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Borders Sexual Health Service Clinical Protocol
Section 4: SYPHILIS

What's new in Version 7:

- The syphilis epidemic in the UK continues. Have a high index of suspicion for symptoms and signs of primary and secondary syphilis, especially in high risk groups.

- Syphilis testing (both serology and PCR testing from suspicious ulcers) should continue to be performed in general practice. Syphilis treatment should be undertaken in the sexual health service.

Background

Syphilis is a contagious disease caused by Treponema pallidum. It is a slender, spiral, motile organism and divides at intervals of 30-36 hours. Humans are its only natural host.

Syphilis transmission is generally through sexual intercourse – through abrasions on epithelial surfaces or mucous membranes. It is transmitted efficiently through oral, as well as penetrative intercourse. 45-60% of partners of those with early syphilis (< 2 years post acquisition) will themselves be infected. Patients with late syphilis (>2 years post acquisition) are not considered infectious.

Mother to child transmission of syphilis can also occur, causing congenital infection as well as other adverse pregnancy outcomes. Transmission risk is highest in early infection.

Syphilis is classified according to its stage and can be either EARLY or LATE.

Symptomatic early syphilis includes Primary and Secondary syphilis:

Primary syphilis: Occurs 10-90 days after exposure and is characterised by an ulcer (the chancre) and associated regional lymphadenopathy. Any ulcer in the anogenital area should be considered to be caused by syphilis until proven otherwise. All patients presenting with ulceration MUST have syphilis serology performed. In single ulcers, tears or fissures, or multiple ulcers that are not typical of herpes simplex (eg are less painful than expected), perform syphilis PCR. Chancres will resolve spontaneously over a few weeks even if left untreated.

Secondary syphilis: usually 3-6 weeks after development of a chancre, within 2 years: Symptoms most often include:

- Rash – maculopapular, can be scaly, often affecting the palms, soles and trunk which is usually not itchy.
- Mucocutaneous lesions-mucous patches, these are painless transient ulcers within the mouth and on the mucous membranes of the genitalia. Condylomata lata-are flat warty lesions on the perianal and vulval skin.
- Generalised lymphadenopathy

- Hepatitis
- Patchy alopecia

Less commonly symptoms of early neurological syphilis can occur and these include:

- Cranial nerve palsies
- Meningitis
- Uveitis
- Otitis
- CVA

Early latent syphilis
Positive syphilis serology with no symptoms and signs within the first two years of infection. Often the diagnosis is made on the sexual history in conjunction with a previous negative serology result within the last 2 years.

Late syphilis is divided into:

Late latent syphilis
Diagnosed when the serological tests are positive but there are no symptoms or signs of syphilis and there is no evidence of negative syphilis serology in the preceding 2 years. ie the infection has been present for more than 2 years. Where the duration of infection is unknown, for example where there is no previous negative syphilis serology, the infection should be treated as late latent.

Symptomatic late syphilis
This will develop in approximately one-third of untreated individuals.
It can be divided into:

- Neurosyphilis
- Cardiovascular syphilis
- Gummatous syphilis

Diagnosis

History

- Symptoms of early syphilis as described above
- Details of previous treatment for syphilis if relevant
- Obstetric history suggesting potential complications of syphilis e.g. miscarriages and still births.
- Blood donation and antenatal screening history
- A history of living in countries where Yaws (Caribbean/Africa)-look for tissue paper scars on the anterior aspects of the legs and Pinta (Central and northern South America) and Bejel (Saharan Africa/Middle East) are endemic.
- Details of previous STI testing including syphilis testing (useful in classifying infection as early/late)

Examination

In early infection:

- Genitalia, oral cavity, anus, skin, mucous membranes and lymph nodes.

In late infection:

- As above plus
- Examination of cranial nerves
- Examination of the cardiovascular and neurological systems to include the eyes
- Exclude papilloedema if lumbar puncture is being considered. If patients with late syphilis have no neurological abnormalities then a lumbar puncture is not required.

Investigations

Routine screening:

- Syphilis IgG (Syphilis EIA on NaSH)

This should be routinely performed on all patients. Positive syphilis serology should be interpreted alongside clinical history.

Suspected syphilis/syphilis contacts:

- Request SYPH on sample form – if screening IgG is positive the lab will automatically run additional tests
- It is NOT necessary to order individual tests on NaSH – you should only ever order Syphilis EIA

- PCR Testing. This can be performed on all ulcers. Take a swab from the base of an area of ulceration using the red topped swab and viral transport medium. Request 'Syphilis PCR' on NaSH. Record the site of the ulcer (anal, penile, vulva etc) on the request form and corresponds with the request on NaSH. A serology sample should always be taken in addition if a PCR sample is being sent.

Interpretation of results

All positive syphilis results should be reviewed by a senior GUM clinician. The following is for guidance only.

Positive syphilis serology

Always repeat positive tests to confirm the result.

Serology should ALWAYS be repeated on the day treatment is initiated to provide a baseline to monitor response to treatment. The RPR titre may rise between the initial diagnosis and the day treatment is started. If this rise is not documented it will be difficult to detect the true post treatment fall in titre and lead to the possible erroneous diagnosis of post treatment failure.

- Patients with a negative RPR in peripheral blood are unlikely to have Neurosyphilis.
- A RPR > 1:32 may predict CSF abnormalities

Biological False Positives:

If only one marker is positive within the range of syphilis screening tests this usually indicates a false positive test. Discuss with Dr. The patient should be informed and asked to provide a follow up sample 2 weeks later. If there is no change in the titre this confirms a false positive.

Negative serology in suspected syphilis

Serology may be negative in the primary stage. If the patient has signs of possible early syphilis with negative serology review after 1 week and repeat the serology.

Otherwise repeat screening is recommended at 4 weeks and then 12 weeks following:

1. High risk exposure,
2. Patient is a contact of syphilis and epidemiological treatment is not given.

Yaws or Pinta can give identical results to syphilis though the RPR is often negative or <1:8. It is not possible to exclude latent syphilis in this situation and therefore patients are managed as though they have syphilis.

Management

All new cases of syphilis should be brought to the attention of a GUM consultant.
All symptomatic cases and suspected neurosyphilis cases: discuss with GUM consultant.

- All patients with syphilis MUST be advised to have screening for other STI's including HIV.
- Patients should be given verbal and written information about syphilis and the long term implications for them and their partners - see syphilis patient information leaflet in document library.
- A standard syphilis letter should be sent to the GP both at diagnosis and at 12 months to document the patients serofast serology

Treatment:

Treatment should be started as soon as possible following diagnosis. The result of the confirmatory test is not required if there is clinical suspicion.

See BASHH guidelines for further treatment options.

Incubating syphilis/Epidemiological treatment:

- *Benzathine penicillin 2.4 MU IM single dose (if non penicillin allergic) or Doxycyline100mg orally bd for 14 days

Early syphilis (Primary, Secondary and Early Latent):

- *Benzathine Penicillin 2.4 mu IM single dose or
- Doxycycline 100mg orally BD for 14 days

Alternative regimes:

- Doxycyline 100 mg orally bd for 14 days
- Azithromycin 2G stat.
- Ceftriaxone 500mgs od for 10 days IM
- Procaine Penicillin G 600 mg (600 000 units) IM daily for 10 days
- Erythromycin 500mgs qds orally for 14 days

Late syphilis (late latent, cardiovascular, gummatous):

- *Benzathine penicillin 2.4 MU IM 3 doses 1 week apart
- Doxycycline 100mg PO bd 28 days

Late syphilis (neurosyphilis):

- Procaine penicillin 1.8-2.4 MU IM od plus probenicid 500mg PO qds 17 days
- *Benzathine penicillin 18-24 MU od (3-4 MU IM 4 hourly) 17 days
- Doxycycline 200mg PO bd 28 days

- Patients should be informed that Benzathine is unlicensed for this indication but has been commonly used for many years for Syphilis treatment and is considered both safe and effective.

Anaphylaxis:
Penicillin is one of the commonest causes of anaphylaxis. All staff should be familiar with the management of anaphylaxis. Facilities for resuscitation should be easily accessed.

Patient Information: reactions to treatment.

Jarisch-Herxheimer Reaction

This occurs most commonly following the treatment of early (secondary) syphilis and ALL patients should be warned about its possibility and how to manage it and this should be documented within the patient record. THERE IS ALSO INFORMATION IN THE PATIENT INFORMATION LEAFLET. Symptoms commence 4 hours after the initiation of treatment for syphilis. Patients with neurological or ophthalmic involvement should be considered for admission to hospital for treatment. They should also be pre-treated with Prednisolone to reduce the risk of complications.

TIME POST TREATMENT	**SYMPTOMS**
4 HOURS	Headache, myalgia
6-8 HOURS	Rigors, chills, worsening of skin lesions
12 HOURS	Peak in temperature
24 HOURS	Recovery

Management

- Paracetamol or Ibuprofen
- Rest

Management of Sexual Partners

- All patients with syphilis should be referred to a health advisor for partner notification.
- In patients with primary syphilis all sexual partners in the past 3 months should be contacted. (50% of contacts of primary infection will also have syphilis)
- In patients with secondary or early latent syphilis partner notification should include all partners in the last 2 years.
- Asymptomatic contacts of early syphilis should have serology performed at presentation and then 4 and 12 weeks after last sexual contact with the index case.
- Epidemiological treatment for asymptomatic contacts of early syphilis should be considered especially when partners are unable or unwilling to attend at 4 and 12 weeks to exclude infection if initial serology is negative.
- In latent syphilis it is helpful to try and locate any previous serology (antenatal clinic, blood donation) or documented treatment. Those with late latent syphilis are usually unable to transmit infection to sexual partners. Although vertical transmission may occur at any time within the first 10 years of infection this becomes unusual more than 2 years after the onset of early syphilis.
- Sexual partners and children born to individuals diagnosed with late latent syphilis of unknown duration should undergo screening to exclude infection.

- Syphilis is an infection that causes risk of serious harm to others. Therefore it may be appropriate to disclose risk of infection to identifiable individuals who may be at risk of infection, without consent of the index patient, if the index patient has not informed them and cannot be persuaded to do so. This should be carried out only after discussion with the index patient's consultant and after informing the index patient. Disclosure to other health care providers-GP, without consent may also be necessary as part of this process.

Follow up

This is to exclude relapse and re-infection.

Early syphilis:
Patients should have repeat syphilis serology at 1month post completion of treatment and then at 3,6 and 12 months, and then 6 monthly until the RPR is negative or serofast.

In treated primary and secondary syphilis the RPR titre should fall by four-fold with in 3-6 months and by eight-fold with in 6-12 months of treatment. Normally the RPR will become negative. Around 15% of individuals with primary or secondary syphilis are expected to fail to show adequate serological response to treatment and may need further investigation.

Late syphilis:
The fall in the RPR is much slower after the treatment of late infection, and although it may eventually become negative, it may also remain positive at low titre (<16).

Serological follow up is 6 monthly until serofast.

Once the RPR is negative or serofast at one year the patient may be discharged.

Relapse and re-infection:
A sustained 4-fold increase in RPR in individuals whose RPR had previously dropped, or recurrence of signs or symptoms in patients who have been treated, where re-infection is thought unlikely should all have retreatment with 3 doses of benzathine penicillin as per late syphilis treatment protocol. (Consider CSF examination)

All post treatment positive syphilis serological tests will be reviewed by a senior doctor – the syphilis serology record can be found on panel view on NASH.

Syphilis and HIV infection:
Patients will require life long monitoring of their syphilis serology.

Letter to GP:

All patients should have a first letter sent to their GP documenting the diagnosis and treatment. A second letter documenting the patients serology after completing follow up should be sent once the patient is serofast - normally 12 months. Please discuss with patients the benefits of GP involvement as their RPR and IgG may remain positive for life. This documentation is required to prevent unnecessary re treatment. The 12 month letter will be sent once the senior doctor has agreed the serology is serofast.

Patients who do not co-operate with follow-up serology at 1 month post treatment and 1 year post treatment are the most important prognostically.
Therefore if patients fail to attend our service for follow up health advisors will attempt contact with the patient and the GP to remind them that serology is required at 1 month and 12 months only.

Additional information

Preparation of benzathine penicillin

Take one vial of Extencilline 2.4 mu aqueous suspension,shake and then perforate the stopper with a needle. Aspirate 8 ml 1% Lidocaine into a syringe and add to the vial. Remove the syringe from the needle and leaving both needles in place shake the bottle to create a homogenous suspension. Carefully aspirate the suspension. Inject half of the volume IM into the upper outer quadrant of each buttock.

(If the pt has a known allergy to Lidocaine then water for injections can be used instead)

Interpreting Results-Staging Syphilis:

The diagnosis of the stage of infection is made on the individuals' history and the clinical features together with serological tests for syphilis. Different stages of syphilis can have the same serological results. Therefore blood results, clinical picture, knowledge of previous infection and treatment and dates of any previous negative testing are needed to accurately stage the infection.

An RPR >8 and a positive IgM suggest early, active syphilis. However these test results are not reliable guides and can be misleading.

Pattern of results of serological tests in different stages of acquired syphilis

VDRL/ RPR	IgG	TPHA/ TPPA	FTA-abs	IgM	Most likely interpretation
+	-	-	-	-	False positive reaction; repeat to exclude primary infection
+/-	+/-	+/-	+/-	+	Primary infection; PCR test from any chancre
+	+	+	+	+	Untreated (or recently treated) secondary or early latent
+/-	+	+	+	-/+	Untreated late or latent; treated or partially treated at any stage
-	+/-	+/-	+/-	-	History of treated syphilis (probably many years previously)

Key: + positive; - negative; +/- usually positive at low titre but may be negative; -/+ usually negative but may be positive at low titre

Management of penicillin allergy

Sometimes it is worth considering desensitisation to penicillin which is performed as an in-patient. With the passage of time after a hypersensitivity reaction to Penicillin, most individuals cease to produce specific IgE and can safely be given the drug. About 10% of people however remain hypersensitive

Penicillin Desensitisation

Penicillin V (Phenoxymethylpenicillin) as an elixir is given orally and increased by doubling the dose every 15 minutes for 14 doses. The desensitisation procedure is performed in hospital with intravenous access and close personal medical supervision for 24 hours. Patients should have regular observations throughout the regimen and following its completion. Mild cutaneous reactions are allowed to resolve spontaneously or are treated with Chlorphenamine 10 mg intravenously over one minute. The injection of Benzathine Penicillin is then given within 30 minutes of completing the final dose of the desensitisation regimen, and the patient is monitored overnight.

Oral desensitisation protocol for Penicillin

PHENOXYMETHYL PENICILLIN DOSE	Amount mg	Volume (ml)	Concentration
1	0.0625mg	0.25ml	0.25mg/ml diluted penicillin syrup
2	0.125mg	0.5ml	0.25mg/ml
3	0.25mg	1ml	0.25mg/ml
4	0.5mg	2ml	0.25mg/ml
5	1mg	4ml	0.25mg/ml
6	2mg	8ml	0.25mg/ml
7	4mg	16ml	0.25mg/ml
8	10mg	0.4ml	25mg/ml
9	15mg	0.6ml	25mg/ml
10	30mg	1.2ml	25mg/ml
11	62.5mg	2.5ml	25mg/ml
12	125mg	5ml	25mg/ml
13	250mg	10ml	25mg/ml
14	500mg	20ml	25mg/ml

- The interval between doses is 15 minutes.
- The desensitisation takes 3 hours and 45 minutes.
- Treatment with Benzathine Penicillin should be started within 30 minutes of dose 14.
- IV access should be established prior to desensitisation.