Identification and Management of Sexual Transmitted Infections

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Disclosure

I have no financial interests or relationships to disclose.

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TOPICS OF DISCUSSION

Sexually Transmitted Infections:

Chlamydia

Gonorrhea

HPV

Syphilis

Herpes

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LEARNING OBJECTIVES

- Pathophysiology of infection
- Clinical manifestations
- Diagnosis
- Treatment

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CHLAMYDIA

- Pathogen - *Chlamydia trachomatis*
- Obligate intracellular parasite
  - Dependent on host cell for energy production
- Can only be grown in tissue culture

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CHLAMYDIA MICROBIOLOGY

Reticular body

Elementary body – infectious form

Two key virulence factors

- Enhanced ingestion by host cells
- Inhibition of phagolysosomal fusion

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CHLAMYDIA: MECHANISMS OF TRANSMISSION

- Sexual contact
- Perinatal

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CHLAMYDIA FREQUENCY

- Most common STI in Western countries
- 3 - 5 x as common as gonorrhea
- Prevalence varies with the population

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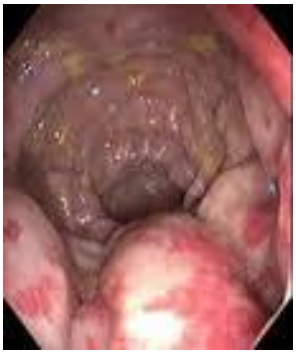
CHLAMYDIA
CLINICAL MANIFESTATIONS IN MEN

- Urethritis
- Proctitis
- Epididymitis



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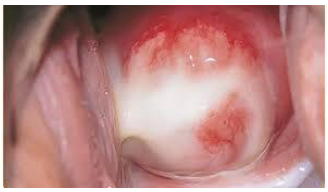
CHLAMYDIA
CLINICAL MANIFESTATIONS IN WOMEN

- Urethritis
- Endocervicitis
- PID
- Perihepatitis – Fitz-Hugh-Curtis Syndrome



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FITZ-HUGH-CURTIS SYNDROME

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CHLAMYDIA DIAGNOSIS

- Clinical examination
- Culture
- Nucleic acid amplification test (NAAT)
  - Urine
  - Cervical discharge

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CHLAMYDIA TREATMENT

Patient and partner should be treated

Risk Category	Recommended Regimen	Alternatives
Adults and adolescents	doxycycline 100 mg orally 2x/day for 7 days	azithromycin 1 gm orally in a single dose **OR** levofloxacin 500 mg orally 1x/day for 7 days
Pregnancy	azithromycin 1 gm orally in a single dose	amoxicillin 500 mg orally 3x/day for 7 days

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CHLAMYDIA SEQUELAE

- Infertility
- Ectopic pregnancy
- Chronic pelvic pain

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GONORRHEA MICROBIOLOGY

Pathogen – *Neissseria gonorrhoea*

Gram-negative diplococcus

Can be cultured in selective media

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GONORRHEA MECHANISMS OF TRANSMISSION

Sexual contact

Perinatal

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GONORRHEA FREQUENCY

- Less common than chlamydia
- Prevalence varies with population

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GONORRHEA CLINICAL MANIFESTATIONS IN MEN

- Urethritis
- Epididymitis
- Proctitis
- Pharyngitis

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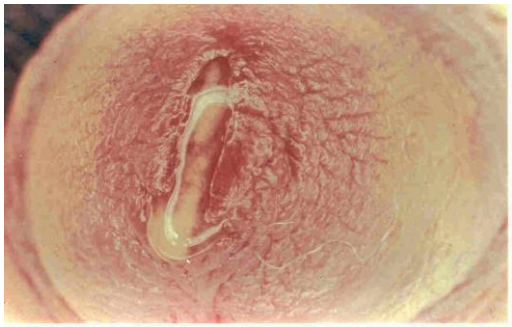
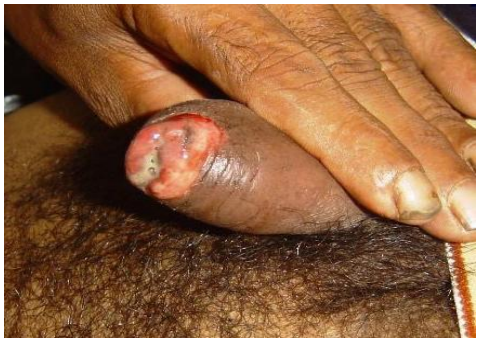
GONORRHEA
CLINICAL PRESENTATION





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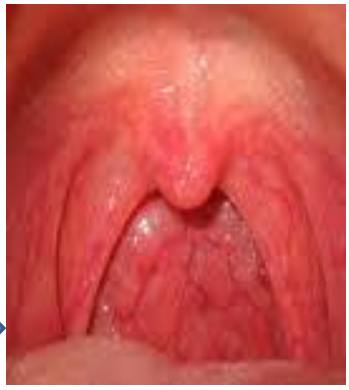
GONORRHEA
CLINICAL MANIFESTATIONS IN WOMEN

- Urethritis
- Endocervicitis
- Proctitis
- PID
- Pharyngitis



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GONORRHEA
DISSEMINATED INFECTION

- Arthritis
- Dermatitis
- Pericarditis and endocarditis
- Meningitis
- Perihepatitis

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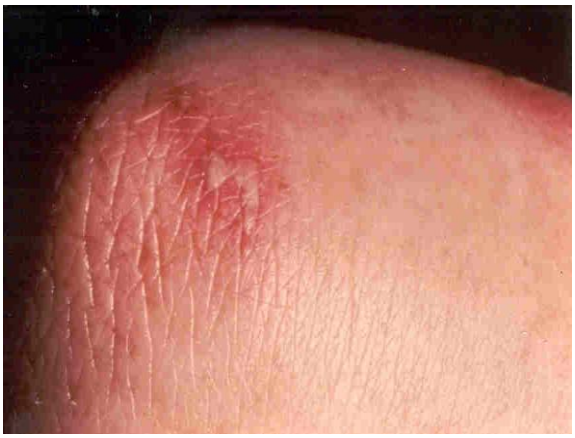
DISSEMINATED GONORRHEA
CLINICAL PRESENTATION



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GONORRHEA DIAGNOSIS

- Clinical examination
- Gram stain
- Culture
- Nucleic acid amplification test (NAAT)
  - Urine
  - Cervical discharge

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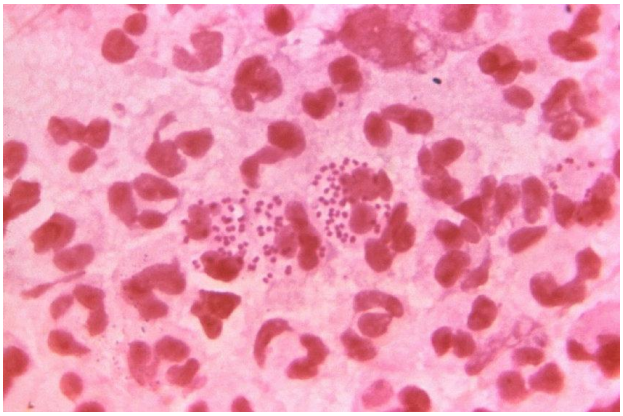
GONORRHEA GRAM STAIN



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GONORRHEA TREATMENT

Patient and partner should be treated

Risk Category	Recommended Regimen	Alternatives
Uncomplicated infections of the cervix, urethra, and rectum: adults and adolescents <150 kg[6]	ceftriaxone 500 mg IM in a single dose[17]	If cephalosporin allergy: gentamicin 240 mg IM in a single dose **PLUS** azithromycin 2 gm orally in a single dose If ceftriaxone administration is not available or not feasible: cefixime 800 mg orally in a single dose[17]
Uncomplicated infections of the pharynx: adults and adolescents <150 kg[6]	ceftriaxone 500 mg IM in a single dose[17]	
Pregnancy	ceftriaxone 500 mg IM in a single dose[17]	
Conjunctivitis	ceftriaxone 1 gm IM in a single dose[18]	
Disseminated gonococcal infections (DGI)[19]	ceftriaxone 1 gm IM or by IV every 24 hours[17]	cefotaxime 1 gm by IV every 8 hours **OR** ceftizoxime 1 gm every 8 hours

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GONORRHEA SEQUELAE

- Infertility
- Ectopic pregnancy
- Chronic pelvic pain

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MYCOPLASMA GENITALIUM

- Pathogen – *Mycoplasma Genitalium*
- Lacks a cell wall
- Slow growing in culture (can take up to 6 months)

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MYCOPLASMA: MECHANISMS OF TRANSMISSION

- Sexual contact

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MYCOPLASMA

- Men-
  - symptomatic and asymptomatic urethritis
- Women-
  - cervicitis
  - PID
  - preterm delivery
  - spontaneous abortion
  - infertility

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MYCOPLASMA DIAGNOSIS

- Who to test?
  - Those with recurrent urethritis, cervicitis
    - Possibly those with PID
- Diagnosis
  - NAAT
    - urine and urethral, penile meatal, endocervical, and vaginal swab samples

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MYCOPLASMA

- Antibiotic resistance
  - Recommend against one dose azithromycin
  - ***pregnancy*** current recommendation is still azithromycin

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MYCOPLASMA TREATMENT OPTIONS

Recommended Regimens if *M. genitalium* Resistance Testing is Available

If *macrolide sensitive:* Doxycycline 100 mg orally 2 times/day for 7 days, followed by **azithromycin** 1 g orally initial dose, followed by 500 mg orally once daily for 3 additional days (2.5 g total)

If macrolide resistant: Doxycycline 100 mg orally 2 times/day for 7 days followed by **moxifloxacin** 400 mg orally once daily for 7 days

Recommended Regimens if *M. genitalium* Resistance Testing is Not Available

If *M. genitalium* is detected by an FDA-cleared NAAT: Doxycycline 100 mg orally 2 times/day for 7 days, followed by **moxifloxacin** 400 mg orally once daily for 7 days

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HUMAN PAPILLOMA VIRUS

Over 120 HPV types:

- >40 infect the mucosa
  - 6, 11 – "genital warts"
  - 16, 18, 31, 33, 45 – "high risk for cervical cancer"

Transmission:

- Direct contact
- Autoinoculation
- ↑in immunosuppressed patients

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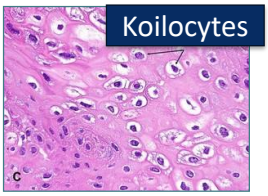
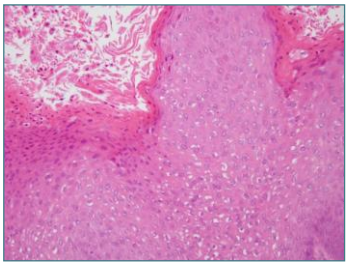
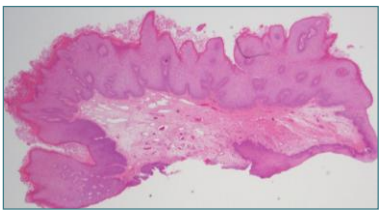
HPV: HISTOPATHOLOGY "WARTS"

- Epidermal hyperplasia and papillomatosis
- Hyperkeratosis and parakeratosis
- Koilocytes







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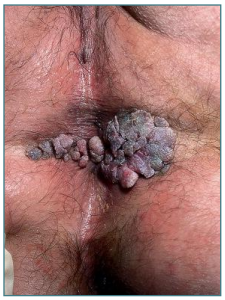
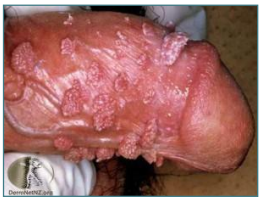
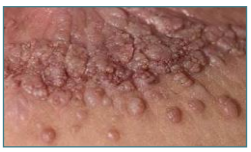
HPV-CONDYLOMA ACUMINATA ANOGENITAL WARTS

- Discrete, papillomatous, exophytic papules
- Sessile or pedunculated
- May form confluent plaques
- Lack the thick horny scale found on cutaneous warts







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CONDYLOMA TREATMENT

Risk Category	Recommended Regimen	Alternatives
External anogenital warts[12]	**Patient-applied**	
	imiquimod 3.75% or 5%[13] cream	
	OR podofilox 0.5% solution or gel	
	OR sinecatechins 15% ointment[13]	
	Provider-administered	
	cryotherapy with liquid nitrogen or cryoprobe	
	OR surgical removal either by tangential scissor excision, tangential shave excision, curettage, laser, or electrosurgery	
	OR trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%–90% solution	
Urethral meatus warts	cryotherapy with liquid nitrogen	
	OR surgical removal	
Vaginal warts[14]	cryotherapy with liquid nitrogen	
	OR surgical removal	
	OR TCA or BCA 80%–90% solution	

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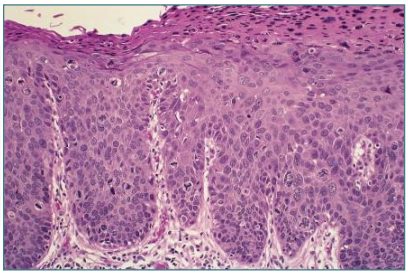
HPV: INTRAEPITHELIAL NEOPLASIA

- Persistent infection with high-risk HPV types represents the most important risk factor for the development of neoplasia
- Cervix, vulva, vagina, penis and anus

Full-thickness atypia
Abnormal keratinocyte maturation
Nuclear pleomorphism
Dyskeratosis



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HPV VACCINES

Helps protect against HPV responsible for genital warts and HPV-related genital cancer

- Cervical, vaginal, vulvar, penile, anal, oropharyngeal

-FDA-approved and CDC-recommended up to age 45

-Pre-teen boys and girls – 11-12 yo (can start at 9 yo)

Series of 3 doses over 6mo

- If vaccine started before 15 yo only need 2 doses

-Injection site reaction – most common side effect

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HPV VACCINES

Gardasil 9
- 2014 – FDA-approved
- HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58

Gardasil
- 2006 – FDA-approved
- HPV 6, 11, 16, and 18

Cervarix
- 2009 – FDA-approved for women and girls
- HPV 16 and 18

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HERPES SIMPLEX VIRUS

HSV1 and HSV2

Transmission:
- Direct contact –
  - mucous membranes or open skin
  - perinatal
- Intrauterine – rare
- HIV-HSV co-infection:
  - ↑risk of transmission

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HSV: CLINICAL

Primary disease:

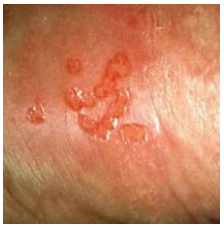
- More severe than recurrent
  - painful ulcerations

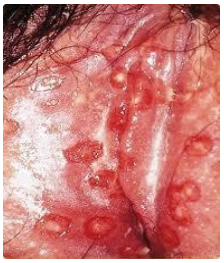
Recurrent disease:

- Milder; prodrome of pain, itching, tingling, paresthesia

Exam:

- Grouped vesicles on an erythematous base
- Round erosions with scalloped borders
- Locations: penis, perineum, anus, female external genitalia, cervix





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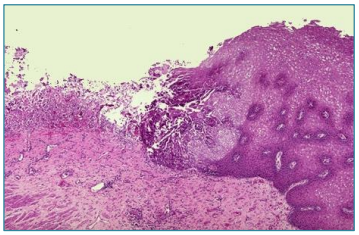
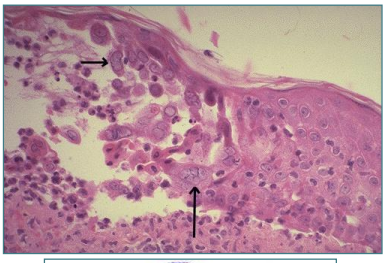
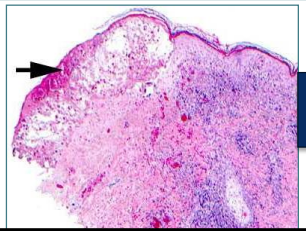
HSV: HISTOPATHOLOGY

- Acantholysis and intraepidermal vesicles
- Ulcer lesions - keratinocyte necrosis and loss of epidermis
- Neutrophilic and lymphocytic inflammation

Ulcer







Keratinocyte necrosis and vesicle

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HSV TREATMENT

Risk Category	Recommended Regimen	Alternatives
First clinical episode of genital herpes[7]	acyclovir 400 mg orally 3x/day for 7–10 days[8] **OR** famciclovir 250 mg orally 3x/day for 7–10 days **OR** valacyclovir 1 gm orally 2x/day for 7–10 days	
Suppressive therapy for recurrent genital herpes (HSV-2)	acyclovir 400 mg orally 2x/day **OR** valacyclovir 500 mg orally 1x/day[9] **OR** valacyclovir 1 gm orally 1x/day **OR** famciclovir 250 mg orally 2x/day	
Episodic therapy for recurrent genital herpes (HSV-2)[10]	acyclovir 800 mg orally 2x/day for 5 days **OR** acyclovir 800 mg orally 3x/day for 2 days **OR** famciclovir 1 gm orally 2x/day for 1 day **OR** famciclovir 500 mg orally once, **FOLLOWED BY** 250 mg 2x/day for 2 days **OR** famciclovir 125 mg orally 2x/day for 5 days **OR** valacyclovir 500 mg orally 2x/day for 3 days **OR** valacyclovir 1 gm orally 1x/day for 5 days	
Daily suppressive therapy of recurrent genital herpes in pregnant women[11]	acyclovir 400 mg orally 3x/day **OR** valacyclovir 500 mg orally 2x/day	

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SYPHILIS MICROBIOLOGY

- Pathogen - *Treponema pallidum*
- Cannot be cultivated in vitro

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SYPHILIS FREQUENCY

- Incidence has increased , especially in females aged 15-24 years
- Highest prevalence - urban blacks and hispanics

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SYPHILIS EPIDEMIOLOGY

- In 2020 the CDC recorded 133,945 cases of syphilis, a 6.8% increase from 2019
- In that same year, the CDC documented 2148 cases of congenital syphilis
  - 149 cases resulted in stillbirths or neonatal deaths

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SYPHILIS
MECHANISMS OF TRANSMISSION

- Sexual contact
  - Highly contagious
  - 50-60% of partners become infected after a single unprotected exposure
- Perinatal

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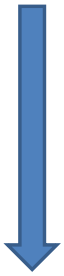
SYPHILIS
CLASSIFICATION

- Primary
- Secondary
- Latent
  - Early
  - Late
  - Indeterminate
- Tertiary
- Neurosyphilis



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SYPHILIS DIAGNOSIS

Clinical examination

Darkfield microscopy – rarely used

Serology – mainstay of diagnosis

- VDRL or RPR – screening test
- MHA or FTA – confirmatory test
- IgM and IgG

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SYPHILIS CONVENTIONAL SEROLOGY

TEST	RESPONSE AFTER TREATMENT
VDRL or RPR	Reverts to negative or decreases to a very low titer Significant elevation in titer indicates re-infection
MHA or FTA	Remains positive for lifetime of patient
IgM IgG	Indicative of acute infection Indicative of chronic infection

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DIAGNOSIS OF SYPHILIS REVERSE SEQUENCE ALGORITHM

T. pallidum antibody

↓

RPR or VDRL

↓

T.pallidum particle agglutination test

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DIAGNOSIS OF SYPHILIS REVERSE SEQUENCE ALGORITHM

- Initial screening test → ***T. pallidum*** antibody
- If negative→ patient is uninfected
- If positive→ reflex RPR
- If RPR is positive→ past or present infection is confirmed
- If RPR is negative→T. pallidum particle agglutination test (TP-PA)
  - If positive→ past or present infection is confirmed
  - If negative→ consider uninfected (false positive)

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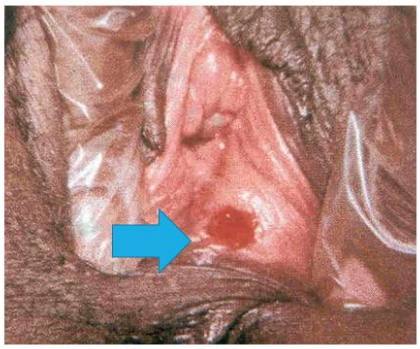
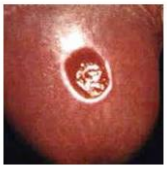
PRIMARY SYPHILIS
PRINCIPAL CLINICAL FINDING

Painless chancre





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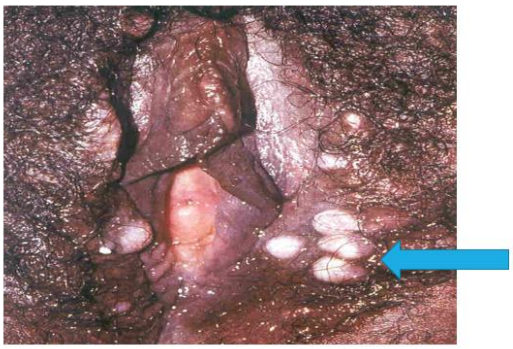
SECONDARY SYPHILIS
PRINCIPAL CLINICAL FINDINGS

Condyloma lata



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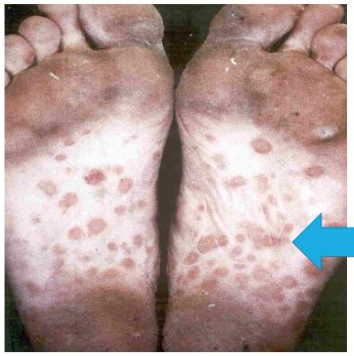
SECONDARY SYPHILIS PRINCIPAL CLINICAL FINDINGS

Rash on palms and soles



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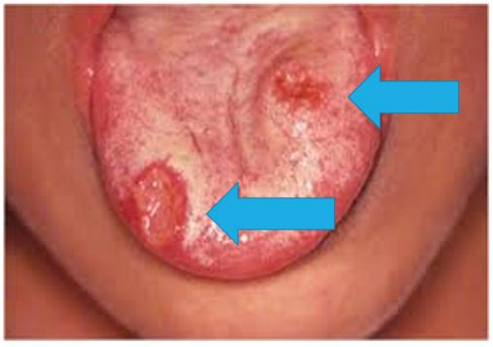
SECONDARY SYPHILIS CLINICAL FINDINGS

Mucous Patches



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LATE-STAGE SYPHILIS
PRINCIPAL CLINICAL MANIFESTATIONS

Destructive gummas

Aortic valve injury

CNS manifestations

- Dementia
- Tabes dorsalis
- Pupillary abnormalities

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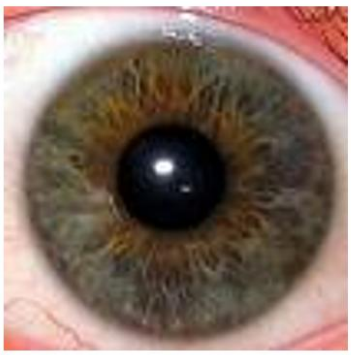
ARGYLL-ROBERTSON PUPIL

Accommodates but does not react



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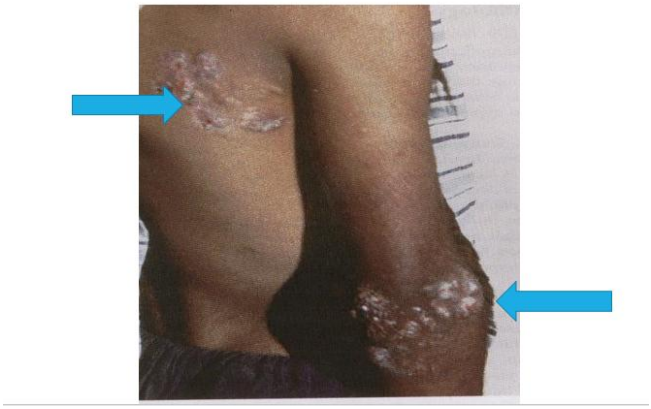
LATE STAGE SYPHYLIS GUMMAS



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CONGENITAL SYPHILIS CLINICAL MANIFESTATIONS

Fetal death

Growth restriction

Multiple anomalies

- Immediately apparent at birth
- Delayed appearance

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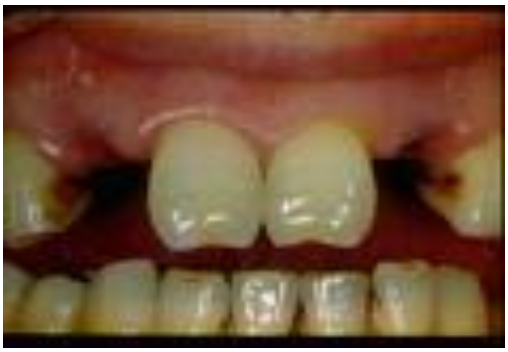
CONGENITAL SYPHILIS
ABNORMAL DENTITION

Hutchinson's Teeth



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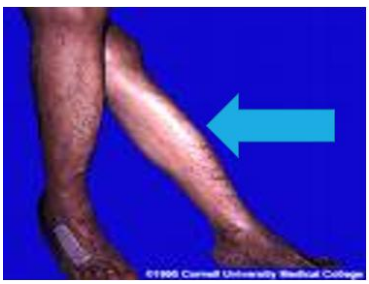
CONGENITAL SYPHILIS
SABER SHINS



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SYPHILIS TREATMENT

Patient and sexual partner(s) should be treated

Antibiotic therapy

- Penicillin – preferred in pregnancy because of proven value in treating fetal infection
- Doxycycline – contraindicated in pregnancy
- Tetracycline – contraindicated in pregnancy
- Ceftriaxone

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SYPHILIS ANTIBIOTIC TREATMENT

Risk Category	Recommended Regimen	Alternatives
Primary, secondary, and early latent: adults (including pregnant women and people with HIV infection)	benzathine penicillin G 2.4 million units IM in a single dose	
Late latent adults (including pregnant women and people with HIV infection)	benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals	
Neurosyphilis, ocular syphilis, and otosyphilis	aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units by IV every 4 hours or continuous infusion, for 10–14 days	procaine penicillin G 2.4 million units IM 1x/day **PLUS** probenecid 500 mg orally 4x/day, both for 10–14 days

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