DECISION MAKING IN SYPHILIS

1 Indications for testing

Clinical indicators:

- Symptoms and signs:
  - rash
  - genital lesion
  - unexplained clinical syndromes or laboratory results

- Clinical context:
  - pregnancy
  - any STI test
  - any HIV test
  - any STI diagnosis
  - any contact with a case of syphilis (must also presumptively treat)
  - PrEP

- Presence of Risk Factors:
  - Behavioural:
    - new partner
    - MSM
    - substance misuse
    - sex work

- Populations:
  - < 30 years old
  - Aboriginal and Torres Strait Islander people
  - Remote communities

- When gaining informed consent before testing, discuss:
  - Preferred gender of healthcare provider
  - Need for an interpreter
  - Reason for test
  - Personal implications of a positive test result
  - Availability of curative treatment

Disclaimer: Guidance provided on this resource is based on guidelines and best-practices at the time of publication. This quick-reference guide is not intended to be a comprehensive list of all available options.

For further information, refer to the Australian STI Management Guidelines for Use in Primary Care: https://sti.guidelines.org.au/sexually-transmissible-infections/syphilis/

CMIA – Chemiluminescent microparticle immunoassay; EIA – Enzyme immunoassay; TPPA - Treponema pallidum Particle Agglutination Assay; TPHA - Treponema pallidum Hemagglutination Assay; RPR - Rapid plasma reagin; VDRL - Venereal Disease Research Laboratory test; NAAT – Nucleic Acid Amplification Test

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2 How to test

To diagnose and determine disease stage of syphilis, diagnosis is by a combination of serology, PCR of lesions, past testing and treatment history and clinical assessment.

Baseline screening, request:

- Syphilis serology - Syphilis antibody
- Syphilis NAAT or PCR swab of lesion.

Further information:

- Laboratory to perform initial syphilis specific antibody (CMIA/EIA) testing and confirmatory testing if positive (TPPA/TPHA)* and RPR as a marker of disease activity and treatment response***.
- Additional test if lesions present. Swab lesion. Must be accompanied by serology.

In addition, recommend comprehensive screening:

- HIV serology
  - Always co-test HIV unless known HIV positive (refer to Australian STI Management Guidelines for Use in Primary Care - HIV)

- Hepatitis B and Hepatitis C serology
  - Unless not required (refer to Australian STI Management Guidelines for Use in Primary Care – hepatitis B & Australian STI Management Guidelines for Use in Primary Care – hepatitis C)

- Gonorrhoea/ chlamydia
  - Standard asymptomatic check-up

3 Interpretation of syphilis serology

Syphilis Antibody (Ab)

- Ab Negative
  - patient does not have and has never had syphilis**
  - REPEAT (if high risk of recent exposure)

- Ab Positive*
  - known past treated syphilis
  - no documented previous treatment
  - possible very early or late latent syphilis**
  - DON'T TREAT

RPR Negative*

- RPR positive
  - documented previous treatment and decline in RPR***
  - past treated syphilis
  - possible very early or late latent syphilis

- RPR negative
  - no documented previous treatment
  - possible re-infection syphilis
  - TREAT

- RPR positive
  - documented previous treatment, RPR declined *** and then increased
  - past treated syphilis
  - TREAT

- RPR negative
  - no documented previous treatment
  - possible very early or late latent syphilis
  - DON'T TREAT

*Positive CMIA/EIA is confirmed by reflex TPPA/TPHA by the laboratory. Uncommonly, positive CMIA/EIA and negative TPPA/TPHA and negative RPR may be a false positive or indicate very early infection. Repeat testing if high index of suspicion.

**Very recent infection may also be antibody negative. Assess for symptoms and signs and repeat serology prior to treating.

*** The RPR is a marker for disease activity and treatment response. It declines after treatment and often reverts to non-reactive. 4-fold change required. Consult with a specialist when RPR is rising, or a 4-fold drop is not achieved by 12 months.
## Disease Staging and Symptoms

<table>
<thead>
<tr>
<th>Disease Stage (often not distinct)</th>
<th>Symptoms and signs (most patients do not have all or most of these)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious</td>
<td></td>
</tr>
<tr>
<td>Primary syphilis</td>
<td>Genital, anal or oral ulcer. Inguinal lymph enlarged.</td>
</tr>
<tr>
<td>Secondary syphilis</td>
<td>Fever, malaise, headache, lymphadenopathy, rash, alopecia, oral, anal or genital lesions</td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td>May arise in context of secondary or less commonly tertiary syphilis. Neurological symptoms or signs: visual changes, tinnitus, deafness, cranial nerve palsies, severe headache or meningitis.</td>
</tr>
<tr>
<td>Early Latent (&gt;2 years) syphilis</td>
<td>Positive syphilis serology no clinical symptoms or signs no evidence of adequate past treatment. Negative test or a 4-fold increase in RPR within past 2 years.</td>
</tr>
<tr>
<td>Non-infectious</td>
<td></td>
</tr>
<tr>
<td>Late latent (&gt;2 years) syphilis</td>
<td>Positive syphilis serology no clinical symptoms or signs no evidence of adequate past treatment. No negative test within 2 years.</td>
</tr>
<tr>
<td>Tertiary syphilis</td>
<td>Destructive skin, cardiovascular or neurological disease.</td>
</tr>
<tr>
<td>Congenital syphilis</td>
<td>Severe multi-organ disease with very high mortality and morbidity in both in-utero and in neonatal periods.</td>
</tr>
</tbody>
</table>

These stages are often not distinct, most patients do not develop all or most of these symptoms and signs.

## Treatment

Refer to sections 3 Interpretation of syphilis serology and 4 Disease staging and symptoms before commencing treatment. Repeat syphilis serology at day of treatment (baseline).

<table>
<thead>
<tr>
<th>Symptomatics</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms or signs of primary or secondary syphilis. Consult with a specialist if not familiar with these. OR documented negative serology in past 2 years OR documented treatment in past 2 years with decline in RPR OR PCR positive</td>
<td>Benzathine benzylpenicillin 2.4 MU (1.8g), stat, given as two injections containing 1.2 MU (0.9g) stat x 1</td>
</tr>
<tr>
<td>All other cases</td>
<td>Benzathine benzylpenicillin 2.4 MU (1.8g), stat, given as two injections containing 1.2 MU (0.9g) weekly x 3</td>
</tr>
<tr>
<td>penicillin allergy or unavailable</td>
<td>seek expert advice</td>
</tr>
<tr>
<td>Pregnant OR Child OR Neurological symptoms or signs</td>
<td>Urgently refer</td>
</tr>
</tbody>
</table>

## Follow-up

- Contraception is unclear.
- Advise no sexual contact for 7 days after treatment is administered.
- Advise no sex with partners from the last 3 months (primary syphilis), 6 months (secondary syphilis) or 12 months (early latent) until the partners have been tested and treated if necessary.
- Contact tracing and presumptive treatment of partners.
- Provide patient with factsheet.
- Notify the state/territory health department according to local procedures.

### Contact tracing:
- Primary syphilis: 3 months plus duration of symptoms
- Secondary syphilis: 6 months plus duration of symptoms
- Early latent: 12 months
- Late latent syphilis: long term partners only

### Repeat syphilis serology at 3, 6 and 12 months. Test and presumptive treatment of all partners of infectious syphilis.

### Consult with a specialist:
- Before commencing on treatment. Interpretation of syphilis serology is complex.
- Diagnosed during pregnancy. Seek urgent specialist advice for congenital syphilis.
- Positive syphilis results in a child. Additionally, discuss results urgently with child protective services.
- Unable to obtain Benzathine benzylpenicillin which is supplied as 1.2MU pre-filled syringes.
- Allergy to principal treatment choice and seeking alternative treatment option.
- Complicated syphilis. Refer those with acute neurological signs, symptoms or suspected tertiary disease to local sexual health or infectious diseases clinic.
- HIV co-infection.
- RPR is rising or a 4-fold drop is not achieved by 12 months.
- Contact tracing is unclear.

### Benzathine benzylpenicillin 2.4 MU (1.8g), stat, given as two injections containing 1.2 MU (0.9g)
- 1.2 MU (0.9g)

### Repeat treatment:
- Benzathine benzylpenicillin 2.4 MU (1.8g), stat, given as two injections containing 1.2 MU (0.9g)
- stat x 1
- weekly x 3