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IMPACTS OF THE LACK OF PENICILLIN SUPPLY ON THE INCIDENCE OF CONGENITAL SYPHILIS IN MATO GROSSO DO SUL

¹Priscila Gonçalves Soares dos Santos, ¹Elenir Rose Jardim Cury Pontes, *¹Valdir Aragão do Nascimento, ³Patrícia Trindade Benites, Ran Shin Tair, ²Virna Liza Pereira Chaves Hildebr, ⁴Dayse Centurion da Silva, ⁴Patrícia Pato dos Santos, ⁵Rosana de Mello Souza Marçola, and ⁶Miréia Rúbia Queiroz

¹Graduate Program in Health and Development in the Mid-West Region, Federal University of Mato Grosso do Sul, 79070-900, Campo Grande, MS, Brazil

²Municipal Secretary of Public Health, Rua Bahia, 280, Jardim dos Estados, 79002-530 - Campo Grande, MS - Brasil

³University Hospital of Mato Grosso do Sul, Nursing Sector, Federal University of Mato Grosso do Sul, 79070-900, Campo Grande, MS, Brazil

⁴Graduate in Environment and Regional Development, The University for the Development of the State and the Pantanal Region

⁵Graduate program in Nursing, Federal University of Mato Grosso do Sul, 79070-900, Campo Grande, MS, Brazil

⁶Graduate in medicine, University of Cuba

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ABSTRACT

Syphilis is still a concern in the area of public and collective health around the world. However, its control is neglected by some countries marked by economic, material and social shortages. This negligence has had a direct impact on the statistical indices, highlighting an increase in the incidence of reported cases and subsequent positive diagnosis. With regard to congenital syphilis, especially in the Mato Grosso do Sul state, it has been highlighted in recent years as one of the main causes of infant deaths, especially among fetal losses. One of the ways of treating the disease is the use of penicillin, a drug that is missing in the state of Mato Grosso do Sul due to lack of supply. Therefore, the manuscript addresses the importance of the drug and the consequences of its lack to the patients.

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INTRODUCTION

The present manuscript is about a bibliographical review about the occurrence of syphilis in pregnant women. The manuscript is organized in three distinct but complementary topics regarding etiology and therapeutics available in cases of positive diagnosis. The first item addressed in the review discusses the characteristics of syphilis, syphilis in Pregnant and Congenital as the symptoms, methods of diagnosis and treatment. On the other hand, the second item deals with the forms of transmission of the disease and emphasizes the lack

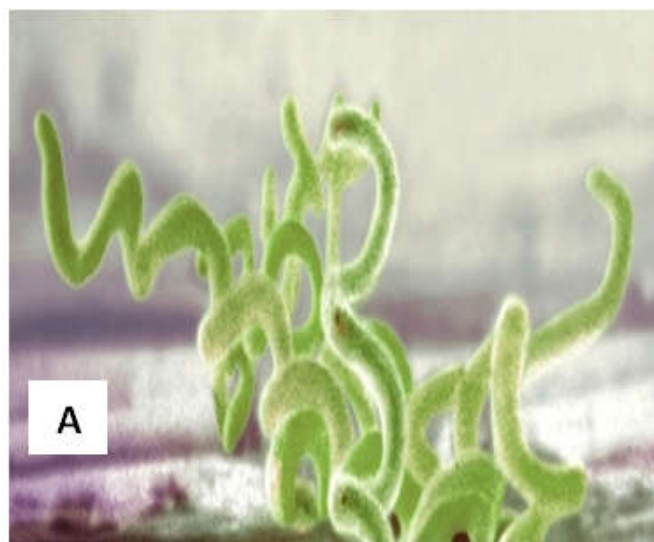
of adequate treatment in the face of the occurrence of the disease and the reasons why the casuistic of the congenital syphilis remains so high in the country and in the world, as well as the treatment. Finally, the third item analyzes the impact of penicillin shortage on the incidence of congenital syphilis in Mato Grosso do Sul and the need for supplementary information on this topic. The importance of quality in treatment and the availability of adequate prenatal medication to prevent vertical transmission of syphilis is the main topic of discussion in this study. The purpose of this discussion is to raise syphilis as an issue that should have been overcome, including, among other things, an increase in prenatal coverage that allows access to rapid testing and low-cost treatment, which could prevent vertical transmission and, consequently,

*Corresponding author: Valdir Aragão do Nascimento, Graduate Program in Health and Development in the Mid-West Region, Federal University of Mato Grosso do Sul, 79070-900, Campo Grande, MS, Brazil

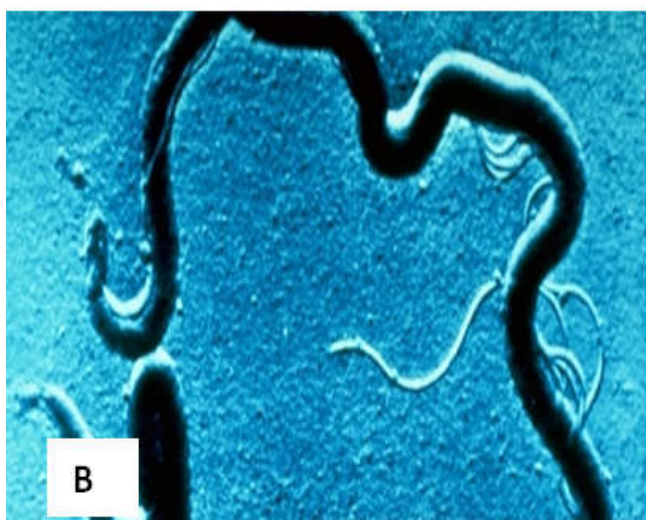
congenital syphilis. However, the representativeness of this disease in the epidemiological scenario of Brazil is still worrying and questions about the quality of syphilis control during the prenatal actions in primary health care.

Literature Review

Syphilis is a chronic, curable infectious disease caused by bacteria that have been challenging humankind for centuries. In the mid-nineteenth century, syphilis had a set of unexplained and non-specific symptoms, being known as a venereal disease, one of the most serious and serious diseases for public health (Bechelli, 1976). There are controversies about the history of syphilis, but according to social-historical analysis, syphilis would have occurred in Europe in the fifteenth century. The discovery of the causal agent of syphilis, *Treponema Pallidum* was performed by Schaudinn & Hoffmann on March 3, 1905 (KÖHLER, 2001). *Treponema Pallidum* presents a rather peculiar development in which its rate of growth is slow (divide transversally every 30 hours), is extremely fragile and has man as its only natural host. Infections in animals have been used to maintain and reproduce the microorganism for experimental studies in laboratories.



A



B

Figura 1. *Treponema Pallidum*. A) computerized illustration showing bacteria grown on mouse skin; B) bacteria observed from an electron microscope

Fonte: <https://www.gettyimages.pt/detail/foto/syphilis>

Syphilis is a sexually transmitted infection (STI) whose control can be effected through public health measures, and can be successful in the presence of sensitive diagnostic tests and the possibility of being effectively treatable at a small cost. However, syphilis is a major public health problem in Brazil (BRAZIL, 2015). Acquired syphilis can be classified as recent (less than one year of evolution) or late (with more than one year of evolution). Recent acquired syphilis may present in primary, secondary, latent and tertiary forms (CDC, 2002). Latent infections do not present clinical manifestations and are detected by serological tests. Latent syphilis acquired in the previous year is referred to as early latent syphilis and all other cases of latent syphilis are latent late syphilis or latent syphilis of unknown duration (CDC, 2002). Regarding the epidemiological aspect, the World Health Organization (WHO) estimates the occurrence of more than one million cases of Sexually Transmissible Infections (STIs) in the world per day. Annually, approximately 357 million new infections are counted, including chlamydia, gonorrhea, syphilis and trichomoniasis. Syphilis affects one million pregnant women annually, leading to more than 300,000 fetal and neonatal deaths, and putting more than 200,000 children at risk of premature death (PAHO, 2017). In the last five years in Brazil, an increase was observed in the number of cases of syphilis in pregnant women, congenital and acquired. Such increase in cases can be attributed in part to the increase in the coverage of testing, with the expansion of the use of rapid tests, reduction of condom use, resistance of health professionals to the administration of penicillin in Primary Care, worldwide shortage of penicillin and etc. In addition, the improvement of the surveillance system may reflect the increase in reported cases (WHO, 2015). The worsening of the syphilis epidemic, with the significant increase in syphilis acquired worldwide, mainly due to unprotected sexual relations, has contributed to the sounding of public health alarms and to make the response to congenital syphilis a priority objective in Brazil. Added to this concern is the occurrence of an increasingly precocious pregnancy among Brazilian girls (BRAZIL, 2015). In the year 2016, 87,593 cases of acquired syphilis were reported, with 37,436 cases of syphilis in pregnant women and 20,474 cases of congenital syphilis, with 185 deaths in Brazil. The highest proportion of cases was reported in the Southeast region of Brazil. When observing the rates individually for each state, the high rates of syphilis in pregnant women found in Espírito Santo, Rio de Janeiro, Rio Grande do Sul and Mato Grosso do Sul are highlighted. In relation to congenital syphilis, the first three states mentioned above remain in evidence, alongside the state of Pernambuco (BRAZIL, 2017).

The coverage of serological tests for the screening of infections during prenatal care for pregnant women in Mato Grosso do Sul is total and occurs for their 78 municipalities and their population coverage among pregnant women is above 95%. Since 2002, the state has the Mato Grosso do Sul Maternity Protection Program (PPG-MS), which carries out the investigation of ten infections (HIV, hepatitis B and C, HTLV I and II, toxoplasmosis, Chagas disease, chlamydia, syphilis, cytomegalovirus, and rubella) and maternal phenylketonuria, using the filter paper technique and post-natal examinations (FIGUEIRÓ *et al.*, 2007). Due to the epidemiological scenario of the increase in cases of syphilis, allied to underreporting of cases, Brazil has not yet started the certification process to eliminate its vertical transmission (BRASIL, 2018). Due to the priority condition attributed to the prevention of vertical transmission of syphilis, the Ministry of

Health developed the Strategic Action Agenda for Reduction of Congenital Syphilis in Brazil, highlighting the collective construction of class associations and various areas of the Ministry of Health to carry out the confrontation of syphilis in Brazil (BRAZIL, 2017).

Clinical aspects, diagnosis and treatment of sifilis in pregnant: Syphilis is divided into several segments according to the particularities of its manifestation. In these subcategories we have primary syphilis; secondary syphilis; latent syphilis and tertiary syphilis. Primary syphilis develops with a single, painless lesion, usually vagina, penis or anus (may be extragenital), called cancer. After a mean incubation period of 21 days the primary lesion begins as a small erosion and ulcer before healing in the period of 3 to 10 weeks, in this case with or without treatment. Primary cancer can go unnoticed and when left untreated, the disease progresses to the secondary stage four to eight weeks after the onset of the primary lesion (WHO, 2016). Untreated syphilis in the primary stage progresses to secondary syphilis. In this stage, hematogenic propagation occurs, in which the treponema invades all organs of the body (BRASIL, 2010). The manifestations that characterize the secondary period of syphilis are represented by the presence of generalized papular mucous cutaneous lesions, distributing bilaterally affecting the palmar, plantar region, oral mucosa and genitalia. Hyperchromic lesions and mucosal ulcers are highly contagious. The systemic symptoms are myalgia, sore throat, alopecia and generalized lymphadenopathy (ROMANELLI *et al.*, 2010, WHO, 2016). These manifestations can be found during the first six months after infection, usually between 6 and 8 weeks. In this period of infection, the lesions are highly infective because they contain large amounts of treponemes on their surface (TAVARES; MARINHO, 2010).

Regarding latent syphilis, the available knowledge about its characteristics asserts that although detected by the serological test, in this period, the infection by treponema does not aggravate clinical manifestations of the disease. Latent syphilis is defined as syphilis characterized by seroreactivity, with no other evidence of primary, secondary, or tertiary disease. Latent syphilis in the first year of evolution is referred to as latent early syphilis and all other cases of latent syphilis are late latent syphilis or syphilis of unknown duration (WORKOWSKY *et al.*, 2015). Tertiary or late syphilis is the destructive stage of the disease affecting approximately one-third of those infected by treponemes that have not received adequate treatment or have not been treated for about 20-40 years after infection (WHO, 2015). Tertiary syphilis can reach any organ and its cardiovascular manifestations include the most frequent picture of syphilitic aortitis, aneurysm and coronary stenosis. Late cutaneous syphilis exhibits gummy and nodular lesions of a destructive nature. In bone syphilis there may be synovitis, gummy osteitis, arthralgias, arthritis and nodules just articulated. Neurosyphilis also occurs at this stage, which may start suddenly (BRASIL 2010; PASQUALOTTO *et al.*, 2006). The diagnosis of syphilis in the absence of clinical manifestations is performed through serological tests. The veneraldisease research laboratory (VDRL) and rapid plasma reagin (RPR) are non-treponemal, quantitative and high sensitivity tests. Tests can be positive for long periods, even after curing the infection. However, there is a progressive decrease in titers until they become unreactive after adequate treatment, in most cases after months or years. On the other hand, the treponemal antibody-absorption (FTA-

ABS), microhemagglutination-Treponema pallidum (MHA-TP), Treponema pallidum hemagglutination (TPHA) and Enzyme-Linked Immunosorbent Assay (ELISA) tests are qualitative and detect antitreponemal antibodies with high specificity. In fact, such tests are useful in excluding false-positive results. However, treponemal serology has a low sensitivity which may result in false-negative exams and, once positive, tend not to become negative even after curing infection (BRASIL, 2006). In relation to the therapy used, the procedures to detect the presence of syphilis during pregnancy are also extended to the sexual partner and should be started as urgently as possible. Since the etiologic agent of syphilis, Treponema Pallidum, is found in the blood of the pregnant woman, she is able to cross the placental barrier and contaminate the fetus at any stage of the gestational process. There is no difference in the pathological changes caused by syphilis in women who are pregnant or not, the difference is related to fetal contagion (BRASIL, 2012). When the pregnant woman's examination indicates the presence of syphilis and there is no adherence to the treatment, there may be some consequences such as prematurity, abortion, fetal death, newborns with or without symptoms.

These latter consequences must be observed, as they may develop congenital syphilis late and may have irreversible consequences and complications. (BRAZIL, 2017). Despite presenting simple diagnosis and effective treatment, gestational syphilis remains a serious public health problem due to the overwhelming prevalence. In addition, syphilis is responsible for high rates of intrauterine morbidity and mortality as a result of congenital syphilis resulting from the hematogenous spread of the infectious agent, from the untreated infected pregnant woman or inadequately treated for its concept, by transplacental route. (Oliveira *et al.*, 2011). Penicillin is the only effective antimicrobial known to prevent maternal transmission to the fetus and treat fetal infection. Syphilis is basically curable in the first stages with a single dose of penicillin. Syphilis carriers for more than one year will receive more doses of the medication. Anaphylactic reactions occur in only 0.01% to 0.05% of patients treated with penicillin, with approximately 2 deaths per 100,000 treatments (BRASIL, 2015). No other treatment besides penicillin proved to be effective in the treatment of syphilis in pregnancy and in the prevention of congenital syphilis (LORENZI *et al.*, 2001).

Clinical aspects, diagnosis and treatment of congenital syphilis: Congenital syphilis is usually acquired by the fetus in the mother's womb of an infected mother when *T. pallidum*, which is disseminated hematogenously, crosses the placenta. The probability of vertical transmission can reach 100%, and it is possible at any stage of gestation, being more likely to occur in the first or second phase of the disease (BRASIL, 2006). Transmission of syphilis from the mother to the baby during pregnancy is a consequence of undiagnosed, untreated or inadequately treated maternal syphilis. As a result of non-treatment, several adverse events can occur in pregnancy, such as abortion, fetal death, low birth weight, neonatal death, or congenital syphilis (PADOVANI *et al.*, 2018). As previously mentioned, congenital syphilis can be classified as recent (cases diagnosed up to the second year of life) or late syphilis (cases diagnosed after the second year of life) and presents a high mortality rate, possibly reaching 40% of infected children 2,3. Congenital syphilis is an easily preventable disease due to the access of the test during prenatal care and to the appropriate treatment of pregnant women with positive tests

and their partners. Despite of the prenatal test, the syphilis has a high prevalence. Congenital syphilis occurs through a dissemination of the spirochete of *Treponema Pallidum* from a pregnant woman who has not been treated or was mistakenly treated for her condition through the placental route, causing the vertical transmission of the disease. Congenital syphilis is characterized by two stages, precocious and late, in which the early stage is asymptomatic (70%), but can be affected by clinical manifestations such as, prematurity, low weight, hepatomegaly, pseudo-paralysis of the limbs, respiratory distress, anemia, convulsion, meningitis, among others. In the late stage the symptoms are rare, due to the cure of the early stage, and it does not have definite affected organ, being able to involve several organs (INSTITUTIONAL TECHNICAL REPORTS, 2008). In the context of congenital syphilis should be used as confirmatory in women the low titer reagent non-treponemal test. On the other hand, for children, only for follow-up at 18 months, when passively acquired antibodies from the mother are no longer detectable by the test. The serological techniques for the detection of commercially available immunoglobulin M (IgM), FTA-AbsIgM, present an excessive number of false-negatives and false-positives, besides being difficult to perform, which does not justify its use in the diagnosis of congenital syphilis. Congenital syphilis (SC) is the transplacental infection of the concept by *Treponema Pallidum* from the untreated or inadequately treated infected mother. It can cause abortion, prematurity and stillbirth. Congenital syphilis is still considered an important public health problem, although it is easily diagnosed and totally avoidable when the treatment of the pregnant woman and her partner is performed adequately (CAMPOS et al, 2012; OLIVEIRA, et al. al, 2011). In view of the various diseases that can be transmitted during the pregnancy-puerperal cycle, syphilis is the one with the highest infection rates through vertical transmission, on average 70 to 100% in the primary and secondary phases, and reducing to 30 % in the latent late and tertiary stages of maternal infection. Regarding the outcomes, spontaneous abortion, stillborn fetus or perinatal death are present in approximately 40% of infected children of untreated pregnant women (BRAZIL, 2017). In Brazil the tests for detecting the causal agent of the disease are performed at the beginning of prenatal care. Thus, the importance of access, as early as possible to information on disease. In this case, also the partner is tested to initiate concomitant treatment, in reactive cases (BRASIL, 2006).

Epidemiological situation of syphilis in Brazil: The compulsory notification of congenital syphilis throughout Brazil was instituted through Ordinance No. 542, dated December 22, 1986; the one of syphilis in pregnant women was instituted by Ordinance n° 33, of July of 2005; and, finally, that of acquired syphilis, through Ordinance No. 2,472, published on August 31 (BRAZIL, 2013). In 2016, 87,593 cases of acquired syphilis were reported in Brazil, 37,436 cases of syphilis in pregnant women and 20,474 cases of congenital syphilis - including 185 deaths. The highest proportion of cases was reported in the Southeast region. The rates of syphilis in pregnant women in the state of Espírito Santo, Rio de Janeiro, Rio Grande do Sul and Mato Grosso do Sul are the highest for each state. In relation to congenital syphilis, the first three states remain in evidence, alongside the state of Pernambuco. Deaths from congenital syphilis in children under one year reached the rate of 18.1 deaths / 1,000 live births in the state of Rio de Janeiro, representing 23.2% of the total observed in the country. In the last five years, there

has been a steady increase in the number of cases of syphilis in pregnant women, congenital and acquired, which can be attributed in part to the increased coverage of testing, health to the administration of penicillin in Primary Care, worldwide shortage of penicillin, and the improvement of the surveillance system, which may reflect an increase in reported cases (BRAZIL, 2017). Although the prevalence of *Treponema Pallidum* infection decreased significantly with the discovery of penicillin in the 1940s from the 1960s, and more markedly in the 1980s, there has been a worldwide trend in syphilis re-emergence between population and, in particular, the cases of congenital syphilis, making it one of the most challenging public health problems of the beginning of the millennium (LORENZI et al., 2001). Goals in the Integrated Health Surveillance Program of the year 2005: VDRL during prenatal /childbirth, based on information from the hospital information system (SIH-SUS) and linked to the payment of the Hospital Admission Authorization for childbirth (AIH-parto), published in ministerial order 766 of December 21, 2004.

Lack of Penicillin

In pregnancy, non-penicillin treatments are inadequate and should only be considered as an option in the absolute contradictions to the use of penicillin. For those women who are proven to be allergic to penicillin, desensitization is recommended in tertiary care according to existing protocols. Pregnant women with confirmed allergies and inability to perform desensitization during gestation should be treated with ceftriazone (Ministry of Health, 2015). Penicillin is the drug considered first-line treatment for syphilis, because it is cheap and effective, but the lack of the drug in health facilities in Brazil has generated concern in recent years, caused by the lack of specific raw material for the production of the drug. However, in an emergency, the Ministry of Health, through technical note 109/2015, prioritized the treatment of syphilis in pregnant women and children with syphilis, recommending the exclusive use of penicillin G benzathine for pregnant women with syphilis and crystalline penicillin for children with congenital syphilis. During the course of this research, it was possible to verify through newsletters, websites and technical notes that crystalline penicillin presented an increasing lack of supply in Brazilian health institutions. Such situations is a calamity, since the medication in question treats children born with syphilis. Until the end of this research there was no supply of medication in pharmacies, increasing the concern of health teams who are replacing benzathine penicillin G with procaine penicillin or ceftriaxone medicines used to treat adults and still does not show a total effectiveness in the treatment of children with congenital syphilis. Because it is a recent fact, we have not found enough material to describe proper references. Therefore, it is necessary to emphasize the importance of quality prenatal care, early treatment in the gestation, health education through actions aimed at clarifying the population the importance of condom use, about the appropriate treatment for the pregnant woman and the partner avoiding the transmission to the concept so that it does not reach the fetal commitment. The Brazilian Ministry of Health has sent an informative note about the lack of penicillin that occurred in 2014, remaining until 2015. Currently, there is a national shortage of penicillins, especially benzathine penicillin due to the lack of specific raw material for its production in the the global market. Therefore, this joint information note prepared by the Secretariat of Health Surveillance and Secretariat of Science, Technology and

Strategic Inputs of the Ministry of Health recommends the exclusive use of penicillin G benzathine for pregnant women with syphilis and of crystalline penicillin only for children with congenital syphilis (BRAZIL, 2015). Since 2005 the WHO has already warned about the inefficient supply of penicillin, and by 2014 there was a lack of penicillin throughout Brazil (WHO, 2005).

Conclusion

The solution of the problem of lack of supply through political forums and the union of efforts between the different levels of public administration is essential in order to promote initiatives to improve care processes and education for professionals who perform prenatal, hearing screening neonatal care and clinical follow-up of these children. In fact, only these initiatives could mitigate the damage and consolidate more effectively the prevention and treatment of this disease. In Brazil, it is essential to reduce the incidence and possibly eradicate congenital syphilis, measures aimed at improving health education for the population, especially in relation to sexually transmitted diseases, better coverage and, especially, the serological screening for syphilis in the first and third trimesters of gestation and at the time of delivery, appropriate interpretation of syphilis serology results in pregnant women, the search for sexual partners and their effective treatment, as well as a better medical knowledge regarding the epidemiological criteria for the diagnosis of the disease are necessary. The quality of the prenatal care received by the pregnant woman is not enough to guarantee the control of congenital syphilis and the reach of the disease incidence goal and that the initial conduct for the detection and treatment of congenital syphilis is not in accordance with the guidelines defined by the Ministry of Health of Brazil.

REFERENCES

- BRAZIL, BOLETIM EPIDEMIOLÓGICO SECRETARIA DE VIGILÂNCIA EM SAÚDE – Ministério da Saúde – Brasil. <http://www.aids.gov.br/pt-br/pub/2017/boletim-epidemiologico-de-sifilis-2017> acesso 18 setembro 2018
- BRAZIL. MINISTÉRIO DA SAÚDE. Boletim epidemiológico sífilis 2015. Ano IV nº 01. Brasília, 2013.
- BRAZIL. MINISTÉRIO DA SAÚDE. Caderno da atenção básica: Gestaç o de Alto risco, Manual t cnico. Bras lia, 2012, p, 139-141. Dispon vel em: <
- BRAZIL. MINIST RIO DA SA DE. Departamento de DST, Aids e Hepatites virais. 2004.
- BRAZIL. MINIST RIO DA SA DE. Secretaria de Vigil ncia em Sa de. Boletim Epidemiol gico S filis. v.48, n. 36. 2017.
- BRAZIL. Minist rio da Sa de. Secretaria de Vigil ncia em Sa de. Programa Nacional de DST e AIDS. Manual de controle das doen as sexualmente transmiss veis. Bras lia: Minist rio da Sa de, 2006.
- BRAZIL. Secretaria de Vigil ncia em Sa de. Secretaria de Ci ncia, Tecnologia e Insumos estrat gico. Nota Informativa Conjunta n.109/2015b/GAB/SVS/MS, GAB/SCTIE/MS. Orienta a respeito da prioriza o da penicilina G. benzatina para s filis em gestantes e penicilina cristalina para s filis cong nita no pa s e alternativas para o tratamento. Bras lia, 28 de outubro de 2015.
- CAMPOS, Ana Luiza de Ara jo *et al.* S filis em parturientes: aspectos relacionados ao parceiro sexual. Rev. Bras. Ginecol. Obstet., Rio de Janeiro, v. 34, n. 9, p. 397- 402, set. 2012. Dispon vel e. acessos em 24 maio 2018. <http://dx.doi.org/10.1590/S0100-72032012000900002>.
- CENTERS FOR DISEASE CONTROL AND PREVENTION. SEXUALLY TRANSMITTED DISEASES TREATMENT GUIDELINES 2002.
- FIGUEIR -FILHO EA, Senefonte FRA, Lopes AHA, Morais OO, Souza J nior VG, Maia TL, Duarte G. Frequ ncia das infec es pelo HIV-1, rub ola, s filis, toxoplasmose, citomegalov rus, herpes simples, hepatite B, hepatite C, doen a de Chagas e HTLV I/II em gestantes, do Estado de Mato Grosso do Sul 2007. http://bvsm.sau.de.gov.br/bvs/publicacoes/gestacao_alto_risco.pdf>. Acesso em: 22.Jul. 2016.
- K HLER W. Zentralblattf r Bakteriologie - 100 years ago: Protozoa as causative agents of smallpox, or: Cytoryctes and no end. Int J Med Microbiol. 2001
- LAFET , K. R. G *et al.* S filis materna e cong nita, subnotifica o e dif cil controle. Rev. bras. epidemiol. [Internet]; v. 19, n. 1, 2016.
- LORENZI, D.; MADI, J. S filis cong nita como indicador de pr -natal. Rio Grande do Sul, 2001, p 647-652.
- MINIST RIO DA SA DE. Caderno de aten o b sica HIV/Aids, hepatites e outras DSTs: Transmiss o vertical da S filis. Bras lia, 2006 p, 75-99.
- OMS (Organizaci n Mundial de la Salud). Orientaciones mundiales sobre los criterios y procesos para la validaci n de la eliminaci n de la transmisi n materno infantil del VIH y la s filis. Ginebra: OMS, 2015.
- OMS (Organizaci n Mundial de la Salud). Orientacion es mundiales sobre los criterios y procesos para la validaci n de la eliminaci n de la transmisi n materno infantil del VIH y la s filis. Ginebra: OMS, 2015.
- PADOVANI, C, OLIVEIRA R.R, PELLOSO, S.M. Syphilis in during pregnancy: association of maternal and perinatal characteristics in a region of southern Brazil. Rev. Latino-Am. Enfermagem. 2018;26:e3019. Dispon vel em: http://www.scielo.br/pdf/rlae/v26/pt_0104-1169-rlae-26-e3019.pdf Acesso em: 3 nov. 2018.
- PAHO (Pan American Health Organization). Elimination of mother-to-child transmission of HIV and syphilis in the Americas. Update 2016. Washington, D.C.: PAHO, 2017 .
- PASQUALOTTO, Alessandro Comar ; SCHWARZBOLD, Alexandre Vargas. Doen as Infecciosas: consulta r pida- Porto Alegre: Artmed, 2006.
- TAVARES, Walter; MARINHO, Luiz Alberto Carneiro. Rotinas de diagn sticos e tratamento das doen as Infecciosas e Parasit rias. 2. ed. S o Paulo: Atheneu, 2010.
- WORLD HEALTH ORGANIZATION (WHO). Investment case for eliminating mother-to-child transmission of syphilis: promoting better maternal and child health and stronger health systems. Geneva; 2012
- WORLD HEALTH ORGANIZATION. Global incidence and prevalence of selected curable sexually transmitted infections 2008. Reproductive health matters, 2012. Dispon vel em: [http://www.rhm-elsevier.com/article/S0968-8080\(12\)40660-7/](http://www.rhm-elsevier.com/article/S0968-8080(12)40660-7/). Acesso em: 22 mar. 2016.