Management of Syphilis in Pregnancy

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Case 1

- 26 years old, G2P1 at 18 weeks POA
- H/O STD 5 years ago and claim given 3 injections at that time
- Current results:

  RPR 1:4

  TPPA positive

Case 1

- How should she be managed?

A. Repeat serology at 28 weeks / delivery
B. She is re-infected, treat her with penicillin now
C. Reassurance with no further workup
D. None of the above
E. I don’t know – refer FMS / Dermatologist

Case 2

- 22 year old, primigravida at 10 weeks POA
- RPR 1:2 and TPPA negative
- No H/O STD
- Husband newly diagnosed HIV and syphilis

Case 2

- How should she be managed?

A. No action, pregnancy can cause false positive
B. Repeat serology at 28 weeks / delivery
C. Repeat serology at 4 to 6 weeks
D. Reassurance, no further workup
E. I don’t know, I will refer

Case 3

- 21 year old lady, G4P3 at 14 weeks POA
- RPR non reactive, TPPA positive
- No H/O receiving treatment for STD in the past
- Physical examination normal

Case 3

- How would you manage?

A. Repeat serology at 28 weeks / delivery
B. Repeat serology at 4 to 6 weeks
C. Reassurance, no further workup
D. Treat her with penicillin

Case 4

- 18 year old lady, G1P0 at 14 weeks POA
- RPR 1:128, TPPA positive
- Husband similar results
- Both were treated as early syphilis with IM Benzathine Penicillin
- Repeated serology 1 month later was 1:256

Case 4

- How would you manage?

A. Re-treat her with penicillin
B. Repeat serology at 4 weeks
C. Ask further history – re-exposure and check for concurrent HIV infection
D. I don’t know, I will refer

My talk will answer the following…

- When should syphilis be suspected in a pregnant lady?
- When should syphilis be tested in a pregnant lady?
- Why should syphilis be tested in a pregnant lady?
- How should syphilis serology be interpreted?
- How do you monitor after treatment?

When should syphilis be suspected in a pregnant lady?

- Sexual / direct contact (infected lesions) with a person who has syphilis
- If the cause is not known for a hydropic or stillbirth newborn -> do postpartum screening

REMEMBER: ALL pregnant women must be assumed to be at risk!

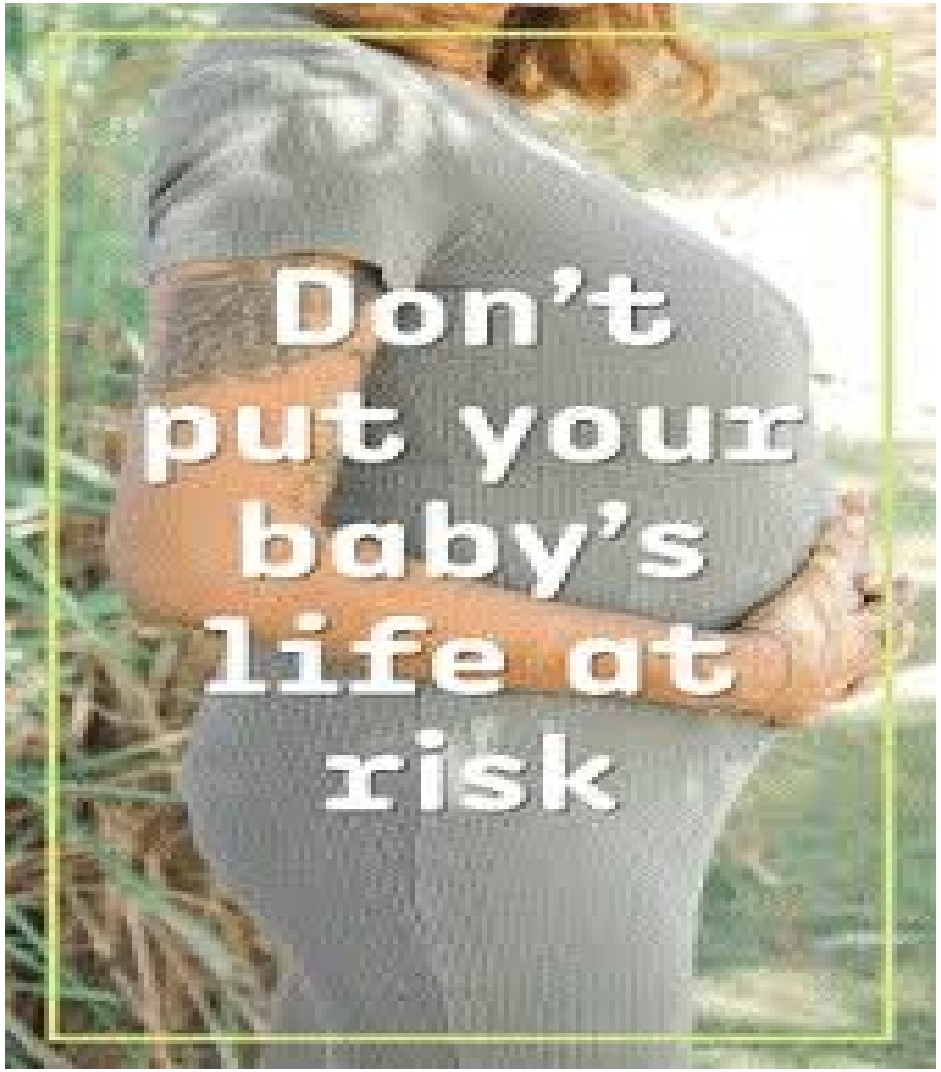
When should syphilis be tested in a pregnant lady?

- All pregnant lady should be screened serologically for syphilis

- When to screen?
  - At first prenatal visit
  - High risk:
    - At 28 - 32 weeks POA
    - At delivery
    - Fetal death at ≥ 20 weeks gestation

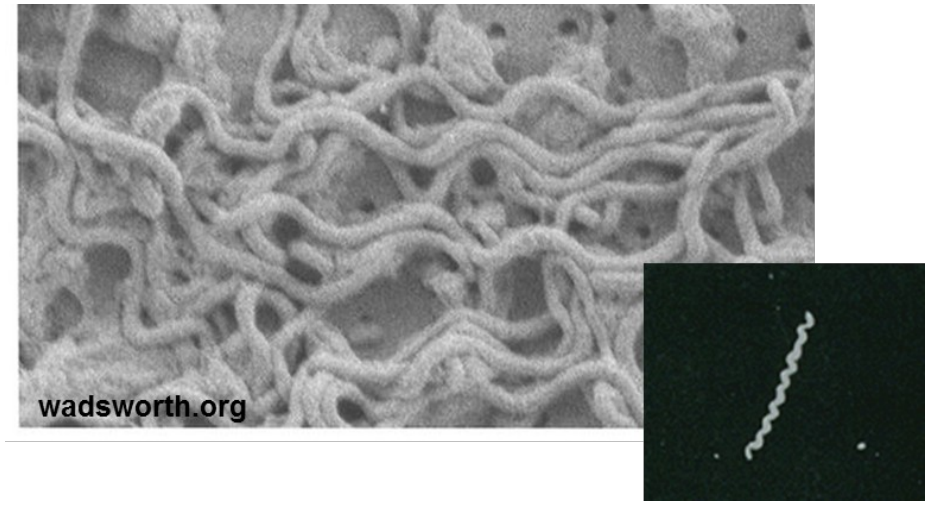
High risk mother

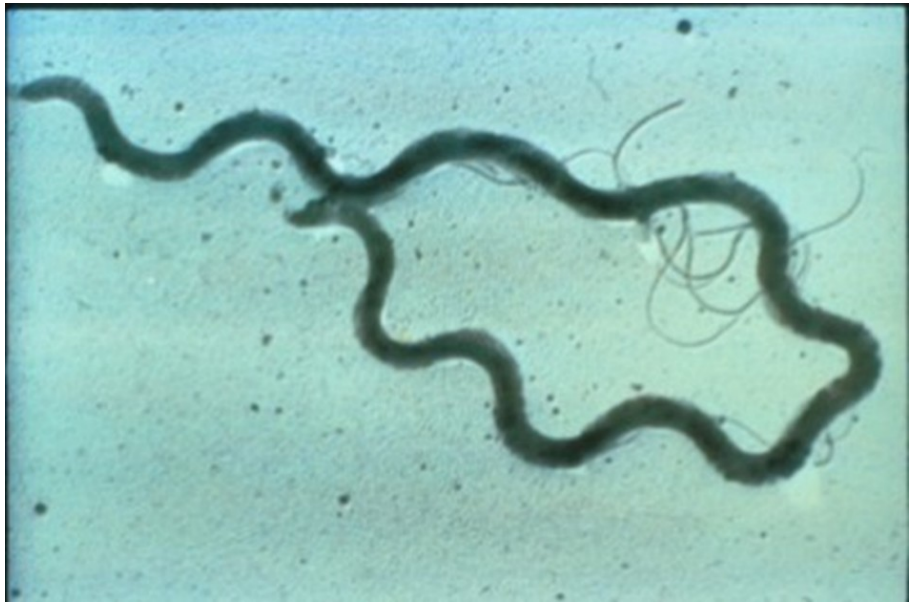
- RPR reactive on booking
- Single mother
- Female sex worker
- HIV positive mother
- Rape case
- History of STI
- Multiple sex partners
- History of stillbirth / miscarriage
- Unbooked / unscreened pregnancy
- Alcohol / drug abuse



Introduction

- Causative organism: *Treponema pallidum*
- Spirochete
- Obligate human parasite
- Transmission
  - Sexual
  - Trans-placental
  - Percutaneous following contact with infectious lesions
  - Blood Transfusion





Syphilis – The “Great Imitator”

- Incubation Period – 21 days (median)

- 3 clinical stages of syphilis
  - Primary:
    - Painless ulcer (chancre) at inoculation site
  - Secondary:
    - Rash, Fever, Lymphadenopathy, Malaise
  - Tertiary:
    - Gumma, cardiovascular syphilis
  - Latent:
    - Asymptomatic

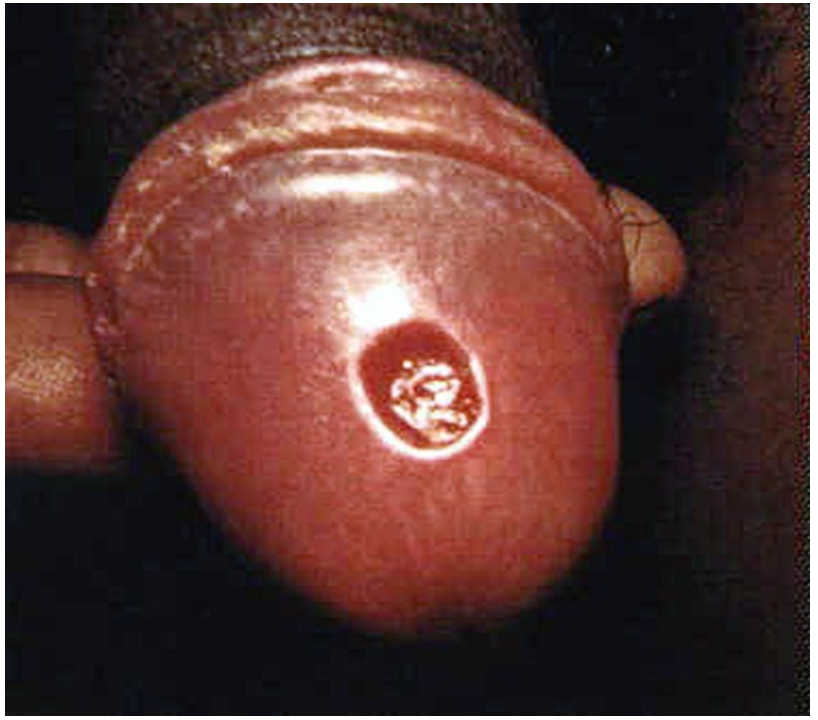
- Neurosyphilis:

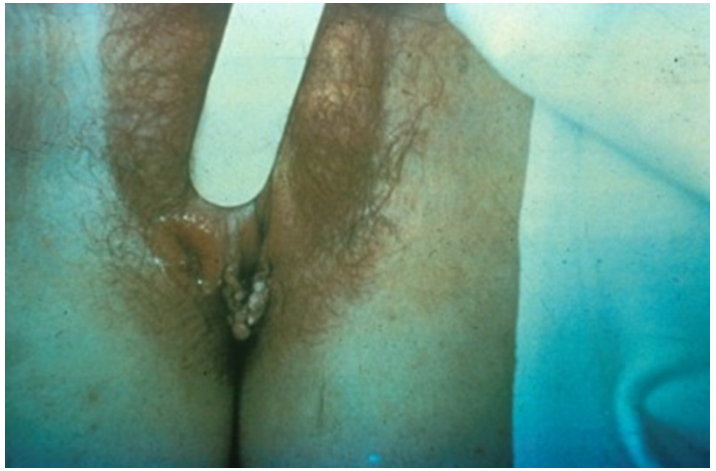
Primary Syphilis

- Incubation period: 9-90 days
- **Chancre**

- painless, indurated with clean base
- Highly infectious
- Typically heals within 3-6 weeks
- Multiple lesions can occur

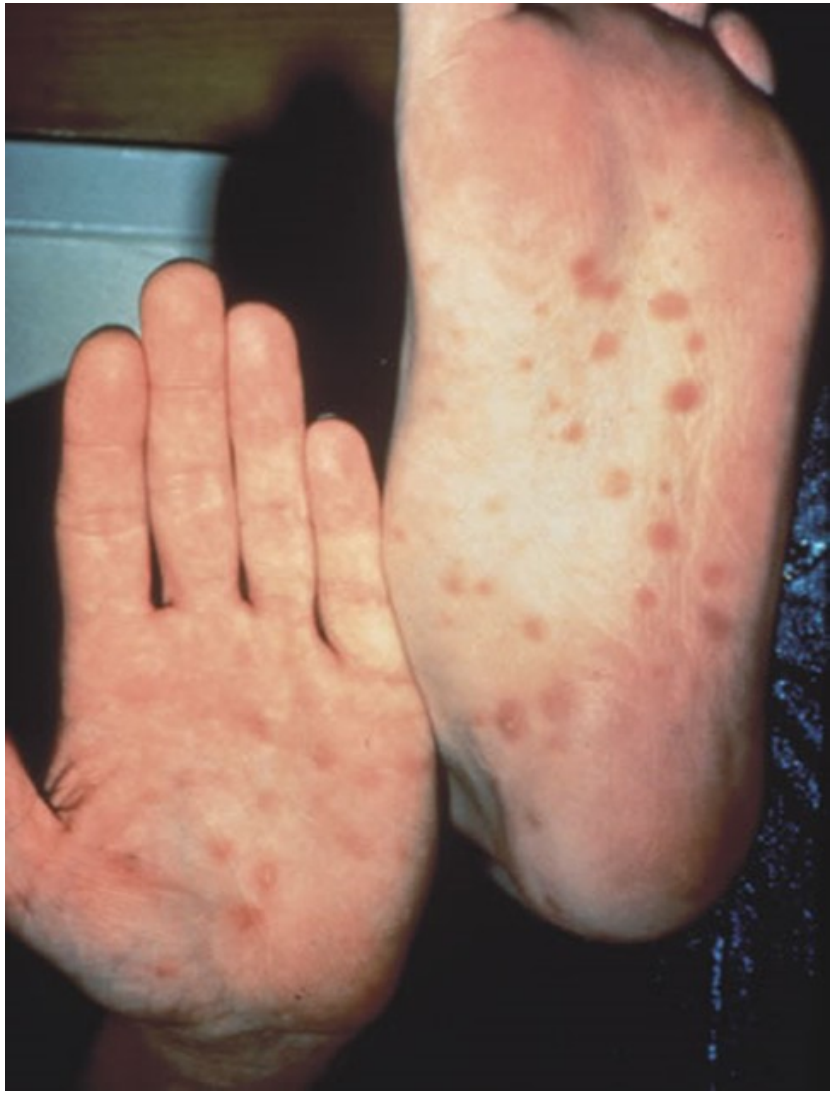
- Regional lymphadenopathy: bilateral, painless
- **Serologic tests for syphilis may not be positive** during early primary syphilis.





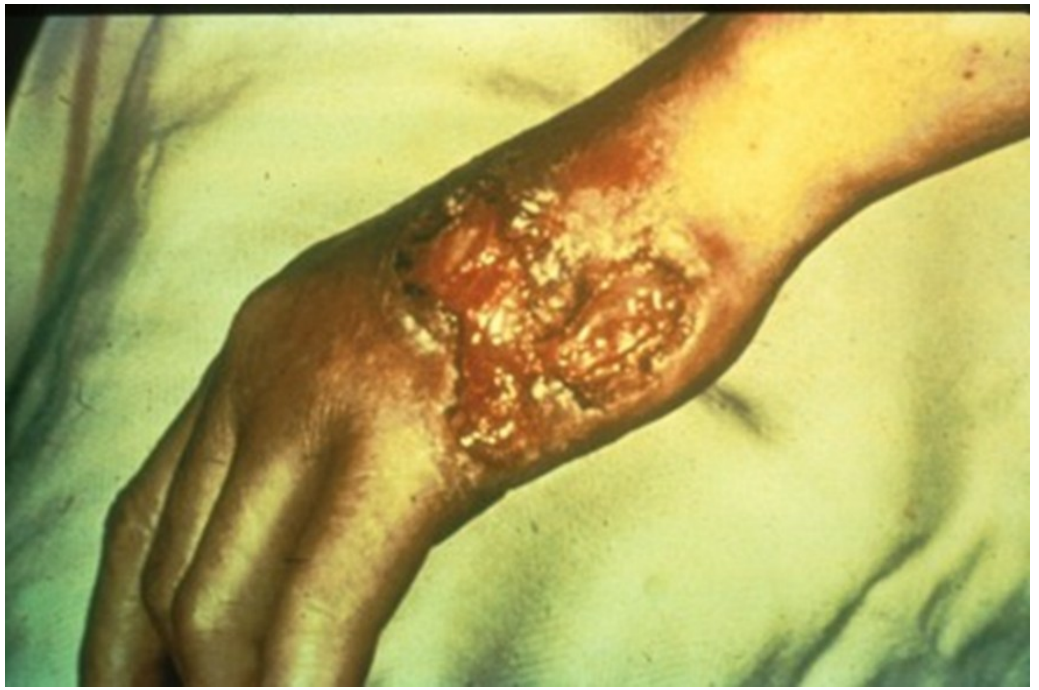
Secondary Syphilis

- Incubation period: 6 weeks to 6 months
- Clinical features:
  - **Rash (75%–100%)**
  - Lymphadenopathy (50%–86%)
  - Malaise
  - Mucous patches (6%–30%)
  - Condylomata lata (10%–20%)
  - Alopecia (5%)
- Serologic tests are usually highest in titer
- Can also be false negative (Prozone effect)



Tertiary Syphilis

- Develop in untreated patient within 1 to 30 years
- Clinical features:
  - Gummatous lesions
  - Cardiovascular syphilis
- Non infectious



Neurosyphilis

- May occur at **any stage of syphilis**
- 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 ocular and auditory involvement
- 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.

Latent Syphilis

- Host suppresses infection, thus **no lesions are clinically apparent**
- Only evidence is a **positive serologic test**
- May occur between primary and secondary stages, between secondary relapses, and after secondary stage
- Categories:
  - Early latent: <1 year duration
  - Late latent: ≥1 year duration

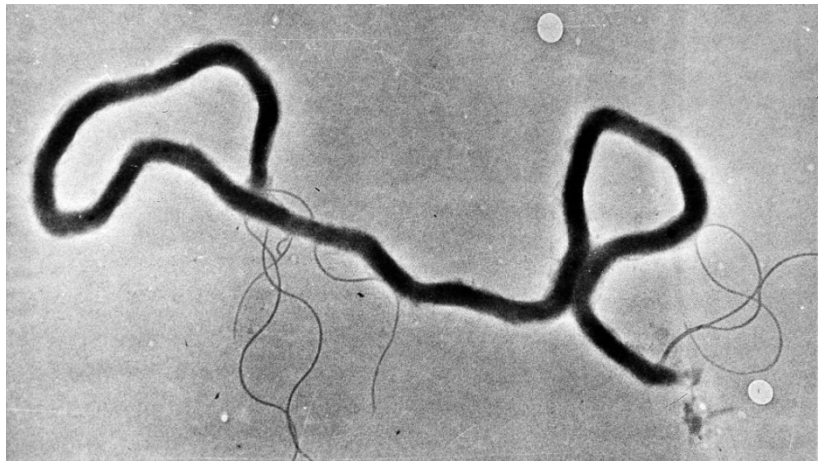
Latent Syphilis

- Criteria for early latent syphilis: The following noted within the year preceding the evaluation
  - Documented seroconversion or 4-fold increase in comparison with a serologic titer
  - Symptoms of primary or secondary syphilis reported by patient
  - Contact to an infectious case of syphilis
  - Only possible exposure occurred within past 12 months

- Patients with latent syphilis of **unknown duration** should be managed clinically as if they have **late latent syphilis.**

Diagnosis

- History
- Physical examination
- **Serology**
  - Mainstay for syphilis testing
  - Two classes of serologic tests
    - Non-treponemal
    - Treponemal



- The use of only one type of serologic test is insufficient for diagnosis

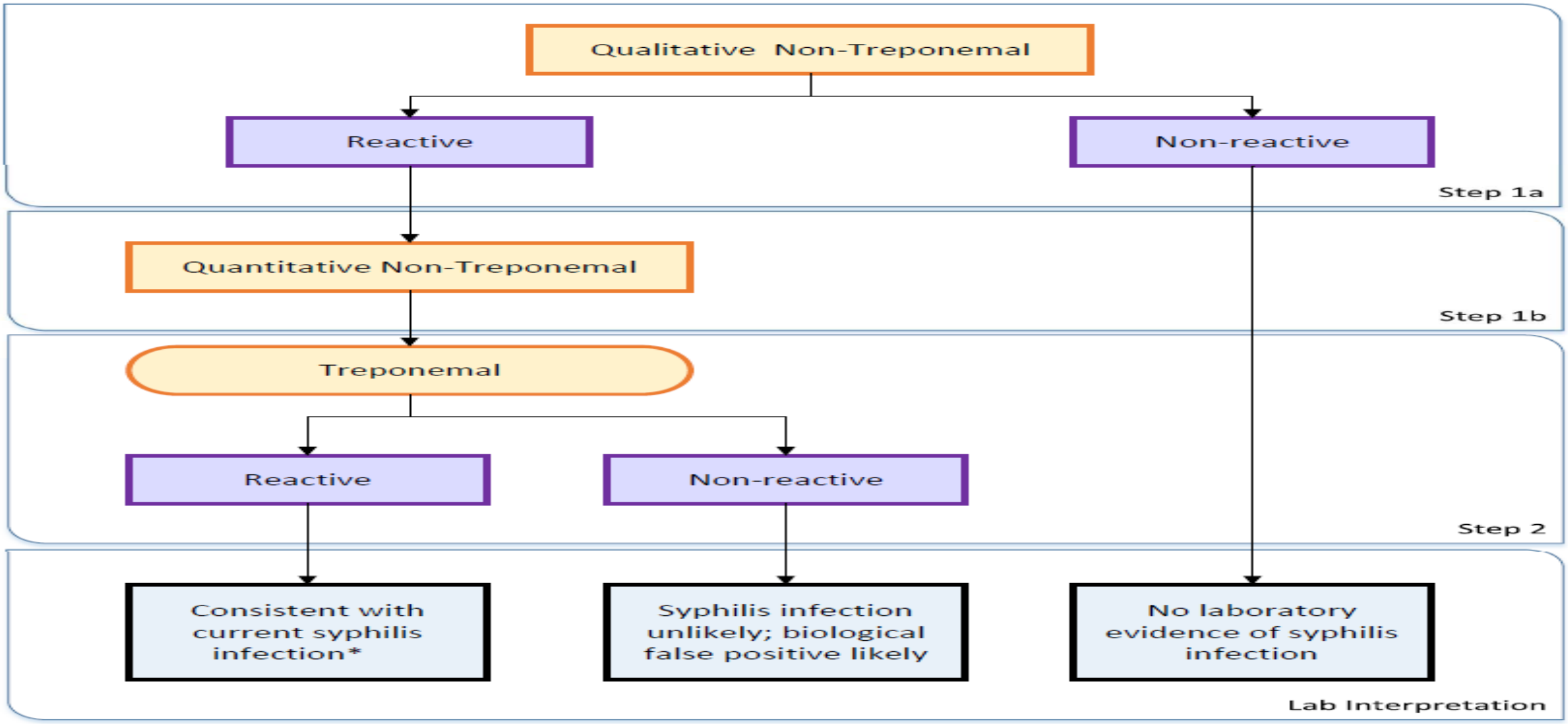
Nontreponemal Serologic Tests

- Principles
  - Measure antibody directed against a cardiolipin-lecithin-cholesterol antigen
  - **Not specific for *T. pallidum***
  - Titers usually **correlate with disease activity** and results are reported quantitatively
  - May be reactive for life, referred to as “serofast”
- Nontreponemal tests include **VDRL, RPR**, TRUST, USR

Treponemal Serologic Tests

- Principles
  - Measure antibody directed against *T. pallidum* antigens
  - Qualitative
  - Usually **reactive for life**
  - Titers should not be used to assess treatment response
- Treponemal tests include **TP-PA**, FTA-ABS, EIA, and CIA
- Cannot differentiate between current and past infection.

Algorithm for Screening



**If titer <1:4 consider these values associated with possible serofast condition.[22] Serofast is used to refer to those persons with early syphilis with non-treponemal titers that neither increase nor decrease 4-fold after treatment.[2,3]*

Interpretation of Serological Tests

Non-Treponemal tests (RPR/ VDRL)	Treponemal Tests (TP-PA/ FTA-ADS)	Possible Explanation
+	+	Syphilis - recent or previous Yaws or pinta
+	—	No syphilis False positive
—	+	Consistent with previously treated or untreated Syphilis Yaws, Pinta, Bejel
—	—	No syphilis Syphilis in incubation period

False Positive Tests

- Viral infections (Infectious mononucleosis)
- Bacterial infections (pneumonia, TB)
- Connective tissue disease (rheumatoid arthritis, SLE)
- Elderly
- Pregnancy

Interpretation of Serological Tests

- **Initial screening may be negative** in early primary syphilis.
  - If the history is strongly suggestive of syphilis then an RPR should be repeated in **3-4 weeks**
- Most people become negative for RPR with adequate treatment.
  - some may maintain a **low titer RPR** (<1:8) for life despite adequate treatment. This is the **serofast state**.
- A **negative RPR test with a positive TPPA**:
  - can be treated or untreated syphilis.
  - **if there is no documentation of treatment for syphilis, the patient must be treated.**
- **Prozone phenomenon**
  - false negative response resulting from overwhelming antibody titers
  - associated with HIV, pregnancy and secondary syphilis

Treatment

Recommended Regimen for Syphilis During Pregnancy

- Penicillin G is the only known effective antimicrobial for treating fetal infection and preventing congenital syphilis.
- Pregnant women should be treated with the recommended penicillin regimen for their stage of infection.

- Patients who are skin-test-reactive to penicillin should be **desensitized** in the hospital and treated with penicillin.

Source: Centers for Disease Control and Prevention. Sexually transmitted infections treatment guidelines 2021.

Treatment

- Primary, secondary and early latent syphilis
  - Benzathine penicillin G 2.4 million units intramuscularly in a single dose
  - Some evidence suggests that additional therapy can be beneficial
    - **a second dose of benzathine penicillin 2.4 million units IM can be administered 1 week after the initial dose**

- Late latent syphilis
  - Benzathine penicillin G administered as 3 doses of 2.4 million units intramuscularly each at 1-week intervals

Source: Centers for Disease Control and Prevention. Sexually transmitted infections treatment guidelines 2021.

Issues related to treatment

- Penicillin allergy: < 1%.....verify and desensitize
- Jarisch-Herxheimer reaction
- In pregnant women, **missed doses are NOT ACCEPTABLE** -> full course of therapy must be repeated if scheduled dose is delayed by >9 days
- All women who have syphilis should be offered testing for HIV infection
- Refer to specialist hospital for delivery
- **Notify** positive case!

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**
- More frequent after treatment with penicillin and treatment of early syphilis
- Antipyretics can be used to manage symptoms, but they have not been proven to prevent this reaction.
- Pregnant women should be informed of this possible reaction, that it may precipitate early labor, and to call obstetrician if problems develop.

Monitoring after treatment

- Preferably serological titers (**RPR / VDRL) monthly until delivery**
- At minimum, serological test repeated at 28-32 weeks and at delivery
- If diagnosed ≥ 6/12 POA, refer for fetal assessment

Causes of treatment failure

- High RPR titre at diagnosis / delivery
- Delivery < 36 weeks
- Short interval during treatment and delivery (< 30 days)
- Re-infection
- Non-penicillin treatment

Indications of treatment failure

- Persistence / recurring signs and symptoms
- Sustained fourfold increase in non-treponemal titer, OR failure of titer to reduce fourfold within 6 months
- Measures:
- Retreat: weekly IM injection of Benzathine penicillin G 2.4 million units for 3/52
- **Test for HIV co-infection**
- CSF examination

REFER DERMATOLOGY AND OBSTETRIC TEAMS!

Management of Sexual Partners

- For sex partners of patients with syphilis in any stage
  - Do syphilis serology
  - Perform physical exam

- For sex partners of patients with primary, secondary, or early latent syphilis
  - Treat presumptively as for early syphilis at the time of examination, unless
    - The nontreponemal test result is known and negative and
    - The last sexual contact with the patient is > 90 days prior to examination.

Postpartum management issues

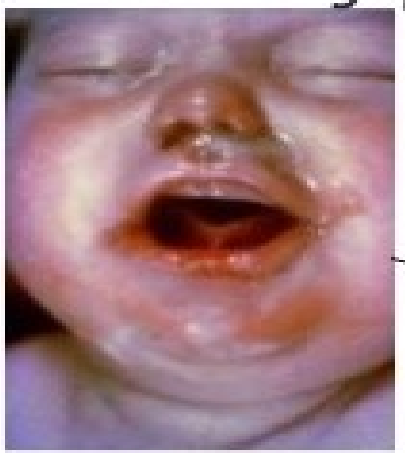
- Even with appropriate penicillin therapy, up to 10% of infants may have congenital syphilis
- Serologic testing of maternal blood at time of delivery is superior to infant blood testing
- Umbilical cord blood testing is not recommended
- A comparison of maternal and infant non-treponemal test titers is very useful to guide therapy
- Neonates should be examined for congenital syphilis.

Congenital syphilis

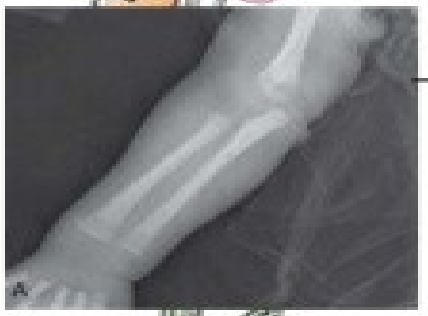
- The risk of vertical transmission depends on the stage of maternal syphilis
  - Untreated primary or secondary syphilis: 70 to 100%
  - Early latent syphilis: 40%
    - The risk is extremely high for the first 4 years after acquisition of infection if not treated
  - Late latent syphilis: < 10%
- Remember: 50% are born asymptomatic, manifestations can first be seen up to 2 years of age

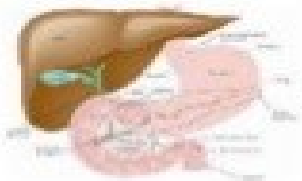
Congenital syphilis (early < 2 years)

Hydrops fetalis



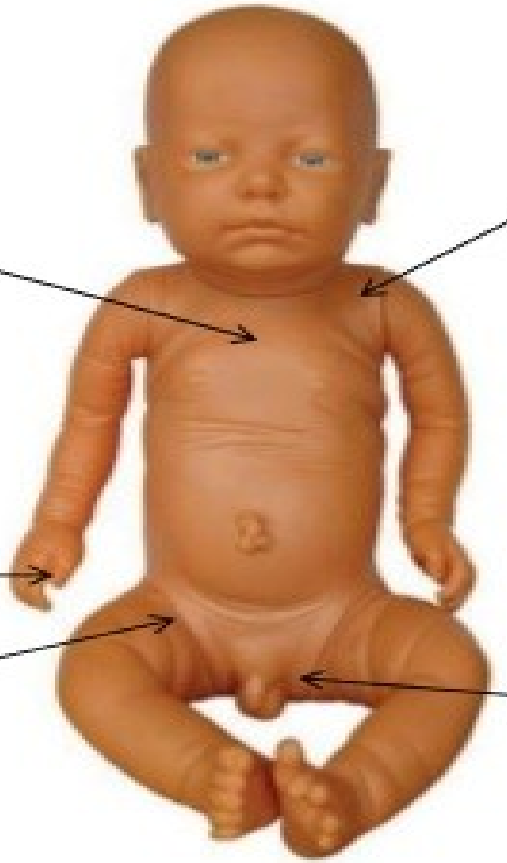
Nasal discharge

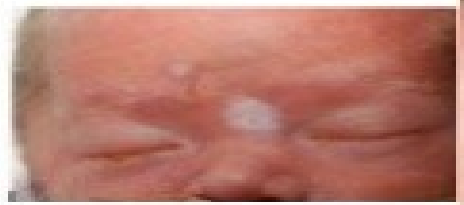


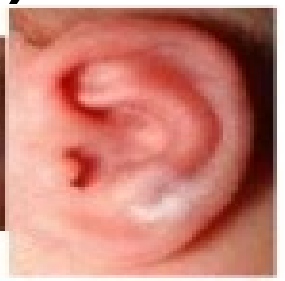


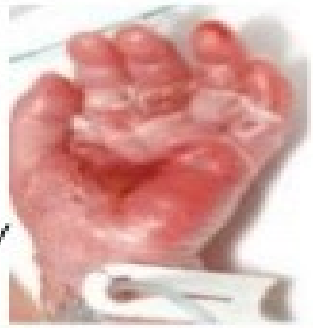
Hepatomegaly

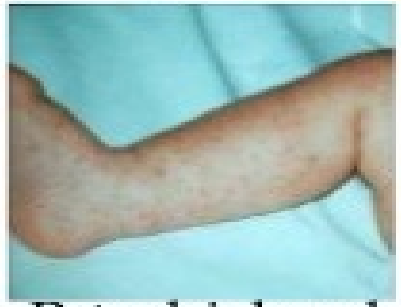
Rash





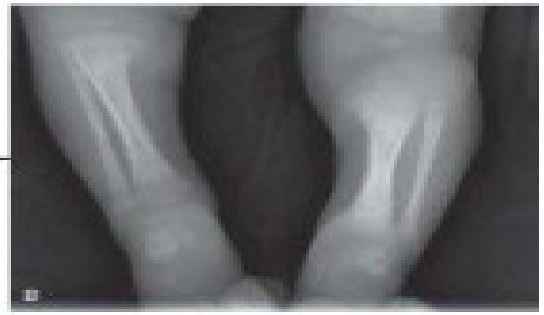






Petechial rash

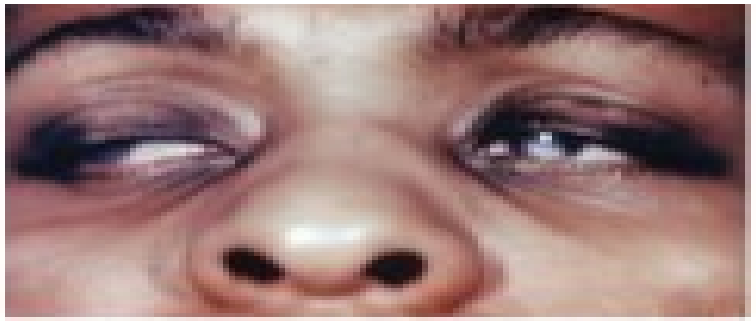
Necrotizing funisitis within the matrix of the umbilical cord



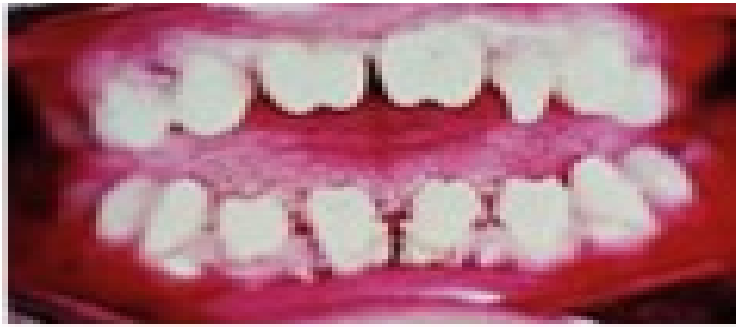
Osfitis ,
Metaphysitis,
Periostitis
Wimberger sign

Congenital syphilis (late > 2 years)

Frontal bossing;
Saddle nose

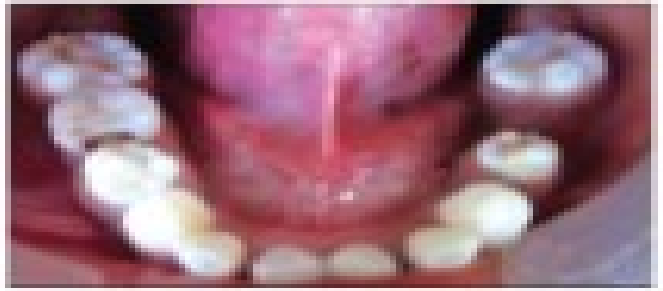


Interstitial keratitis



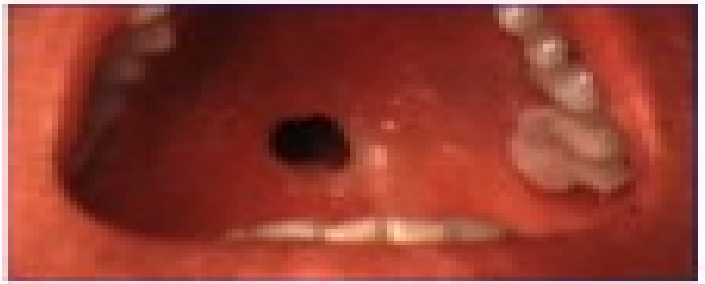
Hutchinson teeth

Rhagades

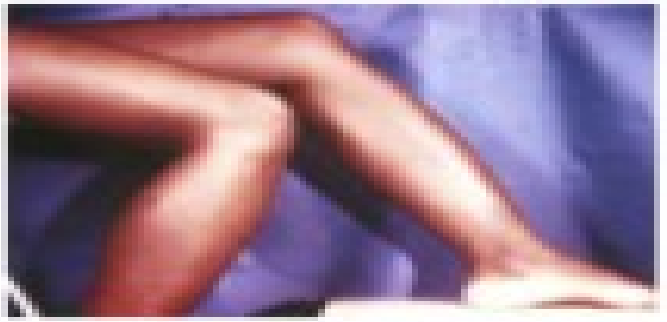


Mulberry molar

Saddle nose



Perforated hard palate



Saber shins

Case 1

- 26 years old, G2P1 at 18 weeks POA
- H/O STD 5 years ago and claim given 3 injections at that time
- Current results:

  RPR 1:4

  TPPA positive

Case 1 answer

- Seropositive pregnant women should be considered actively infected unless an **adequate treatment history is clearly documented** and sequential antibody titers have declined
- Serofast low antibody titers might not require treatment
- Persistent higher antibody titers might indicate re-infection and require re-treatment

Case 2

- 22 year old, primigravida at 10 weeks POA
- RPR 1:2 and TPPA negative
- No H/O STD
- Husband newly diagnosed HIV and syphilis

Case 2 answer

- False positive RPR is common in pregnancy
- However, in high risk patients, serologic testing should be repeated twice in the 3rd trimester at 28 to 32 weeks and at delivery
- **Initial screening may be negative** in early primary syphilis.
  - If the history is strongly suggestive of syphilis then an RPR should be repeated in **3-4 weeks**

Case 3

- 21 year old lady, G4P3 at 14 weeks POA
- RPR non reactive, TPPA positive
- No H/O receiving treatment for STD in the past
- Physical examination normal

Case 3 answer

- Patient should be treated as late latent syphilis
- There is some risk of vertical transmission

Case 4

- 18 year old lady, G1P0 at 14 weeks POA
- RPR 1:128, TPPA positive
- Husband similar results
- Both were treated as early syphilis with IM Benzathine Penicillin
- Repeated serology 1 month later was 1:256

Case 4 answer

- Ask further history – re-exposure and check for concurrent HIV infection
- If no re-exposure and HIV is negative, repeat RPR in 4 weeks time
  - Consider re-treatment if no fourfold decrease in titer

THANK YOU


NOT SURE IF THEY'RE CLAPPING FOR MY PRESENTATION
OR BECAUSE ITS FINISHED