

Amendment to the UK Guideline on the management of syphilis 2015; management of syphilis in pregnant women

4th June 2019

In recent years the incidence of infectious syphilis in the UK has increased dramatically. There was a 20% increase in diagnoses between 2016 and 2017, and a 148% increase relative to 2008¹ and there are several reports of cases of congenital syphilis.²

The guideline authors have provided clinical advice on the management of the babies born with congenital syphilis, as well as regularly providing clinical advice and support to doctors and midwives who are managing pregnant women with positive syphilis serology. We have noted that the continued option of macrolides within the UK guidelines for the management of syphilis in pregnancy, even with the stated caveats and cautions, provides a treatment option that is suboptimal and results in treatment failure with significant adverse outcomes reported. Macrolide antibiotics do not cross the placenta well to treat a foetus that may be affected by syphilis and *Treponema pallidum* has unacceptably high rates of macrolide resistance reported.³⁻⁵

We are therefore making an amendment to the 2015 UK guidelines for the management of syphilis and removing macrolides as a treatment option. This is consistent with the Centres for Disease Control⁶ and International Union Against Sexually Transmitted Infections – Europe⁷ guidelines. World Health Organisation guidelines,⁸ as the UK guideline did until now, continue to offer macrolide treatment as a last option for pregnant women with the caveat the neonates need to be treated at birth. However in our experience, this may result in treatment failure in pregnancy and transmission to the neonate.

For pregnant women who report intolerance or allergy to penicillin or other beta-lactam antibiotics we are making the following recommendations for management which must include consultation with the patient at all stages:

1. A thorough history of drug allergy is taken and substantiated from primary care practitioners
2. If a true allergy history is ascertained refer urgently to immunology/allergy services for testing for allergy to penicillin and ceftriaxone (this is consistent with current NICE guidance⁹). A rapid access referral pathway has been established within Manchester (UK); a high prevalence area with a specialist tertiary foetal-maternal medicine unit which could be adopted in other services.¹⁰
3. If possible following this treat with penicillin (first line) or ceftriaxone (second line)
4. In the rare circumstance of true beta-lactam allergy being confirmed:
 - a. Refer to the tertiary foetal medicine unit for co-management by obstetric, midwifery, paediatric and tertiary GUM (or infection) specialists. Such services exist for the management of HIV positive pregnant women and are best placed to manage such difficult cases.
 - b. Management should be on a case by case and multi-disciplinary basis (including the pregnant woman) where the risk of treatment is balanced against the risk of infection to the neonate and pregnancy loss, still birth or congenital infection and subsequent disability. Factors to consider include the stage of syphilis and any previous treatment history. Such teams also have the ability to monitor mother and baby as needed.
 - c. Desensitisation to penicillin and immediate treatment of the mother with penicillin should be considered and discussed within the team including the mother.
 - d. The authors of this guideline amendment are available for sub-specialist clinical advice and referral within the UK as needed.

Margaret Kingston: Consultant GU Medicine, Manchester University NHS Foundation Trust;

margaret.kingston@mft.nhs.uk

Helen Fifer; Helen.Fifer@phe.gov.uk

Patrick French; Patrick.French@nhs.net

Janet Wilson; janet-d.wilson@nhs.net

Craig Tipple; craigtipple@nhs.net

On behalf of the Clinical Effectiveness Group of BASHH

References:

1. <https://www.gov.uk/government/statistics/sexually-transmitted-infections-stis-annual-data-tables> accessed 31.3.2019
2. Martina Furegato, Helen Fifer, Hamish Mohammed, Ian Simms, Paul Vanta, Sharon Webb, Kirsty Foster, Margaret Kingston, André Charlett, Bhavita Vishram, Claire Reynolds, Noel Gill, Gwenda Hughes. Factors associated with four atypical cases of congenital syphilis in England, 2016 to 2017: an ecological analysis. *Euro Surveill.* 2017 Dec 7; 22(49): 17-00750.
3. Tipple C, McClure MO, Taylor GP High prevalence of macrolide resistant *Treponema pallidum* strains in a London centre *Sex Transm Infect* 2011;87:486-488.
4. Katz, Kenneth A; Klausner, Jeffrey D. Azithromycin resistance in *Treponema pallidum* *Current Opinion in Infectious Diseases:* February 2008 - Volume 21 - Issue 1 - p 83–91
5. Lola V Stamm. Global Challenge of Antibiotic-Resistant *Treponema pallidum*. *Antimicrobial Agents and Chemotherapy* Jan 2010, 54 (2) 583-589; DOI: 10.1128/AAC.01095-0
6. <https://www.cdc.gov/std/tg2015/syphilis-pregnancy.htm>
7. <https://www.iusti.org/regions/europe/pdf/2014/2014SyphilisguidelineEuropean.pdf>
8. <https://apps.who.int/iris/bitstream/handle/10665/249572/9789241549806-eng.pdf;jsessionid=C5C61E6760B8C6F7F6D51A16AD2C2C91?sequence=1>
9. <https://www.nice.org.uk/guidance/cg183>
10. A review of the rapid referrals for allergy investigation in patients with syphilis and self-reported penicillin allergy. J Leighton, T Garcez, A Sukthankar, J Edmonds, M Kingston. Poster Presentation 2018 British HIV Association Spring conference. *HIV Medicine*, 18 (Suppl. S2) and *Allergy* 73, 598-598