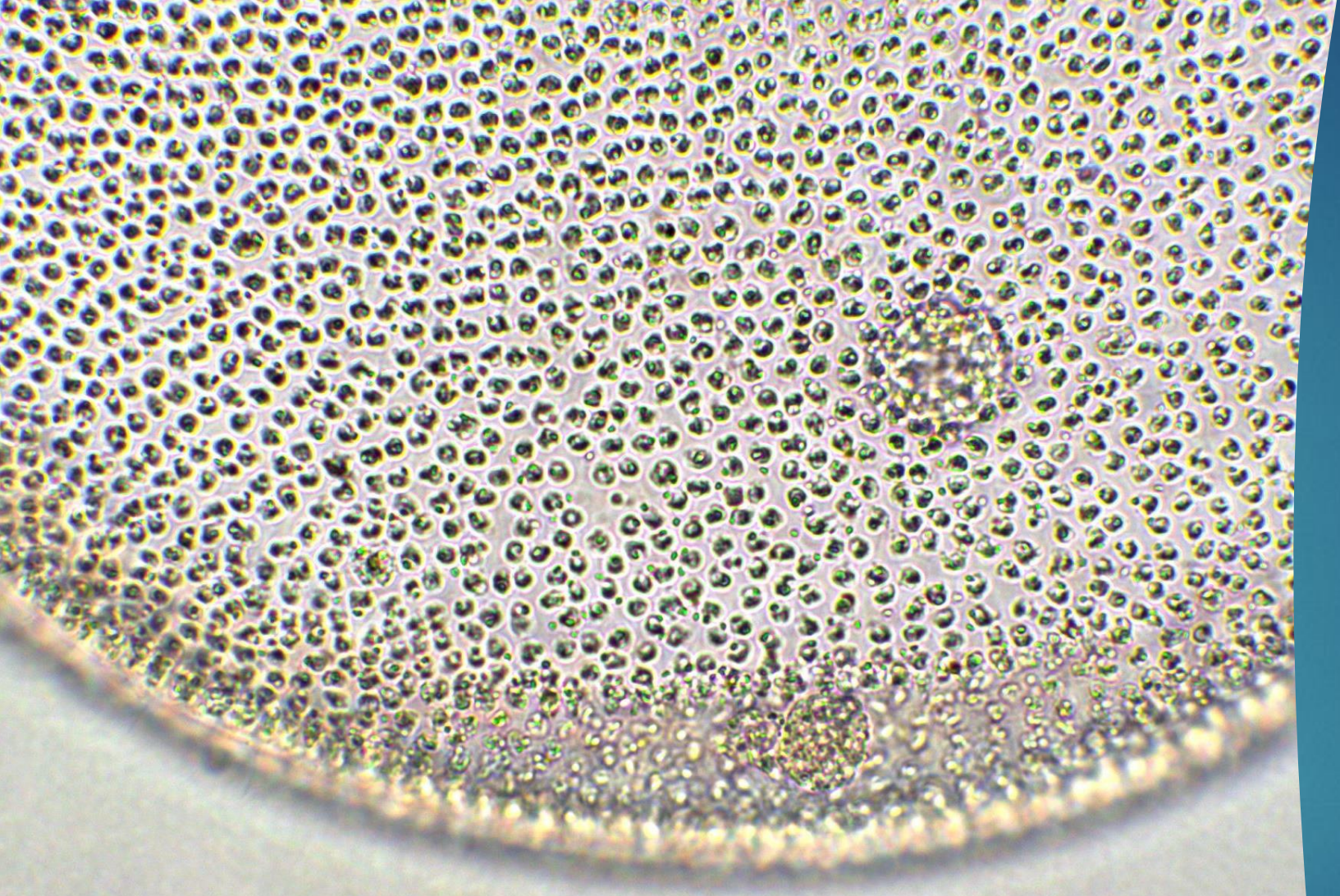


CONGENITAL SYPHILIS

AWACC 20 October 2023

RAY MAHARAJ

SYPHILIS: STD CAUSED BY THE SPIROCHETE TREPONEMA PALLIDUM

Congenital Syphilis :

- **transmitted transplacentally or contact with infectious lesions during childbirth**
- **stillbirth, PTD , LBW, FGI , clinical sequelae**
- **Untreated antenatally :**
  - **⅓ : stillbirth**
  - **⅓ :congenital syphilis**
  - **⅓ : uninfected**
- **WHO: 2nd leading cause of preventable stillbirth globally (2023)**

N.B. Maternal syphilis increases the risk of MTC HIV 2–2.5 times. Maternal HIV- syphilis co-infection has poorer birth outcomes *(Kinikar et al, 2015)*

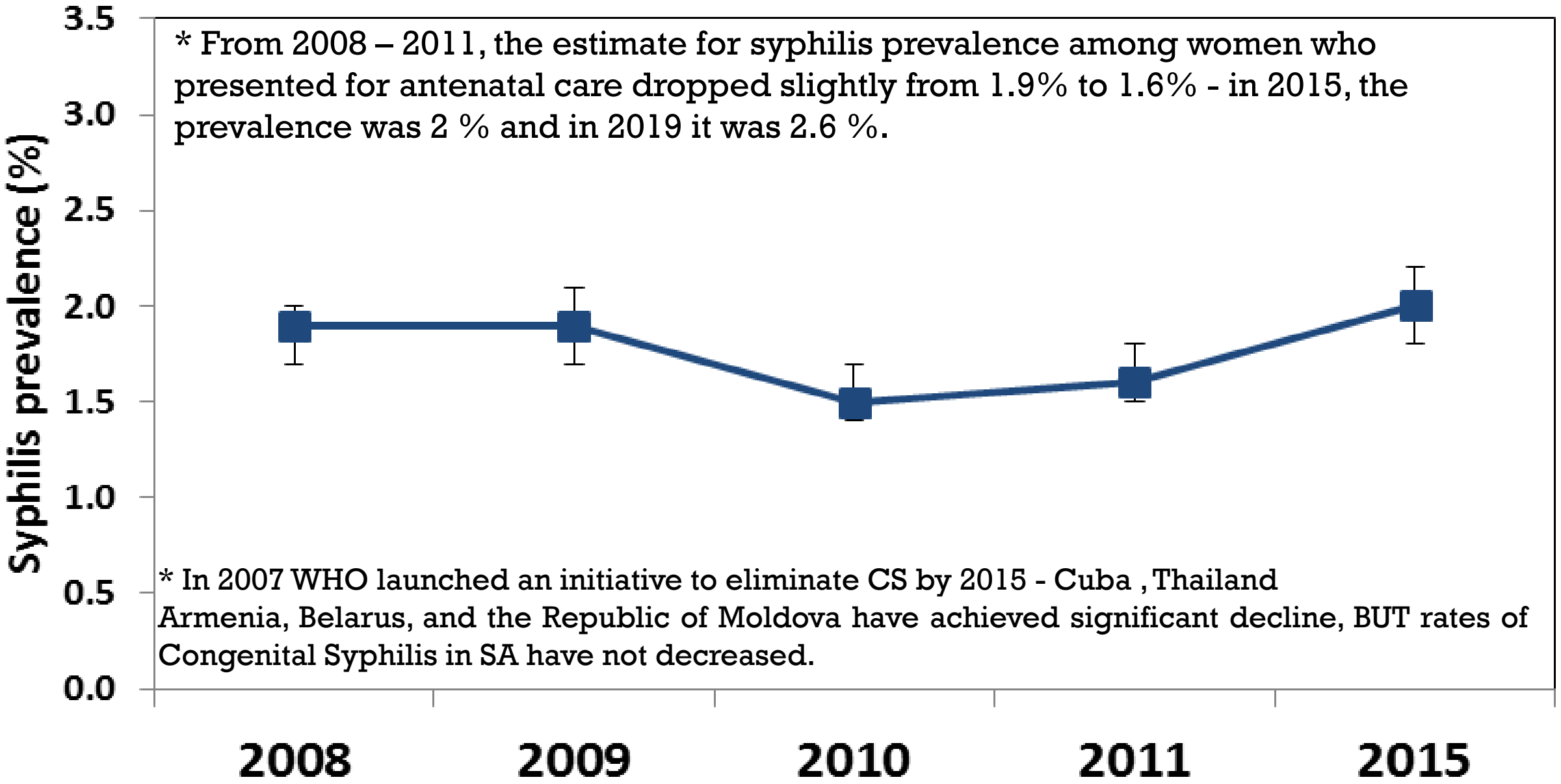
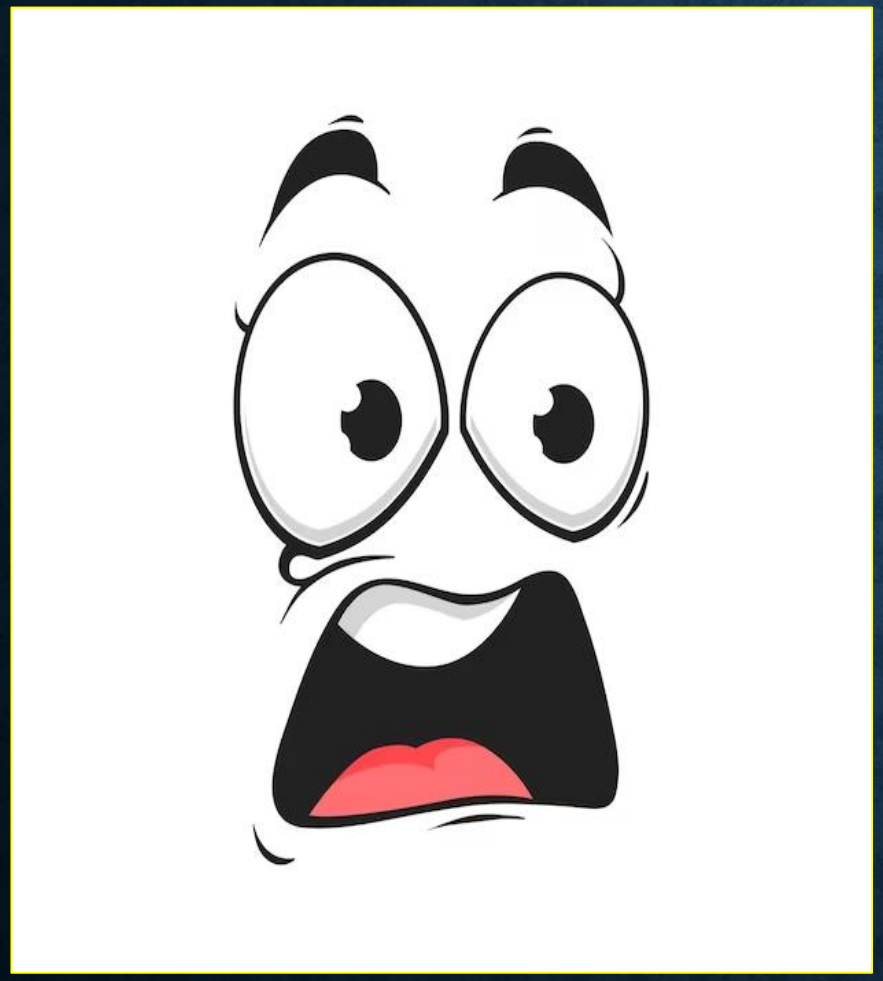


Figure 46: Syphilis prevalence trends among antenatal women, South Africa, 2008 – 2011 and 2015.

Figure 13. Number of specimens received and number of cases notified per quarter between 2017 and 2022

Provincial Notification Trends



Province	All notified cases of congenital syphilis from Q3 2017 to Q2 2022	% of total
KwaZulu-Natal	637	46.5
Western Cape	295	21.5
Gauteng	287	20.9
Northern Cape	42	3.1
Free State	35	2.6
Eastern Cape	32	2.3
North West	23	1.7
Limpopo	12	0.9
Mpumalanga	7	0.5

SYPHILIS

Pathogen

Treponema pallidum

Treatment

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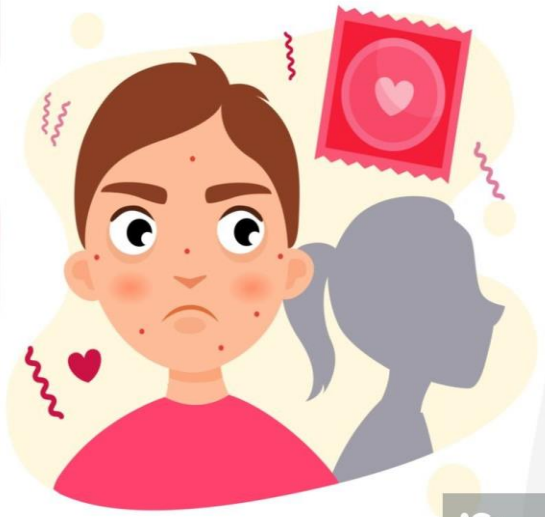
25% of people with syphis die without treatment



Symptoms

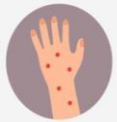
STAGE 1


headache


skin ulcer


muscle pain

STAGE 2


rash


mucosal damage


heat

STAGE 3


dementia and psychotic disorders


internal bleeding


damage to internal organs

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Prevention

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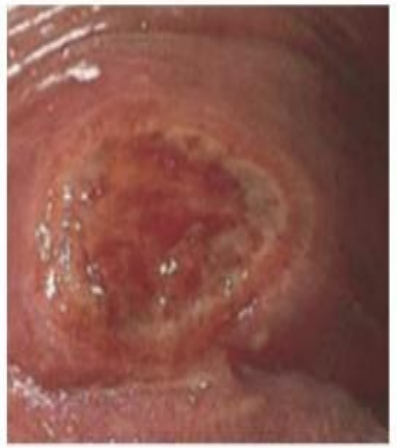
personal hygiene

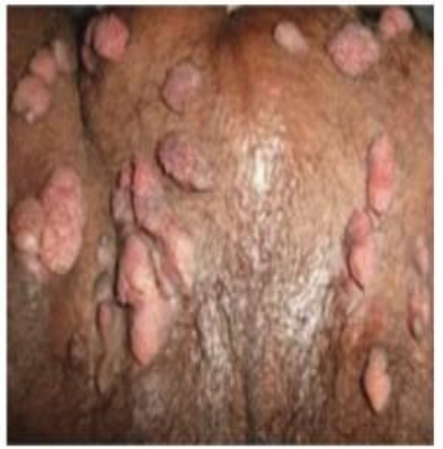

use a condom


syphilis test

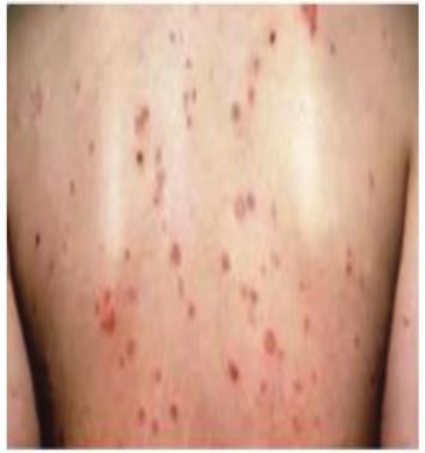

use personal dishes

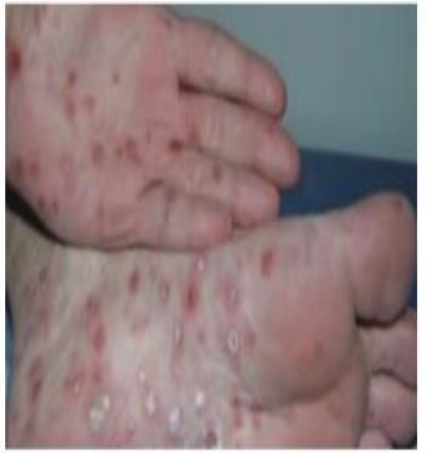

don't kiss sick people





Painless ulcer/chancre and condylomata lata on genitals

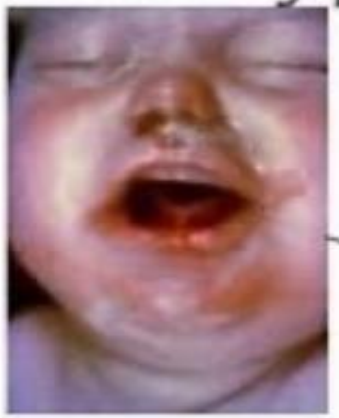




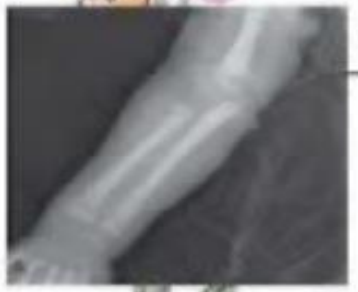
Rash involving palms and soles

Congenital Syphilis

Hydrops fetalis

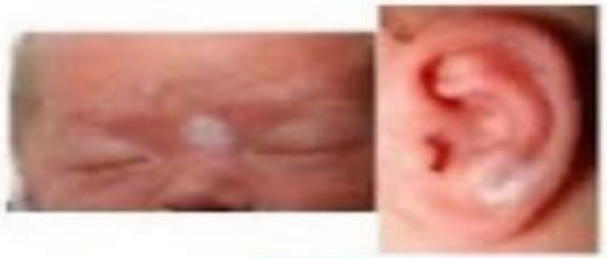


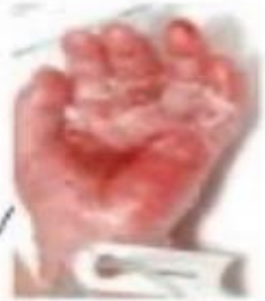
Nasal discharge

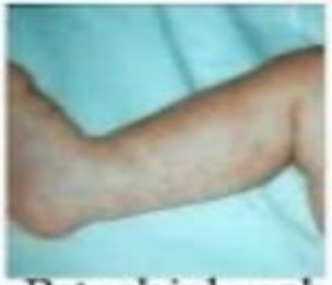


Hepatomegaly

Rash

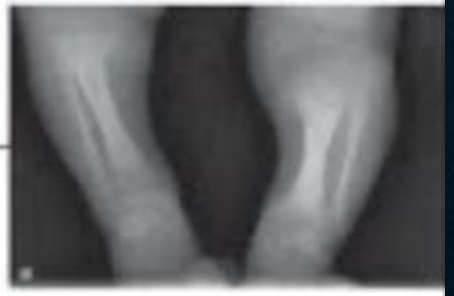




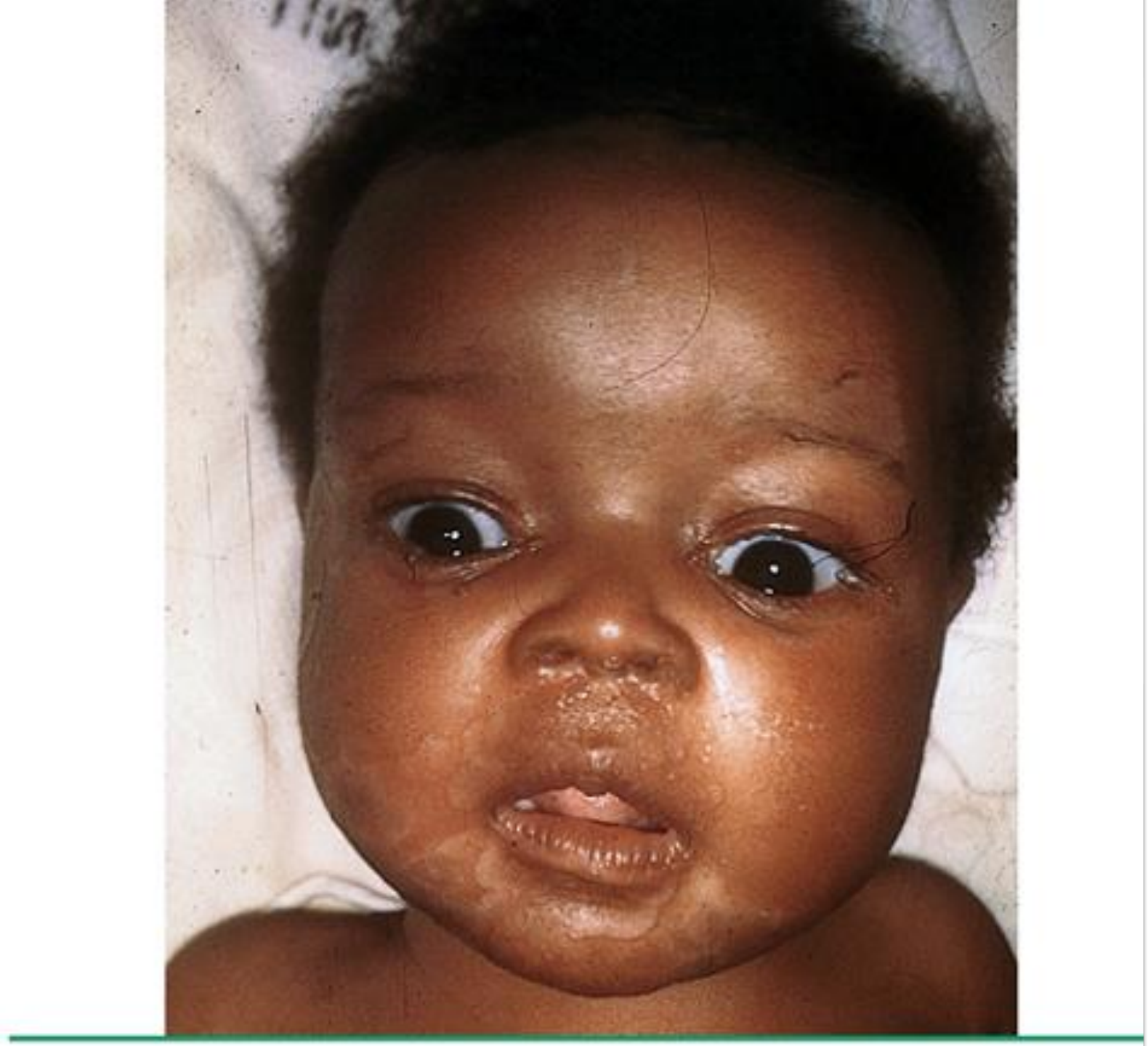


Petechial rash

Necrotizing funisitis within the matrix of the umbilical cord



Ostitis , Metaphysitis, Periostitis Wimberger sign



CHOOSE THE BEST DIAGNOSIS

A. Saddle Nose

B. Cleft Palate

C. Rhintis

D. Saddle nose and rhinitis

E. Cleft Palate and rhinitis

TRANSMISSION AND PATHOGENESIS

T. pallidum is liberated directly into the fetal circulation

Widespread dissemination to bones, liver, pancreas, intestine, kidney, and spleen most frequently

Clinical manifestations result from inflammatory response.

Variable severity from isolated laboratory or radiographic abnormalities to fulminant involvement of multiple organ systems.

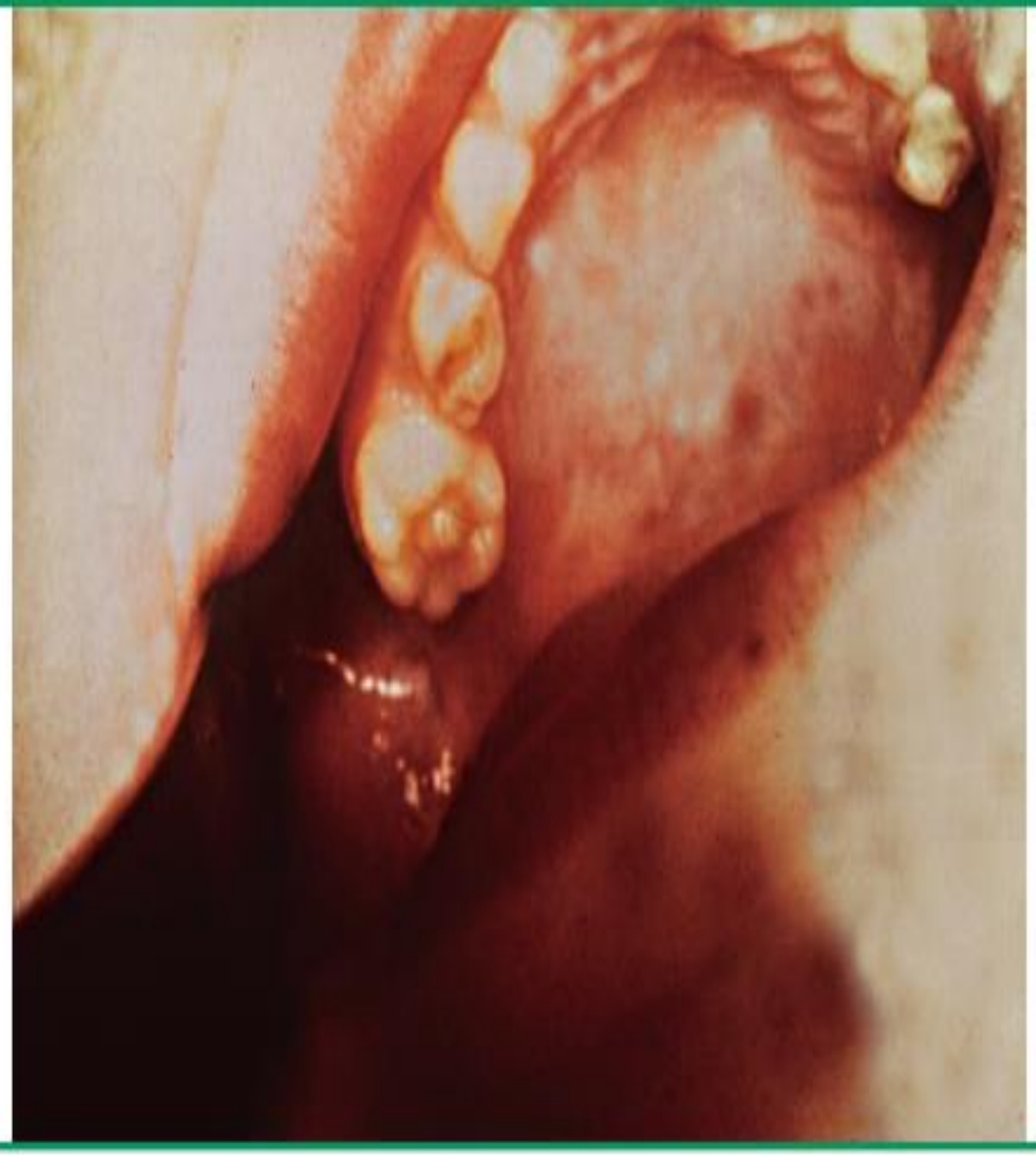
Overt infection can manifest in the fetus, the newborn, or later in childhood

Failure to thrive usually results from gastrointestinal involvement

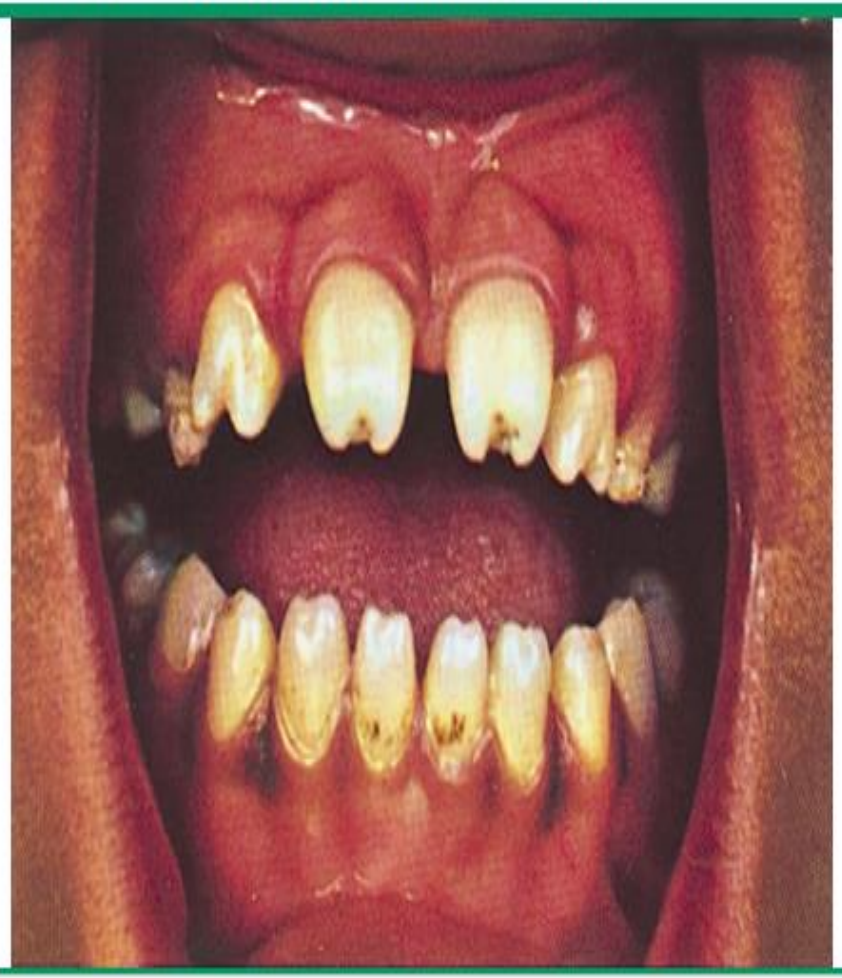
T. pallidum is not transferred in breast milk but may occur if the mother has an infectious lesion on her breast

Vasculitis may lead to infarction and intra-uterine death, premature delivery, or intra-uterine growth retardation.

Congenital syphilis: Mulberry molar



Congenital syphilis: Hutchinson teeth



Hutchinson teeth are smaller and more widely spaced than normal and are notched on their biting surfaces. The sides of the teeth taper toward the biting edges. The upper central incisors of the permanent (not the deciduous) teeth are most often affected.

MAGNITUDE OF THE PROBLEM

- 2016- 988,000 cases of active maternal syphilis globally -60% in sub-Saharan Africa.
- 143 000 fetal deaths, 61 000 neonatal deaths, 41 000 preterm or LBW, 109 000 clinical congenital infections
- The MTCTs is preventable through antenatal screening and treatment.
- The global strategy for the triple elimination of MTCT of HIV, syphilis and hepatitis requires :
- 95% of pregnant women attend antenatal care
- 95% are screened for HIV / syphilis
- 90% tested for hepatitis B
- 95% of infected mothers are treated

Are we achieving these targets – what is your opinion ?
A- yes
B – No

FACTORS ASSOCIATED WITH MATERNAL SYPHILIS POSITIVITY
KUFA ET AL, 2023, SCIENTIFIC REPORTS

- Highest in age 30–34 years
- poor education
- unmarried mothers
- women in Eastern Cape, Free State.
- women attending ANC for the first time
- women higher gravidity (≥ 2)
- women who were HIV + (regardless of ART status)
- peri-urban areas vs rural areas

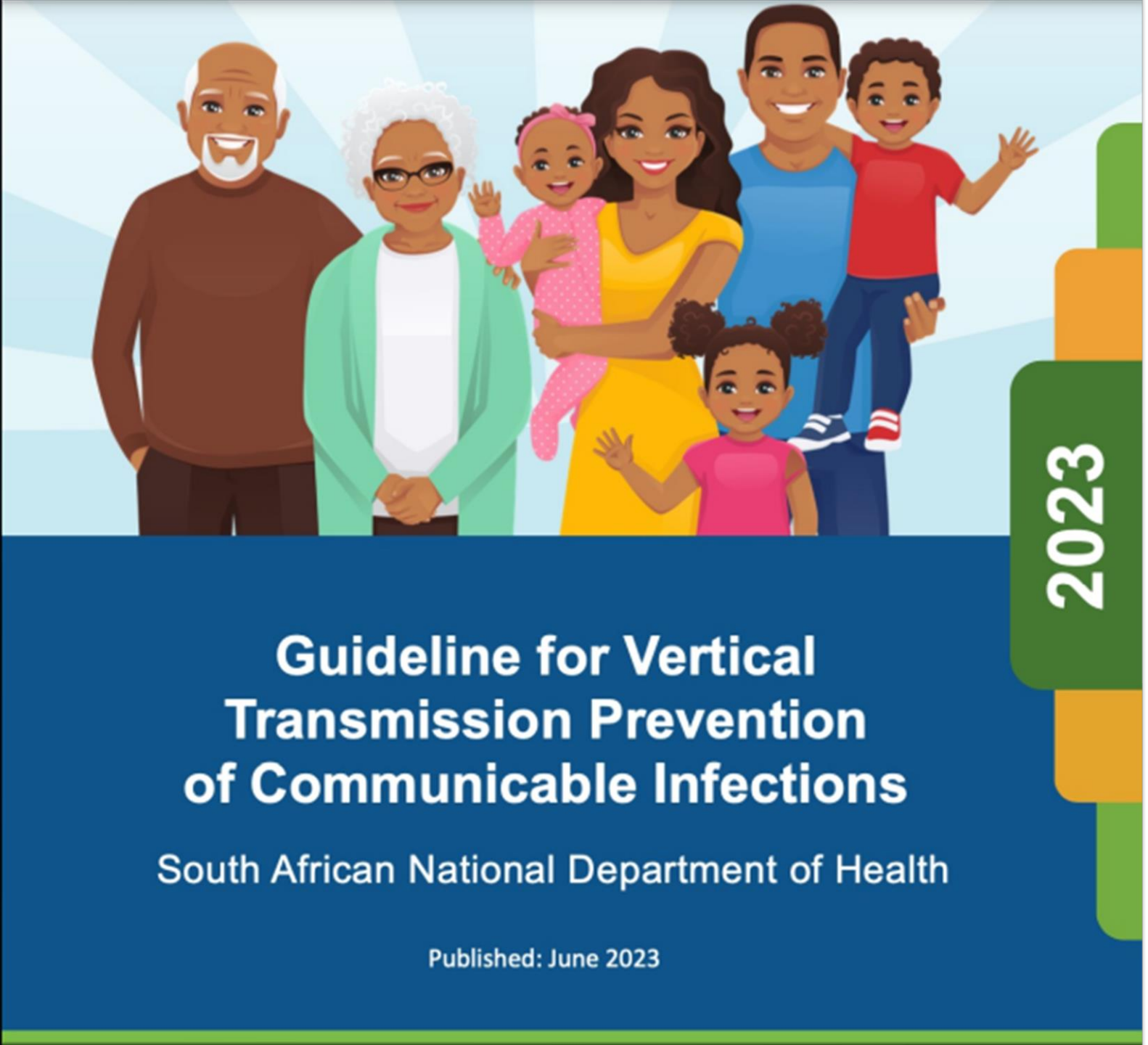
SOME DATA

- national syphilis screening coverage of 96.4%
- lowest proportion of women screened was HIV + pregnant (No ART)
- highest proportion screened were HIV + on ART.
- only 79.6% of mothers screened had documented results
- 2.6% syphilis positive
- treatment with BPG was below the global target for treatment (95%)

2019 ANC survey

- HIV and Syphilis coinfection is common
- Syphilis can increase HIV viral shedding – presence of ulcers
- Syphilis increase HIV -1 viral load and decreases CD4

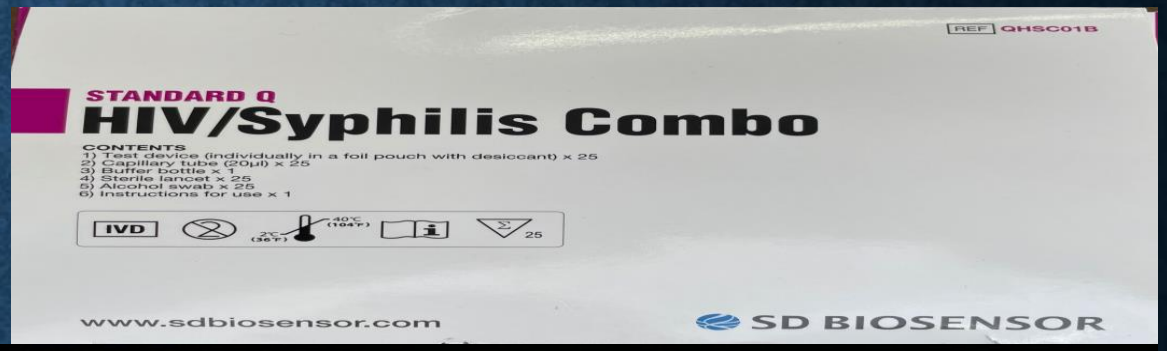
- Useful to manage HIV and Syphilis in tandem

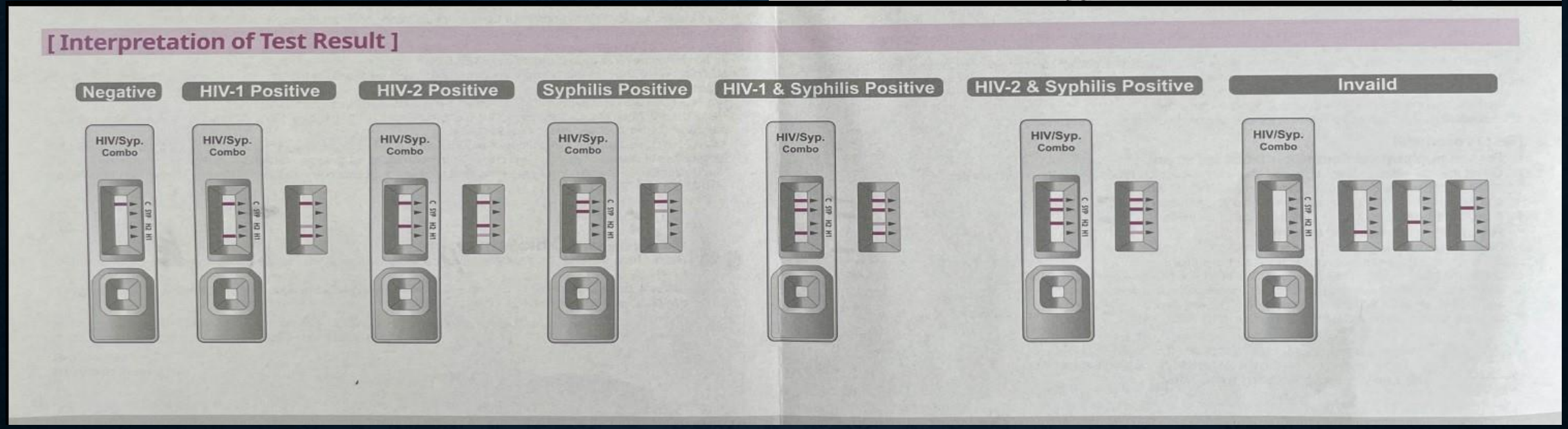


A STEP IN THE RIGHT DIRECTION

TESTING / SCREENING

- Single Rapid tests
- Dual Syphilis and HIV rapid tests





REVISED TESTING ALGORITHM

Frequency of syphilis testing

A pregnant woman should be screened and tested for syphilis

- at her 1st/booking visit in antenatal care.
- If she tests negative, syphilis testing should be repeated:
  - Scheduled antenatal visits, at approximately 4-weekly intervals, e.g., for BANC+ clients, this could be at 20, 26, 30, 34, and 38 weeks gestation
  - During her labour/delivery admission
  - At the time of diagnosis of an intrauterine death
  - At any time, if the mother has clinical symptoms or signs suggestive of syphilis

Syphilis testing should be aligned with the HIV testing schedule:

- If a woman tests positive for HIV, but tests negative for syphilis, repeat syphilis testing should continue at the intervals described above.
- If a woman tests positive for syphilis but tests negative for HIV, repeat HIV testing should continue at recommended intervals

NOTE: If a client is CURRENTLY being treated for syphilis during their current pregnancy, they should NOT be re-tested for syphilis apart from the recommended RPR titre test which is performed a minimum of 3 months after concluding syphilis treatment.

TREATING PARTNERS

- Trace and test partners of women with confirmed syphilis
- Test the partner using a rapid syphilis test if available and assess for symptoms and signs of a genital ulcer or secondary syphilis.
- If the rapid test is positive, and symptoms or signs of syphilis are present, treat the partner for early syphilis using one of the following options:
    - A single immediate dose of benzathine penicillin 2.4 MU IM, if stock levels are sufficient
    - If penicillin stock levels are insufficient, give Doxycycline 100mg 12-hourly orally for 14 days
- If the rapid test is positive and there are NO symptoms or signs of syphilis, send a confirmatory blood sample to the laboratory for an RPR. Do not wait for the results before treating the partner, but be sure to check the results 1 week later. Treat the partner for latent syphilis using one of the following options:
    - Benzathine penicillin 2.4 MU IM, once weekly for 3 weeks, if stock levels are sufficient
    - If penicillin stock levels are insufficient, give Doxycycline 100mg 12-hourly orally for 30 days

MANDATORY NOTIFICATION FOR CONGENITAL SYPHILIS

- **Category 2 Notifiable Medical Condition (NMC):** Health care workers must notify all cases of congenital syphilis through paper-based or electronic case notification forms (CNF) to the National Institute for Communicable Disease (NICD) within 7 days of diagnosis.
- Refer to link: https://www.nicd.ac.za/nmc-overview/notification-forms/
- Test or re-test all negative mothers with miscarriages or stillbirths for syphilis at time of presentation.

CONCLUSION

- Syphilis remains a serious and ongoing challenge
- Prevention strategies: promoting condom (HIV positive and HIV negative women), male medical circumcision, reducing multiple and concurrent sexual partnerships ,partner notification
- Screening and treatment in order to reduce syphilis incidence among men and women of reproductive age.
- Antenatal uptake and screening / treatment of infected pregnant women
- Dual testing
- Avoid Benzathine penicillin G (BPG) stock outs
- Notification and data recording

THANK YOU

Enjoy the conference !

SIGNS AND SYMPTOMS

- Either present at birth or will develop within the first 3 months of life:
  - Rhnitis with mucopurulent bloodstained discharge excoriating the upper lip - Usually develops during first week of life and seldom after the third month. The nasal discharge is white and may be bloody (secondary to mucosal erosion) or purulent if secondary infection. It is more severe and persistent than the nasal discharge of the common cold. The nasal discharge contains spirochetes, is contagious, and can transmit infection by direct contact.
  - A generalised, reddish, maculopapular rash that may desquamate - The rash of congenital syphilis usually appears 1-2 weeks after the rhinitis. Consists of small, initially red or pink spots. Lesions may occur anywhere, but more prominent on back, buttocks, posterior thighs, and soles. The rash generally progresses over 1 to 3 weeks, folloiwed by desquamation and crusting. As it fades, the lesions become dusky red or copper-coloured, and the pigmentation may persist. If present at birth, the rash may be widely disseminated and bullous (pemphigus syphiliticus). Ulcerative lesions and bullous fluid contain spirochetes and are contagious.
  - Other mucocutaneous lesions of the mouth, anus and genitalia, healing with scars, especially the corners of the mouth and on the chin.
  - Involvement of long bones with/without pseudoparalysis of one or more limbs and radiological findings.

SIGNS AND SYMPTOMS

- **Other common findings:**
  - hydrops fetalis
  - thrombocytopaenia
  - anaemia
  - lymphadenopathy – Generalized, nontender. Palpable epitrochlear lymphadenopathy is highly suggestive
  - Hepatosplenomegaly – Hepatomegaly occurs in almost all infants with congenital syphilis. May or may not have splenomegaly, but isolated splenomegaly does not occur. On ultrasonography, hepatomegaly may indicate failure of maternal treatment to prevent fetal infection. Lab findings may include elevated AST, ALT, ALP, and direct bilirubin; delayed prothrombin time; and visible spirochetes on liver biopsy (if one is performed). Abnormalities of liver function may be exacerbated by penicillin therapy before improving. Liver dysfunction generally resolves slowly, even after adequate therapy.
  - jaundice,
  - oedema,
  - condylomata,
  - pneumonia alba,
  - meningitis,
  - nephrosis/nephritis - Nephrotic syndrome is well-recognized complication of syphilis. Onset is usually within first 6 months. Immune complex deposition leads to membranous nephropathy. Adequate antisyphilitic therapy results in complete resolution.
  - interstitial keratitis,

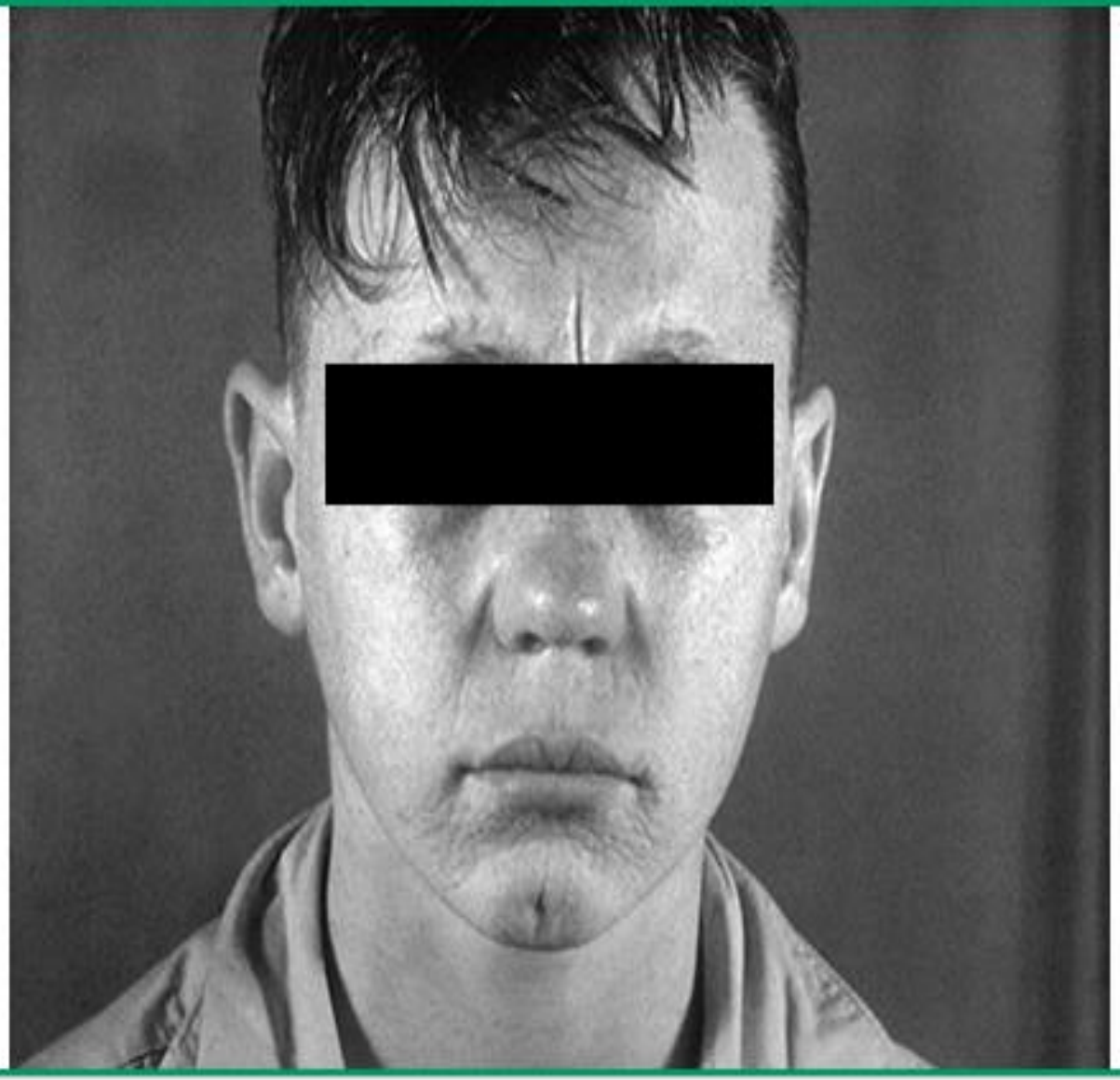
LATE CONGENITAL SYPHILIS

- Manifestations of late congenital syphilis include:
  - Facial features – Frontal bossing, saddle nose, short maxilla, protuberant mandible.
  - Eyes – Interstitial keratitis (bilateral, usually occurs around puberty, but can occur anytime between 4 and 30 years), secondary glaucoma, corneal scarring, optic atrophy.
  - Ears – Sensorineural hearing loss typically develops suddenly at 8 to 10 years of age and often accompanies interstitial keratitis.
  - Oropharynx – Hutchinson teeth (hypoplastic, notched, widely spaced permanent teeth), mulberry molars (maldevelopment of the cusps of the first molars), and perforation of the hard palate (virtually pathognomonic for congenital syphilis).
  - Cutaneous – Rhagades (perioral fissures or a cluster of scars radiating around the mouth), gummas (granulomatous inflammatory response to spirochetes) in the skin or mucous membranes.
  - Neurologic – Intellectual disability, arrested hydrocephalus, cranial nerve palsies
  - Skeletal – Anterior bowing of the shins (saber shins), enlargement of the sternoclavicular portion of the clavicle (Higoumenakis sign), painless arthritis of the knees (Clutton joints).
  - Hematologic – Paroxysmal cold hemoglobinuria.

DIAGNOSIS

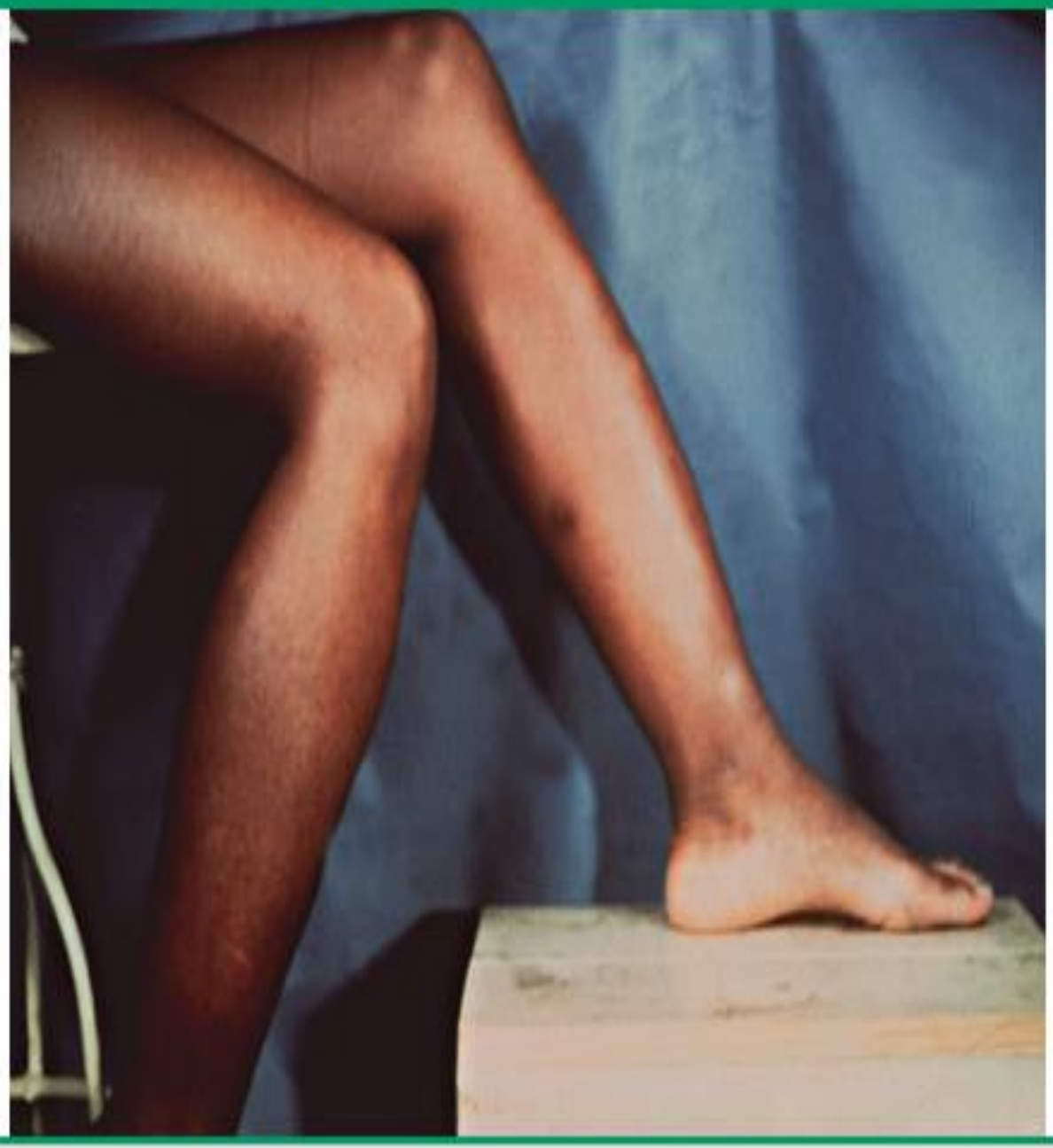
- The only way to make a definitive diagnosis of syphilis is through microscopic identification of *Treponema pallidum* in secretions, by dark ground illumination, or by examination of the pathological tissues.
- Treponemal infection leads to production of both non-specific and specific anti-treponemal antibodies.
- Examples of the non-specific serum antibody tests are:
  - Wasserman
  - Kahn, and
  - Venereal Disease Research Laboratory (VDRL) tests.
- VDRL is most commonly used as a screening test for syphilis and as a quantitative serological method to assess the efficacy of treatment or activity of disease. A disadvantage is false positive reactions, which may be technical or due to other infections or CT disorders.
- Specific antibody tests such as the fluorescent treponemal antibody (absorbed) test (FTA Abs) have proved reliable. Detects both IgG and IgM antibodies.
- A baby born to a syphilitic mother may show positive FTA IgG test merely due to passive transplacental transfer of maternal IgG, but a positive IgM test usually indicates infection of the infant. If syphilis is acquired late in pregnancy, baby may not produce IgM FTA antibody until 3 months of age.
- **TREATMENT**
- **Three once weekly doses of Benzathine penicillin G (BPG) is the standard of care for the treatment of maternal syphilis with the first dose given at least 30 days prior to delivery considered sufficient to prevent MTCTs9.**

Congenital syphilis: Rhagades

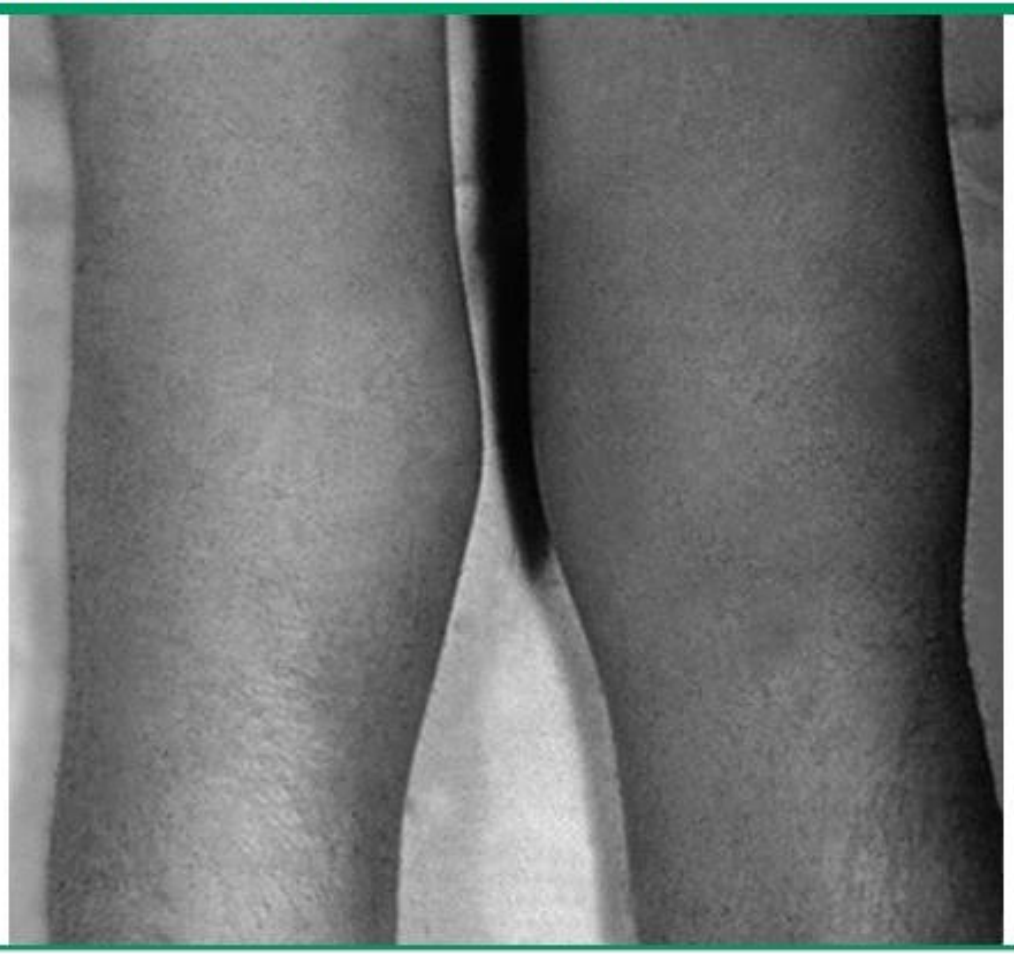


This photograph demonstrates rhagades, which are cracks or fissures in the skin around the mouth, in a patient with late congenital syphilis.

Congenital syphilis: Saber shins



Congenital syphilis: Clutton joints



This patient with congenital syphilis shows "Clutton joints," or symmetrical hydrarthrosis of the knee joint. This is a painless condition that often occurs during the late stages of congenital syphilis.

Inadequate or suboptimal treatment of maternal syphilis

Inadequate therapy
Treatment with a nonpenicillin antibiotic
Treatment less than four weeks before delivery (including treatment with penicillin)
Inappropriate dose for stage of disease
Inadequate documentation of maternal treatment
Lack of performance of serial non-treponemal* antibody titers after maternal treatment
Maternal therapy was not documented
Inadequate response to therapy
Maternal non-treponemal antibody titers did not decline at least fourfold (two dilutions) after treatment
Maternal non-treponemal antibody titers suggest reinfection or relapse (ie, fourfold increase)

* Non-treponemal test: Rapid plasma reagin (RPR) test or Venereal Disease Research Laboratory (VDRL) test.

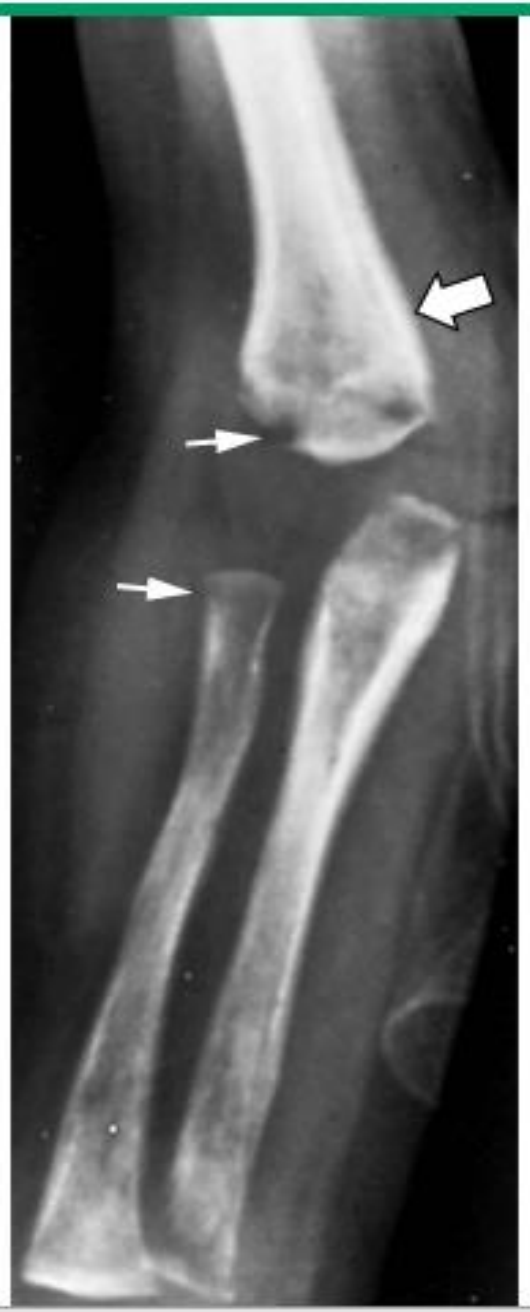
LABORATORY ABNORMALITIES

- Leukopenia or leukocytosis

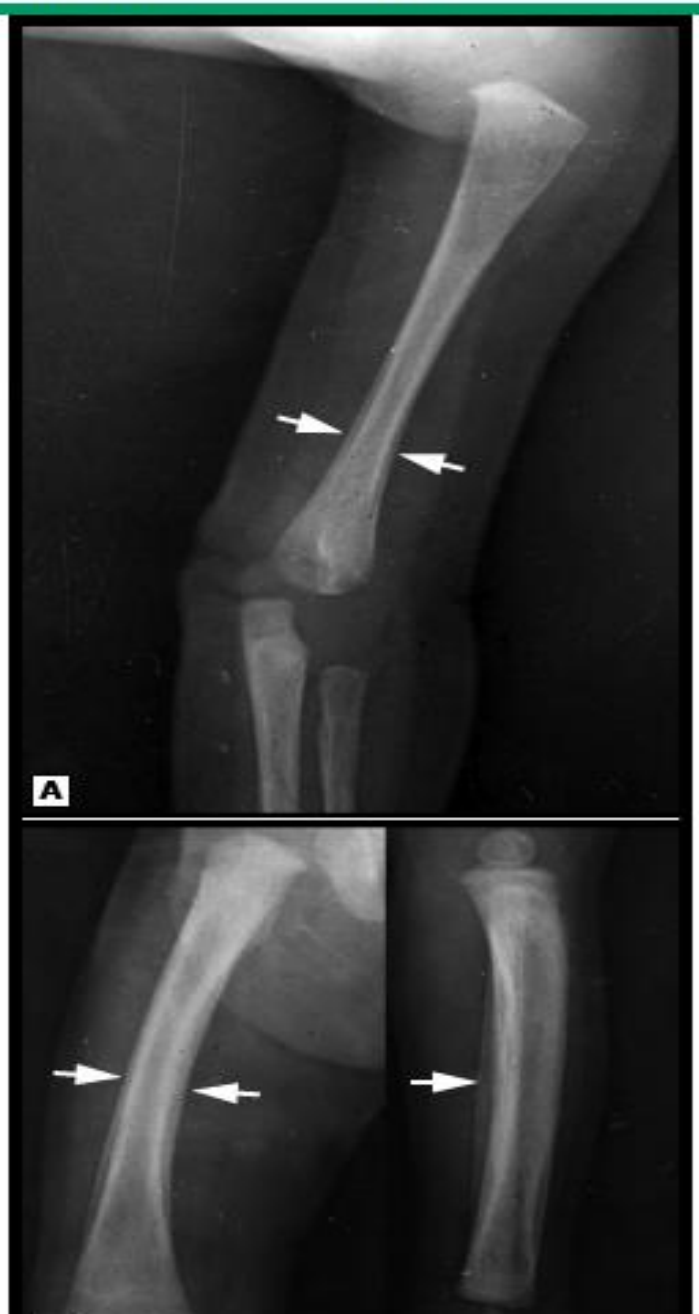
- Hemolysis often accompanied by cryoglobulinemia, immune complex formation, and macroglobulinemia. Does not respond to therapy and may last for weeks.
- **CSF abnormalities** — Laboratory evidence of CNS involvement may include:
  - Reactive CSF VDRL
  - CSF pleocytosis (>25 white blood cells/microL for infants)
  - Elevated CSF protein (>150 mg/dL in term infants and >170 mg/dL in preterm infants)
- Examination of the CSF for *T. pallidum* DNA by polymerase chain reaction may prove more useful for definitive diagnosis of congenital neurosyphilis, but not widely available.

RADIOGRAPHIC ABNORMALITIES

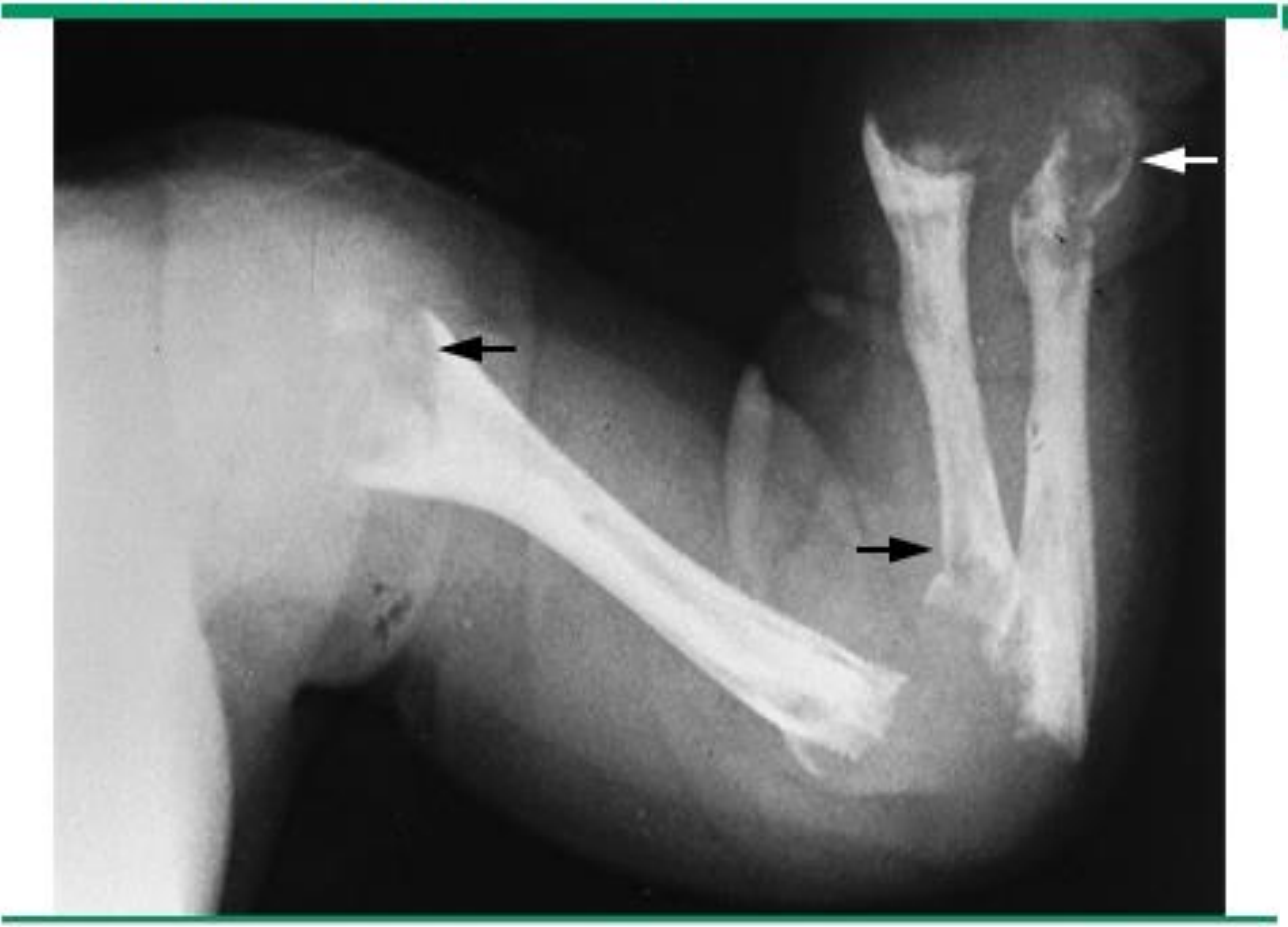
Congenital syphilis: Transverse metaphyseal bands and diaphyseal destruction



Congenital syphilis: Periostitis

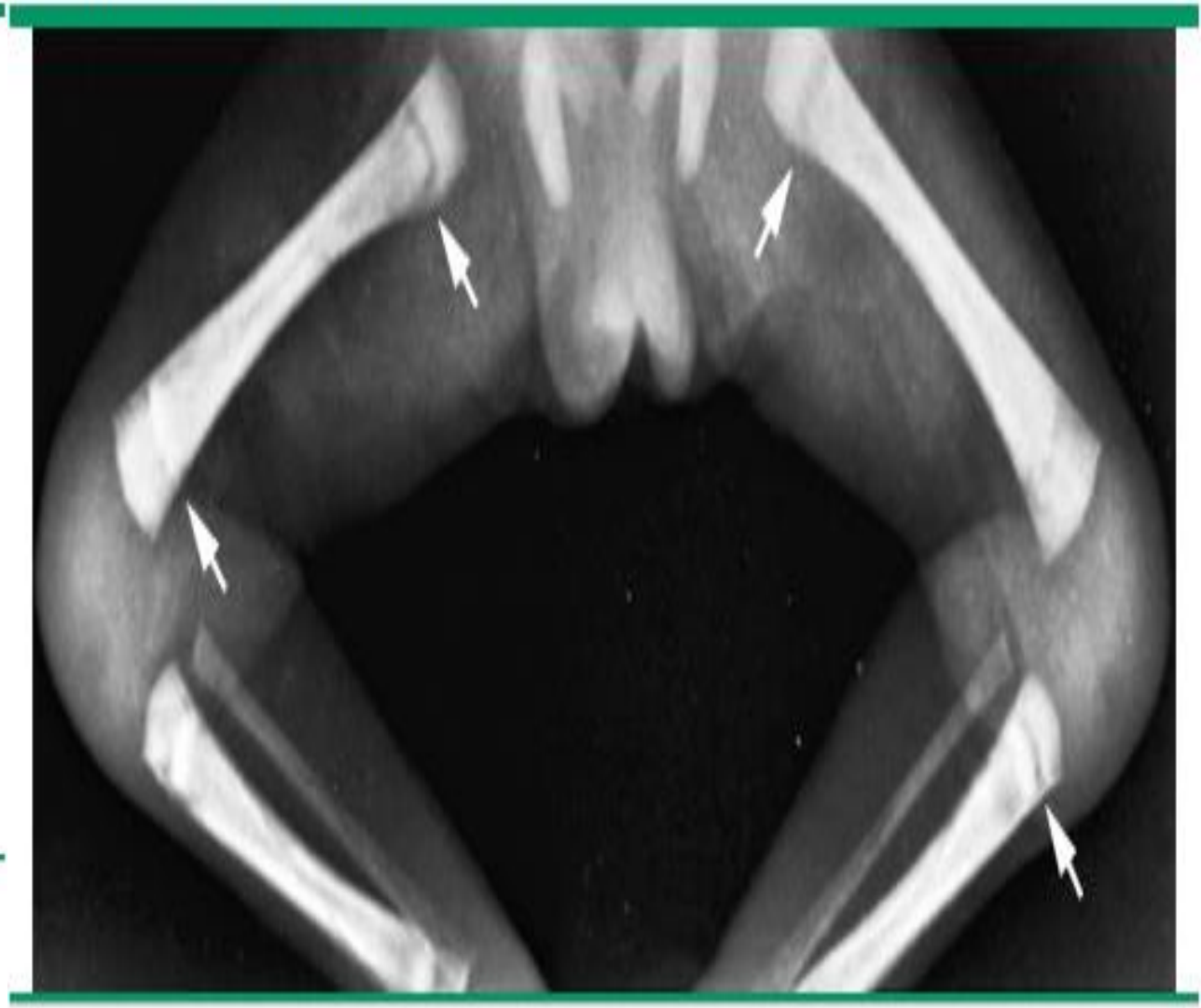


Congenital syphilis: Osteitis



Note the extensive destruction, with metaphyseal (arrows) and diaphyseal radiolucencies throughout the humerus, radius, and ulna. Observe the exuberant periosteal overgrowth, with expansile deformity of the bones of the upper extremity. Syphilitic granulation tissue may extend from the metaphysis to the diaphysis, creating an extension of the infectious focus. Reactive sclerosis often surrounds the osteolytic lesions, with associated periostitis of the long tubular bones.

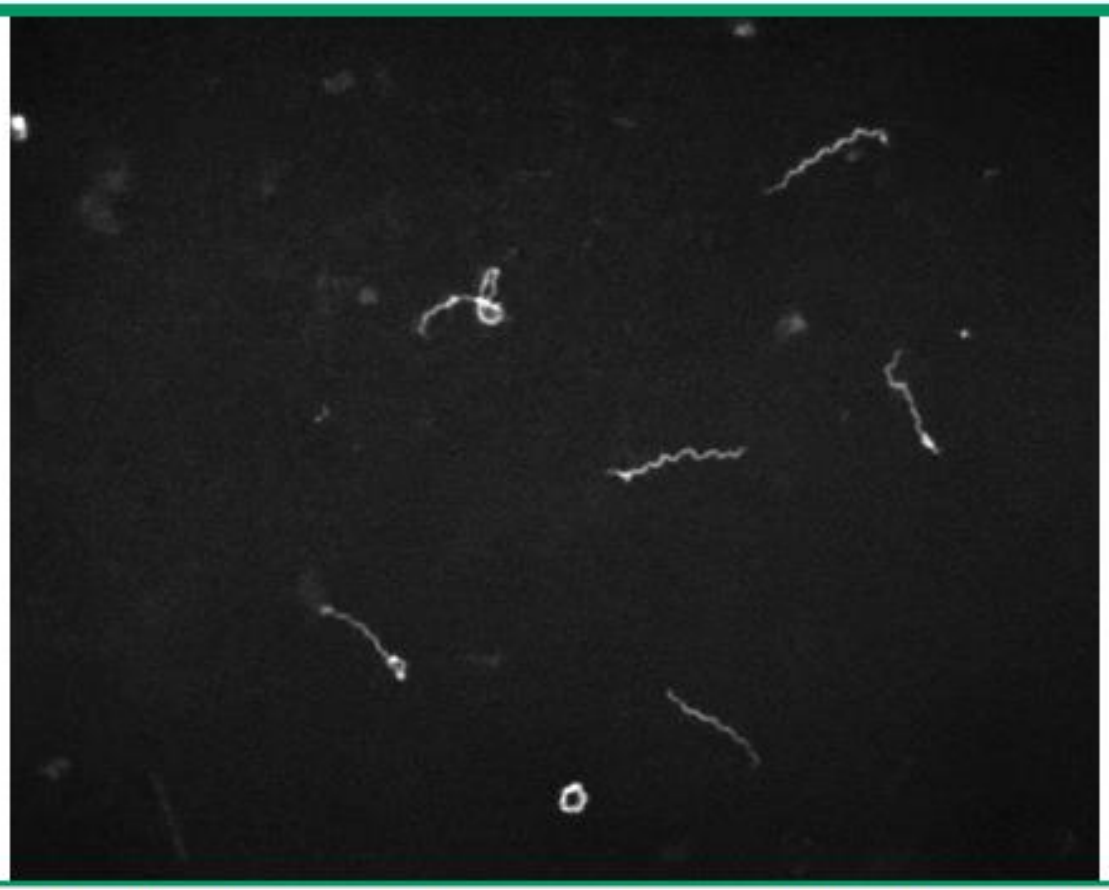
Congenital syphilis: Sclerosis



Diffuse sclerosis with transverse bands of lucency (arrows) in the diaphyses of the femurs and tibias.

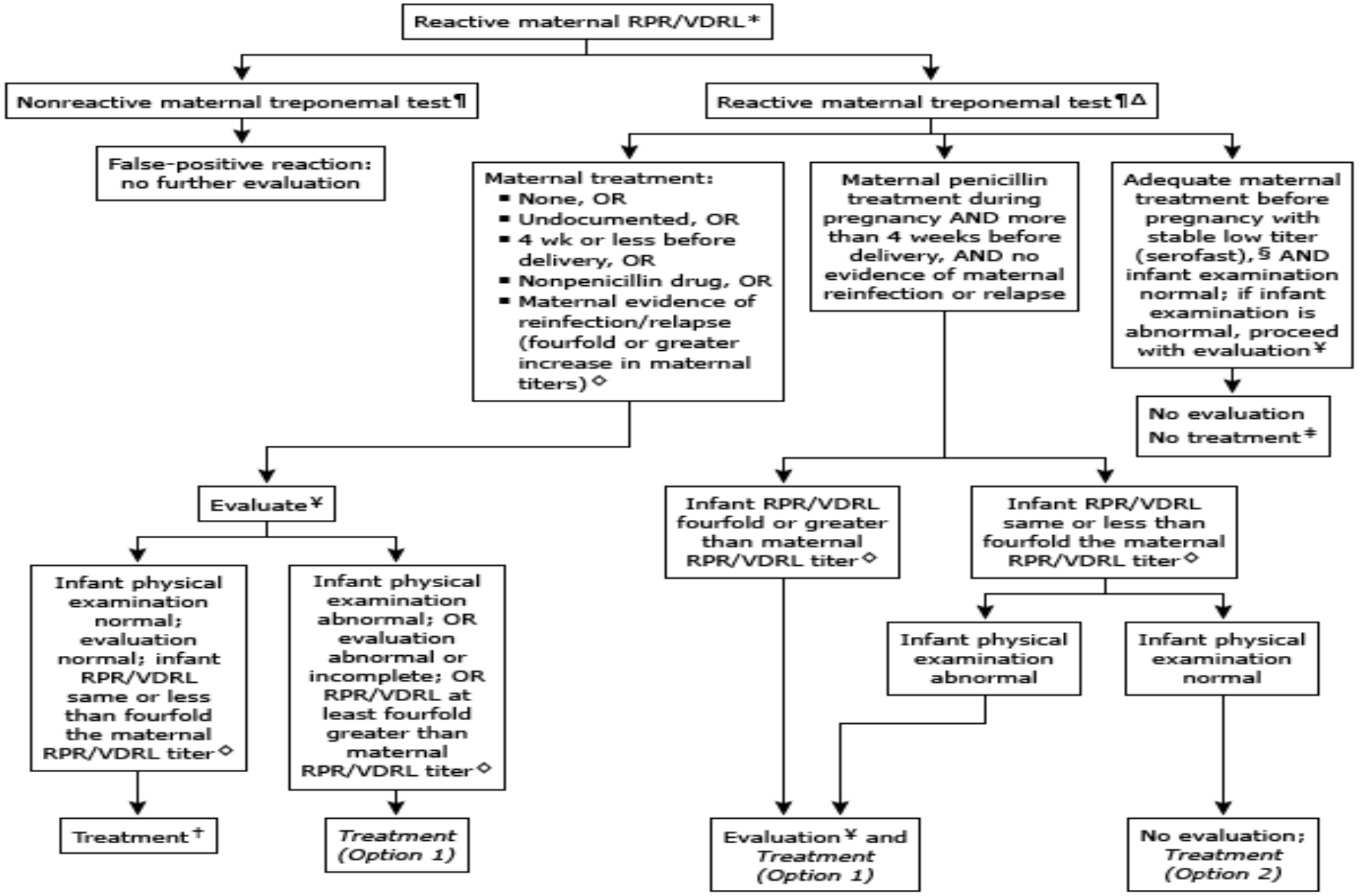
DIAGNOSTICS

Treponema pallidum spirochetes depicted with darkfield microscopy



Using a darkfield microscopy technique, this photomicrograph revealed the presence of *Treponema pallidum* spirochetes, which are the bacterial agents that cause syphilis.

INITIAL EVALUATION NEWBORN



TREATMENT OPTIONS:

1. Aqueous penicillin G, 50,000 U/kg, intravenously, every 12 hours (1 week of age or younger) or every 8 hours (older than 1 week); or procaine penicillin G, 50,000 U/kg, intramuscularly, as a single daily dose for 10 days. If 24 or more hours of therapy is missed, the entire course must be restarted.
2. Benzathine penicillin G, 50,000 U/kg, intramuscularly, single dose.

INITIAL EVALUATION NEWBORN

- **Congenital neurosyphilis** — A lumbar puncture to evaluate CNS syphilis should be performed in infants <1 month whether proven or probable congenital syphilis as well as infants and children who have reactive serologic tests for syphilis.
- Diagnosis of CNS syphilis usually presumed in children with clinical, radiographic, and laboratory abnormalities compatible with congenital syphilis.
- Treated with 10 days of parenteral penicillin.

INITIAL EVALUATION - INFANT

- **Older than one month —**
  - Physical examination
  - VDRL and RPR
  - Darkfield microscopy or fluorescent staining of suspicious body fluids
- If found to have reactive serologic tests for syphilis, maternal serology and records reviewed to assess whether the child has congenital or acquired syphilis.
- Additional evaluation:
  - CSF analysis for VDRL, cell count, and protein
  - FBC) with differential
  - VCT
  - Other tests as clinically indicated – CXR, long-bone X-rays, LFT, abdominal ultrasound, ophthalmic examination, auditory brain stem response, and neuroimaging
- Radiographic abnormalities are more suggestive of congenital than acquired syphilis.
- The possibility of sexual abuse must be considered in children who are determined to have acquired syphilis.

TREATMENT

TREATMENT BASED ON RISK PROFILE

- A positive darkfield or fluorescent antibody test of lesions/body fluid.
- Treatment with 10 days of parenteral penicillin.

- **Possible congenital syphilis —**
  - Neonates with normal physical examination and serum VDRL or RPR titers <fourfold the maternal titer, but whose mothers were not treated or received inadequate therapy are considered to have possible congenital syphilis.t treated or were inadequately treated, even if the mother had nonreactive serology.
  - Treat with single dose IM benzathine penicillin, however consider closely the clinical circumstances.
- **Congenital syphilis less likely —**
  - Neonate has a normal physical examination, serum VDRL or RPR titers are <fourfold the maternal titer, mother received appropriate treatment >4 weeks before delivery, and mother has no evidence of reinfection or relapse.
  - These neonates are at risk and should receive treatment with a single dose of intramuscular penicillin G benzathine. No additional evaluation needed.
- **Congenital syphilis unlikely —**
  - Neonate has a normal physical examination, serum VDRL or RPR titers are <fourfold the maternal titer, mother was adequately treated before pregnancy, and mother's titers remained low (VDRL <1:2; RPR <1:4) and stable before and during pregnancy and at delivery.
  - These infants generally do not require any additional evaluation or treatment.
- A full 10-day course of penicillin should be administered, even if the infant initially received ampicillin for possible sepsis. If more than one day of penicillin therapy is missed, the entire course should be restarted.

EDL MANAGEMENT (A50.9)

TREATMENT >1MONTH

Children diagnosed with congenital syphilis after one month of age (including those with late congenital syphilis) and children with acquired syphilis should be treated with aqueous penicillin G (50,000 units/kg IV every four to six hours for 10 days). If CNS involvement, 10-day course should be followed with single dose of penicillin G benzathine (50,000 units/kg IM).

Child with positive syphilis serology, but no clinical manifestations of disease, and normal CSF - Treat with three weekly doses of penicillin G benzathine (50,000 units/kg IM).

ADVERSE EFFECTS

Jarisch-Herxheimer reaction — Consists of fever 2 to 12 hours after initiation of therapy for active syphilis.

Reaction thought to be produced by the release of endotoxin-like compounds during penicillin-mediated lysis of *T. pallidum*.

Rare in newborns but can occur in older infants and children.

SPECIAL CIRCUMSTANCES

If more than one day of penicillin therapy is missed, the entire course should be restarted. Effective treatment of syphilis requires maintenance of a MIC of 0.03 units/mL of penicillin for 7 to 10 days.

- **Penicillin allergy** — Insufficient data regarding the adequacy of treatment with agents other than penicillins. CDC recommends desensitization and then treatment with penicillin. If non-penicillin agent used - close serologic and CSF follow-up are necessary

FOLLOW-UP

PROGNOSIS

Appropriate treatment of early congenital syphilis within the first three months of life prevents some, but not all, of the late manifestations of congenital syphilis. Interstitial keratitis and anterior tibial bowing (saber shins) may occur or progress despite appropriate therapy.

Syphilis infection may persist for life. Treponemes appear to persist in extracellular loci with little or no inflammatory response elicited. Active disease after reinfection is common, regardless of nontreponemal antibody reactivity.

PREVENTION/SCREENING

Most cases of congenital syphilis are preventable with routine prenatal care, screening of pregnant women for syphilis, penicillin treatment of infected women and their sexual partners, and appropriate monitoring and interpretation of treatment response

negative results of nontreponemal serology is another important limitation. A negative maternal nontreponemal test at delivery does not exclude incubating syphilis or primary syphilis if it is too early for maternal antibodies to have reached detectable concentrations. Infants born in such circumstances continue to escape detection until they become symptomatic, typically at 3 to 14 weeks of

Repeat maternal screening at the first postpartum visit may be warranted for mothers who engage in high-risk behaviors or reside in areas with high prevalence of syphilis.

PRECAUTIONS

SUMMARY AND RECOMMENDATIONS

arbitrarily defined by clinical manifestations with onset after two years of age. Manifestations of late congenital syphilis are related to scarring or persistent inflammation from early infection.

- The diagnosis of congenital syphilis should be suspected in all infants born to women who have reactive nontreponemal and treponemal tests for syphilis and infants/children with clinical findings compatible with congenital syphilis.
- The initial evaluation for congenital syphilis in infants and children should include a quantitative VDRL or RPR titer; physical examination for evidence of congenital syphilis; darkfield microscopic examination or direct fluorescent antibody staining of suspicious lesions or body fluids.
- Measures to prevent congenital syphilis include screening of pregnant women and adequate treatment thereof, contact tracing, contact precautions, and monitoring of close contacts of infectious patients for vclinical or serologic evidence of disease.
- **C**ongenital syphilis is a national notifiable disease. For reporting purposes, congenital syphilis includes stillbirths due to syphilis, cases of congenital syphilis detected in newborns, and cases of congenitally acquired syphilis in infants and children.

WHY IS THE PREVALENCE INCREASING?

Early and regular prenatal care essential for every pregnancy; one test may not be enough

research shows that one in three women who gave birth to a baby with syphilis in 2016 did get tested during pregnancy, but either acquired syphilis after that test or did not get treated in time to cure the infection in the unborn baby and prevent adverse health

CDC recommends that all pregnant women be tested for syphilis at booking. But for many women, one test for syphilis may not be enough. Women at high risk for syphilis or who live in high-prevalence areas should be tested not only at the first prenatal visit, but again early in the third trimester and at delivery.

If sexually active, individuals can lower their risk of getting syphilis by being in a long-term, mutually monogamous relationship with a partner who has been tested for syphilis and using barrier contraception.

MY CHALL ENGE

Ramping	Ramping up support for high burden areas to strengthen local prevention systems and improve our ability to identify and treat pregnant women with syphilis.
Researching	Researching factors contributing to the resurgence of congenital syphilis cases to inform prevention programs.
Increasing	Increasing awareness of congenital syphilis risk factors among pregnant women through partnerships with community organizations.

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National Institute for Communicable Diseases