# Management of Syphilis What every Physician Should Know

THE UNIVERSITY OF THE WEST INDIES

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QUEEN ELIZABETH HOSPITAL
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BARBADOS

# Learning Objectives

Upon completion of this content, the learner will be able to:

1. Three R's of Syphilis
2. Discuss the  usual  and atypical clinical manifestations of syphilis.
3. Methods used in the diagnosis of syphilis. (Clinical Pearls)
4. Recommended treatment regimens for syphilis.
5. Summarize appropriate prevention counseling messages for patients with syphilis.

# History

- Ryan  is a 19-year-old male who presents your office.
- Chief complaint is a penile lesion for 1 week

- Last sexual exposure was 3 weeks prior, without a condom.

- No history of recent travel

- Predominantly female partners (3 in the last 6 months), and occasional male partners (2 in the past year)

- Last HIV antibody test (2 months prior) was negative

# Physical Exam

- No oral, perianal, or extra-genital lesions
- Genital exam discloses a lesion on the ventral side near/at the frenulum. Lesion is red, indurated, clean-based, and non-tender.
- Two enlarged tender right inguinal nodes, 1.5 cm x 1 cm
- Scrotal contents without masses or tenderness
- No urethral discharge
- No rashes on torso, palms, or soles. No alopecia.
- Neurologic exam with normal limits.

# Questions

What is

Which l

?

## Genital Ulcer Diseases — Does It Hurt?

- **Painful**
  - — Chancroid
  - — Genital herpes simplex
- **Painless**
  - — Syphilis
  - — Lymphogranuloma venereum
  - — Granuloma inguinale

# Reference Lab Results

- RPR: Reactive  1:16
- FTA-ABS: Reactive
- HSV : Negative
- Gonorrhea NAAT: Negative
- Chlamydia NAAT: Negative
- HIV antibody test: Negative

Do the reference laboratory results change the diagnosis?

Should you report this case to the MOH?

# Follow-Up

You try tracking Ryan Down unsuccessfully

4 week later because he had travelled about his results .

He said the lesion is gone and he was happy. But he recently developed a rash all over his body and feels very tired. He thinks its due to Zika ……

**What therapy would you commence and what is your next move?**

# Follow-Up

- The RPR was 1:132 on follow up 6 months later.
- What happened?
- Do you retreat?
- Did you get this all wrong?

# Ryan's Sex Partners

Tracy – last sexual exposure 3 weeks ago

Danielle – last sexual exposure 6 weeks ago

Jonathan – last sexual exposure 1 month ago

Tony – last sexual exposure 8 months ago

Carrie – last sexual exposure 6 months ago

**Which of Ryan's partners should be evaluated and treated prophylactically, even if their test results are negative?**

# Sex Partner Follow-Up

Stan’s partner, Tracy, is found to be infected and is diagnosed with primary syphilis. She is also in her second trimester of pregnancy and is allergic to penicillin.

What is the appropriate treatment for Tracy?

- Epidem
- Rapid s
  early st
- Epidem
  return
  - ? en
  - ? A g

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30/07/13 www.barbadostoday.bb Page 9

# Syphilis on the rise

MINISTRY OF HEALTH KEEPS AN EYE ON INCREASING NUMBER OF SYPHILIS CASES

The Ministry of Health is monitoring what seems to be an increase in the number of syphilis cases in Barbados.

Ministry officials disclosed that recent studies have revealed that a growing number of persons were seeking posture for the sexually transmitted infection.

In a recent advisory, health authorities said they were in the process of enhancing their monitoring systems for syphilis and other STIs, as well as gathering data for more detailed analyses that would allow them to determine those who were most at risk.

Syphilis is a bacterium that can cause long-term complications and or death if not adequately treated. It is transmitted from person to person by direct sexual contact with syphilis sores, known as a chancre. It can be easily diagnosed through a blood test. If a person tests positive, treatment will consist of the appropriate antibiotics, which should be prescribed by a physician.

Health authorities also advise sexually active persons to use latex condoms correctly and consistently to prevent the transmission of syphilis and other STIs.

Officials also warn Barbadians to avoid excessive use of alcohol and other mind-altering substances which could impair their judgement and lead to risky sexual behaviour.

"It is important that sex partners talk to each other about their HIV status and history of other STIs so that preventive action can be taken," they advised.

The Ministry of Health has an STI programme as a key component of its HIV response. The mandate of this programme is to prevent and control the spread of STIs in Barbados. This is done through disease surveillance, research and laboratory diagnostics to determine the burden of STIs in Barbados and the provision of treatment.

## Shuttle service available to walkers

Patrons, who attend the Freedom Walk and Historic Tour on Emancipation Day, Thursday, will be able to access a shuttle service after the event.

When the walk and tour end at Independence Square in The City, the shuttles will take patrons to the Sky Mall and the Standard Complex car parks, Haggatt Hall, St. Michael, where parking is available for the event. The shuttle service will be offered at 11 a.m. and 12:30 p.m.

Meanwhile, persons are reminded that they should gather at the Emancipation Statue, ITC Rawsley Roundabout, Haggatt Hall, St. Michael at 6 a.m. for the Emancipation ceremony, which has been organized by the non-governmental organisations.

The walk and tour will begin at 8 a.m. from that location, and walkers will proceed to Independence Square in The City.

At 10 a.m., Minister of Culture, Sports and Youth, Stephen Lashley is slated to give the feature address at the cultural presentation.

Admission is free. Intoxicated persons should register for the Freedom Walk and Historic Tour - From Emancipation to Independence online at www.ticketpal.com.




THE ...sh Medical Journal.

E JOURNAL OF THE BRITISH MEDICAL ASSOCIATION.

LONDON: SATURDAY, JANUARY 6TH, 1917.

...ectures ON ...NOSIS AND TREATMENT ...SYPHILIS.

...EIRA, M.D., F.R.C.P.LOND., ...L.C.S.ENG., ...MENT AND LECTURER ON DERMATOLOGY, ...BY CONSULTANT IN DISEASES OF THE ...ANY HOSPITALS IN LONDON.

...BSTRACT.]

...e of lectures is not to set forth ...dicate certain practical points ...against venereal diseases, and ...which general practitioners and ... the measures introduced by the ... and the county councils. The ...ment of syphilis may be con... ...of view—(1) that of the cure of ...that of preventing the spread of ...ity. The second point of view, ...that which is especially at issue ...that is to say, we are to consider ...e treatment of syphilis as public ...we are dealing with the disease ... the same time endeavouring to ...ual, but as a matter of practice ...s do not quite coincide, for it is ... render an infected patient non-... of his disease. ...ults syphilis must be diagnosed ...ect that we can claim that great ...e in recent years. In the first ... a practice which my experience ...—that is, in a case of doubtful ... until the so-called secondary ...et us always have this in our ... of these secondary manifesta... ...infection. I know that in many ... patient with a chancre he is ...neralized infection, but we must ...itude. We must try and make ...s possible moment. Every day ...nce will help us to know what ...ken to avoid, and by actual ... of the primary lesion we are ...irochaeta pallida in the majority ...s.

...ARY INFECTION.

...may be genital or extragenital, ...rough some crack or fissure of ...nbrane, and an inflammatory ...stent interval. This ...tion is ...ally appears from three to five ...s it may be either ...ater, ...rs and three months. ...n res occur on the side of the ...and glans, and in the sulcus ...es at the meatus urinarius are ...ental chancre may invade the ...syphilitic chancres are not very ...o chancres on the body of the ... the lectures. Occasionally the ...skin of the pubic area or on

In *the female*, the labia majora and minora, the fourchette, clitoris, and meatus urinarius are the most common sites. Chancres on the cervix uteri are not infrequent, but the vaginal wall is rarely the site of a primary lesion.

The primary bubo is a single large indurated gland, with occasional small shotty glands in its neighbourhood. It has no tendency to suppurate.

*Extragenital Chancres.*

These are commonest on the face and fingers. Kissing is the usual cause of lip chancres, but drinking vessels, tobacco-pipes, and blowpipes used in glass-blowing are all known to have conveyed the infection. (During the course four cases of lip chancre were demonstrated.) The next most common sites are the chin, eyelids, nose, cheeks, and ears. In the mouth the tongue and tonsil are most often involved. Finger chancres commonly occur about the nails. I have seen them in doctors, surgical dressers, midwifery nurses, and dentists. I have seen a case of primary chancre of the nipple and anal chancres also occur.

Extragenital chancres are usually larger than the genital sores, and when situated in mucous cavities ulceration occurs early and the surface of the ulcer is often covered with a pseudo-diphtheritic membrane. The primary bubo in extragenital chancres is always large and hard, and has no tendency to suppurate, and these points are often of value in the differential diagnosis. It is, however, of the highest importance to have the serum of a doubtful lesion examined for spirochaetes without delay.

*Diagnosis of the Primary Chancre.*

In a very early chancre there may be little induration, but as a rule when the patient comes for examination the lesion has a characteristic cartilaginous hardness which, with the hard bubo, is sufficient to make a diagnosis. If the lesion has been untreated, the surface may be scraped, or what is better, a fine pipette should be plunged into the substance. The serum obtained is placed on a slide with a few drops of normal saline solution, and examined by a ⅙ in. objective by dark background illumination. The white spirochaetes are seen in motion crossing the field.

Another method of demonstration is to mix the serum with a solution of collargol (collargol 1, distilled water 19) as suggested by Harrison. A film is made by spreading the mixture on another slide and the preparation is allowed to dry. The examination is made with a ⅙ in. oil immersion lens. The spirochaetes shows up white on the dark background of the collargol solution, but it is not so easily recognized as in the former method, as it is not in motion.

The serum may be collected in a capillary tube such as is used for vaccination, and, the ends being sealed, may be sent through the post to a laboratory for examination. I do not recommend this method, which should only be employed if it is impossible to send the patient to the bacteriologist for examination.

The affections which may lead to error in the diagnosis of genital chancres are (1) traumatic ulcer, (2) herpes genitalis, (3) soft sore, (4) lichen planus. All these conditions are distinguished by the absence of induration and of the indurated bubo. Soft sores are usually multiple, the inflammatory reaction is much more acute and appears a few days after infection. The bubo in ulcus molle is usually tender, with surrounding painful swelling, and it tends to early suppuration. In herpes the lesions are superficial. They begin as vesicles which rupture early, producing painful non-infiltrated erosions. They appear

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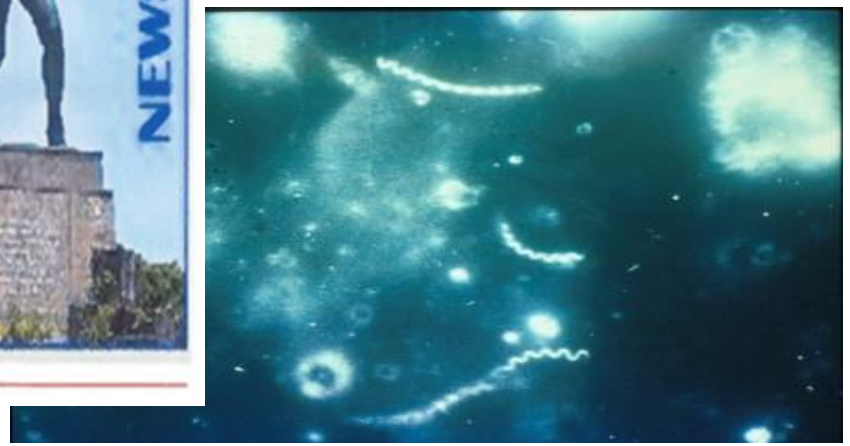


# Preliminary Data MOH




There was a  al number of acute syphilis cases and a further almost 300% increase the following year

# Lesson I:

## The Three R's

## Recognize

## Rx

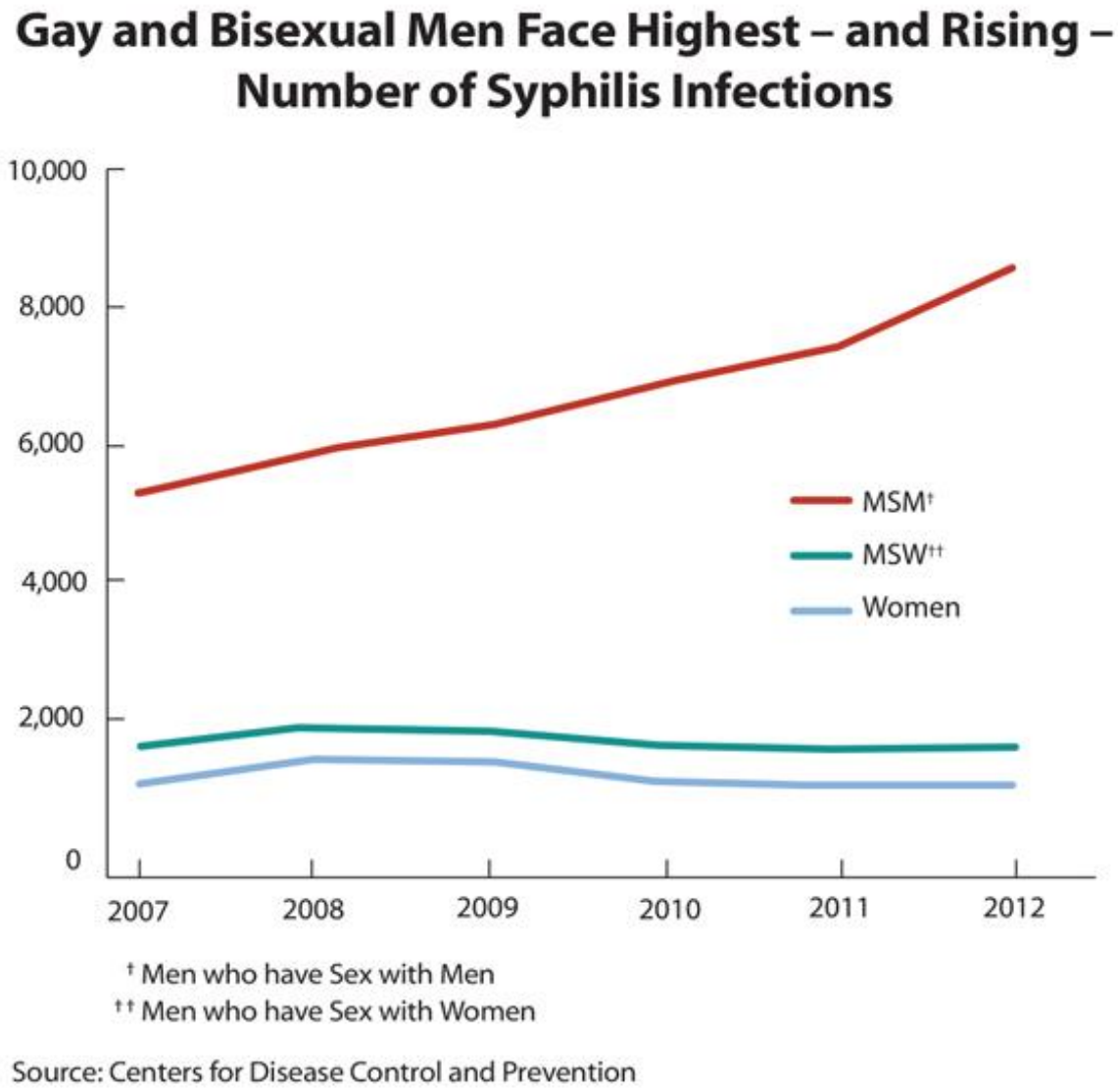
## Research

# Lesson I:
# Recognize Stage

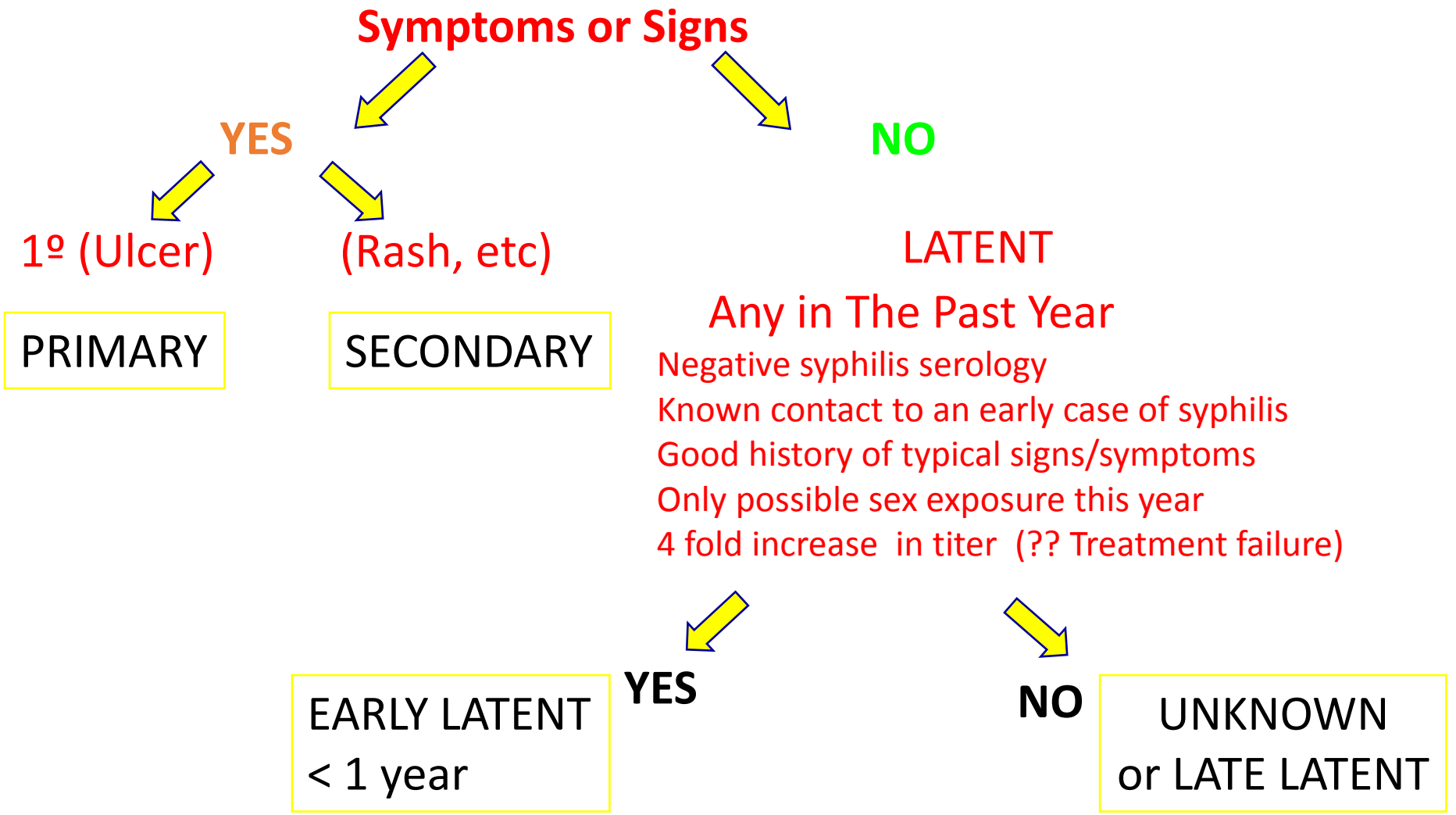
# Syphilis Screening Guidelines

Targeted screening of at risk populations

- Patients with other STDs
- Correctional settings
- Drug treatment settings
- HIV+
- MSMs in outbreak areas or high risk

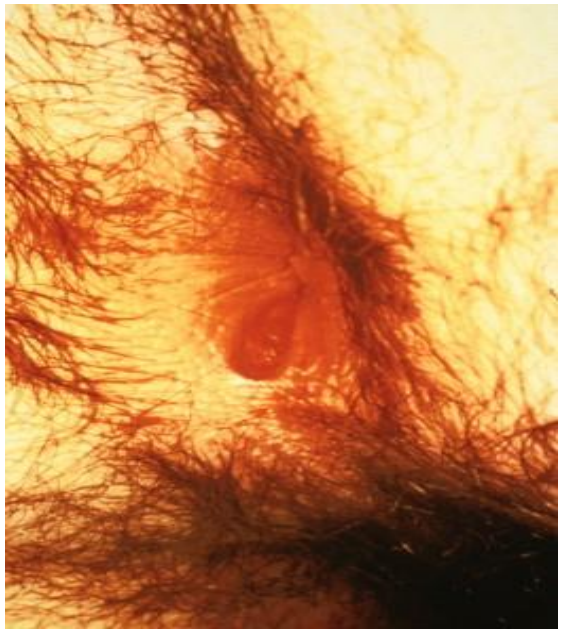


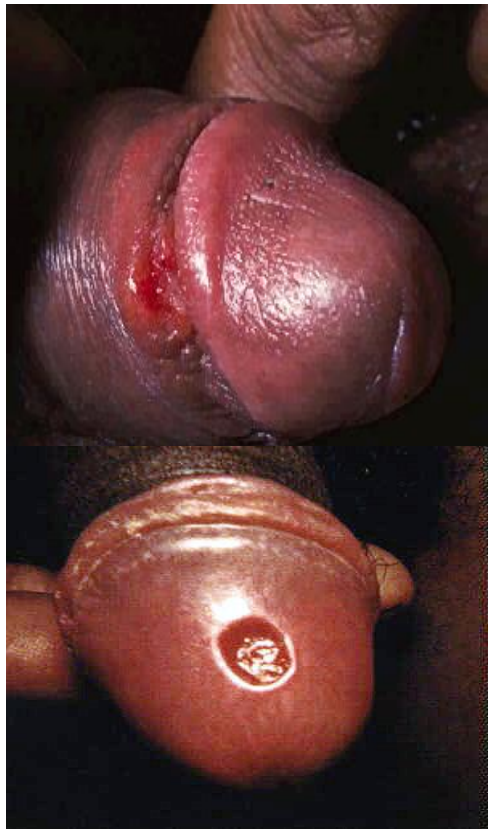
# Syphilis Staging Flowchart

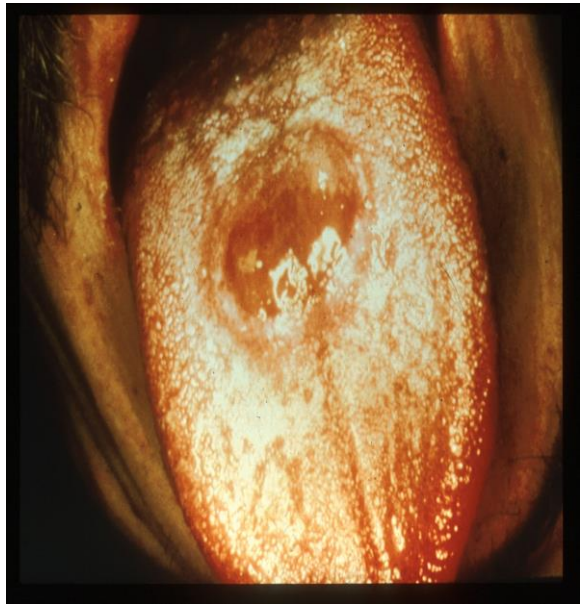


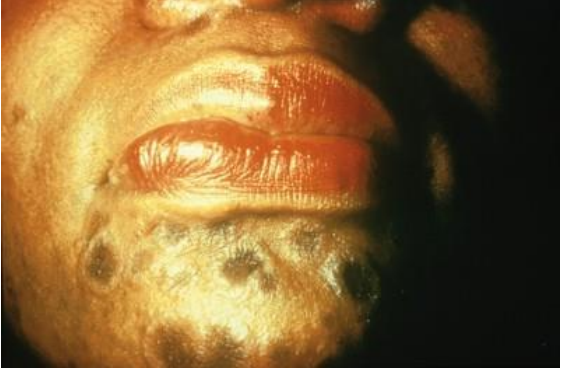
# Primary Syphilis

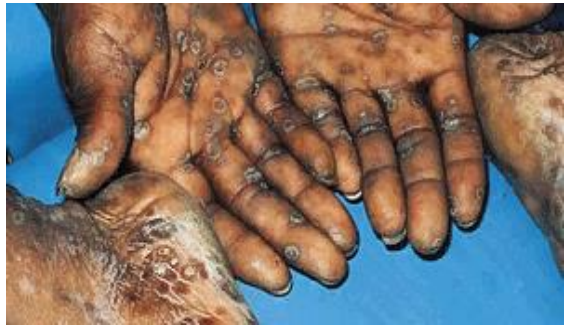
- Chancre:
  - Appears 10-90 days after infection
  - Typically single, painless, clean-based lesion with rolled edges
  - Site of Inoculation





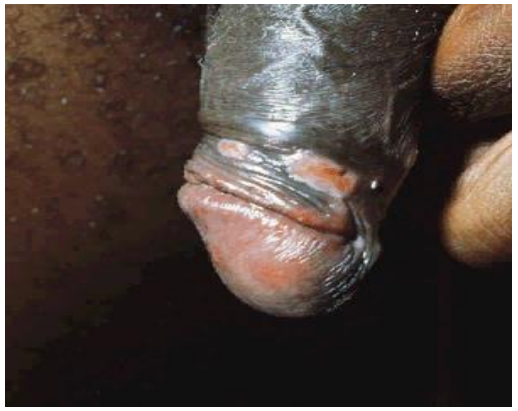


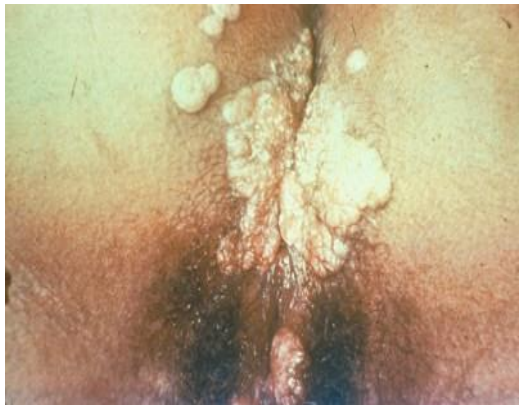




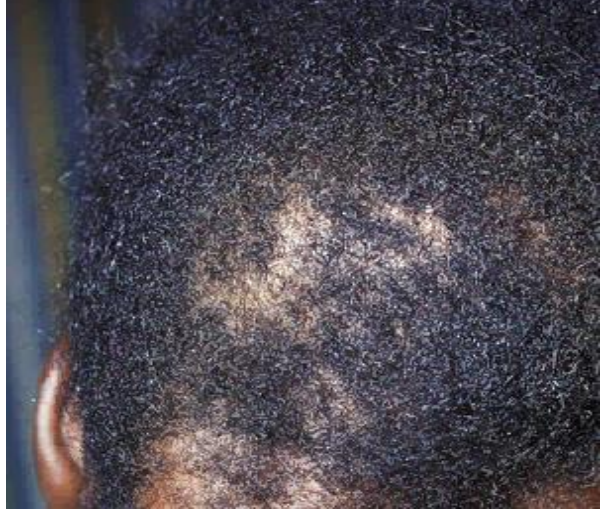
Rash of Secondary Syphilis

Rash (75%–100%)





Condylomata lata (10%–20%)



Moth-Eaten Alopecia (Hair Loss)

Alopecia (5%)

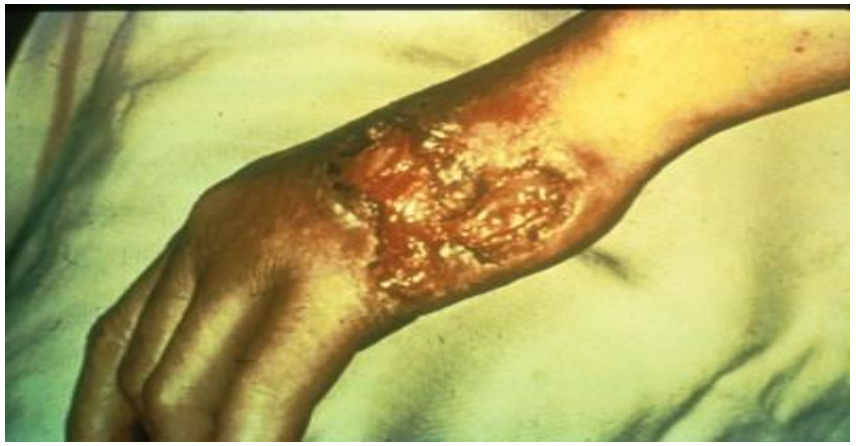
## Other Clinical Manifestations to Bear in Mind:

- Lymphadenopathy (50%–86%)
- Malaise
- Mucous patches (6%–30%)
- Liver and kidney involvement can occur
- Splenomegaly is occasionally present

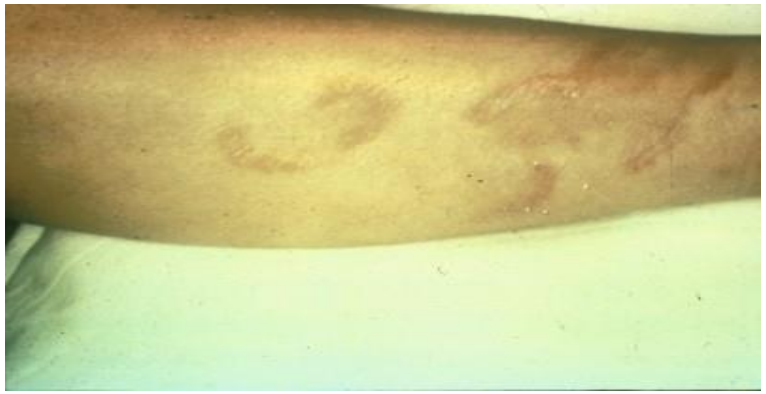
- Serologic tests are usually highest in titer during this stage.

# Tertiary Syphilis

**Late Syphilis - Ulcerating Gumma**

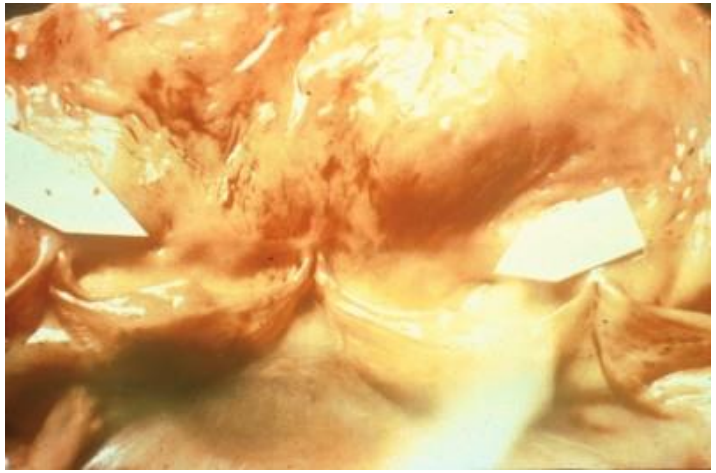


Late Syphilis—Serpiginous Gummata of Forearm



70% of untreated patients remain asymptomatic

Late Syphilis—Cardiovascular



*Source*: CDC/ NCHSTP/ Division of STD Prevention, STD Clinical Slides

# Key Points To Bear In Mind

During early (primary and secondary) syphilis, efficiency of transmission ~ 30%.

Syphilis can infect infants of untreated mothers. Chance of vertical transmission by stage of infection:

-primary syphilis = 50% and early latent syphilis = 40%

-late latent syphilis = 10% and tertiary syphilis = 10%

*If you suspect Latent Syphilis then you MUST:*

*Do a good neurological exam : Take Neuro Out The Picture*

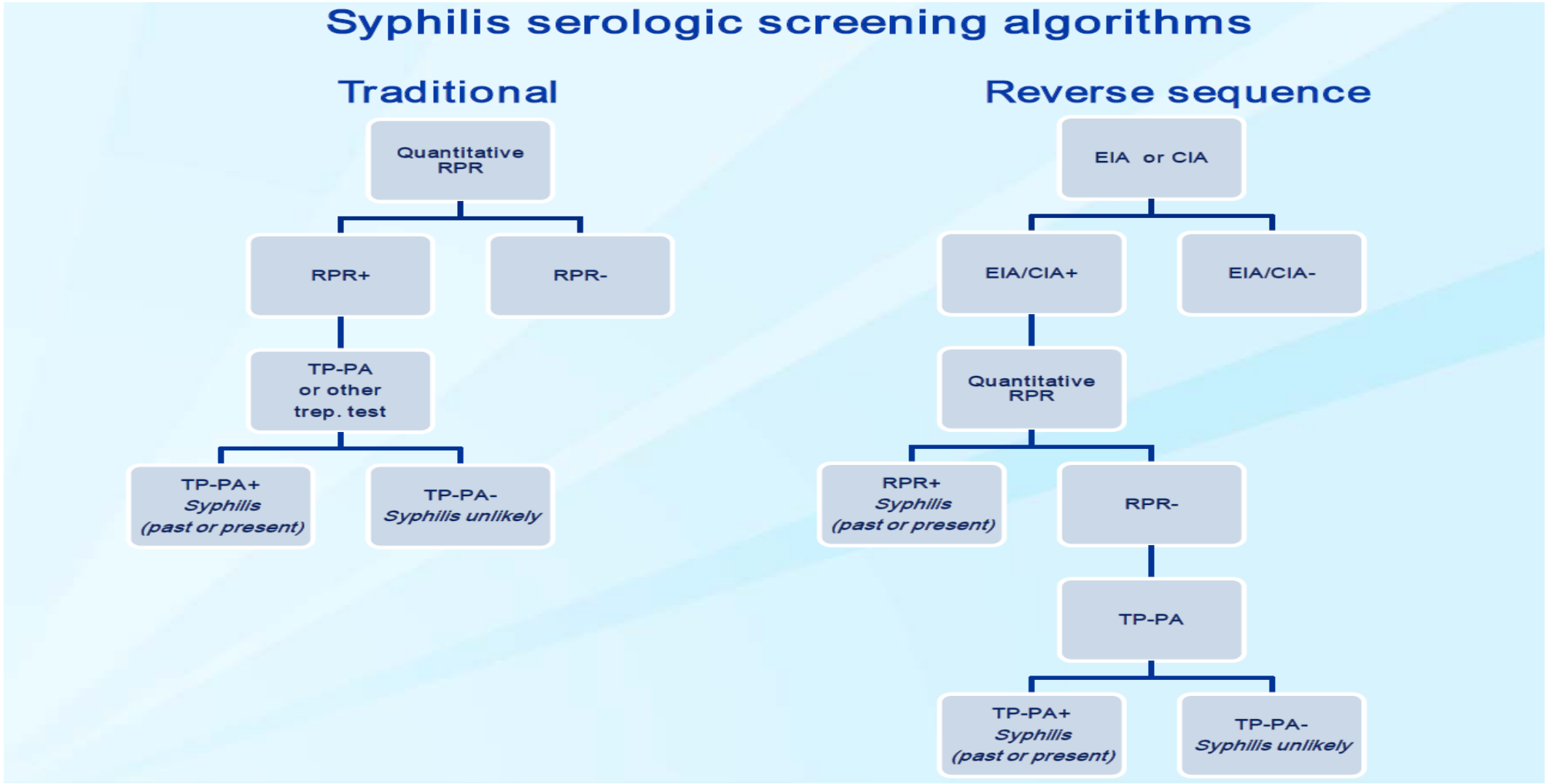
*Do Skin Search: Take primary or secondary disease out the picture: -speculum exam- cervix/vaginal vault, anogenital exam, oral cavity*

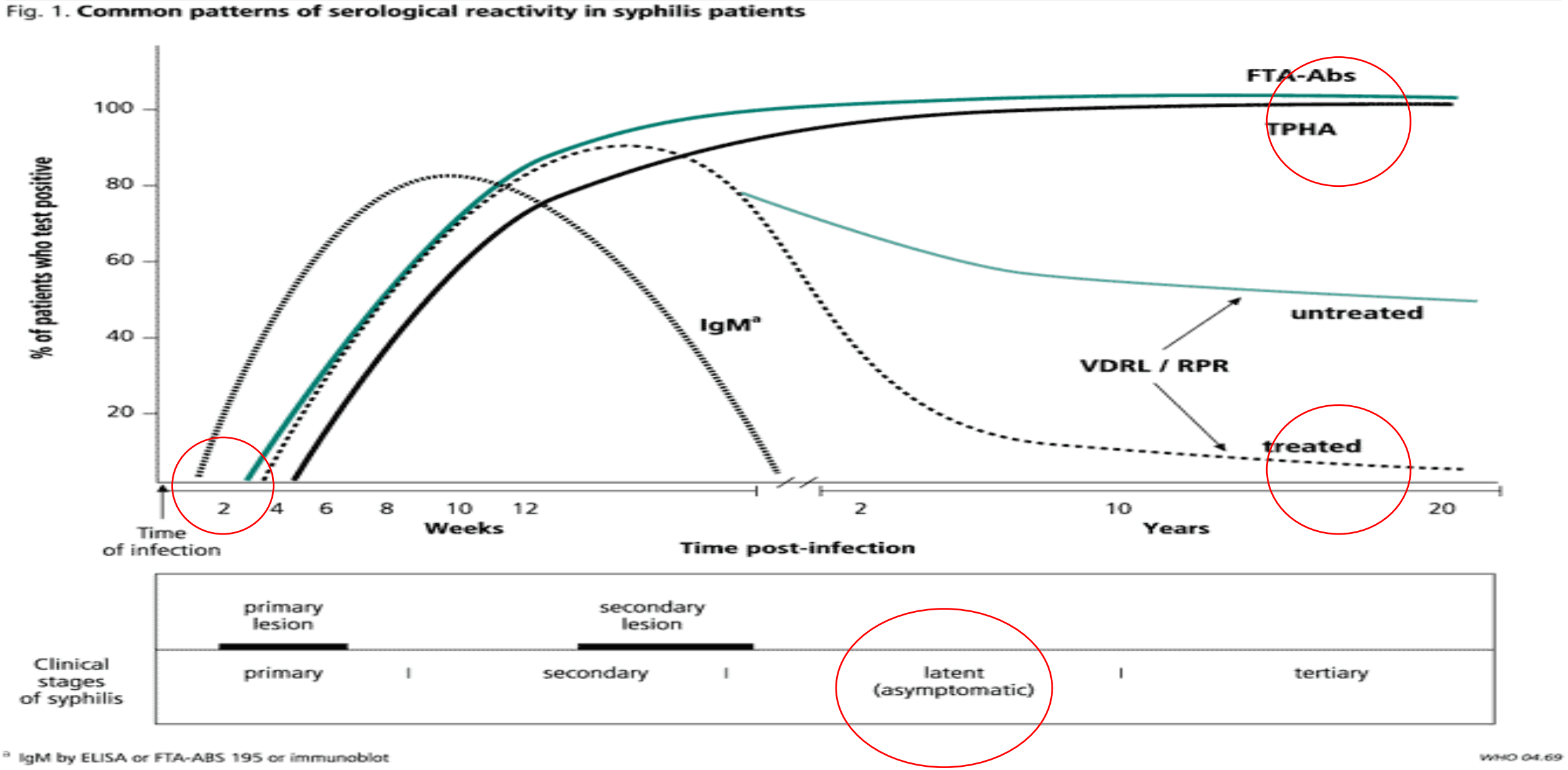
# Lesson I  Recognition

# Know Your Diagnostic Tests

**Now you got that in your head!**

# Know Your Diagnostic Tests






Peeling et al. / Bulletin of the World Health Organization / 2004 / Vol. 82 / No. 6

# Key Points To Bear In Mind:

## Serologic Pitfalls in the Diagnosis of Syphilis

- Negative nontreponemal test may occur early in primary or late in tertiary - check FTA-ABS or TP-PA
- Prozone phenomenon: false negative due to lack of agglutination with high antibody levels
- Serofast: persistent, low-level positive titer after adequate treatment

# Indications for CSF Examination

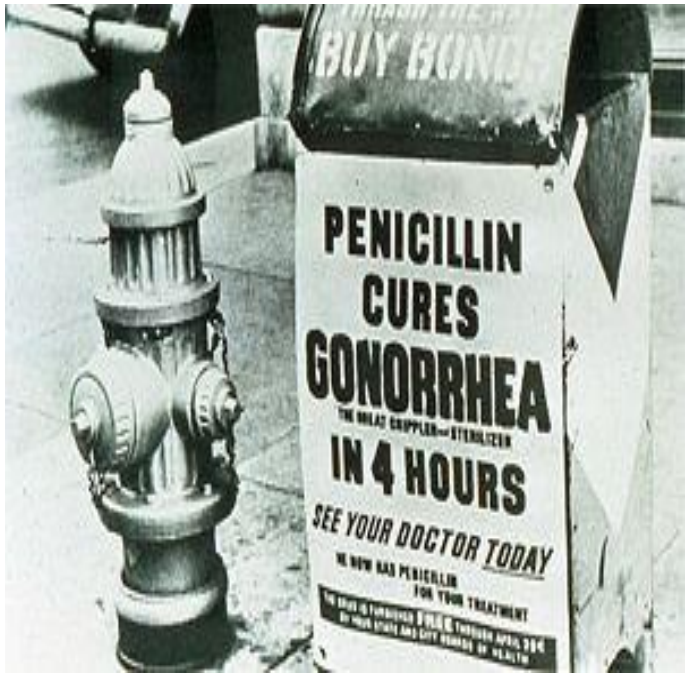
- Patients with syphilis who demonstrate any of the following criteria should have a prompt CSF evaluation:
  - Neurologic or ophthalmic signs or symptoms
  - Evidence of active tertiary syphilis (e.g., gummatous lesions)
  - Treatment failure
  - HIV infection with a CD4 count ≤350 and/or a nontreponemal serologic test titer of ≥1:32
- No test can be used alone to diagnose neurosyphilis.
- VDRL-CSF:  highly specific, but insensitive

# Effect of HIV Infection on Syphilis

- Syphilis and HIV infections commonly coexist.
- Clinical course is similar to non-HIV-infected patients.
- Although uncommon, unusual serologic responses can occur.
- If clinical suspicion of syphilis is high and the serologic tests are negative, then use of other tests (e.g., biopsy of the lesion or rash) should be considered.
- Conventional therapy is effective.

# Lesson II:
# Rx

## Getting the Treatment Right



# Therapy for Primary, Secondary, and Early Latent Syphilis

- Infectious cases (primary, secondary and early latent syphilis), regardless of HIV status, if adherence to treatment and follow-up is uncertain

Benzathine penicillin G 2.4 m.u. IM as a single dose (only option in Pregancy)

**If Adherence To Treatment AND Follow-up Is Expected**

Doxycycline 100 mg PO BID x 14 days

Note:

• A single dose of Benzathine penicillin G long-acting is adequate for HIV positive patients with early syphilis.

*Source*: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2015.

# *Syphilis Resistant to Azithromycin!*

The NEW ENGLAND JOURNAL of MEDICINE

## Macrolide Resistance in *Treponema pallidum* in the United States and Ireland

Sheila A. Lukehart, Ph.D., Charmie Godornes, B.S., Barbara J. Molini, M.S., Patricia Sonnett, B.S., Susan Hopkins, M.D., Fiona Mulcahy, M.D., Joseph Engelman, M.D., Samuel J. Mitchell, M.D., Ph.D., Anne M. Rompalo, M.D., Christina M. Marra, M.D., and Jeffrey D. Klausner, M.D., M.P.H.

N Engl J Med 2004;351:154-8.

# Late Latent, Latent Of Unknown Duration, Tertiary Syphilis (Not Involving The Central Nervous System)

Benzathine penicillin G 7.2 million units total:

Benzathine penicillin G 2.4 m.u. IM weekly x 3 doses

OR

- If penicillin allergic
- Doxycycline 100 mg orally twice daily for 28 days or
- Tetracycline 500 mg orally 4 times daily for 28 days

(Not In Pregnancy)

**In The Event That No Benz Pen Is Available, The Following Treatment Guidelines Are Recommended (Including HIV Infected)**

Alternative treatments Penicillin-G 4 M.U. IV q 4 h x 10 days

OR

Ceftriaxone 1 g IV q 24 h x 10 days

# Key Points:

## Pregnancy

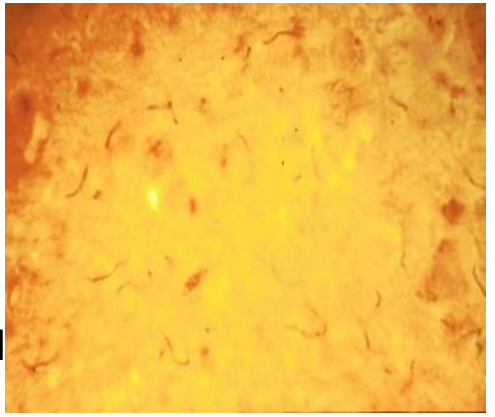
There is no satisfactory alternative to penicillin in pregnancy; strongly consider penicillin desensitization in patients reporting anaphylactic reactions to penicillin

## Jarisch-Herxheimer Reaction

- Self-limited reaction to antitreponemal therapy
- Fever, malaise, nausea/vomiting; may be associated with chills and exacerbation of secondary rash
- Occurs within 24 hours after therapy

Not an allergic reaction to penicillin

# Neurosyphilis



- May occur at any stage of syphilis and can be asymptomatic

- Early neurosyphilis occurs a few months to a few years after infection
  - Clinical manifestations can include acute syphilitic meningitis, meningovascular syphilis, and ocul
- Neurologic involvement can occur decades after infection and is rarely seen
  - Clinical manifestations can include general paresis, tabes dorsalis, and ocular involvement

- Ocular involvement can occur in early or late neurosyphilis.

- Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units intravenously every 4 hours or continuous infusion for 10 to14 days intravenously

- Alternative regimen (if compliance can be ensured)

  - Procaine penicillin 2.4 million units intramuscularly once daily PLUS Probenecid 500 mg orally 4 times a day, both for 10 to14 days

*Source*: Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2010. MMWR 2015;59 (No. RR-12).

# Key Points To Bear In Mind
# Follow-Up

- Primary or secondary syphilis
  - Re: examine at 6 and 12 months.
  - Follow-up titers should be compared to the maximum or baseline nontreponemal titer obtained on day of treatment.
- Latent syphilis
  - Re: examine at 6, 12, and 24 months.
- HIV-infected patients
  - 3, 6, 9, 12 and 24 months for primary or secondary syphilis
  - 6, 12, 18, and 24 months for latent syphilis
- Neurosyphilis
  - Serologic testing as above
  - Repeat CSF examination at 6-month intervals until normal

# Lesson II: Research

# Partner Evaluation for Syphilis Exposure Periods

- All partners within the following time periods require evaluation:
  - 1°: 90 days + duration of symptoms
  - 2°: 6 months + duration of symptoms
  - Early latent: 1 year
- Partners of patients with syphilis of unknown duration and titers ≥ 1:32 should also be evaluated

All patients who have syphilis should be tested for HIV infection.

Consider screening persons with syphilis for other STDs.

# Screening Recommendations

- Screen pregnant women at least at first prenatal visit.
  - In high prevalence communities, or patients at risk
    - Test twice during the third trimester, at 28 weeks, and at delivery, in addition to routine early screening.
  - Any woman who delivers a stillborn infant after 20 weeks gestation should be tested for syphilis.
- Screen other populations based on local prevalence and the patient's risk behaviors.

# Reporting

- MOH Regulations DO NOT require that persons diagnosed with syphilis are reported to public health authorities at this time.
- Reporting laboratory based.
- The follow-up of patients with early syphilis is a public health priority.

# Treatment Failure

- Indications of probable treatment failure or reinfection include:
  - Persistent or recurring clinical signs or symptoms
  - Sustained 4-fold increase in titer
  - Titer fails to show a 4-fold decrease within 6–12 months
- Retreat and re-evaluate for HIV infection.
- CSF examination can be considered.

REFFERAL