Evaluating Patients For Primary Syphilis

SEXUAL HISTORY, RISK ASSESSMENT, & PHYSICAL EXAM

Sexual History, Risk Assessment (past year)
- Gender of partners, number of partners (new, anonymous, serodiscordant HIV status, exchange of sex for drugs or money)
- Types of sexual exposure
- Recent STDs; HIV serostatus
- Substance abuse
- Condom use

History of Syphilis
- Prior syphilis (last serologic test & last treatment)

Physical Exam
- Oral cavity
- Lymph nodes
- Skin
- Palms & soles
- Neurologic
- Eyes
- Genitalia/pelvic
- Perianal

DIAGNOSTIC ISSUES IN PRIMARY SYPHILIS

- **Darkfield** ~ 80% sensitive, varies with skill of examiner; decreased sensitivity as lesion ages
- A negative RPR/VDRL does not exclude syphilis diagnosis; ~75-85% sensitive in primary syphilis
- Use same test (RPR or VDRL) in sequential testing; titers are not interchangeable
- Need both non-treponemal (RPR or VDRL) and treponemal test (TP-PA, FTA-ABS, EIA, CIA) to make syphilis diagnosis
- Treponemal tests can remain positive for life; utility limited in patients with history of prior syphilis, comparison of non-treponemal titers needed

For more details on Treponemal Immunoassays:
www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UseofTreponemalImmunoassays_Syphilis.pdf

Note: Evaluate for neurosyphilis (assess if neurologic, ophthalmic or otic symptoms present, as neurosyphilis can occur at any stage of syphilis)

TREATMENT & FOLLOW-UP

Treatment of Primary Syphilis

Recommended Regimen
- Benzathine Penicillin G 2.4 million units IM x 1

Alternative Regimens for Penicillin Allergic Non-Pregnant Patients:

Efficacy not well established & not studied in HIV+ patients; close follow-up essential:
- Doxycycline 100 mg po bid x 2 weeks or
- Tetracycline 500 mg po qid x 2 weeks

*Pregnant patients with penicillin allergy should be desensitized and treated with penicillin

See CDC STD Treatment Guidelines: www.cdc.gov/std/treatment

California STD Treatment Guidelines Grid:
www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/STD-Treatment-Guidelines-Color.pdf

****Additional Testing and Follow-up**

Note: Also test for HIV, GC/CT, and pregnancy (if female of reproductive age)
- 1-2 weeks: clinical follow-up
- 3, 6, 9, 12, 24 months: serologic follow-up for HIV+ patients
- 6, 12 months: serologic follow-up for HIV- patients
- Failure of titer to decline fourfold (e.g. 1:64 to ≤ 1:16) within 6-12 months from titer at time of treatment may indicate treatment failure. Titer decline may be slower in HIV+ patients.
- Consider retreatment and CSF evaluation if titer fails to decline appropriately

REPORTING & PARTNER MANAGEMENT

- All syphilis cases and presumptive cases must be reported to the local health department within one working day of diagnosis
- Local health departments will assist in partner notification & management
- Contact Number at Local Health Department: 505-467-3611

Patient with new genital lesion or suspicious genital ulcer

SEXUAL HISTORY, RISK ASSESSMENT, & PHYSICAL EXAM

DIAGNOSTIC WORK-UP
- Darkfield (if available)
- Stat RPR (if available)
- RPR or VDRL serology (quantitative)
- Treponemal test[1] (TP-PA/FTA-ABS/EIA/CIA)
- Herpes culture or PCR[2]
- HIV Test

Darkfield
- POSITIVE → **Primary Syphilis[3]**: Treat, obtain quantitative RPR and treponemal tests on treatment date, report to health department, partner management, & follow-up.
- NEGATIVE OR UNAVAILABLE → **Stat RPR**
  - REACTIVE → **Presumptive Primary Syphilis[3]**: Treat, obtain quantitative RPR and treponemal tests on treatment date, report to health department, partner management, & follow-up. (If stat RPR non-reactive, repeat RPR 2 weeks after treatment.)
  - NON-REACTIVE OR UNAVAILABLE → **Risk factors or high clinical suspicion (e.g., MSM)[4]**
    - YES → **Presumptive Primary Syphilis[3]** (same as above)
    - NO → Obtain treponemal and non-treponemal tests at the same time.

Obtain treponemal and non-treponemal tests at the same time.

RPR+/RPR – TP-PA +

Primary Syphilis[3] or Presumptive Primary Syphilis[3,5] with RPR –

Treat, obtain quantitative RPR on treatment date, report to health department, partner mangement, & follow-up.

If RPR non-reactive, repeat RPR 1-2 weeks after treatment.

RPR + TP-PA –
- Repeat RPR/VDRL 2 - 4 weeks after initial visit. If reactive, then repeat TP-PA or FTA-ABS.
- If repeat TP-PA/FTA-ABS is negative, then RPR/VDRL is likely biologic false positive.
- Consider other etiologies.

RPR – TP-PA –
- Repeat RPR/VDRL 2 - 4 weeks after initial visit. If reactive, repeat TP-PA or FTA-ABS.
- Consider other etiologies.

EIA/CIA[5]
- NON-REACTIVE
  - Repeat EIA/CIA test 2 - 4 weeks after initial visit.
  - Consider other etiologies.
- REACTIVE → **Quantitative RPR/VDRL**
  - REACTIVE → **Primary Syphilis[3]**: Treat, obtain quantitative RPR on treatment date, report to health department, partner management, & follow-up.
  - NON-REACTIVE → **TP-PA**
    - REACTIVE → **Presumptive Primary Syphilis with RPR –[3,5]**: Treat, obtain quantitative RPR on treatment date, report to health department, partner management, & follow-up. Repeat RPR 2-4 weeks after treatment.
    - NON-REACTIVE → Reassess patient. If alternate diagnosis favored or confirmed by laboratory testing, no further action.

    If clinical suspicion for syphilis persists then treat, obtain quantitative RPR on treatment date, report to health department, partner management, & follow-up. If treatment date RPR negative, repeat RPR 2-4 weeks after treatment.

[1] Treponemal tests may be more sensitive than non-treponemal tests during primary syphilis.
[2] Also consider culture for Haemophilus ducreyi (chancroid) if exposure in endemic areas or if lesion does not respond to syphilis treatment.
[3] All patients with suspected syphilis should be tested for HIV infection and screened for other STDs. Repeat HIV testing of patients with primary syphilis 3 months after the first HIV test, if the first test is negative.
[4] If the patient is a man who has sex with men (MSM) or has high risk sexual behavior or clinical exam with classic features of a syphilitic ulcer, then standard of care includes presumptive treatment at the time of the inital visit before diagnostic test results are available. Presumptive treatment is also recomended if patient follow-up is a concern.
[5] If the patient does not respond to treatment, repeat RPR/VDRL after treatment and consider other etiologies.

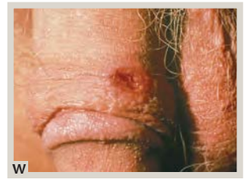
CLINICAL PRESENTATIONS OF PRIMARY SYPHILIS

- Lesion appears 10-90 days after contact at site of exposure; may persist for 2-3 weeks then resolves
- Usually genitorectal but may be extragenital, depending on exposure site
- Clinical presentation, typical or atypical
- Typical: single painless, indurated, clean-based ulcer with rolled edges & bilateral painless adenopathy
- Atypical: can mimic herpes & other genital ulcers
- ~25% present with multiple lesions
- Lesions of primary and secondary syphilis can be present at the same time, especially in HIV positive individuals

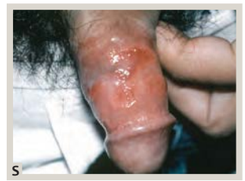
Differential Diagnosis

- Herpes (most common), primary HIV ulcers, chancroid, granuloma inguinale, trauma, and many non-STD infectious and non-infectious causes of genital ulcers
- More than one etiology can be present at the same time

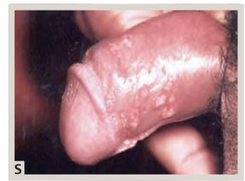
Syphilitic Ulcer, Shaft



Syphilitic Ulcer, Shaft

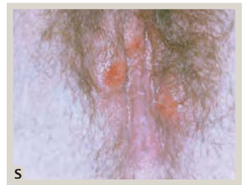


Multiple Syphilitic Ulcers, Shaft

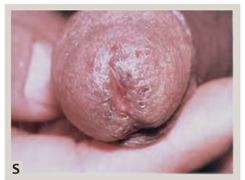


Multiple Syphilitic Ulcers Resembling Herpes

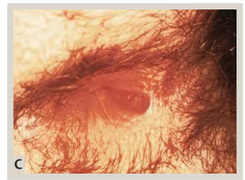
Syphilitic Ulcer, Vulva



Multiple Syphilitic Ulcers, Vulva



Crusted Syphilitic Ulcer, Urethra



Syphilitic Ulcer, Perianal

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To Order Additional Copies
See the online version of the Primary Syphilis Algorithm on the clinical resources page of the CA PTC website: www.californiaptc.com

Acknowledgements
Medical Directors from the National Network of STD Clinical Prevention Training Centers, California STD Controllers Association, Division of STD Prevention of the Centers for Disease Control and Prevention
Revised 7/2018

NEW MEXICO DEPARTMENT OF HEALTH

California PTC

Evaluating Patients For Secondary Syphilis

SEXUAL HISTORY, RISK ASSESSMENT & PHYSICAL EXAM

- I History, Risi< A a 111r•11t (past year)
- Gender of partners
- Number of partners (new, anonymous, serods· cordant HIV status, exchar-.ie of sex for drugs or money)
- Types of sexual expoSIR
- - STDs; HIV serostatus
- substance abuse
- Condom use

History of Syphllls
- Prior syphilis (last serologic test & last treatment)

PhpIcalExam
- Oral cavity
- Lymph nodes
- Skin
- Palms & soles
- Ntu01ogic
- Eyes
- G-.lia/pelvic
- Perlanal

DIAGNOSTIC ISSUES IN SECONDARY SYPHILIS

- RPR/VDRL -100% sensitive in secondary syphilis
  - o Rare caveat: prozone reaction, false negative RPRNDRL from excess antibody interfering with antibody/antigen reaction
  - o Prozone occ..-s <1% of secondary syphilis cases; if suspected ask lab to dilute serum to at least 1/16
- Use same test (RPR or VDRL) in sequential testing; titers are not interchangeable
- Need both non-treponemal (RPR or VDRL) and treponemal test to make syphilis diagnosis
- Treponemal tests (TP·PA, FTA·ABS, EIA, CIA) can remain positive for life; utility limited in patients with history of prior syphilis, comparison of non-treponemal titers needed

For more c1etans on rr.ponemal lmrnunoassays: www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Documen1X20Ubrary/UseofTreponemallmmunoassays_Syphilis.pdf

Note: Evaluate for neurosyphilis (assess if neurologic, ophthalmic, or otic symptoms present, as neurosyphilis can occur at any stage of syphilis)

TREATMENT & FOLLOW-UP

Treatment of Secondary SyphUs

Rocommendrd R•gfmen
- Benzathine Penicillin G 2.4 million units IM x 1

Aftematlw Rogrmens *for* Pfllfcfllfin Alfttgfc Non-Prognant *Patl•nts:*

Efficacy not well established & not studied in HIV+ patients; close follow-up essential:
- Doxycycline 100 mg po bid x 2 weeks or
- Tetracycline 500 mg po qid x 2 weeks

*Pregnant patients with penicillin allergy should be desensitized and treated with penicillin

See CDC SID Treatment Gufdeflnes: www.cdc.gov/std/treatment

California SID Treatment Guldelfnes Grid:
https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Documen1X20Ubrary/STO-Treatment-Guidelines<.olor.pdf

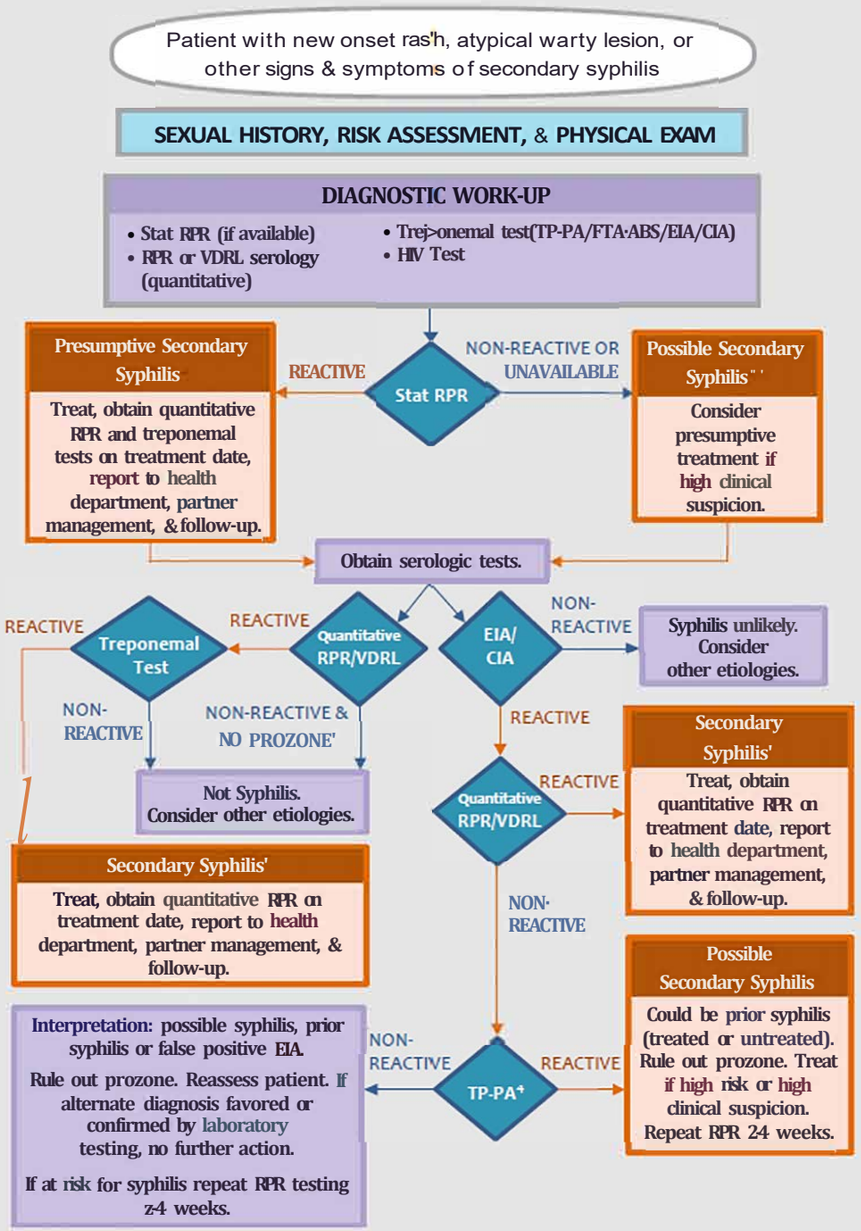
****Addltfonal Testing and Follow-up**

Note: Also test for HIV, GC/CT, and pregnancy (if female of reproductive age)
- 12 weeks: clinical follow-up
- 3, 6, 9, 12, 24 months: serologfc follow-up for HIV+ patients
- 6, 12 months: serologic follow-up for HIV· patients
- Failure of titer to decline fourfold (e.g. 1:64 to s1:16) within 6-12 months from titer at time of treatment may indicate treatment failure. Titer decline may be slower in HIV+ patients.
- Consider retreatment and CSF evaluation if titer fails to decline appropriately

Refer to CDC Treatment Guidelines for management of treatment failure & consult the SID Clinical Consultation Network at www.STDCCN.org

REPORTING & PARTNER MANAGEMENT

- All syphilis cases and presumptive cases must be reported to the local health department within one working day of diagnosis
- Loeal health departments will assist in partner notification & management
- Contact Number at Loeal Health Department:



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, All patients with secondary syphilis should be tested for HIV infection and screened for other STDs. Rep-eat HIV testing of patients with secondary syphilis 3 months after the first HIV test, if the first test is negative.

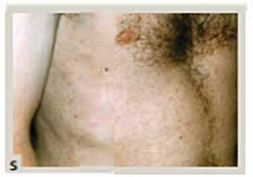
'Pro zone reaction is a false negative RPR or VDRL from excess antibody interfering with the antigen-antibody reaction.

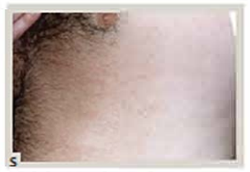
⁴ FTA-ABS is no longer considered the gold standard trep-onemal test given concerns regarding specificity. TPPA should be used for a second treponemal test when EIA/CIA is reactive and RPR is non-reactive.

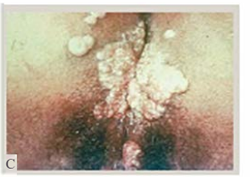
CLINICAL PRESENTATIONS OF SECONDARY SYPHILIS

- Symptoms typically occur 3-6 weeks after primary stage (can overlap with primary); resolve in 2-10 weeks
- 25% may have relapse of signs & -symptoms in first year

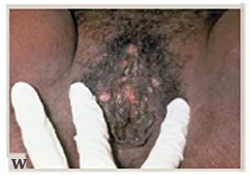
Signs & Symptoms of Secondary Syphilis
- **Rash:** most common feature (75-90%); can be macular, papular, squamous (-scale), pustular (rare), vesicular (very rare) or combination; usually nonpruritic; may involve palms & soles (60%)
- **Lymphadenopathy:** (70-90%); inguinal, epitrochlear, axillary & cesvical sites most commonly affected
- **Constitutional Symptoms:** (50-80%); malaise, fever
- Mucous Patches: (5-30%); flat gray-white patches in oral cavity & genital area
- Condyloma Lata: (5-25%); moist, heaped, wart-like lesions in genital, peri-rectal & rectal areas, & oral cavity
- **Alopecia:** (10-15%); patchy hair loss, loss of lateral eyebrows
- Neurosyphilis: (<2%); visual loss, hearing loss, cranial nerve palsies among other

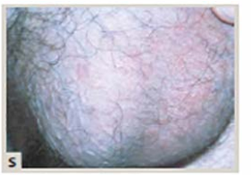

Maculo papular Rash

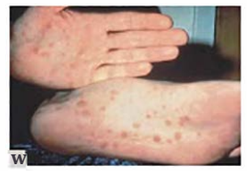

Subtle Macular Rash

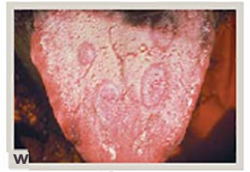

Condyloma Lata

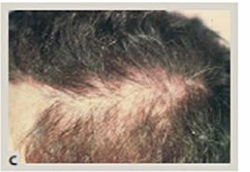

Condyloma Lala


Condyloma Lata


Subtle Scrotal Rash

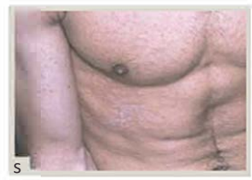

Macula-Rash

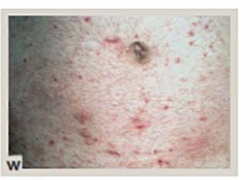

Mucous Patches


Alopecia

Differential Diagnosis of the rash of secondary syphilis includes: pityriasis rosea, psoriasis, erythema multiforme, tinea versicolor, scabies, drug reaction, primary HIV infection


Drug Reaction


Guttate Psoriasis


Scabies

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Revised 7/2018

NEW MEXICO DEPARTMENT OF HEALTH

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