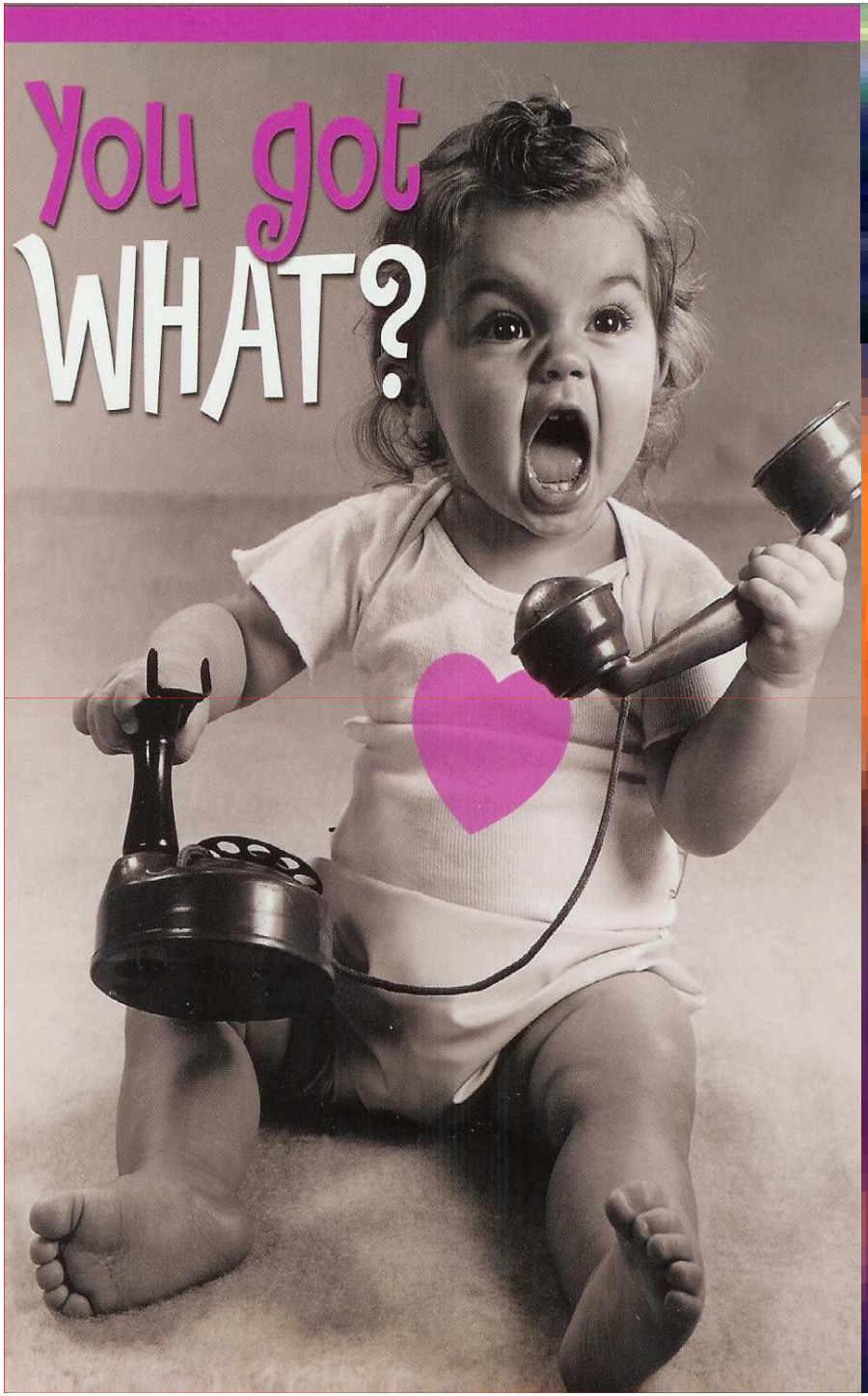

Sífilis congénita: una oportunidad en la prevención

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Nationwide Children's Hospital
The Ohio State University
Columbus, OH

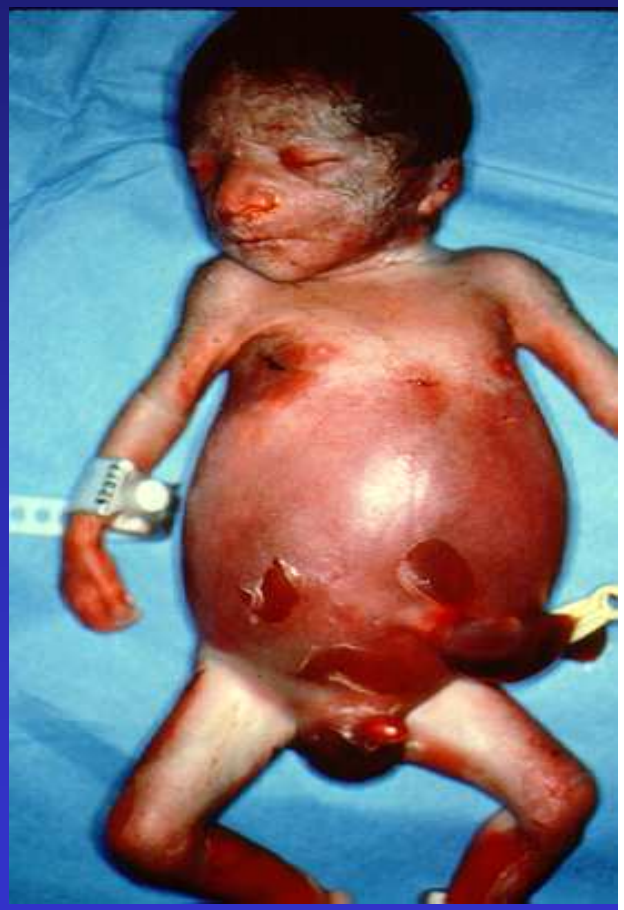
7˚ Congreso Argentino de Infectología Pediátrica
Córdoba, Argentina
April 3-5, 2014

EPIDEMIOLOGY

- Worldwide:
  - Latin America, Africa, Europe
- United States:
  - Racial and ethnic minorities: Blacks
  - South (48%); urban areas
  - Young, unmarried women: lower SEC
  - Congenital cases: inadequate prenatal care
  - Increase in adults since 2001—increase in congenital cases up to 2008, decrease since (322 cases in 2012)

CONGENITAL SYPHILIS: MORTALITY 1992-1998

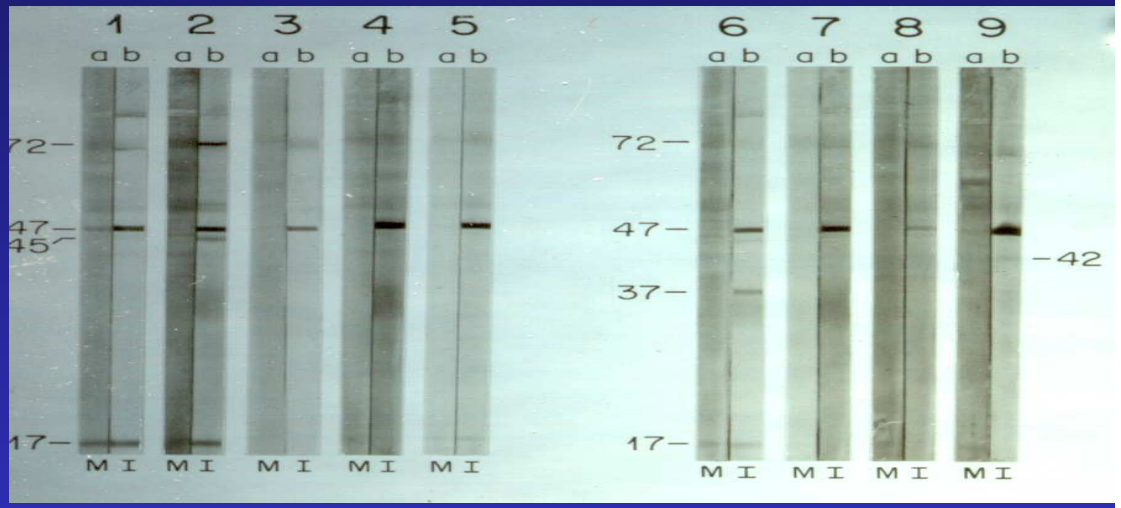
- 14,627 cases of CS (78% decline): 942 deaths, 760 stillbirths
- Case fatality rate: 6.4% (stable)
- 87% of deaths: untreated, inadequately treated, or undocumented treatment during pregnancy
- Less prenatal care: ↑ risk of death
- 52% of deaths occurred by 30 wks of gestation



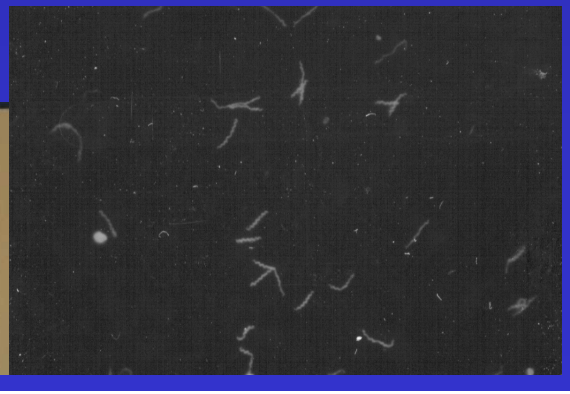
Gust DA et al. *Pediatrics* 2002;109:e79

DIAGNOSTIC STRATEGIES FOR CONGENITAL SYPHILIS

- IgM immunoblot:



- Polymerase chain reaction (PCR)
- Rabbit infectivity test (RIT):



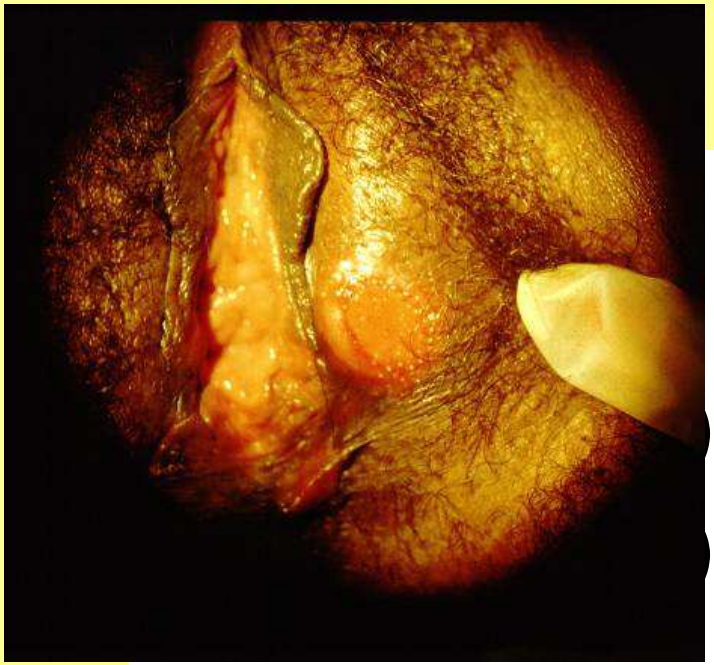
DIAGNOSTIC STRATEGIES FOR CONGENITAL SYPHILIS

- Vertical transmission
- “Asymptomatic” newborn
- Central nervous system invasion
- Evidence-based rationale for the management of infants born to mothers with reactive serologic tests for syphilis (CDC, AAP)

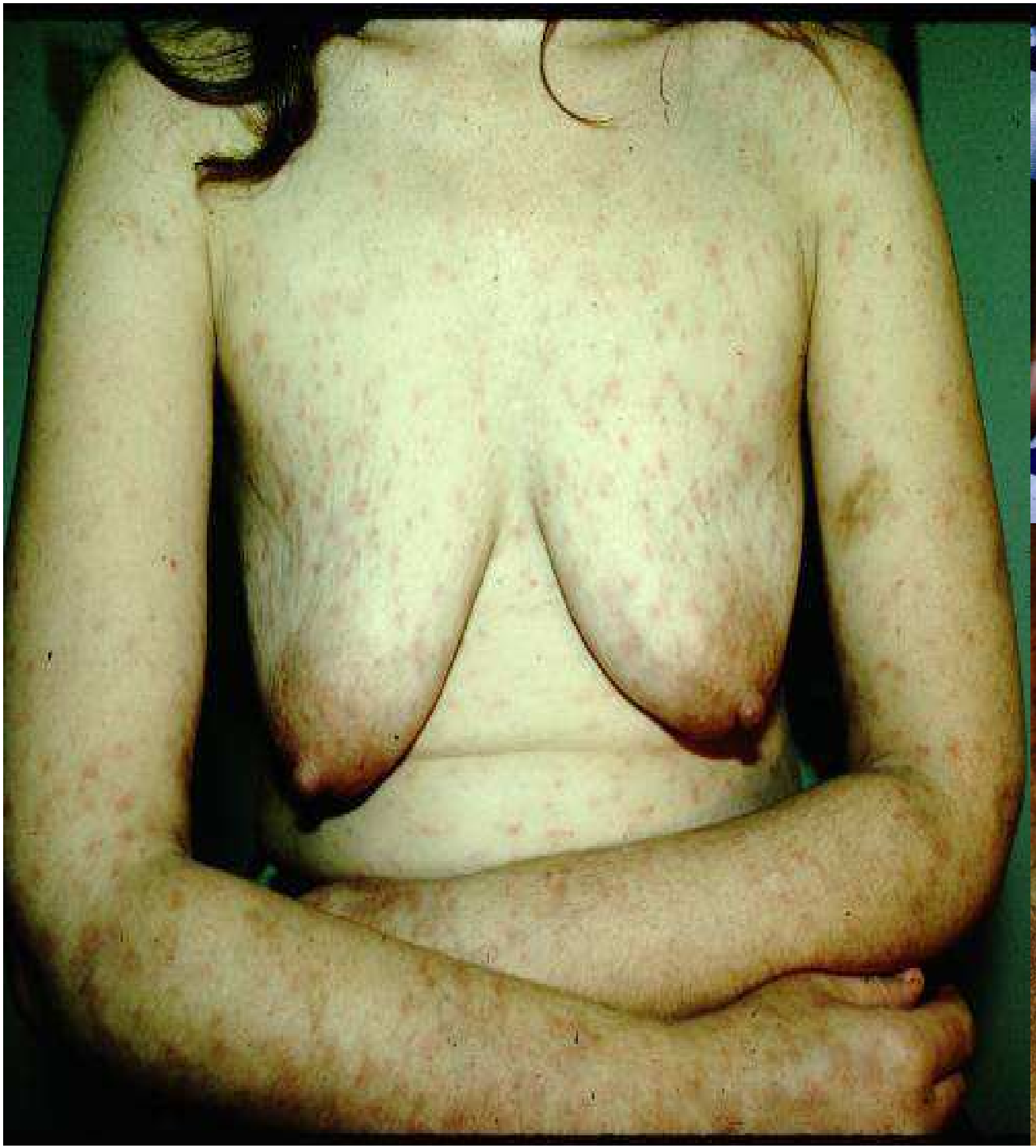
CONGENITAL SYPHILIS: VERTICAL TRANSMISSION

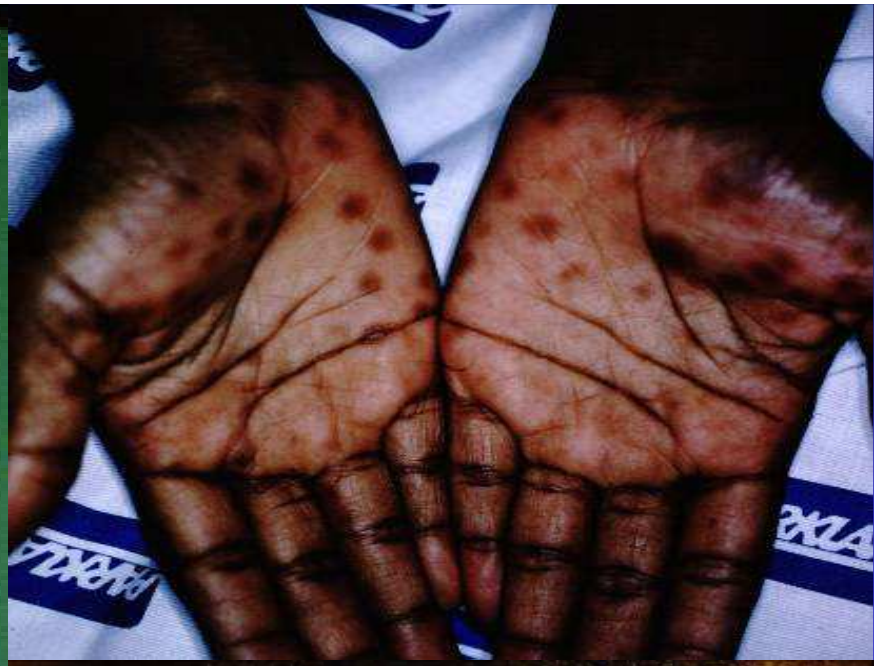
- *In utero*: transplacental route following maternal spirochetemia
- Intrapartum: contact with genital lesion
- Increases as stage of pregnancy advances but can occur at any time in gestation
- Related to stage of maternal syphilis

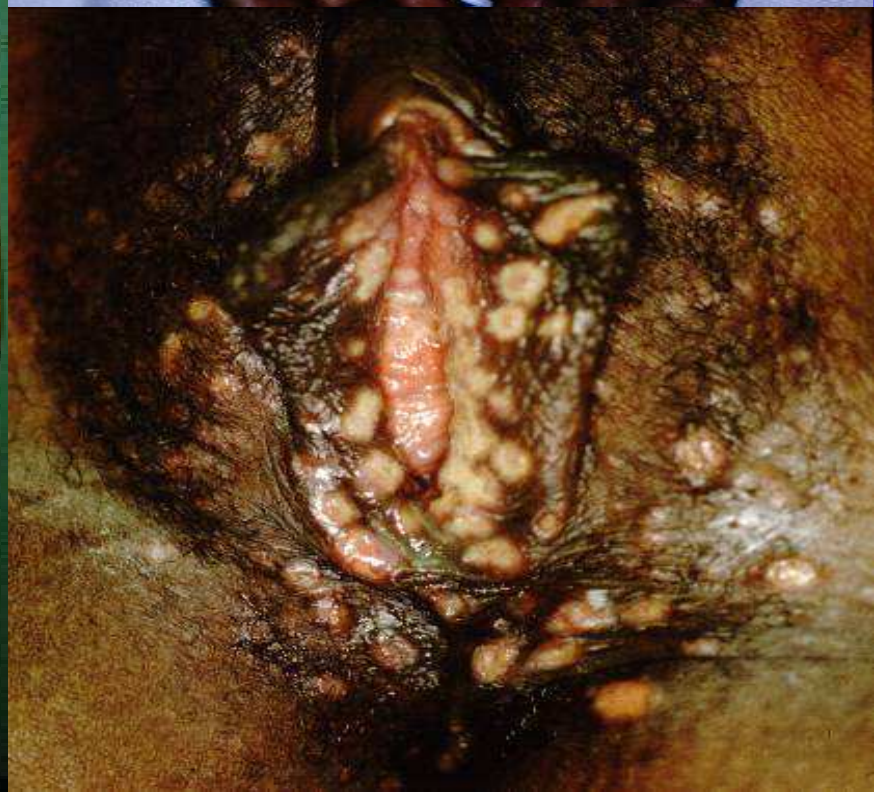
SYPHILIS IN PREGNANCY: THE PARKLAND EXPERIENCE (1988-1998)



			Early Latent	Late Latent
No. of Mothers			145	27
Outcome (%):				
Stillbirth			31 (21)	1 (4)
Congenital Syphilis			21 (14)	1 (4)
Total	6 (23)	32 (60)	52 (36)	2 (7)





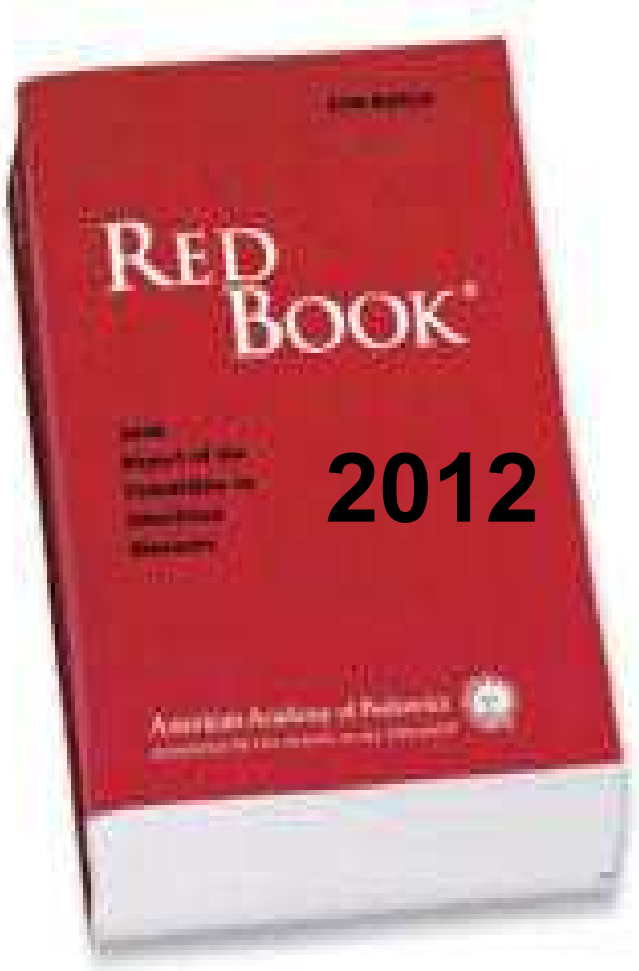


STD

Treatment Guidelines

2010

www.cdc.gov

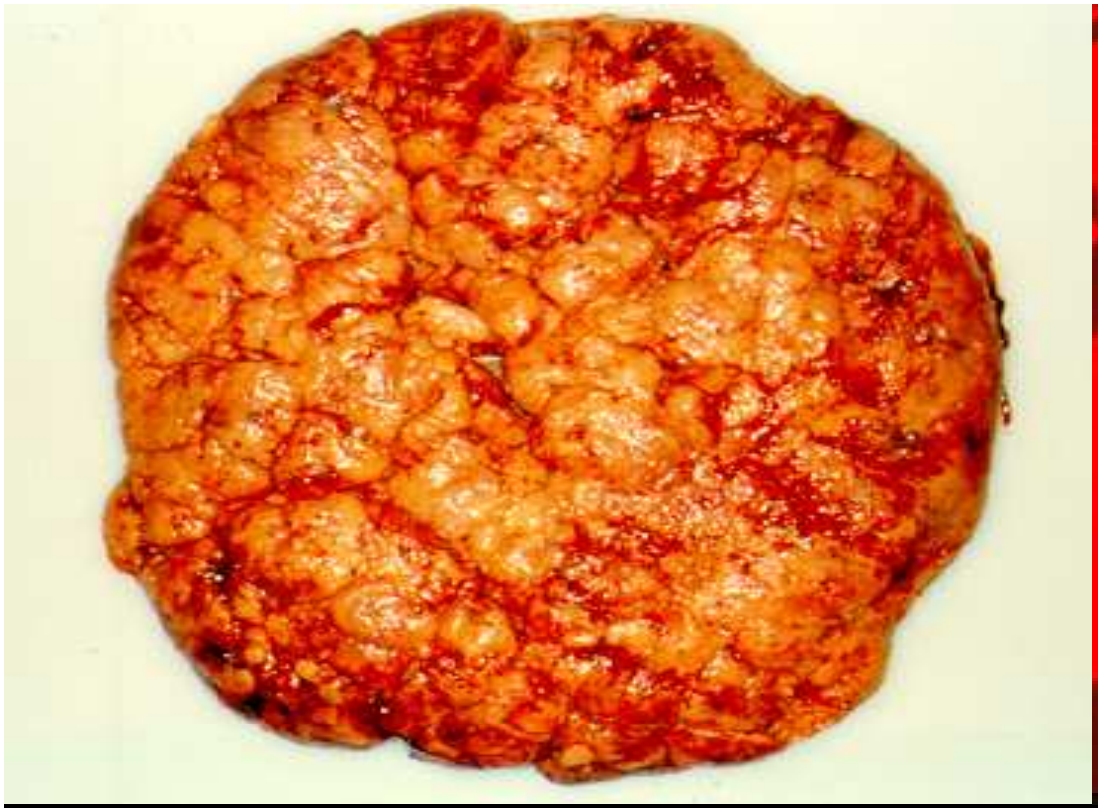


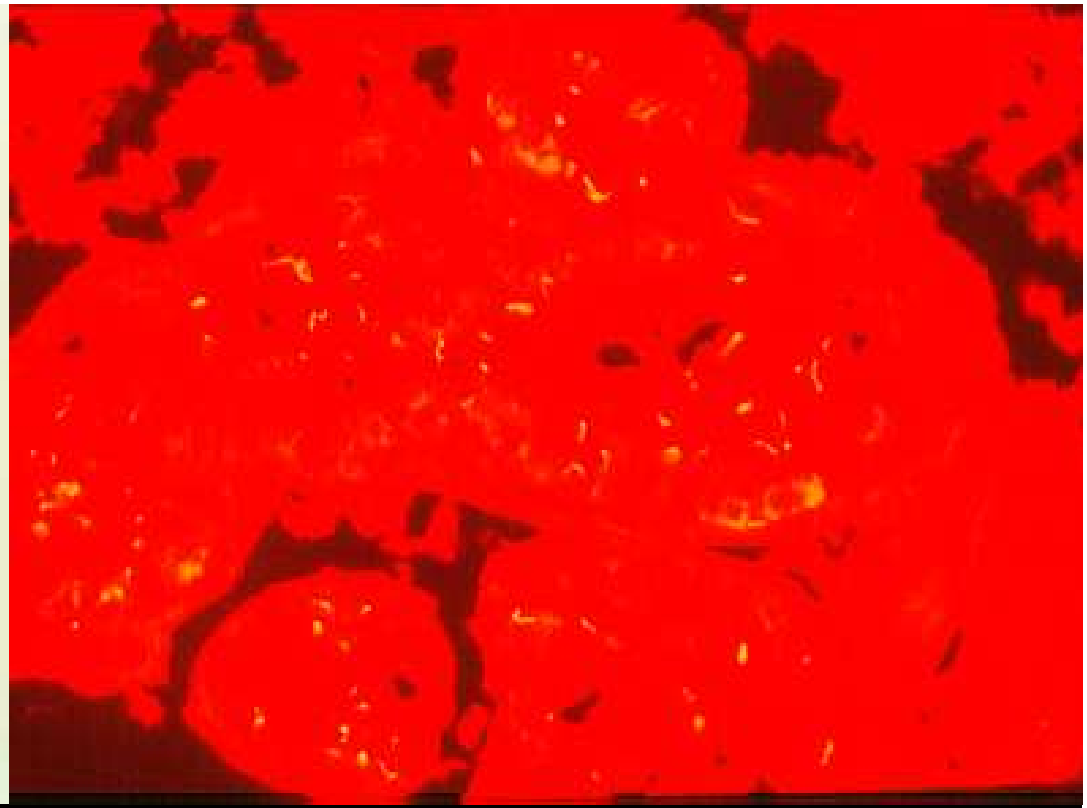
Evaluation and Treatment of Infants During the First Month of Life

SCENARIO 1:
PROVEN OR HIGHLY PROBABLE
SYPHILIS

PROVEN OR HIGHLY PROBABLE SYPHILIS

- Infant physical exam abnormal
- Serum VDRL/RPR ≥4x maternal titer
- Positive darkfield or fluorescent antibody test of body fluid(s)

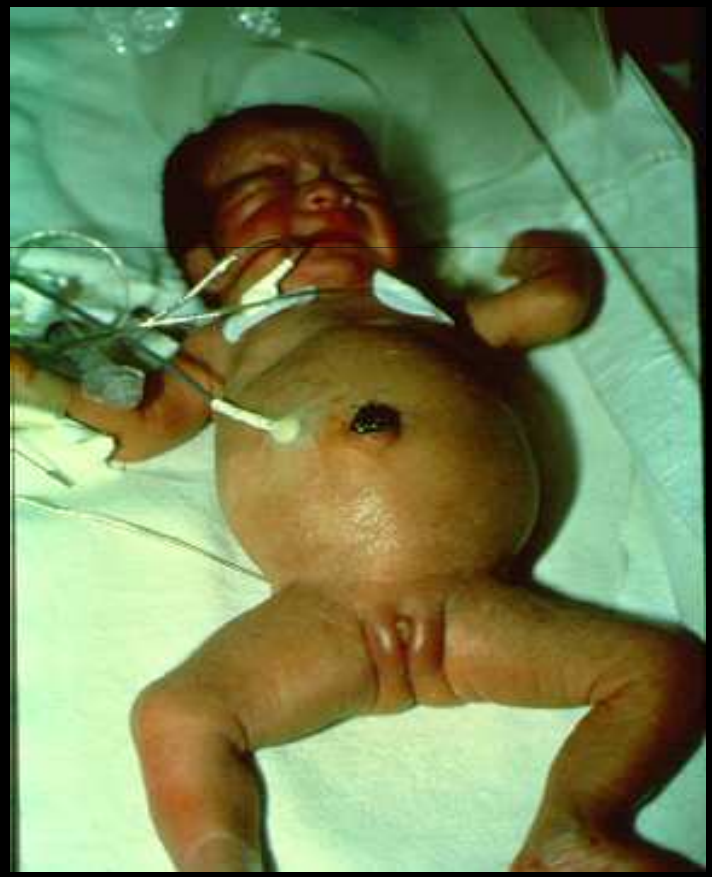


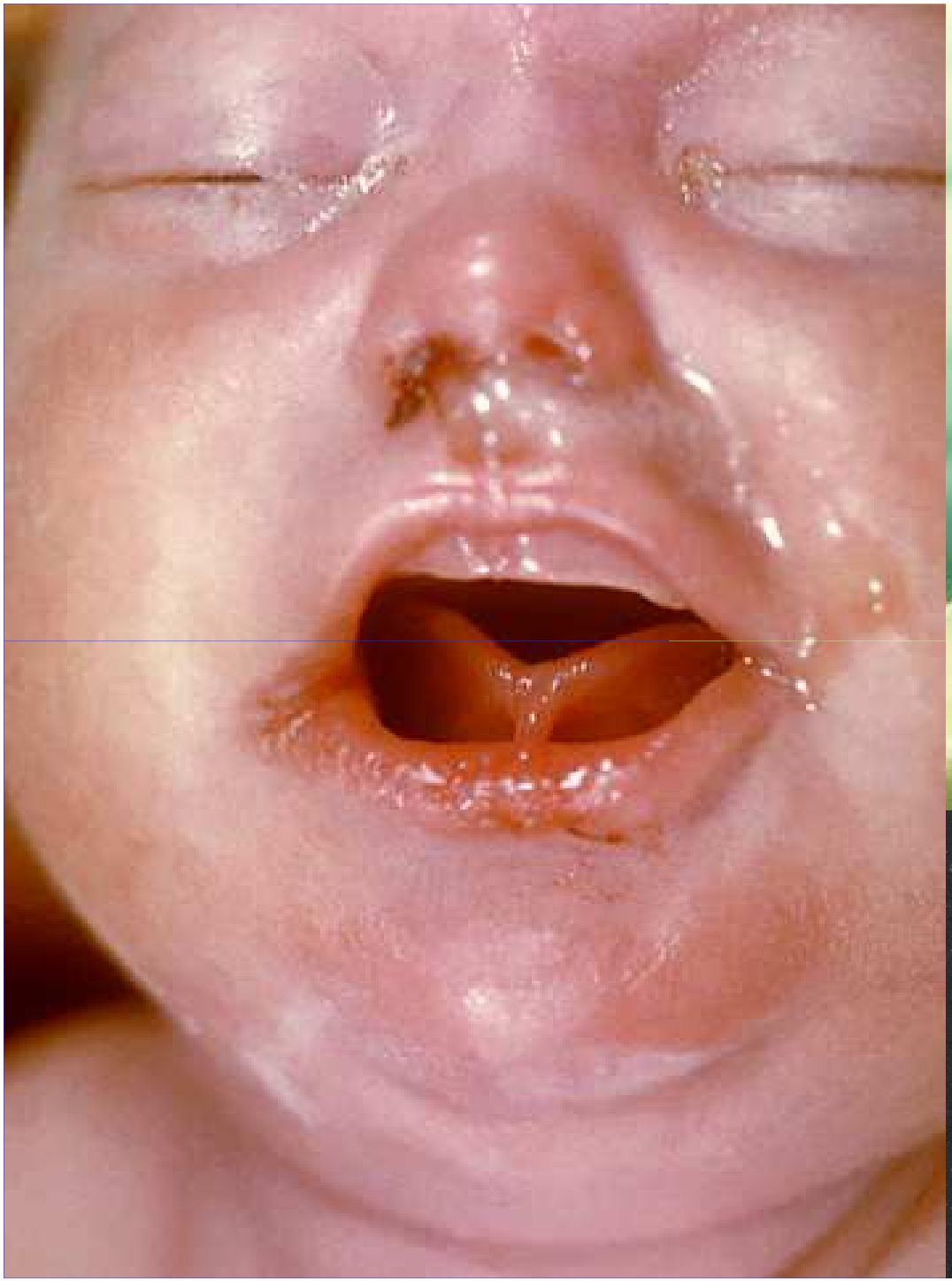


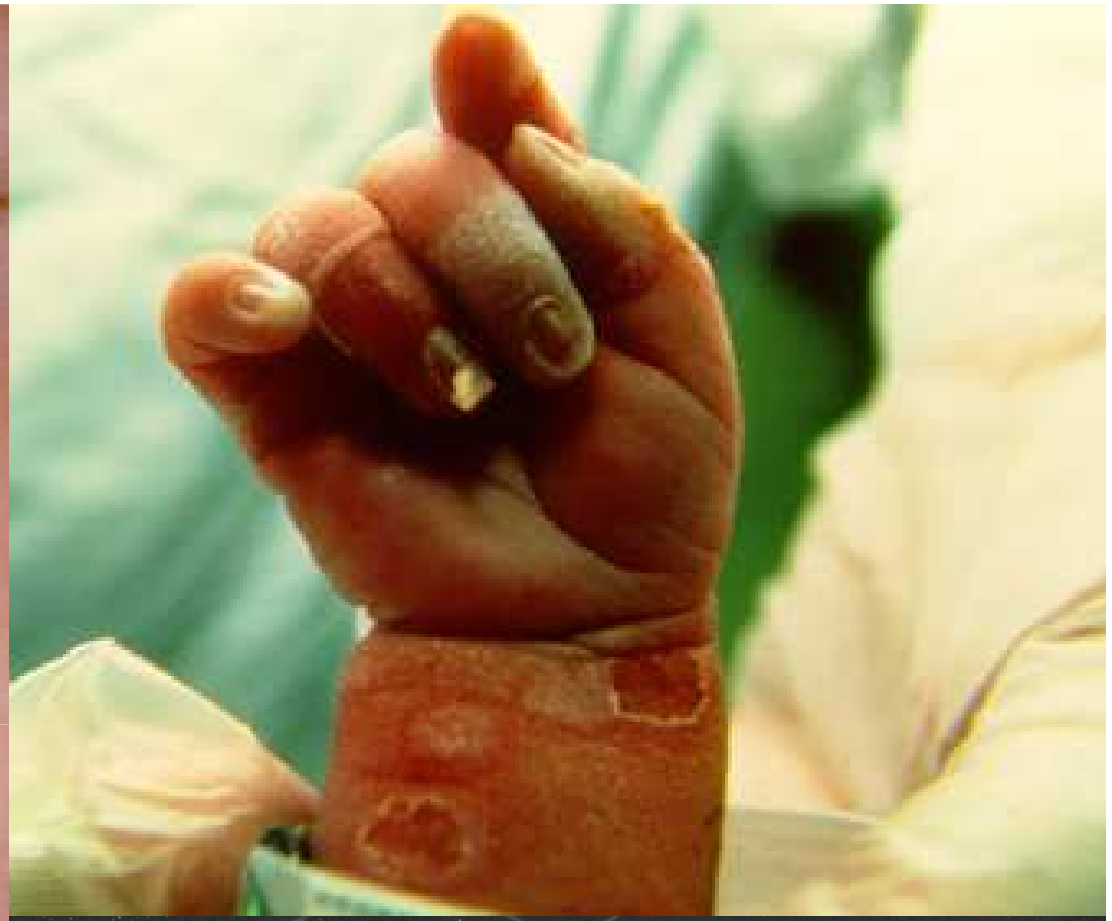
- **Histopathology**: necrotizing funisitis, villous enlargement, acute villitis
- **Increased detection** of congenital syphilis from 67% to 89% in live-born infants, and 91% to 97% in stillborns (Obstet Gynecol 2002:100:126)

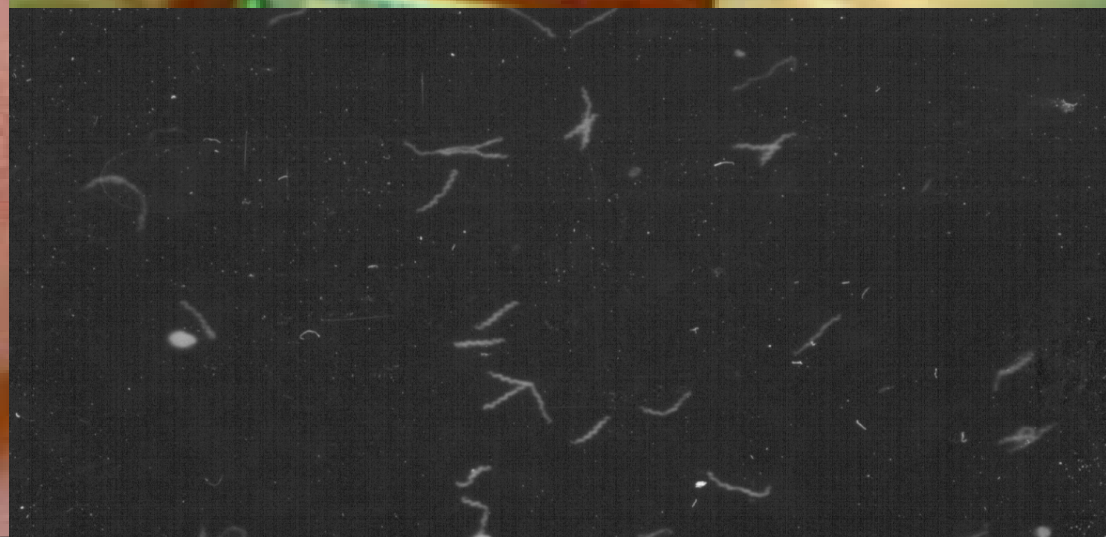
EARLY CONGENITAL SYPHILIS: CLINICAL MANIFESTATIONS

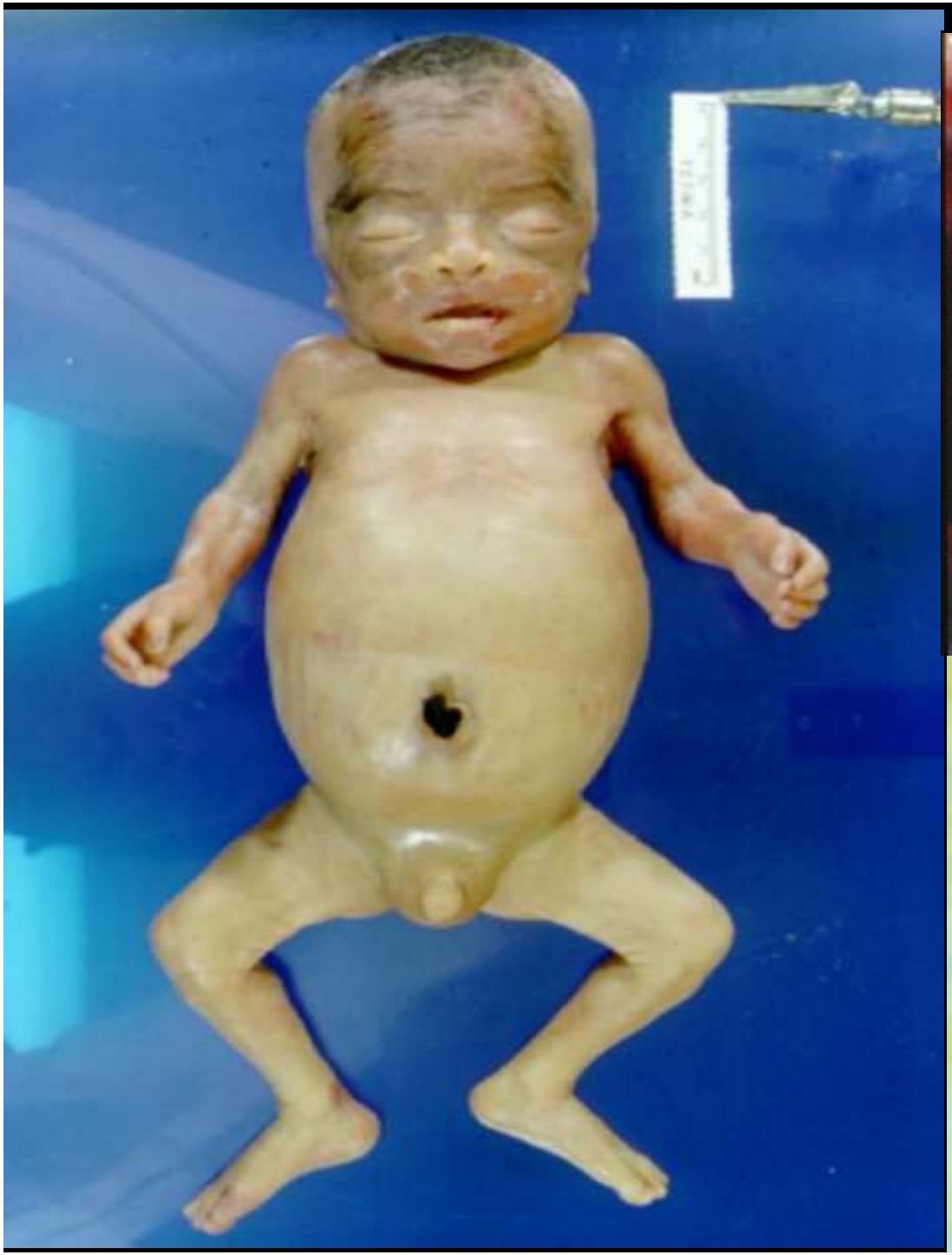
- Hepatosplenomegaly
- Anemia
- Thrombocytopenia
- Hydrops fetalis
- Pneumonia
- Nephrotic syndrome

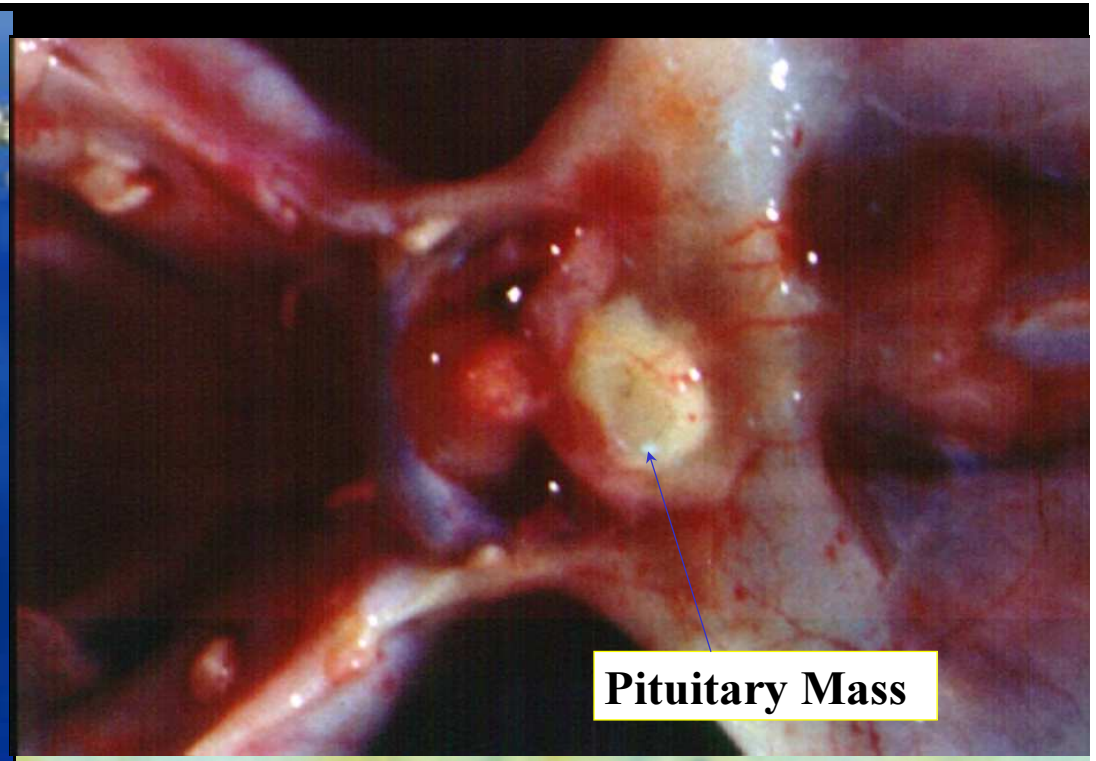


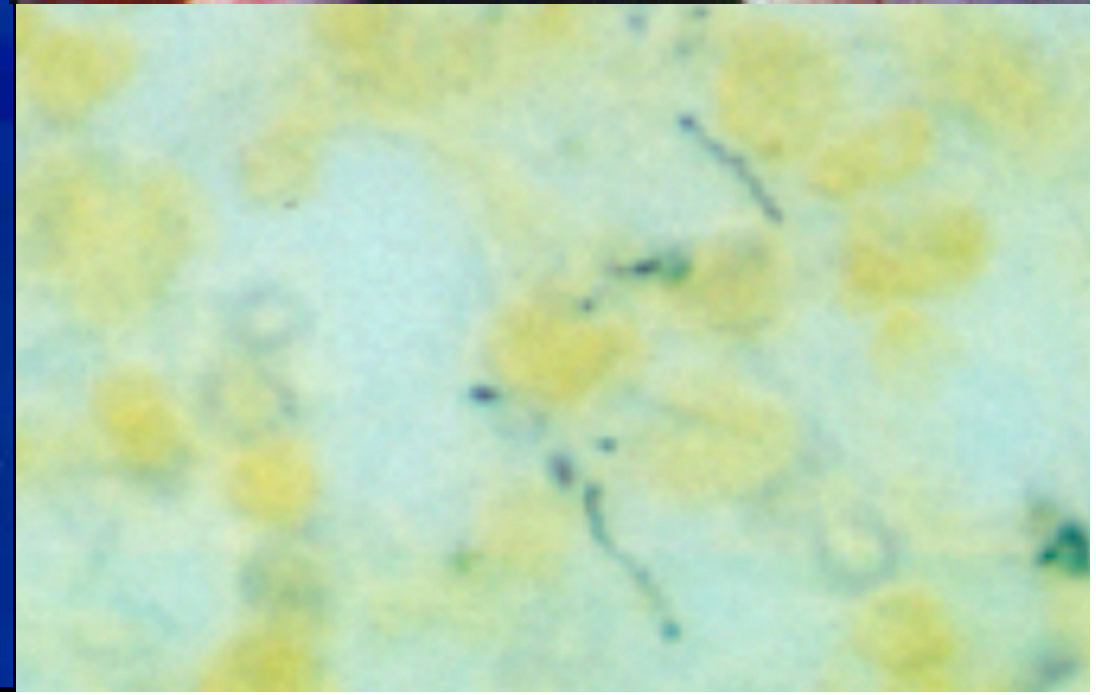









Pituitary Mass

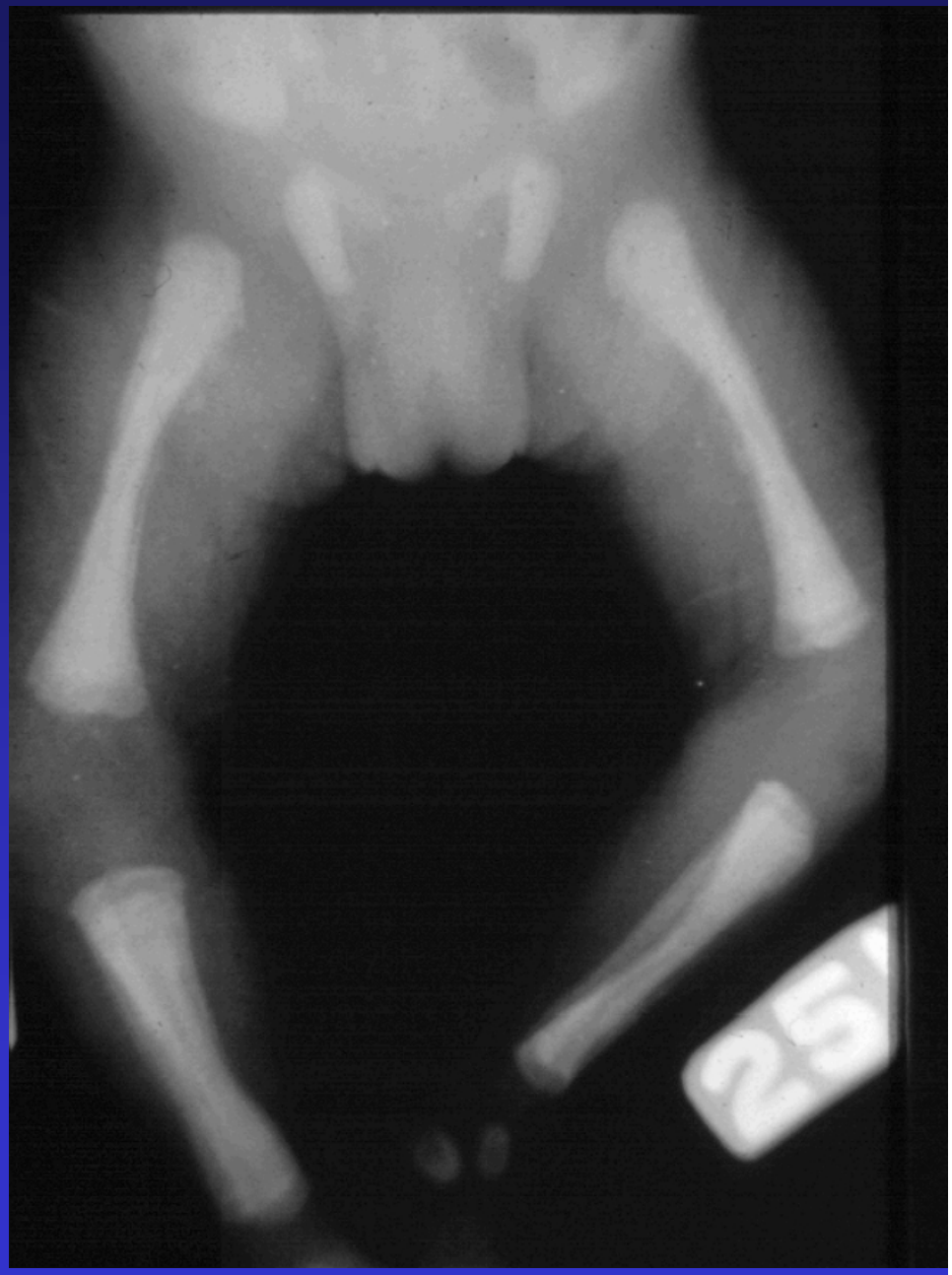


PROVEN OR HIGHLY PROBABLE SYPHILIS: EVALUATION

- Lumbar puncture, CBC / platelet count
- Bone X-rays:
  - CDC: as clinically indicated
  - AAP: unless the diagnosis has been otherwise established
- Other tests (eye exam, LFTs, HUS, ABR, CXR) as clinically indicated

PROVEN OR HIGHLY PROBABLE SYPHILIS: BONE X-RAYS

- Periostitis
- Osteochondritis
- Frequently abnormal: 65% (Houston/Dallas)
- Abnormal findings do not change therapy



PROVEN OR HIGHLY PROBABLE SYPHILIS: EVALUATION

- Lumbar puncture:
  - Why? To establish a baseline for follow-up
  - Why not?

CENTRAL NERVOUS SYSTEM INFECTION IN CONGENITAL SYPHILIS

76 INFANTS, CSF RIT: 17 POS, 59 NEG

- Sensitivity; Specificity:

Reactive CSF VDRL:	53%; 90%
CSF Pleocytosis:	38%; 88%
Elevated CSF Protein:	56%; 78%

Michelow et al. NEJM, 2002

CONGENITAL SYPHILIS: *SYMPTOMATIC* INFANTS

	SERUM/BLOOD (n=46)	CSF (n=39)
POS IgM	98%	41%
POS RIT	57% (20/35)	47% (16/34)

CONGENITAL SYPHILIS: TREATMENT

- Infant VDRL/RPR ≥ 4x Maternal VDRL/RPR OR Physical Exam is *ABNORMAL* OR ⊕ TP body fluid:
  - Aqueous PCN G 50,000 U/kg IV q 8-12 hr x 10 d, or
  - Procaine PCN G 50,000 U/kg IM q day x 10 d

SCENARIO 2

The "*ASYMPTOMATIC*" infant: Why? What is the likelihood that this infant has congenital syphilis?

CONGENITAL SYPHILIS: ASYMPTOMATIC INFANTS BORN TO MOTHERS WITH UNTREATED SYPHILIS

	SERUM/BLOOD (n=86)	CSF (n=68)
POS IgM	16%	3% (2/62)
POS RIT	7%	2% (1/62)

MATERNAL TREATMENT ≤ 4 WKS BEFORE DELIVERY: ASYMPTOMATIC INFANTS

	Blood	CSF
No. of Infants:	23*	21*
⊕ IgM	30%	5%
⊕ RIT	5%	0/19

* 1 Mother HIV-Ab ⊕

CONGENITAL SYPHILIS: EVALUATION AND TREATMENT

- Infant physical exam normal AND VDRL/RPR <4x maternal titer:
  - **Maternal Rx**:
    - None, inadequate, unknown
    - Erythromycin, azithromycin, non-penicillin drug
    - ≤ 4 wks before delivery
  - Mother re-infected (RPR ↑ 4x)

CONGENITAL SYPHILIS: "*Asymptomatic*" INFANT

- Physical exam normal; VDRL/RPR reactive and <4x maternal titer (cont):
  - **Evaluation:** CBC, platelets, LP, bone X-rays
  - **Treatment: options**
    - **Penicillin G** (aqueous/procaine) x 10d: evaluation optional; evaluation abnormal, not done or incomplete
    - **Benzathine PCN G** 50,000 u/kg IM: normal CBC, platelet, lumbar puncture, bone x-rays and follow-up certain

CONGENITAL SYPHILIS: "*Asymptomatic*" INFANT

- Physical Exam NORMAL and serum VDRL/RPR **nonreactive** (cont):
  - **Evaluation:** none (no CBC, x-rays, LP)
  - **Treatment:**
    - **Benzathine PCN G** 50,000 u/kg IM

SCENARIO 3

CONGENITAL SYPHILIS

- Infant physical exam normal AND VDRL/RPR <4x maternal titer:
  - **Maternal Rx**:
    - During pregnancy, appropriate for stage of infection, > 4 wks before delivery
  - No evidence of reinfection or relapse

CONGENITAL SYPHILIS: "ASYMPTOMATIC" INFANT

- No evaluation
- Treatment:
  - Benzathine penicillin G IM x 1
  - "some experts" would not treat but provide close serologic follow-up
    - AAP: follow-up preferably monthly, until RPR NR

Special Considerations

- Penicillin allergy: desensitize, data insufficient to recommend other agents, but if nonpenicillin agent used, close serologic and CSF follow-up
- HIV infection: infants born to mothers coinfected with HIV do not require different evaluation, therapy, or follow-up for syphilis
- Penicillin shortage: penicillin G, procaine penicillin, benzathine penicillin, ceftriaxone

  www.cdc.gov.nchstp/dstd/penicillinG.htm/

CONGENITAL SYPHILIS: FOLLOW-UP

- Serologic testing (RPR) q 2-3 months until nonreactive. Persistent, stable titer beyond 1 yr: retreat?
- Treponemal test: Reactive beyond 18 months indicates congenital infection
- Initial CSF abnormal: Repeat at 6 months and if abnormal, retreat

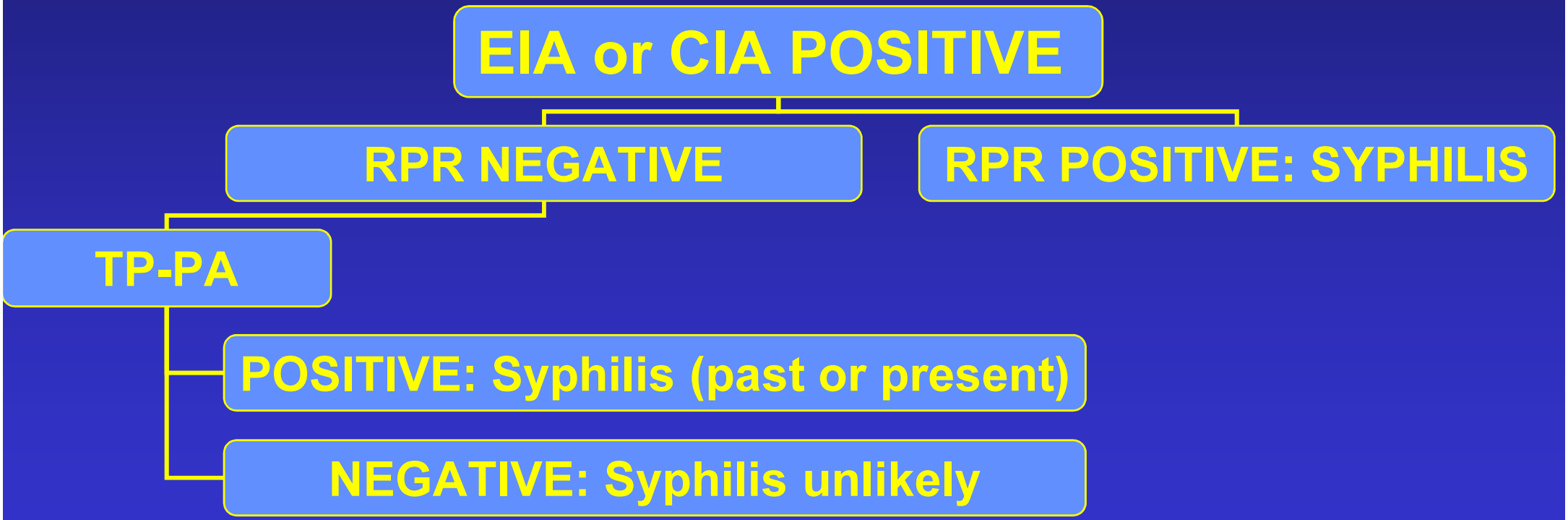
CONGENITAL SYPHILIS: PREVENTION

- Ensure adequate universal prenatal care
- Serologic screening (RPR) at 1st prenatal visit; repeat at 28-32 wks, delivery in high-risk areas
- Screening with treponemal test?

"REVERSE SEQUENCE" SCREENING
MMWR, 2/2011

- 5 laboratories in USA
- 140,176 sera screened with treponemal EIA/CIA
- 3.4% (4834) had reactive test result
- 57% (2743/4834): RPR nonreactive
- 32% (866/2743) NR by TP-PA or FTA-ABS – initial EIA/CIA false-positive?
- Discordant results (NR TP-PA/FTA-ABS) were almost 3x more frequent in low vs high prevalence populations (41% vs. 14%)

"REVERSE SEQUENCE" SCREENING: CDC RECOMMENDATIONS



MMWR, 2/2011

CONGENITAL SYPHILIS: PREVENTION

- Do not discharge infant without maternal serologic status documented at least once during pregnancy
- Report all cases to Health Dept. for contact tracing and identification of core populations and environments


ELIMINATE SYPHILIS
1-866-4EZ-CURE