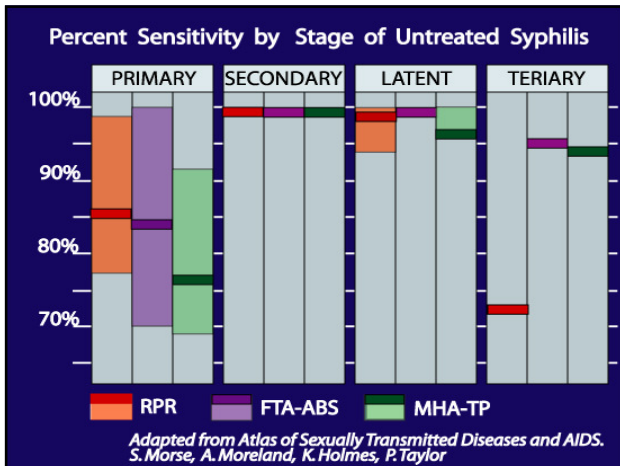
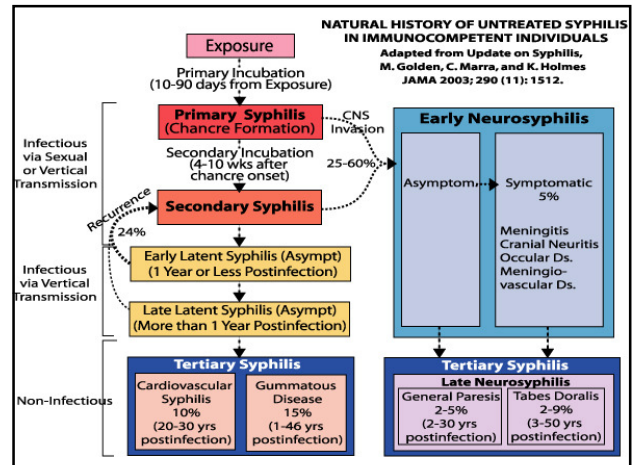


Syphilis: A Case-based Review

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 NYC Department of Health and Mental Hygiene
 Bureau of STD Control



Serologic Interpretation

<p>RPR NonReactive / FTA-ABS NonReactive No Syphilis Diagnosis Incubating syphilis infection → Very Early Primary Syphilis</p>	<p>RPR NonReactive / FTA-ABS Reactive → Very Early Primary Syphilis Secondary Syphilis w/ Prozone Late untreated syphilis w/ sero-reversal of RPR History of Treated Syphilis Syphilis Rxed inadvertently in past False-negative Non-Treponemal test False-positive Treponemal Test (rare)</p>
<p>RPR Reactive / FTA-ABS NonReactive Biologic False Positive False-negative Treponemal Test (rare)</p>	<p>RPR Reactive / FTA-ABS Reactive Positive Syphilis Diagnosis Lyme disease Endemic (non-sexual) treponemal ds</p>

BIOLOGIC FALSE POSITIVE REACTIONS CAUSES

ACUTE (< 6 months)	CHRONIC > 6 months
<u>Physiologic</u>	<u>Physiologic</u>
Pregnancy	Older age
<u>Vaccinations</u>	<u>Chronic Infection (e.g.)</u>
Smallpox	Tuberculosis
Typhoid	Lymphogranuloma venereum
Yellow fever	Malaria
<u>Acute Infections (e.g.)</u>	HIV/AIDS
Herpes varicella-zoster	<u>Autoimmune Disorders (e.g.)</u>
Herpes simplex	Lupus
Infectious mononucleosis	Rheumatoid arthritis
Measles	Autoimmune thyroiditis
Mumps	<u>Other Conditions (e.g.)</u>
Viral hepatitis	Malnutrition
HIV sero-conversion illness	Malignancy
Pneumonia (incl. Mycoplasma)	Hepatic cirrhosis
Lyme disease	Intravenous drug use

Genital Ulcer Disease

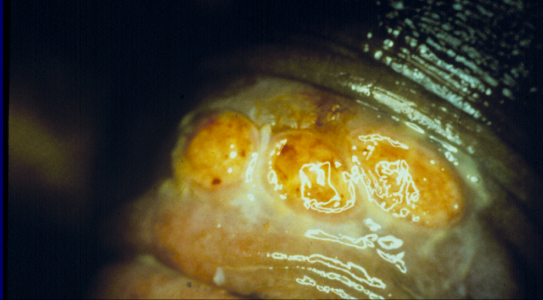
The Usual Suspects

- Genital Herpes-** *Herpes Simplex Virus* type 1 & 2
- Primary Syphilis-** *Treponema pallidum*
- Chancroid -** *Haemophilus ducreyi*
- Lymphogranuloma Venereum (LGV)-** *C. trachomatis*
- Donovanosis-** *Klebsiella granulomatis*

Candidiasis/Balanitis	Lichen Planus (Erosive)
Aphthosis major	Erythema Multiforme
Behcet's disease	Reiter's Syndrome
Fixed Drug Eruption	Trauma
Stevens Johnson Syndrome	Cancer- Squamous Cell

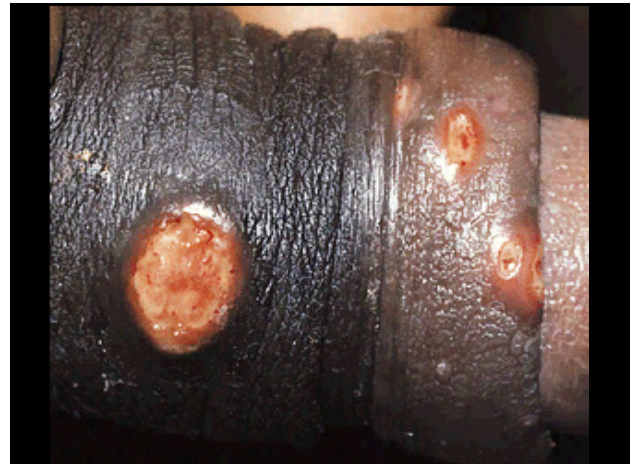
Diagnosis of Chancroid

- Clinical Diagnosis: Bubo c/ painful ulcers
- Important to rule out Syphilis and HSV



Chancroid (*Haemophilus ducreyi*)

- Gram negative coccobacillus with short incubation (3-10 days, average ~5)
- Endemic in regions of sub-Saharan Africa, SE Asia, India, South America, Caribbean
- Men typically present with genital ulceration
- Women usually present w/ non-ulcerative symptoms (Vaginal discharge or bleeding; pain with defecation/urination/sex; ulcers are usually sub-clinical)
- Painful Adenitis in 40-50% cases (80% of Syphilis)
- Systemic symptoms generally absent





LGV: Clinical Presentation

- Primary lesion
 - small non-painful genital papule at site of inoculation after an incubation period of 3 – 30 days, can ulcerate
 - May remain undetected in rectum, vagina
- Secondary clinical manifestations
 - 2-6 weeks after primary lesion
 - Tender inguinal, femoral adenopathy, Uni- or bilateral, may progress to fluctuance (buboes)
 - Proctitis or proctocolitis associated with receptive anal intercourse, often times hemorrhagic
- Tertiary complications
 - Lymphoedema, abscesses, granulomas, strictures

LGV: Treatment

- Consider Presumptive Treatment for LGV
 - Anal receptive sex and signs/symptoms of proctitis especially among MSM
 - Chlamydia + anorectal specimen: S/Sx proctitis or HIV+ status
 - Genital ulcer with extensive lymphadenopathy
- Doxycycline 100mg PO BID x 21 days (preferred)
- Azithromycin 1g PO q week x 3 weeks (lacking clinical data, but probably effective)



Characteristics of Ulcerating Genital Infections

	Syphilis	HSV	Chancroid
Number	Single (60%)	Multiple	Multiple
Edges	Well demarcated Round/Oval	Erythematous Cratered	Irregular Undermined
Depth	Variable	Superficial	Deep/ Excavated
Base	Clean Min. Vascular	Serous Non-vascular	PURULENT Vascular/Friable
Induration	+	-	-
Painful	-	+/-	+++
Nodes	Firm	Firm	Fluctuant

Syphilis Staging

Primary

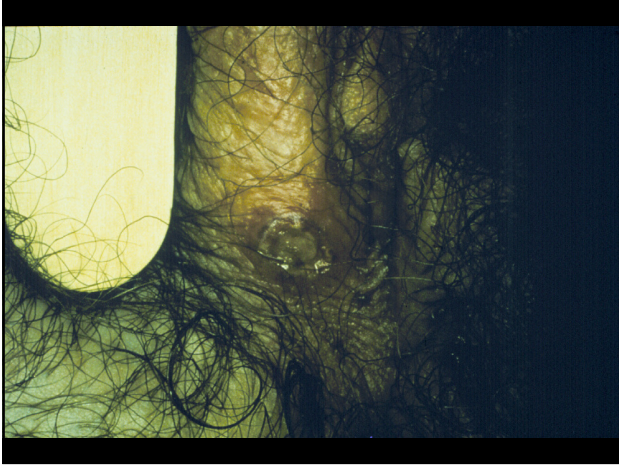
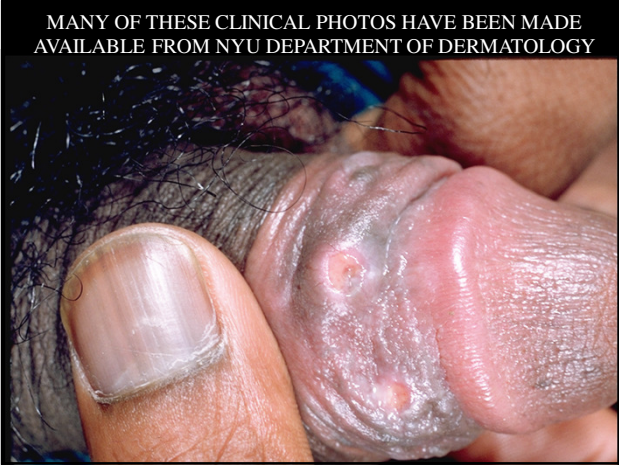
- Muco-cutaneous Ulceration

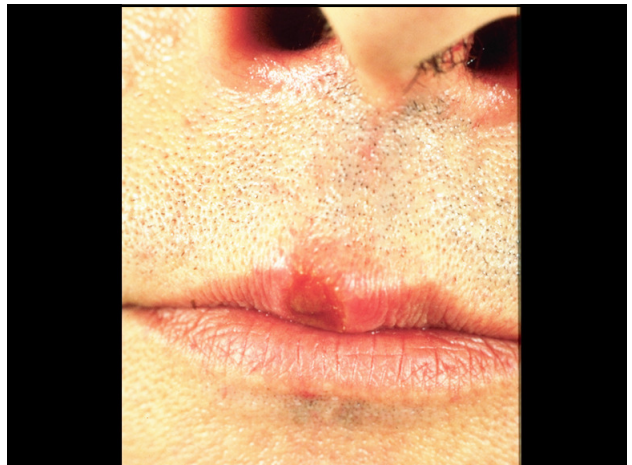
Secondary

- Localized or Diffuse Cutaneous Eruption
- Mucous Patches
- Condyloma Lata
- Patchy Alopecia

Latent

- Asymptomatic at Treatment





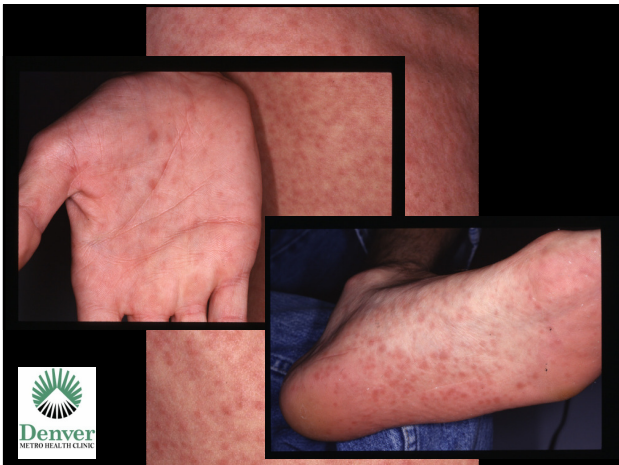


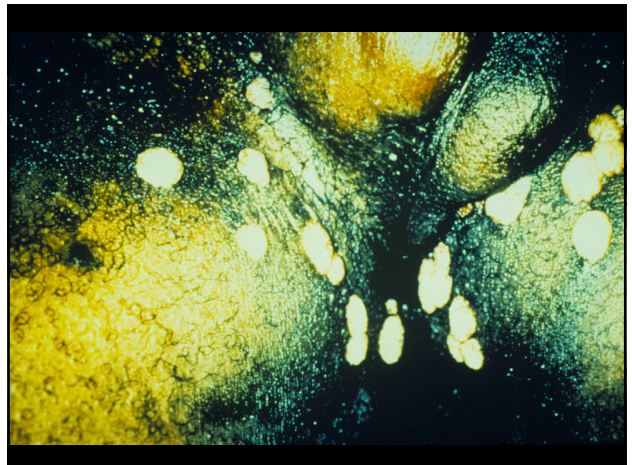
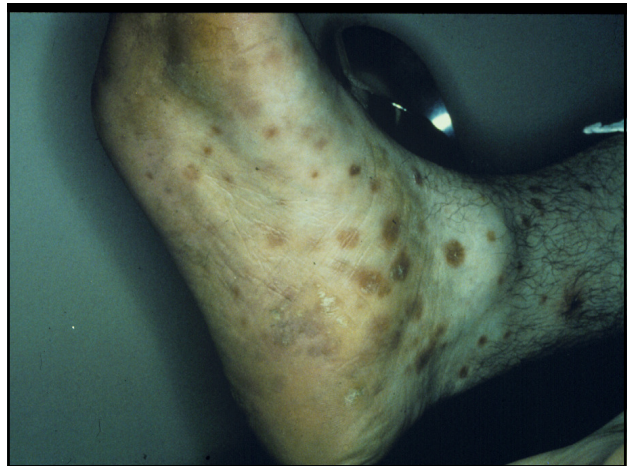
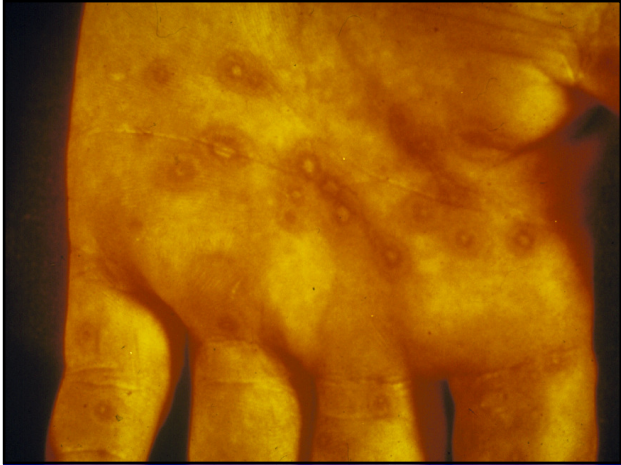


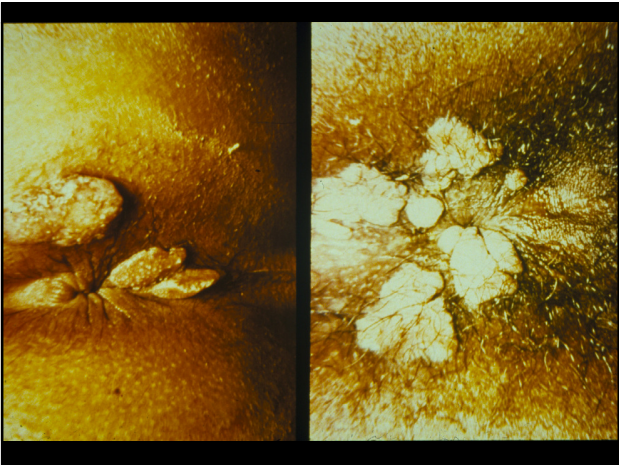
Differential Diagnosis of Secondary Syphilis

- Pityriasis Rosea
- Drug eruption
- Viral exanthem
- Acute HIV
- Sarcoidosis (annular lesions)

- Any Rash of Unknown Origin, especially with systemic complaints









NYU DEPARTMENT OF DERMATOLOGY




Syphilis Staging: Latent Infection

Any of the following during the 12 months prior to Dx = EARLY LATENT

Any of the following > 12 months prior to Dx = LATE LATENT

- Unequivocal Signs/Symptoms
- Serologic Conversion
- Exposure to an infectious case
- Four-fold (2 dilution) rise in titer in a previously treated patient
- Only possible exposure

Relevance of Accurate Staging of Syphilis Infection

	PRIMARY	SECONDARY	LATENT		
			EARLY	UNKNOWN	LATE
Currently Infectious ?	YES		Why?	Possible	No
Duration of Rx	Bicillin LA IM x1 Doxy PO x 2 weeks		Bicillin LA IM x3 Doxy PO x4 weeks		
Management of SexualContacts	Previous 3 months	Previous 6 months	Previous 12 months	?	
Serologic Response to Rx	RPR titer: 2 dilutions in 6 - 12 months		If RPR \geq 1:32: 2 dilutions in 12 - 24 months		
If HIV+: ?LP				YES	YES

New in 2010 CDC Rx Guidelines

Treatment Regimens

Syphilis – Issues Underscored in 2010 CDC Treatment Guidelines

- Must ensure use of Bicillin LA (not C-R)
- Azithromycin (2g oral) not recommended
- Ceftriaxone possible alternative to PCN based on limited clinical studies
 - risk allergic cross-reactivity
 - optimal dose not defined
- Caution- Any non-PCN regimen in HIV+

Based on 2010 CDC Treatment Guidelines

2004 Packaging

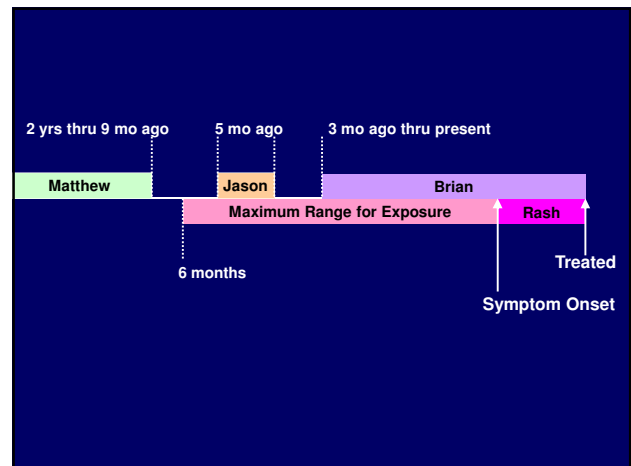


Current Packaging



Relevance of Accurate Staging of Syphilis Infection

	PRIMARY	SECONDARY	LATENT		
			EARLY	UNKNOWN	LATE
Currently Infectious ?	YES		Why?	Possible	No
Duration of Rx	Bicillin LA IM x1 Doxy PO x 2 weeks		Bicillin LA IM x3 Doxy PO x4 weeks		
Management of Sexual Contacts	Previous 3 months	Previous 6 months	Previous 12 months	?	
Serologic Response to Rx	RPR titer: 2 dilutions in 6-12 months		If RPR \geq 1:32: 2 dilutions in 12-24 months		
If HIV+: ?LP			YES	YES	



Response to Therapy by Syphilis Stage

- * **Primary, Secondary Syphilis**
Resolution of symptoms
By 6-12 months- Fall in RPR titer by 2 titers
- * **Early Latent, Late Latent Syphilis**
If RPR titer \leq 1:32 -
Fall in RPR titer by 2 titers
within 12-24 months

??? HIV-infected Patients

Approach to Inadequate Serologic Response to Treatment

- Evaluate for possible re-infection
- Re-screen for HIV
- Consider suboptimal treatment
 - Incorrect staging of infection
 - Non-compliance with oral therapy
- Rule out Neurosyphilis (CSF exam)
- Re-treat with Bicillin 2.4 mU IM x 3

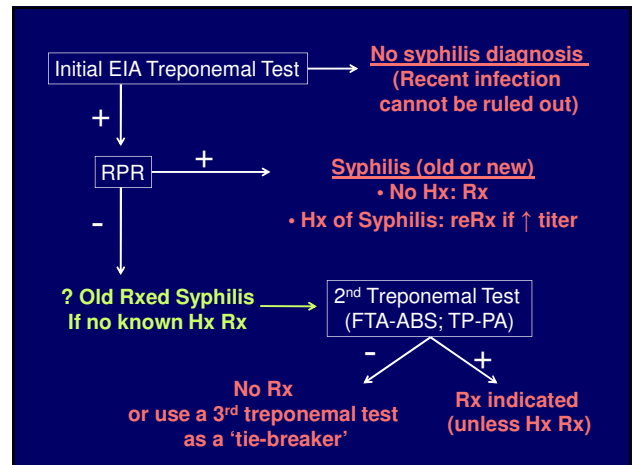
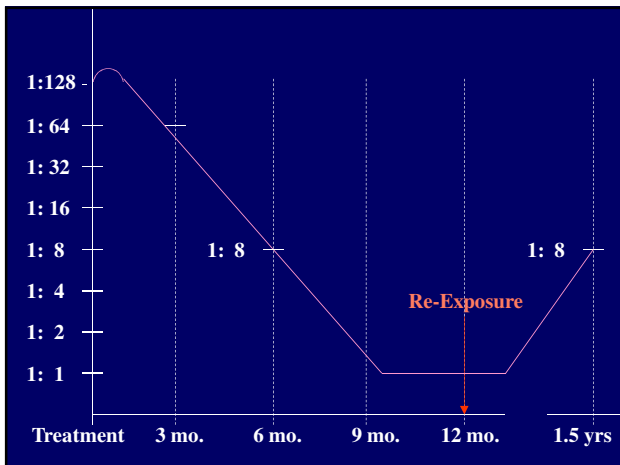
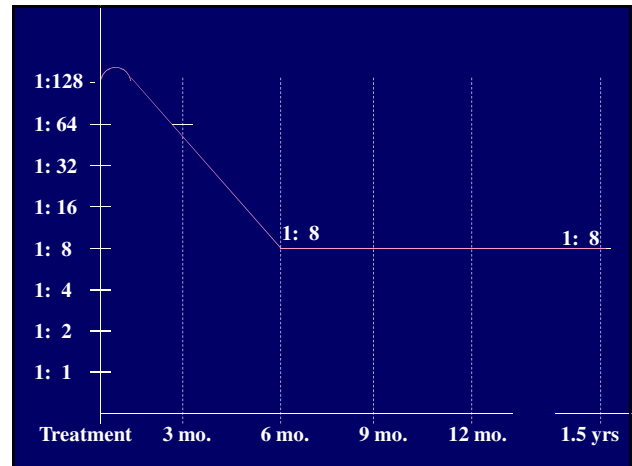
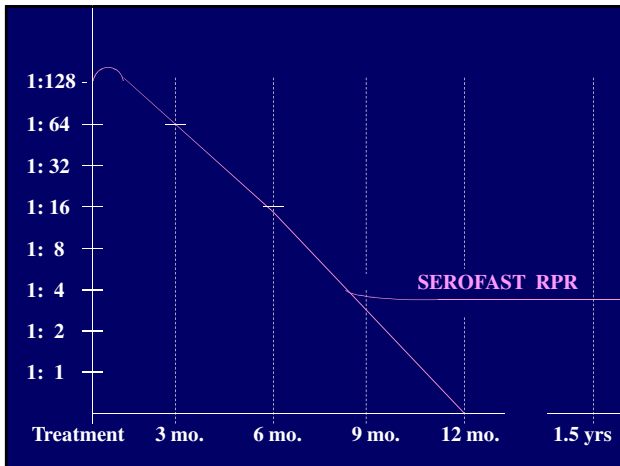
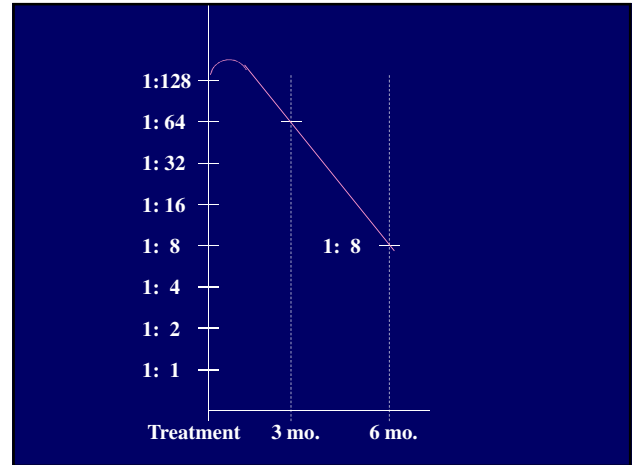
Latent Syphilis: Indications for CSF Exam

- Neurologic or Ophthalmic Signs/Symptoms
- Evidence of Active Tertiary (aortitis, gumma)
- Inadequate Serologic Response to Treatment
- ~~HIV+ with Late Latent or Latent Unknown Dur.~~

- HIV+ patients
- RPR \geq 1:32
 - CD4 \leq 350

Although associated with clinical and CSF abnormalities consistent with neurosyphilis- if asymptomatic, no data that CSF exam \rightarrow improved outcomes

Based on 2010 CDC Treatment Guidelines



Serologic Interpretation

**RPR NonReactive /
FTA-ABS NonReactive**

No Syphilis Diagnosis
Incubating syphilis infection
Very Early Primary Syphilis

**RPR NonReactive /
FTA-ABS Reactive**

Very Early Primary Syphilis
Secondary Syphilis w/ Prozone
Late untreated syphilis
w/ sero-reversal of RPR
History of Treated Syphilis
Syphilis Rxed inadvertently in past
False-negative Non-Treponemal test
False-positive Treponemal Test (rare)

**RPR Reactive /
FTA-ABS NonReactive**

Biologic False Positive
*False-negative
Treponemal Test (rare)*

**RPR Reactive /
FTA-ABS Reactive**

Positive Syphilis Diagnosis
Lyme disease
Endemic (non-sexual) treponemal ds

