Syphilis testing in blood donors: an update

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Syphilis, an ancient disease, is still a public health problem worldwide. The World Health Organization (WHO) estimated that there are 12 million new cases of syphilis each year, with more than 90% occurring in developing nations. Moreover, in the past 30 years, through its association with an increased risk of human immunodeficiency virus (HIV) infection, syphilis has acquired a new potential for morbidity and mortality.

The aim of this review is to update our understanding of various serological tests, their limitations and advantages in order to develop the skill of when and how to order them and interpret their results in an effective and significant manner.

Natural history of syphilis

Syphilis is a chronic infectious disease caused by the spirochaete, Treponema pallidum (T. pallidum). On the basis of its clinical presentation, infectivity and progression, syphilis can be classified into different clinical stages: primary, secondary, early latent, late latent and tertiary syphilis. Primary syphilis is characterised by a painless genital ulcer which develops within 9 to 90 days (average, 21 days) following exposure to infection. About one third of untreated primary cases will progress to secondary syphilis. Secondary syphilis is most clinically apparent and is characterised by a symmetrical macular-papular rash involving the palms and sole and peak bacteraemia with a high load of spirochaetes in the blood. About 50% of untreated secondary cases will progress to latent infection. In general, the latent phase is asymptomatic and a positive serological test for syphilis (STS) is the only indicator of infection. About one third of untreated cases of latent syphilis will progress to tertiary syphilis over a period of 10 to 20 years. Tertiary syphilis typically involves the cardiovascular and/or neurological systems.

Modes of transmission

Syphilis is usually transmitted by sexual contact or from mother to infant, although endemic syphilis is transmitted by non-sexual contact in communities living under poor hygienic conditions. T. pallidum can also be transmitted by transfusion of blood or blood components from donors with active syphilis or when the blood is unscreened.

Transfusion-transmitted syphilis

The first case of transfusion-transmitted syphilis was reported in 1915. By 1941, 138 cases had been reported in the literature. Most reported cases were discovered to have occurred when donors were in the primary or secondary stage of disease. T. pallidum may be found in the blood stream, but levels are variable and bacteraemia is often short-lived even following recent contamination. Moreover, the treponemes are relatively fragile and sensitive to cold; hence the risk of transmission through transfusion of blood stored below 20 °C for more than 72 hours is very low. There is a direct relationship between the amount of organisms present in the blood and the duration of their vitality (infectivity potential). A look-back study involving 98 units of blood from STS-positive donors, which had been quarantined for a minimum of 7 days at 4 °C and transfused into 90 recipients, demonstrated the lack of disease transmission or seroconversion in all tested recipients; in this same study the presence of passively transferred reagins was not detected when the original titre was <1:8, and in those recipients from units with a titre ranging from 1:8 to 1:64, the passively transferred antibodies were no longer detected after 10 days. Platelet concentrates are usually stored at room temperature (22 °C) or transfused within a few hours of collection so they carry a higher risk of transmitting syphilis. The risk of transfusion-transmitted syphilis is particularly high in developing countries with limited blood supplies where the blood is collected from family donors and transfused within hours. A screening test is considered essential to prevent transfusion-transmitted syphilis in such situations. In the past, STS were suggested to provide information on infections caused by other pathogens, such as HIV. However, a recent study showed that STS have no value as a surrogate marker for blood-borne viral infections among blood donors.

When the infection is transmitted to a recipient, signs and symptoms appear a few weeks later; these can include macular lesions on the palms, headache, arthralgia, fever, peripheral lymphadenopathy and, rarely, jaundice. In none of the reported cases did the blood donor have a history of venereal disease or the presence of sores at the time of donation. Thus, syphilis can be transmitted from donors who clinically and biologically do not show any signs of their disease. It is important
rationale of continuing syphilis testing of blood donors has raised questions about the transfusion-transmitted syphilis in recipients among transfusion recipients; and difficulty in diagnosing eligibility screening process; wide use of antibiotics drugs or other payment for sex) through the donor syphilis infection (e.g. subjects who receive money, who are found to have high-risk behaviour for acquiring syphilis infection (e.g. subjects who receive money, drugs or other payment for sex) through the donor eligibility screening process; wide use of antibiotics among transfusion recipients; and difficulty in diagnosing transfusion-transmitted syphilis in recipients. Although the absence of transfusion-transmitted syphilis in many developed countries has raised questions about the rationale of continuing syphilis testing of blood donors, transmission through blood components still occurs in southern Asia. The Standard Operating Procedures of blood transfusion services worldwide do, therefore, include requirements/recommendations for such screening. A new draft guidance for screening, testing and managing blood donors and components was recently distributed by the Food and Drug Administration. Some diseases besides syphilis are caused by other species or subspecies of Treponema: yaws (T. pertenue), pinta (T. carateum) and bejel (T. endemicum). Yaws and pinta may potentially be transmitted by transfusion but very few data are available. Bejel is unlikely to be transmitted or infect individuals by this route. The signs and symptoms of these diseases are usually evident and, therefore, lead to deferral of the potential donors. Various strategies have been proposed by the WHO, International Society of Blood Transfusion and American Association of Blood Banks to prevent transfusion-transmitted syphilis. These include: (i) selection of low-risk donors and screening for the disease using efficient laboratory methods; (ii) application of pathogen reduction technology; and (iii) rational use of blood products. However, blood safety begins with implementation of organised blood centres, a quality system, haemovigilance programmes and adherence to Standard Operating Procedures.

Syphilis and blood donors

Donor selection is based on information about the donor, identifying risk factors in the donor's behaviour, the medical history collected using a questionnaire and physical examination of the donor in order to find clinical signs of the infection. Donor selection is important because donors with high-risk behaviours and other risk factors may be infected by syphilis and compromise the safety of blood used for transfusion. Donors can be deferred during selection, which is particularly useful in the early period of infection when laboratory tests are not efficient.

In developed countries, the prevalence of T. pallidum infection has dropped both in the general population and in blood donors. However, the scenario is different in developing countries of the sub-Saharan region where the prevalence may reach 25%. In such a context, the poor quality of laboratory screening due to the lack of equipment, trained personnel, reagents and standard procedures compounds the need for systematic and better screening for syphilis to help ensure a safer blood supply.

The risk of transfusion-transmitted syphilis is closely related to risk factors in the blood donor, in particular sexual behaviour since the disease is primarily transmitted by the sexual route. The rates of infection are high among homosexual men. Older age, male-male sex, two or more sexual partners, a past history of syphilis treatment and HIV seropositivity are closely related to transfusion-transmitted syphilis. Other risk factors associated with transfusion-transmitted syphilis include prostitution, bisexuality (men having sex with both men and women), intravenous drug use and skin scarification (tattooing, blood rituals). In India, most blood donors are first-time donors. The prevalence of syphilis among blood donors in India was recently reported to be 0.7%. The global incidence of syphilis among blood donors is variable. In a study by Adjei et al., the incidence of syphilis was 7.5% among Ghanaian donors whereas an incidence of 12.7% was noted among Tanzanian donors by Matee et al. and Bhatti et al. found an incidence of 0.75% among Pakistani donors. There are published data indicating that the prevalence of this disease is higher in replacement donors than in voluntary blood donors.

The donor history questionnaire includes questions particularly related to past infection with syphilis. It is also focused particularly on sexual behaviour (past history of sexually transmitted diseases) and sometimes on specific signs observed during the clinical examination. Donors who are reactive for syphilis sometimes persistently continue to donate blood even after post-donation counselling. Certain lacunae remain in donor selection. These could be attributed to difficulty in understanding the questions due to a low level of education and ignorance about infections transmissible by blood transfusion. Furthermore, cultural taboos sometimes prevent donors from disclosing information in response to some kinds of questions. Identified safe
donors must be retained as repeat donors and educated regarding high-risk behaviour and its impact on the safety of the blood supply.

Testing methodologies

The diagnostic methods for syphilis are broadly divided into the following types: (i) direct microscopic examination in the early stage of syphilis when a lesion is present; (ii) indirect treponemal and non-treponemal serological tests; and (iii) molecular biology-based methods.

The basic principle of STS is to measure or demonstrate either specific or non-specific antitreponemal antibodies, hence inferring that the donor has been exposed to T. pallidum. The first serological test for syphilis was described by August von Wassermann in 1906. This was a non-treponemal serum reagin test which has been used for blood donor testing since 1940. Since then a lot of work has been done to refine and take advantage of new developments in devising tests that are more specific and automated. STS are divided into two categories, non-treponemal and treponemal serological tests. They are further divided based on the different methodologies used.

Non-treponemal tests

Non-treponemal serological tests such as the venereal diseases research laboratory (VDRL) and rapid plasma reagin (RPR) tests do not detect specific anti-treponemal antibodies. These tests are based on reactivity, both IgM (also known as reagin) and IgG antibodies, of sera from donors with syphilis to non-specific cardiolipin-cholesterol lecithin antigens. The antibodies are directed at a liquid hapten antigen called cardiolipin which can be found in many tissues as well as within spirochaetes. Serological screening tests have been developed to detect the antibody-cardiolipin complex by using complement fixation, precipitation or flocculation. These tests can be used for monitoring treatment efficacy.

The RPR test is currently the most commonly used non-treponemal test for donor screening. The RPR test uses a combination of cardiolipin antigen and charcoal and measures antilipin antibodies formed in the immune response. Flocculation, as a consequence of the antigen-antibody reaction, indicates a positive (reactive) result. This test usually reverts to negative after successful treatment and can, therefore, be used to monitor response to therapy.

Non-treponemal tests may give false negative results in early primary syphilis in 30% to 50% of cases. False negative results may also occur due to technical errors, such as the antigen being distributed on a sample not previously placed on the entire test area surface. Reagent temperature is also important for sensitivity, especially when testing samples from patients. A false negative result may also be due to the prozone phenomenon. In these cases, specimens will demonstrate a clearly positive reaction when tested after serial dilution, a process that brings the antigen-antibody ratio within the optimal range.

A major problem when using non-treponemal tests is the possibility of biological false positive reactions due to cross-reactivity with other molecules in conditions such as viral infections, pregnancy, malignant neoplasm, autoimmune diseases, and advanced age. The rate ranges from 7% to 50% of positive STS donors and may increase up to 80% in industrialised regions.

When the incidence and prevalence of syphilis in the blood donor population are high and cannot be reduced through donor selection strategies, it may be necessary to consider screening using a non-treponemal assay (e.g. VDRL or RPR) to identify only the highest-risk donors -those with evidence of recent infections.

Treponemal tests

Because of the non-specific nature of non-treponemal tests, further research led to the development of treponemal specific tests. Although treponemal tests do not differentiate between venereal syphilis and endemic syphilis (yaws and pinta), the tests are used as confirmatory tests to verify reactivity in a non-treponemal test. Treponemal tests usually remain reactive for years with or without treatment and treponemal test antibody titres correlate poorly with disease activity. Treponemal tests should not, therefore, be used to evaluate response to therapy, relapse or re-infection in previously treated patients. These tests may serve as diagnostic tests in late syphilis and in patients with reactive non-treponemal tests but with signs and symptoms of late syphilis.

Currently available treponemal tests include the fluorescent treponemal antibody absorption test (FTA-ABS), T. pallidum haemagglutination assay (TPHA) and enzyme immunoassays (EIA). The advantages of treponemal tests include the production of objective results and the facility for automation, making them useful for large blood centres. Treponemal tests are, however, technically difficult to perform and more expensive than non-treponemal tests. As with non-treponemal tests, false positive reactions can occur.

The fluorescent treponemal antibody absorption test

This test is still regarded as the gold standard confirmation of a STS. The FTA-ABS test has been available since the mid 1960s. The test detects two different antibodies: the first, called group antibody, reacts with antigens shared with other treponemes.
Serum samples are absorbed with an absorbent to remove group antibody which allows detection of the treponemal specific antibody. A fluorescein tag is added which results in fluorescent *T. pallidum* and sample fluorescence is calculated against a standard control. While these tests are highly specific and sensitive, they may produce variable results due to variation in equipment reagents and interpretation of test results. Borderline or equivocal readings have less than a 5% chance of being associated with syphilis39.

*T. pallidum* haemagglutination assay

In 1965, haemagglutination assay technology was applied in the development of treponemal-specific testing. The TPHA was modified further to a microhaemagglutination *T. pallidum* (MHA-TP) test. The MHA-TP uses sensitised sheep erythrocytes coated with *T. pallidum* (Nichol’s strain), which agglutinate with anti-treponemal IgM and IgG antibodies39. The MHA-TP test has recently been automated (PK™, TP, Olympus, Irving, TX, USA) eliminating the subjectivity associated with manual test interpretation.

The TPHA test has been replaced by the *T. pallidum* particle agglutination (TPPA) test. The particle agglutination test uses the same treponemal antigen as the MHA-TP test, but has the advantage of using gelatin particles instead of erythrocytes, thus preventing non-specific reaction with plasma samples31. The TPPA test is less expensive and less complicated than FTA-ABS tests and the results can be read with the unaided eye. The TPPA test is a micro-haemagglutination assay for IgM and IgG antibodies32, whereas the FTA-ABS test uses fixed *T. pallidum* to bind IgM and IgG antibodies.

The sensitivity of the MHA-TP and FTA-ABS tests are equivalent except in the primary stage of syphilis when FTA-ABS shows greater sensitivity33. False positive results are uncommon but may occur in patients with collagen diseases, systemic lupus erythematosus and other infections34,35. Despite treatment, most infected individuals, except those treated early for primary syphilis, remain positive for life36.

Enzyme immunoassays

During the 1990s, various EIA that could detect both anti-treponemal IgG and IgM antibodies were commercially available. Earlier assays used microtitre plates of wells coated with wild-type *T. pallidum* antigens and had a clinical sensitivity of 98.4% and specificity of 99.3% when compared with TPHA and FTA-ABS37. An EIA using recombinant antigen instead of wild antigens had a higher sensitivity (99% vs 91.4%; p<0.01)38. A comparative evaluation of ten EIA using either wild-type or recombinant *T. pallidum* antigens for anti-treponemal IgM and IgG antibody detection demonstrated sensitivities of 94.7-99.1% and specificities of 100%39. In a subsequent publication in 1992, the first published in-depth discussion of a treponemal assay-based testing algorithm, the same group proposed that an EIA should replace the VDRL test as the screening test for syphilis40. Since 2000, the options have expanded to include a chemiluminescence assay (CLIA)41 and multiplex flow immunoassay42.

The advantages of EIA include the production of objective results, ability to link EIA plate readers directly to laboratory computer systems (reducing the potential for errors in transcription of results), and the facility for automation. The main drawback of treponemal EIA is that they remain reactive for life in most people and this can be misleading in individuals who no longer have active disease.

Rapid tests

Treponemal tests are also commercially available in formats that can be performed at the point of care. These are either agglutinations tests with latex particles coated with treponemal antigen or immunochromatographic strips on which a positive reaction appears as a coloured line. Most of these tests can be performed using whole blood, serum or plasma. Rapid tests are highly sensitive and specific40. The WHO evaluated the performance of eight rapid syphilis tests in comparison to that of a TPHA/TPPA reference standard and reported sensitivities of 84.5-97.7% and specificities of 92.8-98%43,44.

The advantages of rapid syphilis tests include their cost, minimal training and equipment requirement and availability of results within 5-20 minutes. Results of rapid tests cannot differentiate between active and treated syphilis; false positive reactions can also occur45. Positive results need confirmation with quantitative non-treponemal testing to determine recent infection and response to treatment.

Western blotting

The western blot used to detect syphilis is similar to the western blot used for confirmation of HIV antibodies and provides characteristic molecular banding patterns. Detection of at least three or four major antigens with molecular masses of 15.5, 17, 44.5 and 47 kDa indicate a positive result. This test can detect either IgG or IgM antibodies and is considered a very useful adjunct confirmatory test46. Western blotting is used in some laboratories to resolve questionable results obtained with other treponemal tests.

Polymerase chain reaction

Polymerase chain reaction (PCR) analysis has been extensively used for viruses and is currently employed to detect HIV and other viruses in blood donors. The
The principle of PCR technology is based on successive rounds of *in vitro* replication of nucleic acid sequences using primers complementary to specific targets. Millions of copies of the target genes are made, making it possible to detect minute quantities of a transmissible agent in the blood. PCR tests for syphilis offer a direct method of detection and provide earlier diagnosis of individuals who may present in the serological window period.

The first description of PCR for testing *T. pallidum* DNA dates back to 1990. Since then, several PCR methods have been reported. Each test uses a different target gene, including *tpf-1*, BMP, *tmpA* and *tmpB*, 47 kDa protein gene and 16s rRNA. The 47kDa protein gene is the most commonly reported target for PCR because it rarely cross-reacts with other commensal spirochaetes. The sensitivity of PCR assays varies from the equivalent of $10^{-3}$ organisms, obtained by reverse transcriptase PCR, to 10 to 50 organisms when the gene encoding the 47 kDa protein is used as the target. Thus, reverse transcriptase PCR is a powerful tool for detecting RNA and is more sensitive than DNA PCR because multiple copies of RNA are found per organism, allowing for the detection of less than one genome equivalent.

The most important advantage of PCR is its high level of specificity as compared to serological testing, i.e., its ability to differentiate *T. pallidum* infection from infection by other treponemes and to identify *T. pallidum* infection early when serological tests are non-reactive, especially in primary syphilis. PCR-based diagnosis may provide a more accurate prevalence of infection because of a lower possibility of false positive results. The limitation of PCR testing for *T. pallidum* is its inability to differentiate between the DNA of viable and dead organisms. Given the very stable nature of the DNA biopolymer of *T. pallidum*, it can be detected even in successfully treated cases of neurosyphilis. It is not known how long the dead organisms persist.

Since the introduction of PCR, various studies have been published on the sensitivity and specificity of this technique in the diagnosis of syphilis. One recent meta-analysis and systematic review reported the diagnostic performance of PCR in various biological specimens tested and different clinical stages of the disease. This analysis indicated that the yield of organism was greater from an ulcer or chancre than from blood or cerebrospinal fluid. This could be explained on the basis that DNA extraction from lesions was better than from blood. A study in the United Kingdom found that the sensitivity and specificity of PCR for primary syphilis were 94.7% and 98.6%, respectively, whereas for secondary syphilis they were 80% and 98.6%, respectively.

The presence of *T. pallidum* DNA was assessed by real-time PCR in samples from blood donors with reactive STS. In this study, *T. pallidum* DNA was detected in 1.02% of donors’ samples which were reactive when tested by VDRL, EIA and FTA-ABS. In contrast, donors who were VDRL−, EIA+ and FTA-ABS+ did not demonstrate *T. pallidum* DNA in their blood. This indicates that the former group of donors (VDRL+, EIA+ and FTA-ABS+) were likely to transmit syphilis even though antibodies were present simultaneously. STS may still play a role in preventing the transmission of syphilis via transfusion.

Future studies are required to determine whether seropositivity is predictive of spirochaetemia by detecting the presence of *T. pallidum* DNA and to define the extent to which organisms remain viable and infective in blood components, *T. pallidum* nucleic acid amplification tests are not widely available in clinical laboratories. Thus, serological tests are the foundation of syphilis management, and knowledge of their diagnostic limitations is critical for clinicians.

**Routine blood donor testing**

In India, according to the Drug and Cosmetics Act and Rules 1945, it is mandatory to screen donated blood for transfusion-transmitted infections: the blood should be non-reactive for anti-HIV antibodies, hepatitis B surface antigen, anti-hepatitis C virus antibodies, syphilis and malaria. Currently, only one screening test for syphilis is mandatory. According to the WHO, blood banks may choose VDRL, RPR or treponemal-based EIA due to cost constraints. The U.S. Centers for Disease Control and Prevention continues to recommend the traditional algorithm. The traditional approach to the diagnosis of syphilis begins with a non-treponemal assay, either VDRL or RPR. Since these antibodies are not specific for syphilis, reactive non-treponemal tests must be confirmed with an assay that detects antibodies against *T. pallidum*. The traditional method has several advantages including the fact that it is reliable, especially in high prevalence settings. In addition, this algorithm utilises a rapid, inexpensive screening method that is economical and easily implemented in most hospitals and small clinics. However, this approach also has several limitations, including a low throughput and subjective interpretation of results of non-treponemal assays, which can translate into higher rates of false positive results, especially in low incidence settings.

Because of the limitations of the traditional testing algorithm and the fact that the overall rate of syphilis worldwide is declining, many clinical laboratories have adopted the reverse algorithm for STS, in which sera are initially screened using an automated, treponemal test.
such as an EIA. Samples that are reactive by EIA are then tested by RPR to assess disease and treatment status and provide a supplementary marker of infection. When the results of EIA and RPR are discordant (e.g., reactive by EIA and non-reactive by RPR), the sera may be analysed by the TPPA test\(^5\). A non-reactive TPPA result would suggest that the results of EIA screening were falsely reactive, while a reactive TPPA result would support an interpretation of either past, successfully treated syphilis or late/latent syphilis. The reverse screening algorithm has several advantages including an objective interpretation of screening results, the potential to automate testing, and enhanced sensitivity for the identification of late or latent syphilis. Its disadvantages are high cost and increased detection of samples with reactive screening results. A recent study compared the reverse and traditional syphilis screening algorithms in a population with a low prevalence of syphilis and reported that reverse screening yielded a higher false-reactive rate than traditional testing (0.6% vs 0.0%, respectively; \(p=0.03\))\(^5\). Despite the increased false-reactive rate, the reverse syphilis screening algorithm detected two patients with possible latent syphilis who were not detected by RPR screening. Thus, reverse screening may enhance the sensitivity for detection of early or late/latent disease. Future studies should expand on these findings by directly comparing both algorithms in a population with a high prevalence of syphilis.

There are few publications on the yield of the reverse algorithm in blood bank settings. However, a recent report found that using CLIA as the initial test significantly reduced the false positive rate in Brazilian blood donors\(^6\). Various other studies have also found that the diagnostic performance of syphilis screening is better with the reverse algorithm than with the traditional one, including the detection of infections unlikely to be diagnosed by non-treponemal tests\(^7,9\). The reverse algorithm has also been shown to be highly specific, which is an important quality in screening a low-risk population such as blood donors\(^5,6\).

In India, the routine donor testing algorithm for syphilis should also include the use of a treponemal test to confirm initial serological reactive non-treponemal test results such as those from the RPR test. The sensitivity of various treponemal tests varies from 93 to 99% depending on the phase of the disease and their specificity ranges from 93 to 95.6%\(^6\). The sensitivity of all STS increases as time from exposure increases. There is debate in literature regarding the earliest positive results for syphilis when comparing non-treponemal with treponemal tests. Studies evaluating this issue found that treponeme-specific antibody is detected at the same time as the non-specific antibody and possibly slightly sooner\(^1,2\).

**Management of donors with a positive syphilis test**

There is an additional public health benefit from serological screening for syphilis in blood banks. All blood donors with reactive serological blood tests are notified and referred for specialised medical care in public centres for sexually transmitted diseases where they receive treatment and advice on prevention for themselves and their partners. Neto et al.\(^8\) found that less than one-third of blood donors with a past syphilis infection had previously been referred for treatment; very few remembered having any symptoms. In contrast, Orton and colleagues in the USA found that half of blood donors reactive at screening with an automated specific treponemal test for syphilis (PK\(\text{TM}\)) and with a confirmed, positive FTA-ABS test reported a past, treated syphilis infection\(^9\). Blood donors with past disease who have not received medical treatment can be in a late latent phase and, if not treated, may develop tertiary syphilis. In our experience, none of the donors reported a history of medical treatment or recognised symptoms of syphilis during post-donation counselling. We have published a study on donor notification and management of donors who test reactive for RPR after blood donation\(^10\).

A report on platelet concentrates and serum samples from blood donors with PK\(\text{TM}\)+, FTA-ABS+, STS, tested for T. pallidum DNA and RNA, was presented at the Blood Products Advisory Committee Meeting in Bethesda, MD (USA) in September 2000. At least 100 samples (50 RPR+ and 50 RPR−) were tested by each method. All samples tested were negative for evidence of T. pallidum DNA and RNA. With this lack of demonstrable T. pallidum DNA and RNA, the probability of these blood donors, who were reactive for syphilis in serology, transmitting the disease was 0 to 3\%\(^11\). These data contrast with those reported from analyses of two syphilis outbreaks in the USA in which T. pallidum DNA was detected in the blood of untreated infected individuals during all phases of syphilis infection\(^12,13\).

**Biological false reactivity**

The relevance of a confirmed positive syphilis test result in an apparently healthy blood donor is an issue today. Although there is ample literature addressing false positive test results associated with specific conditions when using current testing methods, these conditions may not be relevant to the contemporary interpretation of positive STS in blood donors. At the same time, disclosing results to the donors' sexual partners or spouse is a critical component of disease control and prevention as early identification and treatment of contacts can potentially prevent the continued spread of infection. While performing the post-donation counselling in such
donors, the implications of false positive test results on future donations and what factors cause such test results remain unknown. However, some false positive results occur without association with conditions mentioned in literature. It is known, however, that the majority of blood donors (90%) with confirmed positive syphilis test results continue to test confirmed positive at subsequent donations.

Conclusion

Although there are various tests for diagnosing syphilis, a gold standard method is still lacking because no test is ideal for all stages of syphilis. The ideal test for syphilis should have both high sensitivity and specificity, be suitable for monitoring response to treatment, give a negative result after adequate therapy and also give a clear indication of re-infection. In addition, sensitivity and specificity should be calculated and compared relative to the standard test in use at that time, rather than by testing large groups of samples from clinically diagnosed individuals. The test for syphilis was the first test to be introduced in blood banking and has been used for many years, and yet data are inadequate to ascertain whether it accounts for the current rarity of transfusion-transmitted syphilis. Laboratories are switching from the traditional testing algorithm to a newer one. Future studies are required to ascertain the significance of the reverse algorithm in low-risk populations. Interpretation of syphilis serology results is complex and relies on careful consideration of laboratory and clinical findings. The main aim of algorithms, whichever used, is to achieve better prevention and control of syphilis.

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