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# Deceptive Venereal Disease Research Laboratory Test in Pregnancy: A Clinical Case Report

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## Abstract

In Portugal, during pregnancy monitoring, syphilis screening is carried out using the venereal disease research laboratory (VDRL) test, despite pregnancy being a known cause of false-positive VDRL results. This case describes a 34-year-old woman in a stable relationship for about five years. She attended a consultation with a probable seven-week pregnancy, and first-trimester blood tests were requested. Two weeks later, during a maternal health consultation at a gestational age of nine weeks and one day, she presented the results, which revealed a positive VDRL test. New tests were requested for both the pregnant woman and her partner, including VDRL, rapid plasma reagin (RPR), and *Treponema pallidum* hemagglutination assay (TPHA), all of which were negative in both individuals. A false-positive VDRL result was therefore considered the most likely explanation, and both the pregnant woman and her partner were reassured. Pregnancy is a challenging period, and a positive analytical result indicating a sexually transmitted infection can be disturbing for both the pregnant woman and the couple's relationship. This case highlights the importance of informing patients, when requesting VDRL testing during pregnancy, about the possibility of false-positive results.

**Categories:** Obstetrics/Gynecology, Family/General Practice
**Keywords:** false-positive test, family medicine, pregnancy, syphilis screening, vdrl

## Introduction

Pregnancy monitoring is essential to ensure appropriate maternal and fetal health. In Portugal, for low-risk pregnancies, the first prenatal consultation should be scheduled no later than 12 weeks of gestation [1]. Following the initial consultation, regular prenatal follow-up is recommended to provide early detection of potentially harmful conditions for the mother and/or the baby, of which syphilis is one.

Syphilis is a systemic sexually transmitted infection (STI) characterized by different stages, with different clinical manifestations, varying from local symptoms, as in primary syphilis, to multisystemic and debilitating consequences, such as the cardiac and neurologic effects of tertiary syphilis. However, syphilis can also be transmitted from mother to child during pregnancy (with an infection rate above 70%), leading to congenital syphilis [2], which is associated with relevant and chronic sequelae, such as bone deformations, scarring, and gumma (a noncancerous, granuloma-like growth specific to syphilis) formation [3]. Considering the debilitating consequences of congenital syphilis and the long periods during which the mother can remain asymptomatic, it is a priority to screen all pregnant women for syphilis [4].

Syphilis is usually screened for by measuring one of the following: treponemal tests (TTs), such as the *Treponema pallidum* hemagglutination assay (TPHA), which detects antibodies against specific *Treponema pallidum* antigens, and non-treponemal tests (NTTs), such as the venereal disease research laboratory (VDRL) test, which detects nonspecific antibodies against cardiolipin antigens present in, but not limited to, the membrane of *Treponema pallidum*. This predisposes NTT to become reactive in other conditions, such as infections and autoimmune reactions, requiring a reflex TT to confirm the diagnosis. In Portugal, syphilis screening during pregnancy is recommended using the VDRL test during the first and third trimesters [1]. Pregnancy is a recognized cause of false-positive VDRL results, making it essential to distinguish between a false-positive result and a true syphilis infection [2].

Throughout pregnancy, healthcare professionals, particularly those involved in prenatal care, develop a close therapeutic relationship with the pregnant woman. This allows them to provide support during the physical and emotional adaptation to pregnancy while also addressing the challenges that may arise for the couple during this period. Therefore, an unexpected positive test result suggesting an STI may have a significant emotional impact, not only on the pregnant woman but also on the couple's relationship. Accurate interpretation of VDRL results and clear communication are therefore essential to avoid unnecessary distress and provide appropriate reassurance and support. Given the lack of literature on the emotional impact of false-positive results in pregnancy, we present a case report that illustrates a false-positive VDRL result during pregnancy, highlighting how to manage it and the importance of clear communication with the patient and her partner. Written informed consent for the publication of this case report was obtained from the couple.

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## Case Presentation

A 34-year-old Portuguese woman attended a consultation with her family physician due to amenorrhea and a beta-human chorionic gonadotropin (β-hCG) level of 488 mIU/mL (Table *1*). Although she was uncertain of the date of her last menstrual period, she was estimated to be approximately seven weeks pregnant and had started taking 5 mg of folic acid daily.

| Consultation date | Sample collection date | Gestational age (dating method) | Test | Method | Result | Reference range | Clinical interpretation |
|---|---|---|---|---|---|---|---|
| Pregnant woman | | | | | | | |
| 16/09/2024 | 02/09/2024 | 7 weeks (LMP) | β-hCG | ECLIA | 488 mIU/mL | Non-pregnant ≤ 5 mIU/mL | Positive; confirms pregnancy. LMP was uncertain, so gestational age was established by ultrasound dating. |
| 30/09/2024 | 25/09/2024 | 9+1 weeks (ultrasound) | VDRL | Agglutination with titration | Reactive, with titer 1:2 | < 1:2 | Non-treponemal test reactive; confirmatory testing required |
| | | | Toxoplasmosis (IgG and IgM) | ECLIA | IgG: < 1 kUI/L IgM: Non-reactive | IgG: Non-immune ≤ 6 kUI/L IgM: n/r | No other infection identified on the screening panel |
| | | | HIV-1 and HIV-2 antibodies | ECLIA | Non-reactive | n/r | |
| | | | HBsAg | ECLIA | Non-reactive | n/r | |
| | | | HCV antibody | ECLIA | Non-reactive | n/r | |
| 14/10/2024 | 02/10/2024 | 11+1 weeks (ultrasound) | VDRL | Agglutination with titration | Non-reactive | < 1:2 | Repeat non-treponemal tests non-reactive and treponemal test negative: initial VDRL result interpreted as a biological false positive |
| | | | RPR | Charcoal particle flocculation | Non-reactive | n/r | |
| | | | TPHA | Hemagglutination | Non-reactive | n/r | |
| 17/04/2025 | 12/03/2025 | 33+1 weeks (ultrasound) | VDRL | Agglutination with titration | Non-reactive | < 1:2 | Persistently non-reactive VDRL in the third trimester; supports a false-positive result |
| Partner | | | | | | | |
| 14/10/2024 | 10/10/2024 | n/a | VDRL | Agglutination with titration | Non-reactive | < 1:2 | No serological evidence of syphilis in the partner |
| | | | RPR | Charcoal particle flocculation | Non-reactive | n/r | |
| | | | TPHA | Hemagglutination | Non-reactive | n/r | |

**TABLE 1: Laboratory results and clinical course of the couple.**

LMP, last menstrual period; β-hCG, beta-human chorionic gonadotropin; ECLIA, electrochemiluminescence immunoassay; n/a, not applicable; VDRL, venereal disease research laboratory; Ig, immunoglobulin; n/r, not reported; HIV-1, human immunodeficiency virus type 1; HIV-2, human immunodeficiency virus type 2; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; RPR, rapid plasma reagin; TPHA, *Treponema pallidum* hemagglutination assay

First-trimester blood tests were requested, and she was referred to the hospital in her area of residence to undergo first-trimester combined screening. Two weeks later, she attended a maternal health consultation,

where her gestational age, established by dating ultrasound, was nine weeks and one day. She presented the laboratory results, which revealed reactive VDRL, non-immune toxoplasmosis, non-reactive human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) antibodies, non-reactive hepatitis B surface antigen (HBsAg), and non-reactive hepatitis C virus (HCV) antibody (Table *1*). She arrived at the consultation very worried about the positive result. She was also anxious about the possibility of infidelity by her partner and about the future of the baby, and she cried during the consultation. Through empathy and active listening, she felt heard and supported, and her distress and concerns were acknowledged.

Following the reactive VDRL result, a complete physical examination was performed to exclude clinical signs of syphilis. The skin and mucous membranes were carefully inspected, with no rash (including on the palms and soles), no oral lesions, and no condylomata lata. The genital, anal, and perianal regions showed no ulcers or other lesions suggestive of a primary chancre. There was no palpable lymphadenopathy, and the neurological examination was normal, with no neurological symptoms reported. Cardiopulmonary auscultation was also performed and was normal. Her vital signs, routinely measured by the family nurse at every consultation, were always within normal limits.

An explanation was provided, and the possibility of a false-positive result was discussed given the absence of clinical signs of syphilis. It was proposed that, if the patient felt calmer and her partner agreed, he could also be tested and that she would be retested as well. She was a healthy woman, with no significant past medical history, no laboratory abnormalities in the previous pregnancy, no previous STIs, and up-to-date vaccinations. She worked as a human resources consultant and had been in a stable relationship for five years, with whom she had a two-year-old child.

To clarify the situation, new tests were requested at a different laboratory for both the pregnant woman and her partner, who agreed and considered it appropriate to be tested as well. Given the clinical context, the couple's investment in the issue, and the fact that the results would be sent swiftly, the medical team opted to wait for the results before treating for possible syphilis.

Two weeks later, the pregnant woman returned for a follow-up consultation and presented the results, which were non-reactive VDRL, non-reactive rapid plasma reagin (RPR), and non-reactive TPHA in both individuals. The initially reactive VDRL was considered a probable false-positive reaction, supported by the follow-up laboratory results (Table *1*) and by the absence of clinical signs of syphilis, relevant past medical history, or evidence of laboratory error. The couple was visibly relieved that both were well and, above all, that the baby was not at risk. Reassured, they were finally able to enjoy this new phase of their lives.

## Discussion

Pregnancy can be a challenging time for a couple, and especially for the expectant mother. In the case presented, we can see how regular screening with a positive result can contribute to this. This result, at nine weeks of gestation, demanded a second evaluation with a TT, in accordance with European guidelines [2], in addition to a new VDRL evaluation, which was interpreted as evidence of a false-positive result. We must also mention certain caveats to this conclusion, such as the different blood analyses taking place in different laboratories and the inability to say with 100% certainty what the cause of the false-positive result was (although pregnancy seems to be the most likely explanation). Following this incident, the couple continued their follow-up with their primary care team, with the woman's third-trimester screenings, including VDRL, all returning negative results. She would eventually deliver a healthy baby boy, now two years of age, who was apparently healthy and otherwise well.

Analyzing the approach to syphilis screening, and as introduced above, both TT and NTT can be used to screen for syphilis. TT have the advantage of usually being more sensitive in detecting early syphilis. However, these tests do not distinguish between active infections and previously treated infections, since they remain positive even after treatment, and provide a high number of false-positive results. As for NTT, not only can they help distinguish between past and current infections, based on changes in their titers from previous measurements (equivalent to a minimum fourfold change) and clinical context, but they can also be used to monitor active infections, based on the evolution of titers. However, these are less sensitive than TT in detecting syphilis and can, as previously mentioned, become positive in other contexts, albeit at low titers (<1:4) in most cases [2]. These contexts vary from chronic conditions, such as chronic liver disease, HIV infection, and autoimmune diseases like systemic lupus erythematosus, to temporary conditions, such as recent vaccination, acute febrile illnesses, and pregnancy itself. In the latter cases, the titers decrease over a period of up to six months [5].

Based on their advantages and disadvantages, screening can be done with either of them, with positive tests requiring a reflex test. Nonetheless, the most recent Portuguese guidelines for the follow-up of low-risk pregnancies recommend screening for syphilis via VDRL measurement in the first and third trimesters, as well as at preconception appointments, whenever possible [1]. It is thus important to know how to distinguish between a false-positive result and an actual syphilis infection during pregnancy. This can be achieved by performing a TT in conjunction with a new NTT measurement, which will not only confirm or exclude the diagnosis but also evaluate the disease's activity [2]. Figure *1* presents a flowchart based on the most current European guidelines on syphilis screening [2].

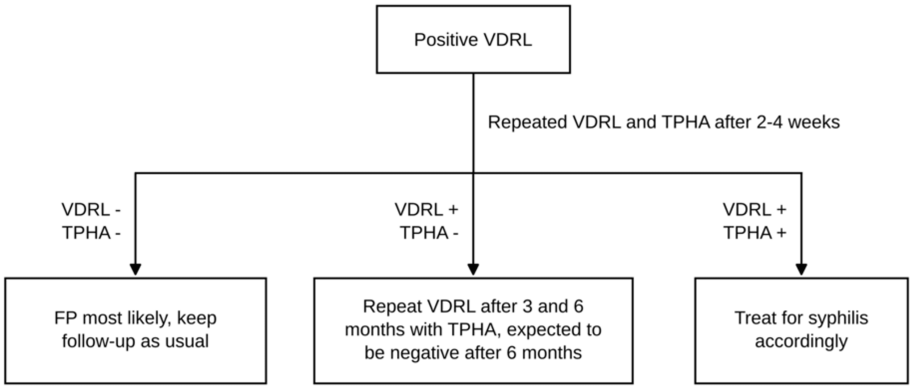



**FIGURE 1: Flowchart for the management of a positive VDRL result during regular pregnancy follow-up.**

VDRL, venereal disease research laboratory; TPHA, *Treponema pallidum* hemagglutination assay; FP, false-positive; "−", negative; "+", positive

One can, thus, wonder if an initial TT screening would be better suited for pregnancy screening, based on the many causes of false-positive results in NTT screening and their similar sensitivity in non-primary cases. To answer this, we need to provide some context based on the literature, which cannot be obtained from a single clinical case. To begin, in the Portuguese context, we must consider that, even though Portugal has one of the highest rates of syphilis incidence in Europe, with a growing trajectory, it is still low by global standards, which favors the use of NTT screening [6,7]. Moreover, in a cost-effectiveness analysis review of both screening methods, it was concluded that NTT screening is better suited for smaller laboratories that serve low-risk populations [8]. This is the setting found in Portugal, where the analytical follow-up is performed in small, individual laboratories in the community.

Given that NTT screening seems to be better suited for the Portuguese pregnancy follow-up system, strategies to mitigate the psychological impact of a false-positive result, not only on the expectant mother but also on the relationship between the soon-to-be parents, given the implicit assumption of possible infidelity by one of them, are necessary. For this, a solid healthcare professional-patient relationship is fundamental in preventing these consequences. In a study comparing individual prenatal care with group prenatal care, women reported higher levels of trust when the follow-up was performed by the same healthcare professional (as it is done in Portugal, where the family doctor follows the pregnancy) compared with different healthcare professionals [9]. The study also highlighted the importance of group prenatal care in emotional support and patient education, reinforcing the importance of the prenatal classes our institution provides to expectant mothers in the community.

## Conclusions

Syphilis can be vertically transmitted during pregnancy, highlighting the importance of appropriate screening. In Portugal, pregnant women are screened for syphilis using the VDRL test, despite the possibility of false-positive results during pregnancy. Therefore, distinguishing a false-positive result from a true syphilis infection is essential and requires confirmation with a TT in conjunction with a repeat NTT, without delaying either the physical examination or treatment whenever there is a high clinical suspicion.

It is crucial that physicians explain the possibility of false-positive results when ordering a VDRL test, as these results can cause uncertainty and anxiety for both pregnant women and their partners. This case illustrates how clear communication and a relationship of trust and proximity between the physician and the patient can help manage these situations in a more reassuring way as part of regular pregnancy follow-up.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Joana Castelão, Sara Meireles, João Pedro V. Patrício, Samuel R. Ângelo, Ana Henriques

**Acquisition, analysis, or interpretation of data:** Joana Castelão, Sara Meireles, João Pedro V. Patrício,

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**Critical review of the manuscript for important intellectual content:** Joana Castelão, Sara Meireles, João Pedro V. Patrício, Samuel R. Ângelo, Ana Henriques

**Supervision:** Joana Castelão, Sara Meireles, João Pedro V. Patrício, Samuel R. Ângelo, Ana Henriques

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