Infants: A positive FTA-ABS test for IgM was regarded as indicating fetal infection. An FTA-ABS test was performed on the cerebrospinal fluid of all newborn infants with IgM antibodies. If the result was positive the infant was treated with penicillin G 100 000 U/kg/d for 10 days. Penicillin G is used because it crosses the blood-brain barrier. A single dose of benzathine penicillin 50 000 IU/kg was given to infants with a negative cerebrospinal fluid FTA-ABS test result.

Results

Five hundred antenatal patients were included in the study, their ages ranging from 16 to 43 years (mean age 26,2 years). Of the group, 19,4% were nulliparas, 69,2% had 1 - 4 children and 11,4% 5 or more. Three per cent were under 12 weeks, 17% 12 - 20 weeks, 42,1% 21 - 30 weeks, 36,6% 31 - 36 weeks, and 1,1% 37 or more weeks pregnant. The mean gestational age was 28,1 weeks, and the parity 2,1.

Results of the serological tests are shown in Table I. All 3 tests were negative in 373 patients (74,6%). Fifty-one patients (10,2%) had a positive RPR test, while in 57 (11,4%) positive TPHA results were obtained. One hundred and fifteen patients (23%) had a positive FTA-ABS test for IgG; 37 of these (7,4%) had positive IgM-specific FTA-ABS test results.

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TABLE I. RESULTS OF THE SEROLOGICAL TESTS

	RPR +ve				RPR −ve					
	TPHA +ve		TPHA −ve		TPHA +ve		TPHA −ve		Total	
FTA-ABS	No.	%	No.	%	No.	%	No.	%	No.	%
+ve IgG, +ve IgM	30	6,0	0		7	1,4	0		37	7,4
+ve IgG, −ve IgM	7	1,4	8	1,6	4	0,8	59	11,8	78	15,6
−ve IgG, −ve IgM	3	0,6	3	0,6	6	1,2	373	74,6	385	77,0
Total	40	8,0	11	2,2	17	3,4	432	86,4	500	100

The results of the RPR and TPHA tests correlated well ($\phi = 0{,}58$; $P < 0{,}001$), differing in only 5,6 % of all cases. Diagnostic indices for the two tests (Table II) show that the TPHA and RPR tests have similar potential for diagnosing syphilis. The low sensitivity indicates that less than half of all patients with syphilis are diagnosed on the basis of the RPR and TPHA tests.

TABLE II. DIAGNOSTIC INDICES FOR THE TPHA AND RPR TESTS

	TPHA	RPR
Sensitivity	**41,7%**	**39,1%**
Specificity	**97,7%**	**98,4%**
False-positive rate	**15,8%**	**11,8%**
False-negative rate*	**15,1%**	**15,6%**
Validity	**84,8%**	**84,8%**

*The TPHA test did not miss any cases of active syphilis.

Of the 115 babies born to mothers with positive serological tests for syphilis, 83 were lost to follow-up. Results of the FTA-ABS test on cord blood of the remaining 32 babies are shown in Table III. Fourteen of the infants with a positive serological IgM-specific FTA-ABS test did not show evidence of neurosyphilis, as the cerebrospinal FTA-ABS test was negative in these babies.

TABLE III. FTA-ABS TEST RESULTS IN THE NEWBORN INFANTS

	No.	%
+ve IgG, +ve IgM	**15**	**46,9**
+ve IgG, −ve IgM	**2**	**6,2**
−ve IgG, −ve IgM	**15**	**46,9**
Total	**32**	

Discussion

A number of serological tests are available for the diagnosis of syphilis. These tests detect two basic types of antibodies, to (*i*) non-treponemal lipoidal antigens; and (*ii*) specific treponemal antigens. In category (*i*) we have flocculation tests (VDRL), complement fixation tests (Wassermann reaction) and agglutination tests (RPR). In category (*ii*), the *T. pallidum* immobilization (TPI) test is generally regarded as the most sensitive, but is an expensive and laborious procedure. For all practical purposes, the FTA-ABS test is regarded as being diagnostic of syphilis. The overall prevalence of syphilis in this study of syphilitic contact and active infection was 23%. The prevalence of active syphilis was 7,4%. These figures are extremely high, and indicate that 1 in every 13 patients presenting at the antenatal clinic has active syphilis.

One of the surprising features of this study was the high incidence of IgM-specific antibodies (indicating active infection) in the newborn infants of mothers who had syphilis. It is generally accepted that if the mothers are treated in early pregnancy the infant is usually cured. Despite treatment of the mothers, whose average gestational age was 29 weeks at the time of diagnosis, 15 of the 32 babies who had diagnostic tests had an active infection. Holder and Knox[3] have shown that although treatment will cure the spirochaetaemia in the fetus, it does not entirely prevent the late development of the stigmata of congenital syphilis. It is therefore possible that the fetuses were mature enough to produce IgM antibodies, which were detected at birth. Alternative explanations for the high incidence of IgM antibodies are that treatment may have been inadequate, or may have been given too late in pregnancy.

These results in the newborn make a strong case for the treatment of all newborn infants of syphilitic mothers where facilities are not available for the performance of specific tests to confirm or refute a Wassermann or RPR test in the newborn. A positive Wassermann reaction and RPR test in the newborn signifies a passive transfer of antibodies from the mother or an active infection.

The RPR test not only showed a high false-positive rate of 11,8% but also failed to detect 7 (18,9%) of the 37 patients diagnosed as having active syphilis with the IgM-specific FTA-ABS test. This shortcoming is surprising because the reagin tests are reported to detect mainly IgM-type antibody. Therefore although the RPR test showed a validity of 84,8% with the FTA-ABS test (Table II), its sole use for the screening of syphilis in this study shows definite drawbacks.

In comparison with the FTA-ABS test, the TPHA test also showed a validity of 84,8% (Table II). In comparison with the RPR test, the results of TPHA testing were 94,4% true, but the TPHA test did not miss any of the 37 cases of active syphilis (Table I). The incidence of false-positive results was 15,8%, slightly higher than that of the RPR test.

From the results of this study it would seem that the RPR or the TPHA test alone would have a high incidence of false-positive results, and that the RPR test will not detect approximately 20% of cases of active syphilis. We therefore recommend that:

1. All pregnant patients have a TPHA test performed on admission as a screening test. This would certainly decrease the false-negative result rate. The FTA-ABS test should be used as a confirmatory test.
2. The TPHA test should be repeated late in pregnancy, after the 36th week, in order to detect patients who have contracted the disease during or late in pregnancy.
3. Although adequate therapy with penicillin for the mother probably prevents congenital syphilis, nevertheless ideally all infants of syphilitic mothers should have IgM- and IgG-specific FTA-ABS antibody tests performed. If the FTA-ABS test is positive the infant should have a cerebrospinal fluid examination.
4. Because of the high incidence of syphilis at King Edward VIII Hospital, all unbooked patients should have a TPHA test on admission. All babies born of unbooked mothers should be investigated to exclude congenital syphilis.
5. The FTA-ABS test should be used to detect syphilis in patients with unexplained stillbirths, neonatal deaths and abortion.

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