WEST OF SCOTLAND GUIDELINE *APPROVED September 2022*

Syphilis

CONTENTS:

WHAT'S NEW:

There have been no changes to this guidelines since the last update.

ANY CASES OF SUSPECTED OR CONFIRMED SYPHILIS SHOULD BE DISCUSSED WITH A SENIOR DOCTOR (e.g.: Associate Specialist, Specialist Registrar, Consultant)

INTRODUCTION

All patients diagnosed with Syphilis should be given a detailed explanation of their condition and this should be reinforced with the offer of written information.

Syphilis in Pregnancy

Refer to BASHH guidelines (beyond the scope of this document)

History taking and Surveillance

Major outbreaks of syphilis (mostly in MSM) have been reported in London, Manchester, Brighton and Dublin as well as Glasgow and Edinburgh. Ask about sex in scene venues (saunas, back rooms) and geographical location of sex partners. Record this location in the notes.

There have also been recent outbreaks of syphilis affecting young heterosexual males and females in Scotland.

A national surveillance scheme exists for all early infectious syphilis. This uses laboratory data and clinician-initiated reports. Each clinic should be aware who completes these forms in their area. These forms should be completed proactively. Completion of this form should be recorded in the patient clinical notes.

Clinical and laboratory assessment:

- Testing for Syphilis **always** involves blood tests. **In addition** if there are suspicious lesions then dark ground microscopy and PCR should be performed where possible (see under primary syphilis)
- Blood tests for syphilis are either known as ‘Treponemal’ or ‘non-treponemal’ tests for syphilis:
    - Treponemal tests include TPPA, Treponemal total antibody EIA and Inno-LIA. These should not be used to assess disease activity and remain positive for life in most patients
    - Non-treponemal tests include VDRL and RPR and are quantitative. They are important for monitoring response to treatment and possible reinfection
- The initial screening test is a Treponemal total antibody EIA. If the screening test is found to be positive, further tests will be required and requested. These may include VDRL/ RPR, TPPA, Inno-LIA blot and specific IgM. These tests may be done locally or sent to the regional virus laboratory, Glasgow Royal Infirmary or The Royal Infirmary of Edinburgh Microbiology/Virology Lab or Colindale.

- Inno-LIA blot is recommended when the confirmatory test does not confirm the positive treponemal screening test result
- All positive tests should be repeated on a second specimen for confirmation
- If syphilis is suspected **clinically**, indicate this clearly on the request form
- Full clinical examination, with particular emphasis on the skin, genitals, lymph nodes and mucosa is essential in all patients found to have positive syphilis serology. Cardiovascular and neurological examination is required in late syphilis and in those with relevant symptoms
- **HIV testing** should be recommended to all patients diagnosed with syphilis
- **A full STI screen** should be recommended to all patients diagnosed with syphilis. In addition the need for Hepatitis B vaccination should be assessed
- **It is important that on the very first day of of t**reatment **(DAY 1 of treatment), VDRL/RPR titre is taken, allowing accurate assessment of response to treatment**. It is also important to ensure that when assessing response to therapy, results being compared are from the same lab.

HIV infection and Syphilis

- Serological tests for syphilis in patients with both syphilis and HIV are generally reliable although false negative tests and delayed appearance of sero-reactivity have been reported
- HIV infected patients with early syphilis ***may*** be more likely to develop multiple/ large or deeper genital ulcers
- HIV infected patients with early syphilis ***may*** have an increased risk of neurological involvement, unusual neurological manifestations, and higher rate of treatment failure
- HIV infected patients may have neurological abnormalities that may be difficult to differentiate from neurosyphilis. Limited case review data suggests higher risk of neurosyphilis in HIV+ if VDRL/RPR >=1:32
- A lumbar puncture is recommended in **all HIV positive patients with:**

  a) Serological treatment failure

  b) Neurological or ophthalmological signs/ symptoms

  c) VDRL/RPR >=1:32 at any stage

  d) Consider in those with late syphilis and CD4<350
- HIV infected patients may also be more likely to have rapid progression to gummatous syphilis

- All HIV infected patients co-infected with syphilis should have the choice to have a neurosyphilis treatment course whatever their syphilis infection stage. The decision may involve their attitude to further complications, injection discomfort and the likely ease of follow up. These difficult treatment decisions must be made by a senior HIV-experienced doctor
- HIV infected patients may have a slower rate of decline of VDRL/ RPR after treatment
- HIV co-infected patients should be followed up for life with at least six monthly serology (consider 3-monthly in an outbreak situation)

1. Incubating Syphilis / Epidemiological treatment

If a patient is asymptomatic and reports exposure to infectious syphilis, discuss the option of:

- Immediate epidemiological treatment before any results have been received, or
- Waiting for a positive result, repeating the serology at monthly intervals for three months

In an outbreak situation epidemiologic treatment should be given especially if there is a chance the patient will not return.

Epidemiologically treated patients still require serological follow-up.

***Benzathine penicillin 2.4MU intramuscular**

For administration, see appendix 1

(as*Extencilline 8ml) *(NB unlicensed medication, named patient form may be needed)*

PENICILLIN ALLERGY: Doxycycline 100mg twice daily orally for 14 days

Note: there have been some reports of azithromycin resistance for syphilis – so it should not be used!

2. Primary Syphilis

Incubation period 21 days (9-90 days).

Symptoms and Signs

- **Characterised by an ulcer known as "*the chancre*", in genital and non-genital sites, with localised lymphadenopathy**
- The chancre is often painless with a clean base and indurated edges, BUT can be multiple and painful
- Depending on the site, chancres may go unnoticed and heal spontaneously
- **Any anogenital ulcer should be considered to be syphilis until proven otherwise**

Diagnosis

Dark ground microscopy, PCR testing and serology can help in the diagnosis of primary syphilis.

- Where possible/ available perform **dark ground microscopy** of the serous exudate from any visible ulcers - slide taken to lab **immediately**. (Know if your laboratory can do dark ground microscopy) ***(NB: Dark ground microscopy is of no value in intra-anal or oral lesions. Only take a dark ground if you know how, get help if you don't)***

- If dark ground microscopy is not available then consider sending the patient to the appropriate centre

- If a suspicious lesion is dark ground negative, consider bringing the patient back for up to two more dark grounds and repeat serology one week later

- **PCR testing** is available via the Regional Virus laboratories in Glasgow and Edinburgh: place the swab in viral transport medium and send to your microbiology department who will forward to the relevant virus lab. PCR is the preferred method for oral and other lesions where contamination with other commensal treponemes is likely. PCR is not a replacement for dark ground microscopy due to the time taken to get the result but should be done alongside dark ground microscopy if it is available.

  Please note all PCR ulcer swabs should be tested for HSV1/2 and *T.pallidum*

Serological tests in primary syphilis

- May be **negative** at this stage (usually become positive 2 weeks after the chancre appears)
- If initial serology is inconclusive and there is a clinical suspicion, arrange repeat serology a week later and ideally at 6 weeks and 3 months
- Avoid the use of antibiotics if possible at this stage if the diagnosis remains uncertain **and the patient reports no exposure to syphilis.** Treatment at this stage may prevent a serological response. Likewise **if the patient is requiring antibiotics for another reason then this may affect syphilis serology**

Management

Treatment must be initiated **as soon as a diagnosis is reasonably established** to limit infectivity and reduce risk of progression to secondary syphilis. Do not defer therapy because someone is uncertain about HIV testing or to bring patients back for further confirmatory tests. If you are happy with the clinical picture and the dark ground/ PCR is positive then start treatment **immediately**.

***Benzathine penicillin G** 2.4 MU **intramuscular**

For administration see appendix 1

(as*Extencilline 8ml) *(NB unlicensed medication, named patient form may be needed)*

PENICILLIN ALLERGY: Doxycycline 100mg twice daily orally for 14 days

Complications of Treatment

1) Jarisch Herxheimer reaction may occur at approximately 8 hours. This is an acute febrile illness with headache, myalgia, rigours which resolves in 24 hours and is common in early infection (advise rest, paracetamol). Usually this is not clinically important unless there is neurological or ophthalmogical involvement or if the patient is pregnant. In these situations prednisolone and further monitoring may be advised (discuss with consultant)
2) Anaphylaxis – facilities for resuscitation must be present. Refer to local policy for further guidance

Patients should remain on the premises for 15 minutes after receiving their 1st injection to allow observation for immediate adverse reactions.

Partner Notification

All patients diagnosed with syphilis need specialist input and to be seen by a sexual health adviser experienced in partner notification for Syphilis at diagnosis and at each follow up visit, until partner notification and any local surveillance is documented as complete. Sexual partners within the last 3 months should be notified.

Follow-up

- Clients should refrain from sexual contact until any lesions are fully healed and 2 weeks following treatment completion
- Assess clinically at the end of treatment. Repeat serology at 3, 6 and 12 months after the end of treatment regime then if indicated, six monthly until VDRL/ RPR is negative or serofast
- If VDRL/RPR was positive at presentation expect a four-fold drop (2 dilution steps) in titre by six to twelve months.
- If VDRL/RPR titre does not fall, or at any stage shows a >2-fold rise, discuss with senior doctor
- Discharge only at 12 months if VDRL/RPR negative or if VDRL/RPR is serofast and has appropriately decreased as above
- Ask permission to write to GP to confirm treatment complete, give patient a written summary of treatment with discharge serology (SEE APPENDIX LETTER)

3. Secondary Syphilis

Develops in 25% of untreated patients, typically 3 months after infection acquired.

Symptoms and Signs

- **Multi-system involvement within the first 2 years of infection**
- Often associated with a generalised rash affecting palms and soles, muco-cutaneous lesions, condylomata lata (confluent wart like lesions) and generalised lymphadenopathy and fever
- Less commonly: patchy alopecia, anterior uveitis, meningitis, cranial nerve palsies, hepatitis, splenomegaly, periosteitis, arthritis and glomerulonephritis.

Diagnosis

Dark-ground microscopy and PCR: from mucous patches or condylomata lata

Serological tests: invariably all positive

Other tests: Full blood count, liver and renal function tests

Rapid tests: Some centres have a small supply of Abbott Determine TP fingerprick tests. These are especially useful for confirming clinical suspicion of secondary syphilis. Discuss with Senior Doctor and see pack for instructions on how to use. They are insufficiently sensitive to exclude syphilis completely and should not replace formal serological testing.

Treatment, Complications & Follow-up

As for primary syphilis, **unless** the patient is pregnant or has neurological/ opthalmological signs/ symptoms.

For those with neurological/opthalmological symptoms and signs (and those who are pregnant) discuss management with GUM Consultant (**and** the relevant speciality) as imaging, lumbar puncture, pre-treatment steroids and admission for antibiotic treatment may be recommended.

SEE section on neurosyphilis.

DO NOT defer therapy if a single blood test is positive and the clinical picture fits: start treatment and take a confirmatory blood test.

<u>Partner notification</u>

Partner notification may need to extend to 2 years.

4. Early Latent Syphilis

Syphilis serology is positive, person is asymptomatic and is within the first 2 years of infection.

Diagnosis

1. Serological tests are positive (on two separate occasions)

   AND

2. Known to have been syphilis serology negative within the last two years **OR** has positive specific IgM with likelihood of infection in the last two years

   AND

3. Patient is asymptomatic, with no clinical evidence of disease

Treatment, Complications & Follow-up

As for primary syphilis.

<u>Partner notification</u>

Partner notification may need to extend to 2 years.

5. Late Latent Syphilis

Syphilis serology is positive, patient is asymptomatic and has no known negative serology within the last 2 years.

See below for investigations required.

Examination

- All patients need a careful clinical cardiovascular and neurological history **recorded in the notes**.
- Auscultation must be performed in patients with late latent or tertiary syphilis.
- Patients who have signs or symptoms of cardiovascular involvement should have a full cardiovascular assessment. Consider an echocardiogram +/- chest x-ray before starting therapy to exclude aortic valve disease. Patients with clinical or radiological evidence of aortic valve disease must be referred to a cardiologist for further assessment
- Patients should have a thorough neurological examination if they have symptoms suggestive of neurological involvement
- The BASHH 2015 guidelines discuss the necessity of CSF examination in asymptomatic patients. Asymptomatic patients with no clinical findings consistent with neuro-syphilis do not need a lumber puncture. CSF examination **should** be done in those who have:
    - Neurological/opthalmological signs/symptoms
    - VDRL/RPR >=1:32
    - Those with treatment failure

Treatment – LATE LATENT SYPHILIS

There is much less urgency in treating late syphilis and it is better to plan treatment so that it can be reliably completed

_Benzathine penicillin G** 2.4 MU intramuscular on day **1** & **8** & **15**
(as Extencilline 8ml)

For administration, see Appendix 1

OR

****Procaine penicillin** 600,000units intramuscular
once daily for **14** days

*(**unlicensed medications, named patient form may be needed)*

PENICILLIN ALLERGIC (or declines parenteral):

Doxycycline 100mg twice daily orally for 28 days

Complications

- Jarisch Herxheimer reaction is less common than in early syphilis
- Procaine reaction. This is caused by inadvertent IV injection of procaine penicillin which is minimised by the aspiration technique of injection. Lasts for less than 20 minutes and is characterised by feelings of impending death +/- seizures. Anaphylaxis should be excluded and the patient should be reassured and calmed. Sedation may be required for seizures
- Anaphylaxis – facilities for resuscitation must be present. Refer to local policy for further guidance

Patients should remain on the premises for 15 minutes after receiving their 1st injection to allow observation for immediate adverse reactions.

Partner Notification LATE LATENT SYPHILIS

- All patients to see sexual health adviser

Follow-up

- 4 weeks after end of treatment regime - to check compliance and partner notification
- 3 months - to repeat serology ± HIV test
- VDRL/RPR is often negative in late syphilis but this does not exclude the need for treatment. Follow up is to ensure adherence and for completion of partner notification. Discharge at 3 months if VDRL/RPR remains negative.
- If VDRL/RPR titre was raised prior to treatment, repeat at 3,6,12 months until VDRL/RPR negative or reduced and serologically stable on two occasions
- Ask permission to write to the patient's GP to confirm treatment complete and give patient a written summary of treatment and discharge serology **(SEE APPENDIX LETTER).**

6. Neurosyphilis

Can be early (secondary) or late (tertiary) in the course of disease.

The management and investigation of neurosyphilis should be made with a Consultant in Genitourinary Medicine/ Infectious Diseases and a consultant neurologist.

Meningovascular: may be associated with early or late syphilis.

Parenchymatous: General paresis and/or tabes dorsalis.

Patients should have a thorough neurological examination to rule out focal neurology or papilloedema that may indicate raised intracranial pressure and relevant radiological imaging of the head requested if these signs are present **prior** to lumbar puncture. Neurological imaging must be considered if there are neurological signs or symptoms.

LUMBAR PUNCTURE

In order for CSF tests to be interpreted correctly the CSF should not be macroscopically contaminated with blood.

CSF tests should include:

1) Cell count
2) Total protein
3) Oligoclonal bands
4) A treponemal test
5) A non-treponemal test
6) TPHA index. This requires CSF albumin and CSF IgG (but not widely available)

If the CSF is abnormal then CSF examination should be repeated between 6 weeks and 6 months after treatment.

TREATMENT FOR NEUROSYPHILIS

Prednisolone 40-60mg orally once daily for three days, starting anti-treponemal treatment 24 hours after commencing prednisolone.

For ENT or optic atrophy complicating syphilis infection, a longer prednisolone course may be considered. Refer for ENT/Ophthalmology Consultant opinion.

Procaine penicillin 2.4MU intramuscular once daily for **14** days

(Unlicensed medication, named patient form may be needed)

PLUS

Probenecid 500 mg 4 times daily orally for 14 days

OR

Benzylpenicillin 10.8g-14.4g daily given as 1.8g-2.4g intravenously every 4-6hours for **14** days

PENICILLIN ALLERGIC (or declines parenteral): Doxycycline 200mg twice daily orally for 28 days

In tertiary neurosyphilis partner notification and follow-up as for late latent syphilis.

7.Tertiary syphilis: Cardiovascular Syphilis

Asymptomatic: diagnosed on clinical, radiological and echocardiographic changes.

Symptomatic: usually from aortic valve disease, aneurysmal changes of the aorta or coronary ostial occlusion.

Requires assessment by Cardiologist before treatment. Discuss with senior doctor before referring.

TREATMENT FOR CARDIOVASCULAR SYPHILIS

Treatment as for late latent syphilis plus **Prednisolone** 40-60mg orally once daily for three days, starting anti-treponemal treatment 24 hours after commencing prednisolone.

Partner notification and follow-up as for late latent syphilis but will also need long-term follow up with cardiology. Cardiovascular lesions may progress despite adequate treatment for syphilis.

8. Tertiary syphilis: Gummatous Syphilis

Gummatta can occur anywhere but most often affecting skin and bones. Gummatta should be managed alongside the appropriate specialist.

References

1. BASHH UK National Guidelines on the Management of Syphilis 2015 accessed via www.bashh/org/guidelines
2. 2014 European guideline on the management of Syphilis

Appendix 1: *Preparation Instructions for Extencilline 2.4MU*

To reduce the pain experienced by patients receiving benzathine and procaine penicillin injections, 1% lidocaine (lignocaine) can be used as an alternative diluent to water for injections (unlicensed indication).

Benzathine Dose: 2.4 Mega units IM weekly for up to 3 weeks.

Presentation: Powder for suspension for injection.

Reconstitute the vial with 8 ml of 1% lidocaine hydrochloride BP solution. Split the resultant suspension into two equal volumes.

The suspension should be administered by deep intramuscular injection in two different sites.

Contraindications

Allergy to penicillin or lignocaine. Concomitant anticoagulant therapy. Bleeding diathesis (e.g. Haemophilia).

Precautions

For patients with penicillin allergy, cross reactivity to other beta-lactams such as cephalosporins should be taken into account.