Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2024, 14, 102-109
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

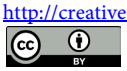
Infectious Disease Update in Obstetrics: A Modern Approach to the Patient with a Positive Screening Test for Syphyilis in Pregnancy

Papa Essilfie

Wigan, Wrtinghton and Leigh Teaching Hospitals, Wigan Lane, Wigan, UK
Email: papaessilfie@doctors.org.uk

How to cite this paper: Essilfie, P. (2024) Infectious Disease Update in Obstetrics: A Modern Approach to the Patient with a Positive Screening Test for Syphyilis in Pregnancy. *Open Journal of Obstetrics and Gynecology*, **14**, 102-109.
https://doi.org/10.4236/ojog.2024.141011

Received: October 1, 2023
Accepted: January 21, 2024
Published: January 24, 2024



Abstract

Screening for maternal syphilis has been an essential component of routine antenatal screening tests in most countries for many years. This is not only because of the virulence of the spirochete which causes the infection but also because of its vertical transmission rate and the potential severe adverse complications/morbidity that can result from its transmission to the fetus. Although the incidence of maternal syphilis and its fetal sequalae in low-income countries has been considerable for several years, the disease has been almost non-existent in high income countries with wide antenatal screening coverage and effective treatment programmes for Syphilis. The recent alarming increase in the incidence of maternal syphilis in high income countries has spawned a renewed public health interest in the infection, with several countries updating and strengthening public health guidance in an attempt to stem this dramatic trend. This is a short clinical update for the practising obstetrician on how to manage the antenatal patient with a positive syphilis screening test.

Keywords

Treponema Pallidum, Chancre, Condyloma Lata, Gummas, VDRL Test, RPR Test, Revere-Sequence Testing, Jarisch-Herxheimer Reaction

1. Introduction

For decades this century, congenital syphilis was considered a disease of the past in many developed countries. Whilst the burden of disease has remained considerable in Sub-Saharan Africa and other developing countries, congenital syphilis

has been a condition largely confined to textbooks in several western countries where Antenatal screening tests for maternal syphilis are often well-developed.

In 2016, the WHO estimated global maternal syphilis prevalence to be 690 per 100,000 women. The global rate for congenital syphilis for the same year was 473 per 100,000 [1] [2]. As might be expected most of these cases were recorded in low-income countries. Over the last few years however, there has been a steady increase in the prevalence and incidence of Syphilis even in high income countries. This increase has led to a dramatic rise in the incidence of congenital syphilis. From 2012 to 2020, the USA reported a nearly 7-fold increase in the incidence of Congenital syphilis (from 8.4 per 100,000 births to 57.3 cases per 100,000 births) [3] [4]. In England, there were 7982 diagnoses of Syphilis in 2019, a 200% increase since 2010 [5]. Although most of the cases in England were recorded in Gay and bisexual men (Men who have sex with men, MSM), the diagnosis of Syphilis in heterosexual women increased by at least 35% between 2013 and 2018 [6] [7]. This rise in incidence in the heterosexual population is reflected in the increased incidence of congenital syphilis in the UK and indeed across Europe.

These alarming statistics make it imperative for public health systems to maintain vigilance in the screening, treatment, and appropriate follow up of pregnant women who test positively for Syphilis infection.

This is a short update for the obstetrician on the modern approach to a pregnant woman with a positive syphilis screening test in a high-income country setting.

2. Clinical Features

Syphilis is caused by the bacterium Treponema Pallidum, subspecies Pallidum. It is a sexually transmitted infection. Infection can also occur through vertical transmission when the pathogen is passed from mother to child before or shortly after birth.

The infection begins when the bacterium penetrates dermal micro-abrasions or intact mucous membranes, often resulting in a chancre (a firm ulcerative painless lesion) and enlarged local lymph nodes at the site of inoculation. The chancre can appear around the external genitalia *i.e.*, on or around the penis, vagina, cervix, or anus. It may also appear in the rectum or in the mouth. It's painless nature and occasional cryptic location can sometimes delay the diagnosis of the infection at this stage. There are four recognized stages of the infection: Primary stage, Secondary stage, Latent stage, and Tertiary Syphilis.

The first stage (Primary Syphilis) is characterized by a chancre and local lymphadenopathy. This asymptomatic chancre often heals spontaneously without scarring within 3 to 6 weeks if left untreated. If treated the lesion heals within days.

The second stage (Secondary Syphilis) occurs between 1 to 3 months after the initial infection if a patient is not treated. Symptoms at this stage may include a

flu like illness with headache, sore throat, generalized lymphadenopathy, myalgia, and arthralgia. Skin manifestations include a generalized maculopapular rash involving the palms/soles, and Condylomata Lata (wart-like lesions usually found on the genitals or in the perineum). Symptoms of secondary syphilis usually resolve over 3 to 12 weeks.

The Latent stage of Syphilis is further divided into 2 substages, early Latent stage (less than 1 year of infection) and Late Latent stage (more than 1 year of infection). Latent stage syphilis occurs when Secondary syphilis is left untreated. During the Latent stage there are no symptoms, and the infection can only be detected by serological tests.

The fourth stage (Tertiary Syphilis) occurs 15 to 20 years after the initial infection if an infected patient receives no treatment. It is caused by an immune response to low level chronic infection and is characterized by cardiovascular signs (aortic aneurysm, aortic valvular disease or coronary artery disease), gummas, condyloma lata or late neurosyphilis.

3. Diagnosis

Treponema Pallidum bacteria can be identified with darkfield microscopy of exudate (fluid) from a syphilitic lesion. Diagnosis can also be confirmed by a PCR test, immunohistochemistry, or special staining of lesions from infected tissue. Because these tests are largely unavailable in many clinical settings, the cornerstone of diagnosis of syphilis infection is serological testing.

There are 2 groups of serologic tests for Syphilis-Treponemal and Nontreponemal tests.

Non treponemal tests (VDRL and RPR) measure concentrations of total immunoglobulin antibodies against lipoidal antigens released from damaged host cells as a result of T. Pallidum infection. In many developing countries as well as some developed countries (eg Netherlands), antenatal screening tests for syphilis are non-treponemal tests. Non-treponemal tests can be quantified using a titre. Titre levels are used to monitor the response to treatment and to detect the presence of new infections. Adequate treatment usually results in a fourfold reduction of titres within 12 - 24 months. False positive RPR tests can occur in certain infections (Epstein-Barr Virus, Hepatitis, HIV, Varicella, measles, tuberculosis, and endocarditis), Malaria, certain connective tissue disorders, and lymphoma [3]. Interestingly, pregnancy can also cause a false positive RPR result. It is therefore essential that positive non-treponemal tests are confirmed by Treponemal tests. False negative RPR tests can occasionally occur in early, incubating syphilis when there is a very high concentration of antibodies that block the antigen-antibody reaction to RPR. This phenomenon, known as the Prozone reaction occurs when the high antibody titre interferes with the formation of the usual antigen-antibody lattice necessary to visualize a positive flocculation test.

Treponemal tests detect antibodies against Treponema pallidum. In these tests surface antigens of T. Pallidum are combined with a patient's serum to show a

reaction to specific antibodies. Treponemal tests include Treponema Pallidum agglutination test (TP-PA test), fluorescent treponemal antibody absorption test (FTA-ABS test), Treponema Pallidum Enzyme immunoassay (TP-EIA test) and Treponema Pallidum Chemiluminescence test (TP-CIA test). Treponemal tests will generally remain positive for the rest of a patient's life despite successful treatment. In a few patients (15% - 20%), these tests may become negative (revert to non-reactive Treponemal test status) in 2 - 3 years if the infection is treated at the primary stage [3]. Although they are more specific than non-treponemal tests, treponemal tests can also occasionally be falsely positive in certain rare infections e.g., Borrelia Burgdorferi infections or other non-venereal trepanomatoses [2]. In the UK, Public health England (PHE), recommends that an initial positive treponemal test should be confirmed by a second (confirmatory) test using an alternative treponemal antibody.

3.1. Mother to Child Transmission

Transplacental transmission of Syphilis can occur at any stage of the disease and at any gestational age of the pregnancy. The rate of transmission depends on the stage of the disease in pregnancy. It also depends on the gestational age at which infection occurs, with increased transmission rates when infection occurs in the 2nd half of pregnancy. Generally, transmission rates of 40% - 90% are quoted for primary or secondary maternal syphilis whilst latent stage disease has lower rates of transmission (with 40% transmission rate for early latent phase and <10% transmission rate for Late, latent stage disease) [2]. It is important for patients to understand that transmission is still possible several years after the initial infection. In the United Kingdom, vertical transmission is rare because of the high uptake of maternal syphilis screening (>99%). It is worth noting, that globally, an estimated 40% of infected babies will either be still-born or die in the neonatal period because of Syphilis infection [6]. To reduce world-wide transmission rates, all pregnant women who are syphilis seropositive should be offered penicillin treatment.

3.2. Fetal Complications of Maternal Syphillis Infection

Untreated maternal syphilis can result in various adverse fetal outcomes. From as early as 14 weeks gestation, spirochete bacteria can cross the placenta and cause fetal infection leading to fetal loss [6].

In the 2nd and 3rd trimesters, fetal infection can cause fetal hepatic dysfunction and hepatomegaly. Placental involvement may lead to placentomegaly (which can be detected on obstetric ultrasound scan). Fetal thrombocytopenia, anaemia and ascites may result from the infection. Where the infection is severe, Fetal hydrops may occur as a result of disseminated damage to endothelial cells with consequent fluid shifts. Severe infection may also result in distorted fetal long bones.

Fetal growth restriction, Preterm delivery, intrauterine fetal death (IUFD) and

the delivery of a small for gestational age baby (SGA) may all result from Maternal Syphilis infection.

3.3. Management of the Pregnant Patient with a Positive Treponemal Test

The approach to the pregnant patient with a positive syphilis screening test must be multidisciplinary. The patient must be managed by a team consisting of Antenatal screening midwives, an Obstetrician with a special interest in infectious diseases in pregnancy, fetal medicine specialists, genitourinary medicine specialists (GUM Physicians), microbiologists and paediatricians. Regular correspondence between these specialists is essential for the appropriate care of the patient. In our Unit (as well as in many other Hospitals in the United Kingdom), the antenatal screening test of choice for Syphilis is the Treponemal antibody test. A confirmatory test with an alternative Treponemal antibody is requested once an initial test is reported as positive. When both tests are positive, a qualitative non-treponemal test (RPR) is performed. This is followed by a quantitative RPR test to obtain titre levels. The process of initially obtaining a Treponemal test, followed by a non-treponemal test is referred to as reverse-sequence testing.

The patient must be informed of the positive test result in a sensitive manner. In the UK, Hepatitis and HIV screening forms part of routine antenatal screening tests. Vaginal swabs to rule out other STD's (sexually transmitted diseases) should be performed. Immediate referral to GUM services is always arranged after a positive Syphilis test. Initial treatment, contact tracing/partner notification and further testing is supervised by GUM physicians. In the UK, high risk patients with suspected infection who decline testing or those with confirmed syphilis who decline treatment and then knowingly transmit the infection (via sexual or non-sexual contact) to others are liable to prosecution by the Crown Prosecution service (CPS).

Fetal medicine specialists should be notified of the test results. Characteristic features of fetal infection that may be noted on the Mid-trimester routine Obstetric fetal anomaly ultrasound scan include placentomegaly, hepatosplenomegaly, intrahepatic calcifications, and ascites. These features must be looked for on the routine mid trimester fetal anomaly ultrasound scan in a woman with a positive syphilis test. Where there is a significant chance of fetal infection (e.g., in Primary, secondary, or early latent infection), it may be prudent to arrange Obstetric fetal growth scans as fetal growth restriction or a small for gestational age baby (SGA) may be the only manifestations of fetal infection.

3.4. Treatment

A woman who tests positive for syphilis in pregnancy should be treated as early as possible. Treating maternal syphilis 30 days (or earlier) before the delivery of the baby greatly reduces the risk of vertical transmission and perinatal

mortality [6]. In our unit, treatment is supervised by the local GUM department.

Parenteral Penicillin G is the recommended treatment for Syphilis. The duration of treatment depends on:

1) the stage of infection

and

2) the gestational age at which infection occurs.

Whilst the WHO recommends a stat dose of 2.4 million units Intramuscular penicillin G for early-stage disease, latent and tertiary syphilis require a longer duration of treatment. In the USA, the CDC (Centre for Disease Control) recommends 3 weekly doses of Benzathine Penicillin G (2.4 million units per week) for late latent phase, unknown-duration, or tertiary Syphilis [1].

Penicillin is the only antibiotic that crosses the placenta in sufficient levels to prevent or treat infection in the fetus [3]. In early gestations (1st and 2nd trimester), a single dose is regarded as adequate treatment for early-stage disease. In the 3rd trimester a second dose is recommended when treating early-stage disease because of lower serum concentrations of the drug and the potential risk of treatment failure. Because penicillin is the only drug known to prevent congenital syphilis, desensitization in a hospital setting should be considered in patients who report sensitivity to the drug. When major allergy makes it impossible to use the drug, cephalosporin can be used as an alternative. The dosage suggested by BASHH (British association of sexual health) is intramuscular (IM) ceftriaxone 500 mg daily for 10 days [6].

An occasional complication of the treatment of syphilis is the Jarisch-Herxheimer reaction. This reaction may complicate some 45% of treatments in pregnancy [6]. It occurs as a result of the killing of a large number of T. Pallidum spirochaetes. This leads to the production of nonendotxin pyrogens, spirochaetal lipoproteins, and a subsequent acute inflammatory reaction. The complication is commoner in the treatment of early-stage disease, with the highest incidence in treatment of secondary syphilis. Symptoms usually occur in the first 24 hours of treatment and include fever, chills, myalgia, headache, hypotension, and a skin rash. In pregnant women uterine contractions and preterm labour can occur. Management of this complication is largely supportive as all the symptoms are self-limiting. Because of the risk of preterm labour in patients who develop this complication, pregnant women with early-stage disease should be informed and educated about this reaction before treatment is commenced. They should be given advise on the importance of close access to in-patient hospital facilities during treatment. For preterm pregnant patients who live in remote areas, a short period of hospital admission when treating early-stage syphilis (particularly secondary syphilis) may be necessary. This would facilitate the prompt administration of intramuscular steroids (for the prevention of neonatal respiratory distress) and peri-partum Magnesium sulphate (for fetal neuroprotection) if threatened preterm labour ensues.

3.5. Neonatal Considerations

The importance of keeping paediatricians informed when treating a pregnant woman with a positive syphilis test cannot be overemphasized. Multidisciplinary meetings (and regular correspondence) between relevant specialists (Obstetricians, GUM physicians, paediatricians, screening midwives etc.) are essential in providing a platform necessary for formulating an appropriate management plan for the baby once it's born.

Congenital syphilis is classified as early disease (occurring from birth to 2 years of life) or late disease (occurring after 2 years of age). Signs and symptoms of early disease include hepatosplenomegaly, haemolytic anaemia, uveitis, Optic atrophy, generalized lymphadenopathy, a disseminated bullous rash, thrombocytopenia, periostitis, desquamation involving the palms and soles, meningitis, and interstitial keratitis. A comprehensive examination of the neonate by a paediatrician looking for any of these signs should be performed soon after birth. It is important to note that 70% of infected neonates may be asymptomatic.

Where the index of suspicion is high in spite of a normal physical examination (e.g., when the mother contracts primary/secondary syphilis in pregnancy or where there were Obstetric ultrasound features in the antenatal period suggestive of fetal infection), serological investigations are recommended. Neonatal serology can be complicated by the presence of transplacentally acquired IgG antibodies from the mother. However, a neonatal non-treponemal antibody titre more than 4 times the maternal titre would support active infection as such a high ratio is unlikely to be achieved by passive transfer [5]. Other investigations that may be indicated include PCR tests of nasopharyngeal aspirates, full blood count, liver function tests, serum inflammatory markers, lumber puncture, and long bone X-rays. Occasionally specialist ophthalmologic reviews and hearing tests may be useful.

4. Conclusion

In 2019, Public Health England (PHE) published an action plan to address the rapid increase in the incidence of Syphilis in England. In addition to targeting the highest risk group (Men who have sex with men, MSM), the plan also stressed the importance of maintaining high antenatal screening coverage and improving vigilance in the detection of the infection throughout antenatal care. Current guidelines in England recommend screening for syphilis once in the first trimester. It is interesting to note that there have been several cases of congenital syphilis where a mother screened negatively at her routine first trimester screening test. This is not surprising as the infection can be contracted much later in the pregnancy, (*i.e.*, after the first trimester screening test has been reported). For this reason, PHE recommends in its current guidance, that women who are deemed high risk (e.g., those with multiple sex partners, sex workers etc.) be offered repeat testing every 3 months throughout the entire pregnancy. Until such recommendations become routine practice in England, clinicians

should remain alert and at the very least consider the infection as a differential diagnosis in neonates who have suggestive symptoms and signs (even where the initial antenatal first trimester screening was negative).

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

[1] Gullete, D. and Hopkins, K. (2021) Syphilis: An Elusive Diagnosis. *The Journal for Nurse Practitioners*, **17**, 189-193. https://doi.org/10.1016/j.nurpra.2021.10.003

[2] Keuning, M., Kemp, G.A., Schonenberg-Mienema, D., Dorigo-Zetsma, J., Van Zuiden, J.M. and Pajkrt, D. (2020) Congenital Syphilis, the Great Imitator: Case Report and Review. *The Lancet Infectious Diseases*, **20**, 73-79. https://doi.org/10.1016/S1473-3099(20)30268-1

[3] Fang, J., Partridge, E., Bautista, G.M. and Sankaran, D. (2022) Congenital Syphilis Epidemiology, Prevention and Management in the United States: A 2022 Update. *Cureus*, **14**, e33009.

[4] Haroon, S., Sithermbiso, V., Yasmin, G., Nike, A., *et al.* (2004) The Prevention and Management of Congenital Syphilis: An Overview and Recommendations. *Bulletin of World Health Organization*, **6**, 424-430.

[5] Fifer, H., Hughes, G. and Ladhani, S. (2021) Shining the Light on Congenital Syphilis: From TORCH to SCORTCH. *Archives of Disease in Childhood*, **106**, 937-938. https://doi.org/10.1136/archdischild-2019-318503

[6] Dewick, L., Jayaprakasan, K. and Raouf, S. (2020) Syphilis in Pregnancy: Identifying and Managing a Historic Problem on the Rise. *The Obstetrician & Gynaecologist*, **22**, 209-216. https://doi.org/10.1111/tog.12669

[7] Teles, H., Cachao, J., Olivera, I. and Neves, V.H. (2020) Symptomatic Congenital Syphilis: Still a Reality. *BMJ Case Reports*, **13**, e234812. https://doi.org/10.1136/bcr-2020-234812