Chapter 22

Vulvovaginitis, Sexually Transmitted Infections, and Pelvic Inflammatory Disease

Prepared and lectured by

Oday Hamad , MD

Teaching assistant , AUG

Reproductive Tract Infections



- Infections of the vulva, vagina, and cervix (lower reproductive tract) and the uterine corpus, fallopian tubes, and ovaries (upper reproductive tract) are common gynecologic problems. Many of these infections are sexually transmitted and require partner treatment for effective care.

- The term sexually transmitted infection (STI) is replacing sexually transmitted disease (STD) as a more accurate and appropriate term for these frequently asymptomatic disorders , emphasizing their infectious nature and the need for screening, early recognition, and treatment. A person with an STI may be infected and infect others without actually " having a disease."

- The most common STIs are chlamydia, genital herpes, human papillomavirus (HPV), and gonorrhea.

Chapter 22

Vulvovaginitis, Sexually Transmitted Infections, and Pelvic Inflammatory Disease

- Vulvovaginitis is a common pelvic infection caused by yeast, bacteria, or trichomonads, and pelvic inflammatory disease (PID) is the most serious form of upper reproductive tract infection. PID is frequently a consequence of an unrecognized or inadequately treated lower tract STI.

- PID is a common cause of infertility and is the reproductive tract infection that is most likely to require hospitalization and even surgery for adequate treatment.

Normal Physiology and Microecology of the Vagina



- The vagina is lined by nonkeratinized stratified squamous epithelium, which is powerfully influenced by estrogen and progesterone. The vagina of the newborn is colonized by aerobic and anaerobic bacteria acquired while passing through the birth canal.
- The newborn's vaginal epithelium is strongly estrogenized and rich in glycogen, which supports growth of lactic acid–producing lactobacilli.
- This results in a low Ph (<4.7), which promotes further growth of acidophilic protective microflora.
- Within days of birth, estrogen decreases, and the vaginal epithelium becomes thin, atrophic, and largely devoid of glycogen. In this environment, the pH rises, and acidophilic organisms no longer have a selective advantage. As a consequence, the predominant vaginal microflora becomes diverse gram-positive cocci and bacilli.

- With the onset of puberty and ovarian steroidogenesis, the vagina again becomes estrogenized, and the glycogen content increases. Lactic acid– and hydrogen peroxide (H_2O_2)–producing lactobacilli again predominate, resulting in a self-sustaining vaginal pH of between 3.5 and 4.5.

- Even so, a wide variety of aerobic and anaerobic bacteria can be cultured from the normal vagina. Most women harbor at least three to eight types of bacteria at any given time. Lactic acid, H_2O_2, and other substances produced by “healthy” lactobacilli provide some protection in the lower reproductive tract from STIs, including human immunodeficiency virus (HIV).

- Multiple factors may alter this protective microflora.

- Antibiotics suppress growth of commensal organisms, which can allow pathogenic strains (e.g., yeasts) to predominate.

- Douching with water or nonbuffered solutions may transiently alter the pH or selectively suppress endogenous bacteria.

- The presence of a foreign body (e.g., forgotten diaphragm or tampon in adults) dramatically disrupts normal vaginal cleansing mechanisms and may lead to secondary infection.

PHYSIOLOGIC VAGINAL FLUIDS



- Vaginal fluid is a mixture consisting of cervical mucus (the major component), endometrial and oviductal fluid, exudates from the Bartholin's and Skene's glands, transudate from the vaginal squamous epithelium

- Together with exfoliated squamous cells, and metabolic products of the microflora. Vaginal fluid is composed of proteins, polysaccharides, amino acids, enzymes, and immunoglobulins. Physiologic increases in vaginal and endocervical fluid occur during pregnancy, at mid menstrual cycle, and during intercourse. In postmenopausal women (not using estrogens), vaginal fluid may become markedly decreased, which predisposes to infection with various exogenous microflora (e.g., Escherichia coli and staphylococcal, and streptococcal species).

- Patients with a vaginal infection frequently complain of a non bloody vaginal discharge. The characteristics of the discharge (e.g., color, texture, viscosity, and odor) are helpful in making the correct diagnosis. Normal vaginal fluid has a pH of less than 4.7 in ovulatory women.

- Vaginal pH can be easily determined by using pH paper with an appropriate pH range (3.5 to 7.0).

- Testing for the presence of an amine odor (referred to as a positive whiff test) is performed by putting a few drops of 10% potassium hydroxide (KOH) in the spoon of a vaginal speculum after it is removed from the vagina. With healthy vaginal fluid, no odor is noted.

- An “amine” or “fishy” odor suggests trichomoniasis or bacterial vaginosis (BV)

- A wet-mount preparation of the discharge should be evaluated. Using a cotton-tipped applicator, a sample of vaginal discharge from the posterior fornix is suspended in 2 mL of normal saline. A drop of this solution is placed on a glass slide, covered with a coverslip, and examined under the microscope. Motile trichomonads may be seen on this type of wet mount .

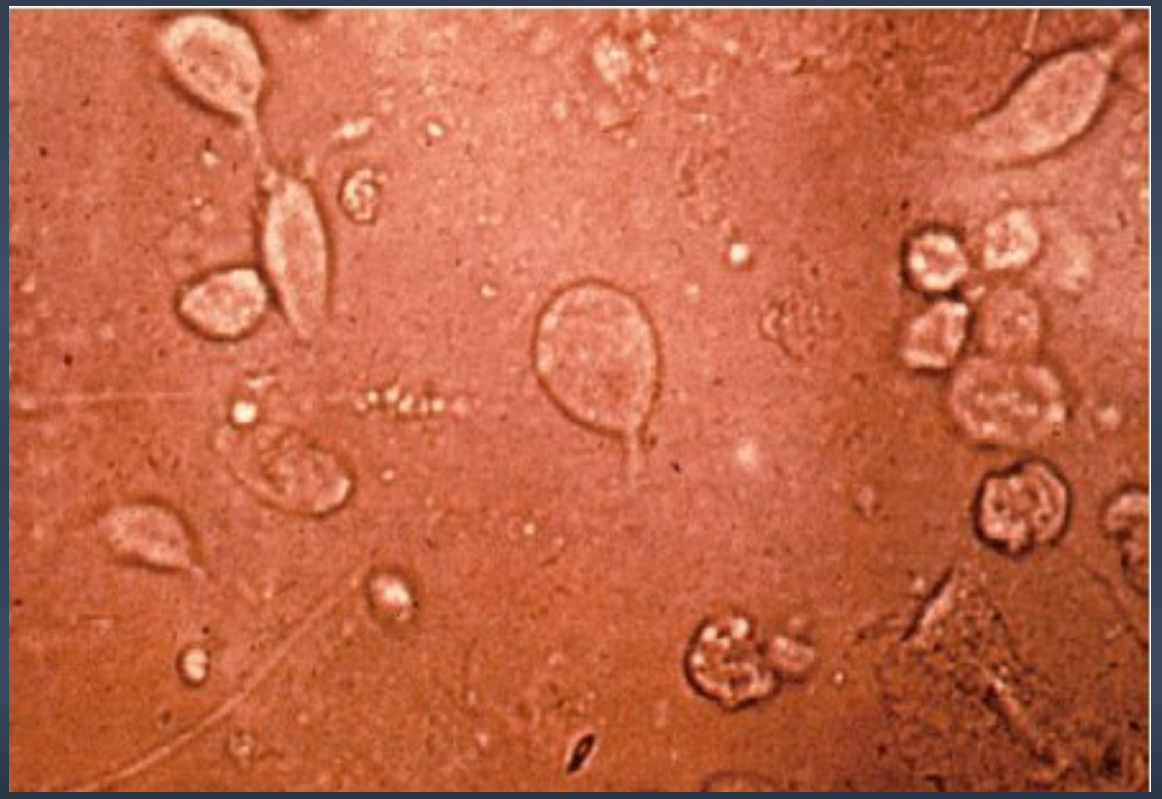


FIGURE 22-1 Microscopic view (high power) of a trichomonad in a saline wet-mount preparation. The organisms are usually motile in this type of preparation.

- Also, epithelial cells with irregular, granular edges (clue cells) are indicative of clumped bacteria on the cell wall and are highly suggestive of BV if present in more than 20% of epithelial cells.

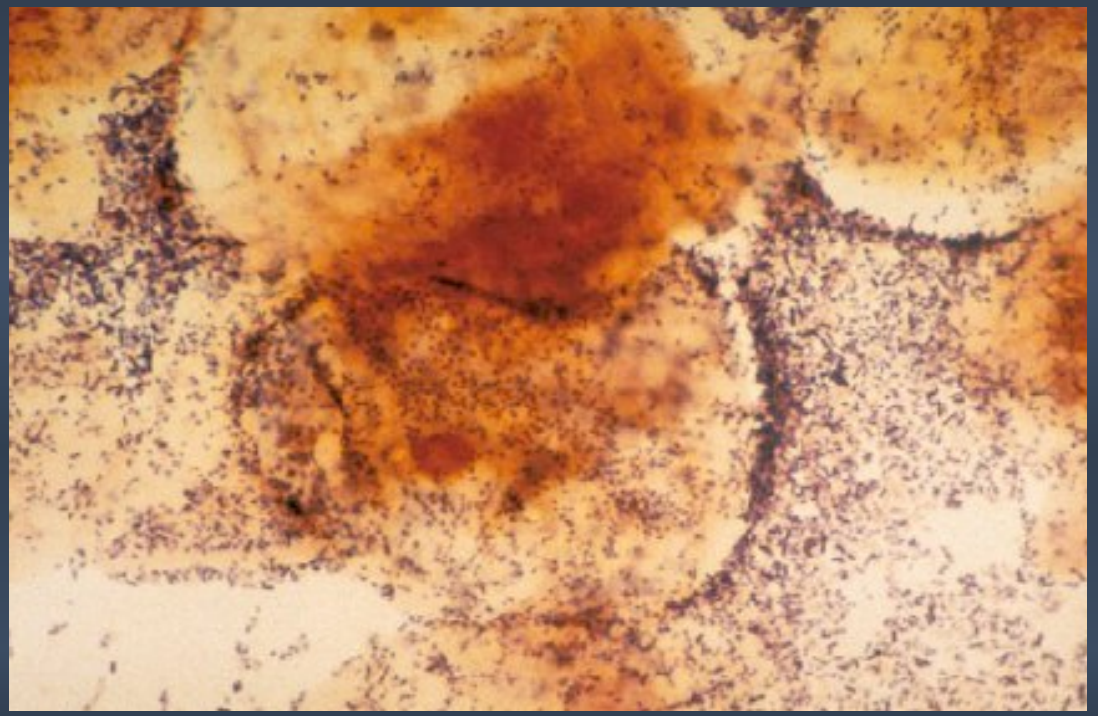


FIGURE 22-2 Microscopic view of clue cells in a saline wet-mount preparation. Note the irregular or serrated cell walls.

- If the cells are not sufficiently separated, an aliquot of fluid is placed in a drop of saline or 10% to 20% KOH (to eliminate cellular and other debris while leaving mycelia) and examined microscopically, to visualize the pseudohyphae or spores of Candida infection. In complicated or atypical cases, bacterial and yeast cultures are required.

Vaginal Discharge Etiology

Chapter 22

Vulvovaginitis, Sexually Transmitted Infections, and Pelvic Inflammatory Disease

- Vaginitis and complaints referable to the vagina (e.g., discharge, pruritus, burning, and “late” dysuria) are common. A correct diagnosis can be difficult because symptoms and signs may be nonspecific, patients frequently self-medicate with OTC products, multiple causes may be present, and accurate diagnostic tools are either not available or not properly employed.
- Up to 90% of cases of vaginitis appear to be caused by three conditions. Bacterial vaginosis accounts for 40% to 50%, vulvovaginal candidiasis (VVC) for 20% to 25%, and trichomoniasis for 15% or less of cases.
- Mucopurulent cervicitis (“mucopus”) caused by chlamydia, Neisseria gonorrhoeae, mycoplasma, or BV associated bacteria may also cause vaginal



FIGURE 22-6 Uterine cervix at the time of speculum examination with mucopus protruding from the os.

Less common types include atrophic vaginitis (overgrowth with aerobic or anaerobic microflora in the absence of lactobacilli and with hypo estrogenized tissues), foreign-body vaginitis, genital ulcer diseases such as herpes and syphilis, desquamative vaginitis (most commonly group B Streptococcal overgrowth), and lichen planus.

BACTERIAL VAGINOSIS

BV is the most common cause of vaginal discharge but is often without other symptoms. BV occurs subsequent to a significant disruption of “healthy” vaginal microflora, (typically Lactobacillus jensenii and Lactobacillus crispatus) by a characteristic set of BV-complex microorganisms: Gardnerella vaginalis, genital mycoplasmas (Mycoplasma hominis, Ureaplasma urealyticum) and vaginal anaerobic bacteria, including Prevotella, Bacteroides, and Mobiluncus species.

Risk factors for acquisition of BV include smoking, intrauterine device (IUD) use, and frequent douching.

Classic features of BV discharge include a profuse, milky, nonadherent discharge that demonstrates an amine or fishy odor after alkalization with a drop of KOH (positive whiff test).

The presence of BV heightens a nonpregnant woman's risk for PID, postoperative infections (e.g., after hysterectomy or pregnancy termination), and HIV transmission.

Partner treatment is generally not recommended.

VULVOVAGINAL CANDIDIASIS

- VVC is the second most common cause of vulvovaginal- related symptoms.
- Wide use of OTC antifungal products for self-diagnosed candidiasis has resulted in a decreased frequency of doctor visits, but women who do present are less likely to present with textbook findings.
- Candida albicans formerly caused more than 90% of cases of VVC, but now less azole-susceptible species, such as Candida glabrata, are recognized as causative agents in 15% of cases. These less susceptible yeasts necessitate prolonged or alternative treatments. Because of Candida's requirement for estrogenized tissues, VVC becomes more common after menarche and less common after menopause.

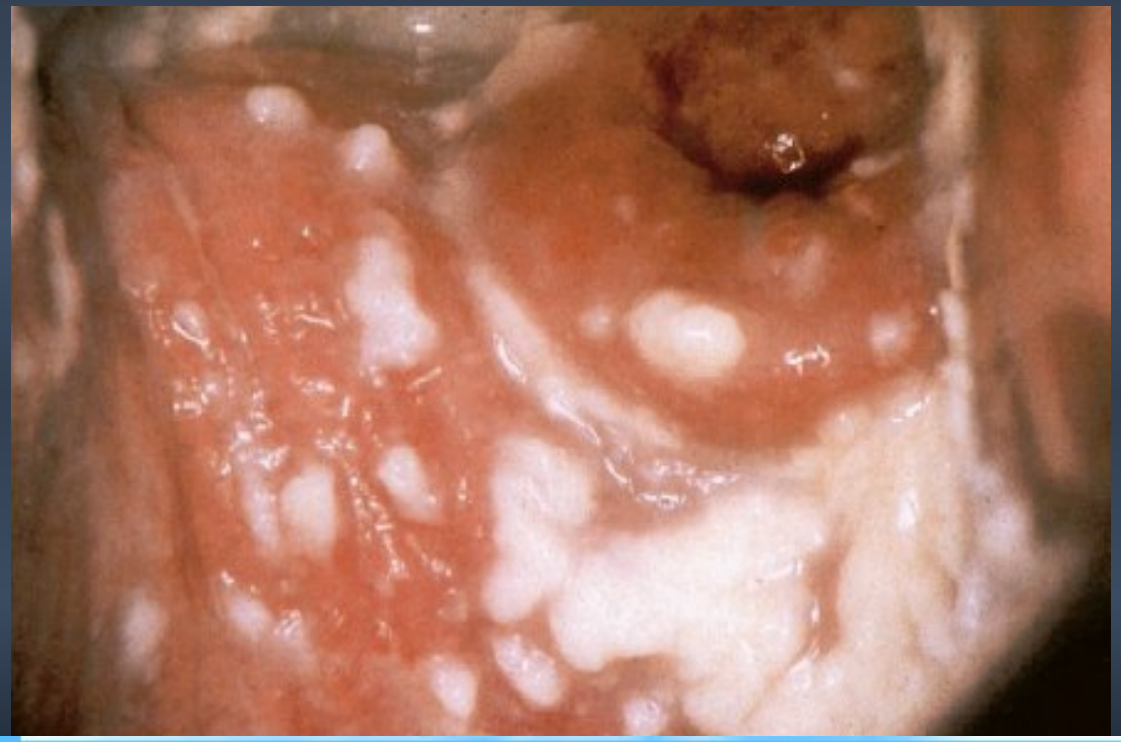


FIGURE 22-3 Cottage cheese or curd-like appearance of vaginal discharge is typical of vulvovaginitis due to yeast.

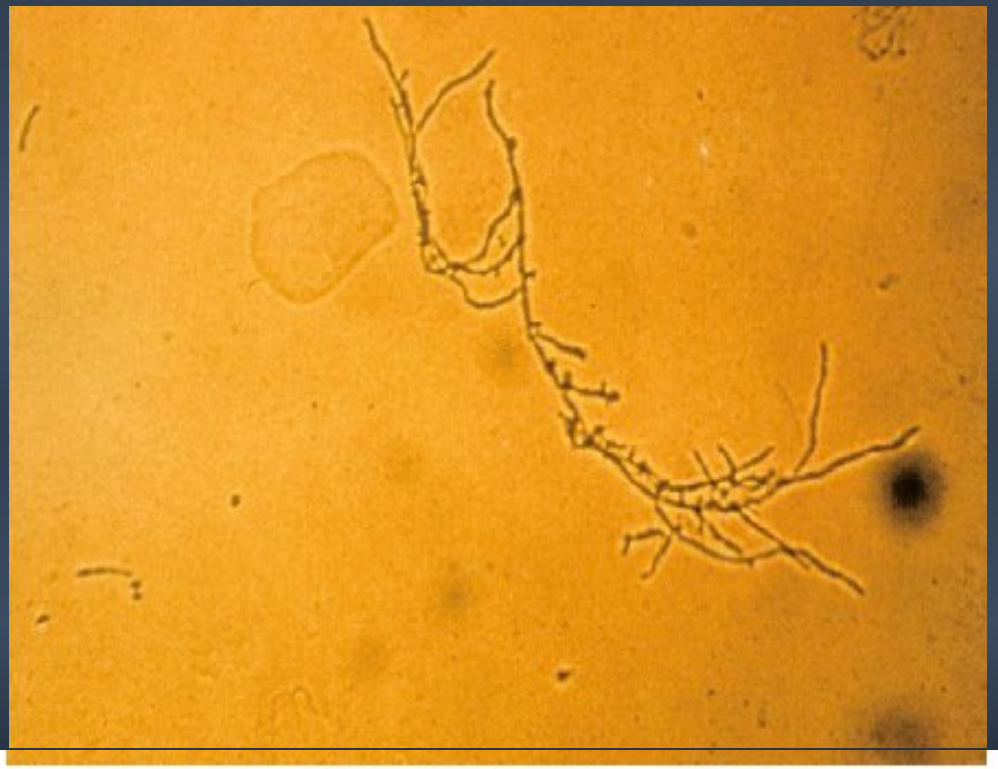


FIGURE 22-4 Mycelial tangles of yeast pseudohyphae in KOH wet-mount preparation.

- First-line treatments include topical or oral antifungal (imidazole) agents. Documented cases of recurrences can be effectively treated by confirming the diagnosis and treating with weekly suppressive doses of topical imidazoles .

- Boric acid (600 mg vaginal gelatin capsules) 3 times daily for 1 week is an effective treatment for imidazole-resistant species.

- Although VVC is not thought to be sexually transmitted in most cases, male partners sometimes reinfect their partners and are routinely treated by some practitioners.

TRICHOMONIASIS

Trichomoniasis (cervicitis, vaginitis, and urethritis) is caused by the protozoan T. vaginalis. About 50% of cases in women and men are asymptomatic. Symptomatic infection is classically manifested by a green yellow, frothy vaginal discharge, with a “musty” odor. Dyspareunia, vulvovaginal irritation, and occasionally dysuria may be present. Male partners are often asymptomatic even though they demonstrate nongonococcal urethritis on direct examination.

- The diagnosis of trichomoniasis in patients and their sexual partners should be followed by screening for other prevalent STIs and empiric treatment of partners.

- Diagnosis is usually made on clinical grounds and can be confirmed by seeing the characteristic motility of trichomonads on a saline wet mount. Much more sensitive techniques, including culture, polymerase chain reaction (PCR), and antigen testing, are becoming available.

- In addition to vulvovaginitis and urethritis, trichomoniasis is associated with upper reproductive tract symptoms, an increased risk for adverse pregnancy outcomes (prematurity, low birth weight), and increased transmission of HIV infection.

Metronidazole (2 g single oral dose) is the recommended treatment. Patients should not consume alcohol for 2 days after treatment.

Although metronidazole is not known to be teratogenic in recommended dosages, it has been traditionally avoided during the first 12 weeks of pregnancy. Prompt early treatment during pregnancy relieves symptoms, reduces the risk for HIV transmission, and may improve pregnancy outcomes. Trichomoniasis should be treated before vaginal surgical procedures.

Metronidazole resistance is increasing and may be overcome by using tinidazole or using higher doses of metronidazole (2 g daily for 7 days). Reversible side effects of metronidazole include an “Antabuse-like reaction” with alcohol exposure, neutropenia, and peripheral neuropathy

ATROPHIC VAGINITIS

- Atrophic vaginitis is the most common cause of vaginal irritation among climacteric patients. As the term indicates, the atrophy of the vaginal epithelium results in secondary infection. The vulva and introitus quickly become involved because of the associated discharge, and the situation may be exacerbated by a foreign body (such as a pessary).

- Patients complain of vulvar irritation and discharge, which may be clear or purulent and yellow but occasionally will be blood tinged.

- Associated symptoms of frequency, urgency, and stress incontinence may occur.

COMMON CAUSES OF VULVOVAGINITIS

Infection	Symptoms/Findings	Diagnosis	Treatment
Yeast	Vaginal burning, itching, irritation; curdy white discharge	Wet prep and/or KOH microscopic examination shows pseudohyphae, or budding yeast	Butoconazole 2% cream*, 5 g intravaginally for 3 days, or fluconazole, 150 mg orally in a single dose†
Bacterial vaginosis	Asymptomatic, or vaginal odor; odor after intercourse, or increased discharge	Wet prep "clue cells"; release of amine odor; positive whiff test with KOH; vaginal fluid pH > 4.5	Metronidazole, 500 mg orally twice a day for 7 days or clindamycin cream 2%, one applicator (5 g) intravaginally at bedtime for 7 days†
Trichomoniasis	Asymptomatic, or increased thin or thick, green or yellow foul-smelling discharge; frothy in 2% to 3% of cases; strawberry cervix in 2% to 3% of cases	Motile trichomonads on microscopic examination of wet mount	Metronidazole, 2 g orally in a single dose or tinidazole, 2 g orally in a single dose (for resistant cases)†

Vaginitis

Chapter 22

Vulvovaginitis, Sexually Transmitted Infections, and Pelvic Inflammatory Disease

	Bacterial Vaginosis	Trichomoniasis	Vulvovaginal Candidiasis
Microbiology	- Shift in vaginal flora away from lactobacilli, to diverse bacteria including anaerobes - *Gardnerella vaginalis* predominant	- Protozoan *Trichomonas vaginalis* infection	- Overgrowth of *Candida albicans* (part of normal vaginal flora) - Other *Candida* also possible (ie glabrata)
Risk	- Sexual activity - Frequent douching	- Unprotected sex (passed person-to-person via sexual contact)	- Diabetes mellitus, antibiotic use, immunocompromised states
Clinical	- Odor, increased discharge	- Increased discharge, odor, pruritus, dysuria	- Vulvar pruritus, with possible burning, irritation
Exam	- Homogenous thin gray-white discharge	- Erythema of the vulva and vaginal mucosa - Punctate hemorrhages of upper vagina/ cervix ("Strawberry cervix") - Profuse, malodorous yellow-green discharge	- Erythematous, excoriated vagina - Thick, white, discharge with curdy texture without odor
pH	> 4.5	5.0-6.0	4.0-4.5
Whiff test	Positive	Occasionally positive	Negative
Wet Mount	Clue cells (epithelial cells with bacteria)	Motile trichomonads (bigger than WBC, smaller than epi cells)	Pseudohyphae
KOH Prep	Negative	Negative	Positive (pseudohyphae)
Management	PO Metronidazole (500 mg PO BID 5-7 days) Topical Metronidazole (5 days) (Vaginal or oral Clindamycin can also be used)	PO Metronidazole or Tinidazole (single dose) * Partners should also be evaluated and treated	PO Fluconazole (1 time) or topical azoles * Cases of recurrent disease may require longer PO or topical regimens * Glabrata treated with intravaginal boric acid
Other	Amsel Criteria (≥ 3/4): Classic vaginal discharge, elevated pH, clue cells, fishy odor		

AfraTafreeh.com

Other Common Sexually transmitted Infections
GENITAL HERPES



- Genital herpes is the most prevalent STI in the United States, with an estimated 50 million adults infected (active or latent) with herpes simplex virus (HSV) and about 1.5 million new cases occurring every year. It is a chronic lifelong viral infection with the potential for rare to frequent recurrences. This infection may have devastating emotional and social consequences.

- Unfortunately, only 10% to 20% of infected persons know that they are infected, and 70% of transmissions are from asymptomatic viral shedding from infected partners with no visible lesions. Individuals who are infected with HSV are at increased risk for acquiring and transmitting HIV.

- HSV has two serotypes, HSV-1 and HSV-2.

- HSV-1 is most commonly associated with oral lesions (cold sores), but about 30% of primary genital herpes is due to HSV-1.

- HSV-2 is the cause of 70% of primary genital herpes and 95% of recurrent genital herpes.

- The frequency of recurrences is much higher after a primary infection with HSV-2 than HSV-1. The virus enters the body through mucosa or micro abrasions in the skin and follows the sensory nerves to the dorsal spinal ganglion, where it remains dormant until reactivated.

- Transmission occurs through intimate genital, or oral. An infected mother can transmit the virus to her infant during delivery resulting in significant

- Primary genital herpes infection occurs when the infected person has no HSV-2 or HSV-1 antibodies.

- The usual clinical presentation is multiple, bilateral, and painful anogenital vesicles or ulcers with an erythematous base. Systemic symptoms may also be present, such as fever, headache, malaise, and lymphadenopathy.
- Acute cervicitis may be present. The lesions heal without scarring in 14 to 21 days.

- Recurrent genital herpes infection occurs when the infected person has HSV antibodies to the same serotype. The lesions are fewer, unilateral, and less painful. Systemic symptoms and lymphadenopathy are rare. The lesions heal without scarring in 5 to 7 days in immunocompetent individuals.

Laboratory tests that are used to confirm the diagnosis include

(1) viral culture that requires live cells from a lesion, which is expensive, time-consuming, and has a relatively low sensitivity (50% to 80%);

(2) PCR, which is expensive and very accurate, is very useful for testing cerebrospinal fluid, but is not used routinely on genital lesions;

And (3) type-specific serologic tests for HSV-1 and HSV-2 antibodies. These are highly sensitive and specific tests that can identify infected individuals who are asymptomatic.

- The goals of treatment for genital herpes are symptom relief, acceleration of lesion healing, and a Decrease in frequency of recurrences.

- The antiviral agents (acyclovir, famciclovir, and valacyclovir) are safe and effective for treating primary and episodic outbreaks and for providing suppressive therapy for Patients with chronic disease.

- No treatment can eradicate the latent virus from the dorsal ganglia of the spinal cord. Work is underway to develop an HSV vaccine.

HUMAN PAPILLOMAVIRUs (HPV)

- Genital HPV is a common viral STI with an estimated 20 million infected persons in the United States and 5 million new cases every year.

- Most HPV cases are latent infections with no visible lesions and are only diagnosed by DNA hybridization testing performed in the evaluation of an abnormal Pap smear.

- Subclinical infections have lesions that are only visible during colposcopy. Clinical infections are characterized by readily visible “warty” growths called condylomata acuminata on the vulva, vagina, cervix, urethra, and perianal area.

- There are about 1 million new cases of these external genital (venereal) warts every year in the United States.
- HPV infection usually clears spontaneously within 2 years, but recurrences are common. There are about 200 HPV subtypes. Some have been strongly associated with genital neoplasia and cancers, especially cervical cancer
- Biopsies of atypical or persistent lesions are needed to rule out neoplastic disease. Because these growths may also mimic condylomata lata, syphilis must be excluded if the lesions are atypical or do not respond to treatment.
- Transmission of HPV can occur even when there are no visible lesions.
- During pregnancy, condylomata may increase in number and size, but transmission from mother to infant is rare.

- An HPV-like particle vaccine (Gardasil) is now available that protects against four HPV serotypes (6, 8, 16, and 18), which together are responsible for 70% of cervical cancers and 90% of genital warts. This Vaccine was licensed in 2006 for use in females aged 9 to 26 years.

- Another vaccine against HPV types 16 and 18 only (Cervarix)
- These vaccines are highly effective (>95%) in women who have not been exposed to these HPV types.

The reasons for treating genital warts are to relieve symptoms (pain an
bleeding) and to ameliorate psychological and cosmetic concerns of th
patient. Multiple therapeutic modalities are available, and all are comparable.

Provider-applied topical therapies include

(1) podophyllin resin 10% to 25% in tincture of benzoin and

(2) trichloroacetic acid (TCA) or bichloracetic acid (BCA) 80% to 90%.

Patient-applied topical therapies include

(1) podofilox 0.5% solution or gel and

(2) imiquimod 5% cream.

Surgical therapies include
(1) cryotherapy,
(2) surgical excision,
(3) electrocautery,
(4) laser vaporization,
and (5) intralesional interferon.
Podophyllin, podofilox, and imiquimod should not be used during pregnancy.

CASE

Hx: A 24-year-old woman presents with a 3-day history of unpleasant-smelling, continuous vaginal discharge.She is sexually active with 1 partner for 3 years and is currently 10 weeks pregnant.

PE: External genitalia normal; Opaque copious vaginal discharge present with an amine odor; Underlying vaginal walls and cervix appear normal.



Labs

A sample of the discharge has a pH of 6.5; Addition of KOH produces a fishy odor and reveals no fungal elements on microscopy; A saline prep reveals:



- What would you do next?
- A. Start metronidazole 500 mg bid × 7 days.
- B. Start metronidazole 2 g × 1.
- C. Start clindamycin 300 mg bid × 7 days.
- D. No treatment. Have her return in her 2nd trimester and treat if still symptomatic.

Vaginosis and Vaginitis



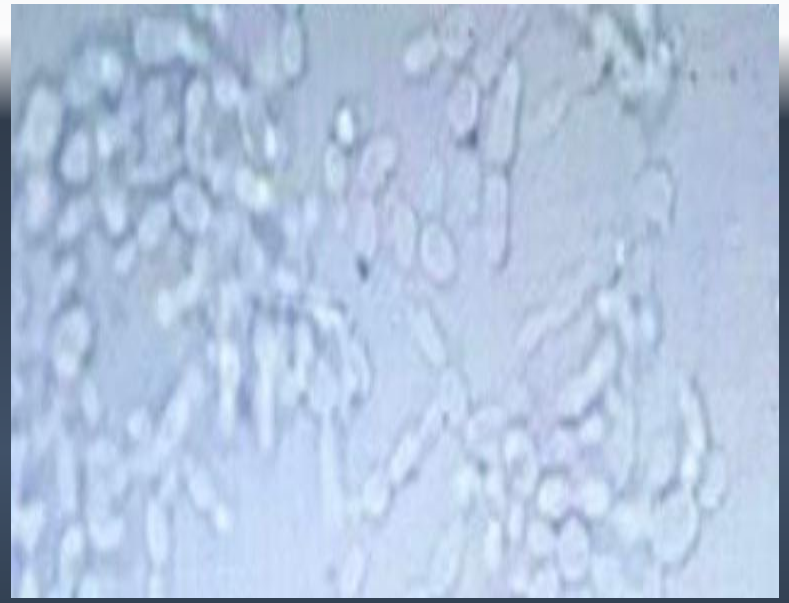
- Bacterial vaginosis
  - Lactobacillus replaced by anaerobes
    - Mobiluncus, Gardnerella
- Clinical: Amine odor, no irritation
- Vulvovaginal candidiasis
  - C. albicans
    - Clinical: Pruritus, white plaques on red base
    - If recurrent: R/O DM and HIV
- Trichomonas
  - Trichomonas vaginalis
  - Clinical: Profuse discharge,+ or - foul

Vaginosis and Vaginitis Diagnostic T

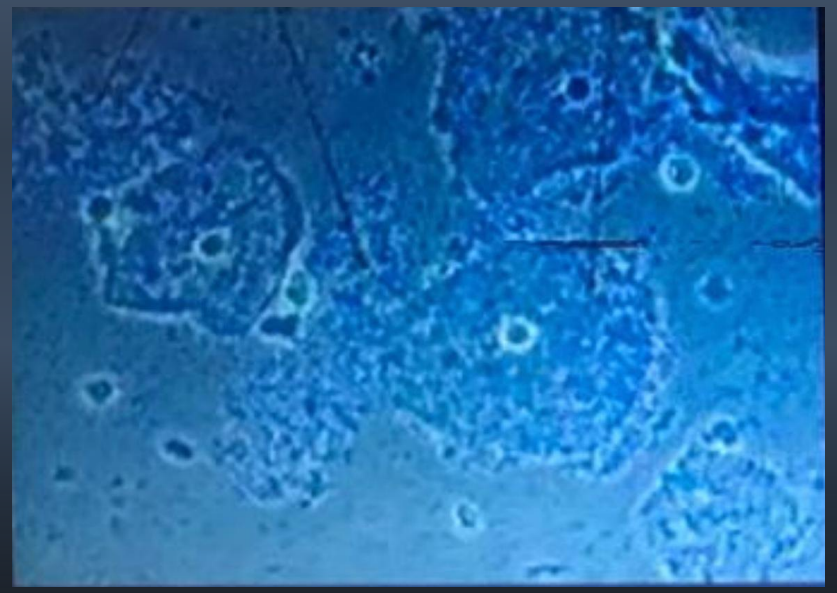
	Vaginal pH	Wet Prep	KOH Prep
Bacterial	> 5.0	Clue cells	Amine odor
Candida	< 5.0	Fungal elements	Fungal elements
Trichomonas	> 5.0	Trichomonads	Not diagnostic

Chapter 22

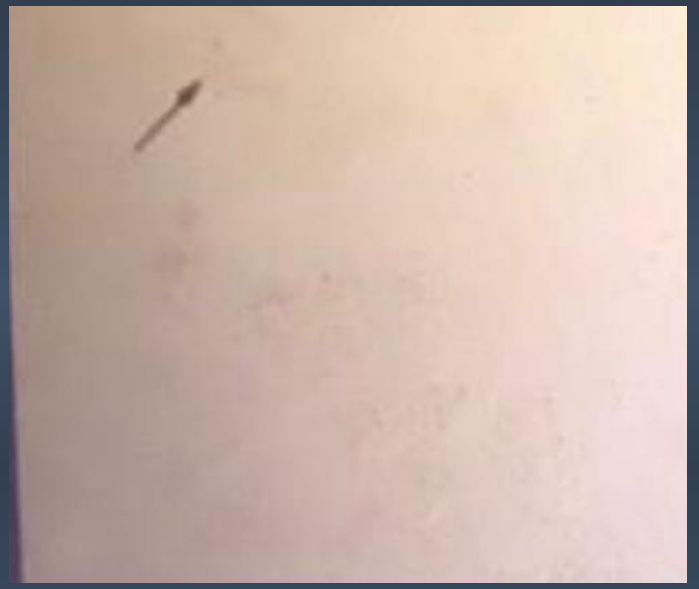
Vulvovaginitis, Sexually Transmitted Infections, and Pelvic Inflammatory Disease



Candida



Clue cells



Trichomonas

Vaginosis and Vaginitis Treatment

	1st Line	Other	Pregnancy
Bacterial		Clindamycin	Same
Candida	Fluconazole	Topical	Topical
Trichomonas	Metronidazole PO or gel × 7 days	Tinidazole 2 g × 1	Same clotrimazole or miconazole

Metronidazole in 1ST Trimester

- The Study
  - Meta-analysis 1966-1996
    - 4 cohort (2 prospective), 1 case-control
  - N = 199,451
- The Results
  - Malformations
    - Exposed = 189/2,524 (7.5%)
    - Not exposed = 30,887/196,927 (15.7%)
    - p = 0.32

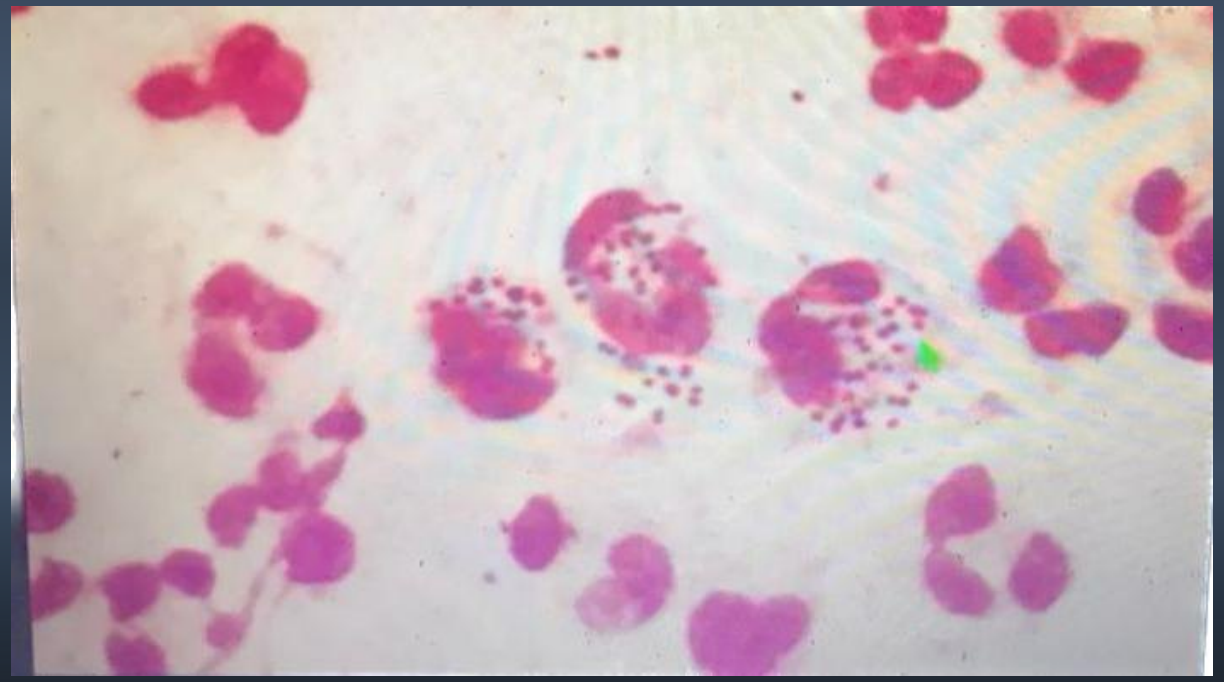
CASE

Hx : A 19-year-old man comes to your office complaining of severe burning with urination for 2 days. He noted pus from his urethra today. He had vaginal intercourse without protection with a new female partner 4 days ago. She has no symptoms and denies any prior STIs.

PE: Exam normal except for easily expressible pus from the urethra

Labs

Nucleic acid amplification testing (NAAT) is not available in your office. A Gram stain of the urethral pus is performed and is also sent for culture. (See below.)



Gram-negative coccobacilli

WHAT should be done next?
A. Send him to ED for NAAT prior to treatment.
B. Start ceftriaxone 250 mg IM × 1.
C. Start ceftriaxone 250 mg plus azithromycin 1 g PO × 1.
D. Start azithromycin 1 g PO × 1.

Neisseria gonorrhea in Men

Chapter 22

Vulvovaginitis, Sexually Transmitted Infections, and Pelvic Inflammatory Disease

Purulent, painful urethritis (rarely asymptomatic)
Incubation period 3-7 days

- Complications

Epididymitis, prostatitis

- Diagnosis

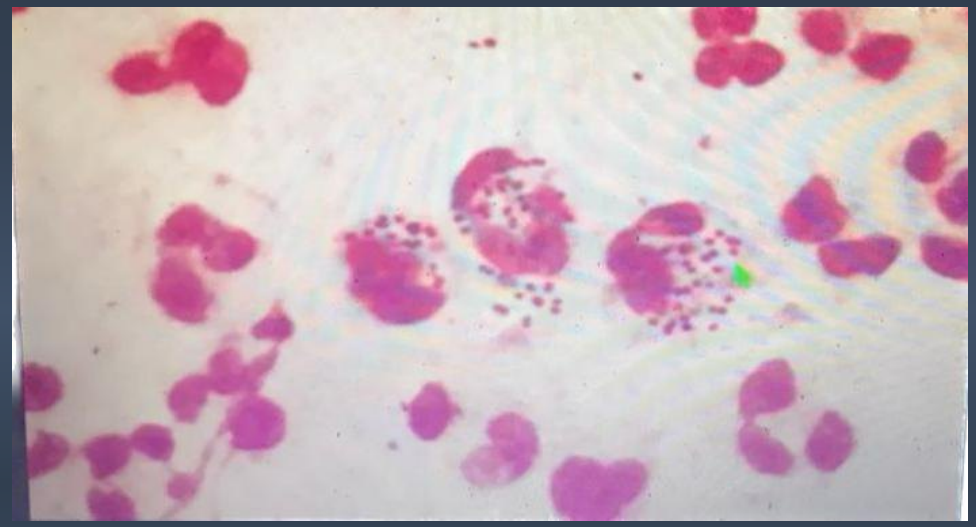
-Gram stain or discharge: Useful and diagnostic
-Sens = 90-95%, Spec = 95-100%
-NAAT of urine
- Culture if above not (+)

- Treatment (test for cure in 3 months)

- Ceftriaxone 250 mg IM x 1 and
- azithromycin 1,000 mg PO x 1

- Screening (annual)

- MSM



Neisseria gonorrhoeae in Women



- Primary site = Endocervix (80% asymptomatic)
- Secondary spread to vagina, urethra, rectum
- Complications
- Pelvic inflammatory disease
  - TOA, sterility, periurethral abscess
  - Rx: Foxy/doxy vs. clinda/gent
- Disseminated infection
- Oligoarthritis and cutaneous pustules

Neisseria gonorrhoege in Women



•Diagnosis

- Gram stain of endocervix: Not useful

• Sens = 50-70%, Spec = 80%

- NAAT of urine/vaginai swabs or cuiture required(80-90% sensitive)

• Treatment (test for cure in 3 months)

Uncomplicated

• Ceftriaxone 250 mg IM × 1 and azithromycin 1,000 mg PO × 1

Disseminated

•Ceftriaxone for 3 days, then total7- to 10-day course

• Screening (annual)H/O STI, new/multiple partners, unsafe sex, sex for drugs/money



chlamydia trachomatis

Epidemiology

The most common bacterial STI

• Majority of women are asymptomatic

- continuous reservoir

Clinical manifestations (7- to 14-day incubation)

Women: Cervicitis > acute urethral syndrome,> PID, > perihepatitis

Men: Urethritis > epididymitis

Diagnosis

- NAAT of urine

Treatment if uncomplicated (test for cure in 3 months)

Azithromycin 1 g PO × 1

• Screening (annual)

Men: MSM

Women: >24; > 24 new/multiple partners, h/o STI, unsafe sex, sex for drugs/money

Gonorrhea and Chlamydia Co-Infection Rates

The Study

Prospective study of the prevalence of STIs in all high schools in the U.S.

- 20,000 participants

•Prevalence

- Chlamydia = 4.19%

Gonorrhea = 0.43%

Co-infection

• Chlamydia if GC = 69.97%

• GC if Chlamydia = 7.29%

CHLAMYDIA



- Chlamydia has the highest incidence of any bacterial STI in the United States. Most cases (75%) are found in individuals who are younger than 25 years.
- Chlamydia trachomatis is an obligate intracellular bacteria that grows in vitro only in tissue culture. It can infect the columnar epithelium of the endocervix, urethra, endometrium, fallopian tubes, and rectum. This organism can persist for long periods in an asymptomatic carrier state.
- There is no vaccine available, and even though chlamydia antibodies are produced, they do not protect against reinfection.
- Most cases in males and females are asymptomatic.
- In those cases in which symptoms are present, the clinical manifestations of lower genital tract chlamydia infection are (1) mucopurulent cervicitis or mucopus, which is a yellow discharge coming from a swollen, red, friable cervix that bleeds easily, and (2) acute urethritis with dysuria but minimal frequency and urgency and a negative urine culture.

Various laboratory tests are used to confirm the diagnosis of chlamydia:

(1) tissue culture,

(2) (2) antigen tests, which are inexpensive and rapid with high sensitivity and specificity

(3) DNA hybridization tests and nucleic acid amplification tests (PCR and ligase chain reaction), which are rapid and very accurate. These newer DNA amplification tests can be done on urine specimens as well as cervical swabs and therefore they are very convenient for screening purposes.

Selective screening should be performed at least annually on all sexually active females younger than 26 years and all women with risk factors (e.g., unmarried, multiple partners, inconsistent use of barrier contraception, previous history of any STI, and all pregnant women).

Treatment

It is estimated that 30% of untreated chlamydial Cervicitis will progress to PID. Aggres
screening and appropriate early treatment have been shown to decrease the incidence of PID.

General treatment guidelines for lower genital tract chlamydial infection include the following:

(1) presumptive treatment with appropriate antibiotics (e.g., azithromycin, 1 g orally in a single dose, or doxycycline, 100 mg twice a day for 7 days);

(2) treatment of all sexual contacts within the 60 days before diagnosis;

(3) testing for other STIs, including chlamydia, syphilis, hepatitis B, and HIV.

Chlamydial infection during pregnancy can cause adverse outcomes for both mother and infant.

These include preterm labor, chorioamnionitis, and postpartum endometritis.

Intrapartum transmission to the infant can cause neonatal conjunctivitis and pneumonia.

GONORRHEA



- N. gonorrhoeae is the second most common bacterial STI in the United States.
- The organism is a gram-negative diplococcus, and it infects the same columnar epithelium as chlamydia.
- There is no vaccine available, and no immunity is conferred even though antibodies are produced.
- Most infected women, but as few as 5% of infected men, have no symptoms. If symptoms are present, the clinical manifestations of lower genital tract gonococcal infections are the same as for chlamydia and usually a negative urine culture in women.

- Laboratory tests that can be used to confirm the diagnosis include Gram stain of the discharge or cervix , which is rapid and inexpensive. The presence of gram negative diplococci in the leukocytes is very sensitive in men; however, in women, the sensitivity is only 50%.

- Thayer-Martin or Transgrow media culture is inexpensive but takes longer with a sensitivity of 90% and a specificity of 97%.

- DNA hybridization test is inexpensive and rapid, with high sensitivity and specificity, and nucleic acid amplification tests (PCR and ligase chain reaction [LCR]) are more expensive and rapid with high sensitivity and specificity. These tests can be done on urine or cervical swabs.

- Because most women with gonococcal cervical infection are asymptomatic, selective screening of high-risk persons is essential in attempting to control the progression and spread of this disease.
- Resistant strains of gonorrhea include penicillinase-producing N. gonorrhoeae, chromosomal mediated– resistant N. gonorrhoeae, tetracycline-resistant N. gonorrhoeae, and quinolone-resistant N. gonorrhoeae.

General treatment guidelines for lower genital tract gonococcal infection include

(1) treatment with appropriate antibiotics (e.g., cefixime, 400 mg orally in a single dose, or ceftriaxone 125 mg intramuscularly in a single dose);

(2) simultaneous treatment for chlamydia (i.e., 1 g of azithromycin orally in a single dose is indicated because 20% to 40% of gonococcal cervical infections also have chlamydia);

(3) treatment of all sexual contacts within the 60 days before diagnosis;

(4) testing for other STIs, including chlamydia, syphilis, hepatitis B, and HIV.

Gonococcal infection during pregnancy can cause adverse outcomes for both the mother and the infant.

These include preterm labor and delivery, chorioamnionitis, postpartum endometritis, and neonatal conjunctivitis (ophthalmia neonatorum).

Pelvic Inflammatory Disease

- More than 10% of reproductive-aged women report a history of PID.
- The most important single-agent causes of PID include C. trachomatis, N. gonorrhoeae, and genital mycoplasmas (M. hominis, U. urealyticum, and Mycoplasma genitalium).
- M. hominis, U. urealyticum, and M. genitalium are widely recognized causes of nongonococcal urethritis in males and females.

- PID develops in 15% to 30% of women with inadequately treated gonococcal or chlamydial cervicitis.

- The highest rates of chlamydial cervicitis occur in sexually active adolescents and young adults between the ages of 20 and 25 years. The largely asymptomatic nature of chlamydial cervicitis in women and urethritis in men makes routine screening and treatment for chlamydia necessary for the prevention of PID.

- The most common microbial isolates recovered from patients at laparoscopy or at drainage of pelvic abscesses are endogenous lower reproductive tract or gastrointestinal microflora, including E. coli, Bacteroides and Prevotella species, G. vaginalis, and anaerobic streptococci. These common sexually transmitted and endogenous agents should be covered during antibiotic treatment for PID.

SYMPTOMS

Women with symptomatic PID commonly have lower abdominal pain and tenderness, abnormal vaginal discharge, chills, and fever. Less common symptoms include irregular vaginal bleeding, dysuria, nausea, and vomiting. No specific combination of symptoms is consistently associated with PID. Some women are asymptomatic.

SIGNS

- Clinical signs in women with laparoscopically confirmed PID most frequently include lower abdominal tenderness, with or without rebound tenderness; uterine and adnexal tenderness to palpation and motion; and findings of mucopurulent cervicitis .
- Fever is the least common finding.
- A pregnancy test should be performed when symptoms or signs of pregnancy are present.

COMPLICATIONS

- Women with clinical PID were 6 times more likely to have an ectopic pregnancy and 14 times more likely to have tubal factor infertility than women without PID.

- Women with a history of PID were 6 to 10 times more likely than healthy controls to have the diagnosis of endometritis, suffer from chronic pelvic pain, or require a hysterectomy. Women with prior salpingitis are at increased risk for premature labor.

INVESTIGATIONS



- Nucleic acid, antigenic, or culture tests should be done to detect chlamydial and gonococcal infections. Confirmatory laboratory evidence includes leukocytosis, increased erythrocyte sedimentation rate, or C-reactive protein level, and microscopic or leukocyte esterase test evidence of purulent cervical discharge (mucopus).

- Pelvic ultrasonic studies may show enlarged, tender fallopian tubes as well as cul-de-sac fluid.

TREATMENT



- Empiric antibiotic regimens should be aimed at treating likely causative agents, that is, N. gonorrhoeae, C. trachomatis, genital mycoplasmas, and BV-associated endogenous microflora. The latter include anaerobic (Bacteroides and Prevotella species and anaerobic streptococci) as well as aerobic organisms (G. vaginalis, E. coli, and facultative streptococci). Except for N. gonorrhoeae and some anaerobes, resistance is not yet a clinical problem.

- The need for hospitalization is an important treatment decision . Women with severe infections or an inability to take and absorb oral antibiotics (nausea, vomiting, possible peritonitis, and ileus) should be hospitalized and treated until clinical improvement is evident.

- Similarly, women with a questionable diagnosis, pregnancy, or unreliability, should be admitted initially and treated with parenteral agents to ensure compliance and treatment efficacy, as should those who fail to respond to outpatient therapy.

TABLE 22-2

CENTERS FOR DISEASE CONTROL AND PREVENTION RECOMMENDED TREATMENTS FOR PELVIC INFLAMMATORY DISEASE, 2006*

Regimen A	Regimen B
INPATIENT TREATMENT	
Cefoxitin, 2 g IV q6hr *or* Cefotetan, 2 g IV q12hr *plus* Doxycycline, 100 mg IV q12hr until improved, followed by doxycycline, 100 mg orally twice daily, to complete 14 days	Clindamycin, 900 mg IV q8hr *plus* Gentamicin, 2 mg/kg IV once, followed by 1.5 mg/kg IV q8hr until improved, followed by doxycycline, 100 mg orally bid, to complete 14 days
OUTPATIENT TREATMENT	
Ceftriaxone, 250 mg IM in a single dose, plus doxycycline, 100 mg twice daily, to complete 14 days *with or without* Metronidazole, 500 mg orally twice daily for 14 days	Cefoxitin, 2 g IM single dose, and probenecid, 1 g orally, *plus* Doxycycline, 100 mg twice daily, to complete 14 days *with or without* Metronidazole, 500 mg orally twice daily for 14 days

PREVENTION

- Single-dose regimens, such as azithromycin, 1 g orally (for chlamydial infections), and cefixime, 400 mg, or intramuscular ceftriaxone, 125 mg, simplify treatment and ensure greater compliance.

- To minimize the risk for reinfection, partners for the past 60 days should be identified, diagnosed, and given specific treatment or treated empirically for both chlamydial infection and gonorrhea.

- Most infected male partners are asymptomatic. This practice should minimize recurrence and reinfection that can lead to permanent adhesions.

TUBO-OVARIAN ABSCESSs (TOA)



- TOA involving fallopian tubes, ovaries, bowel, and possibly other pelvic structures is a potentially lethal complication of PID. Inflammatory complexes also represent severe infection but do not contain Significant amounts of pus and are more easily treated with antibiotics.

- TOAs occur in about 10% of women hospitalized for PID. A TOA in the course of the initial episode of PID represents severe infection in which the host is unable to localize tissue damage. Some TOAs are caused by reactivation of past infection or repeated infections, whereas others may occur as a result of postpartum or postoperative infections.

Rupture of a TOA causes spreading peritonitis, which can be rapidly lethal in the absence of expeditious surgical drainage, antimicrobial treatment, and systemic vital organ support. TOAs may cause considerable long-term morbidity from irreversible tubal and ovarian damage, with subsequent infertility, chronic pain, and gonadal failure. Rarely, death results from uncontrolled sepsis

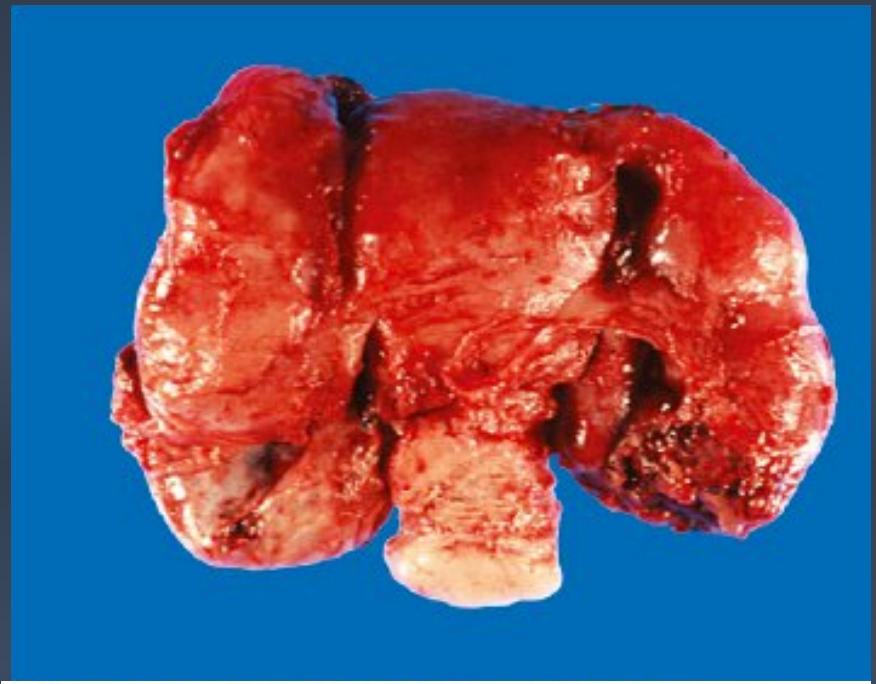


FIGURE 22-8 Gross appearance of bilateral tubo-ovarian abscesses. *(From Kumar V, et al: Robbins and Cotran Pathologic Basis of Disease, 7th ed. Philadelphia, Saunders, 2005.)*

A TOA is distinguished from uncomplicated endometritis or salpingitis by the presence of a tender inflammatory adnexal mass.

Confirmation of the diagnosis may require the use of imaging techniques such as ultrasonography, computed tomography, or magnetic resonance imaging, as depicted in the figure .

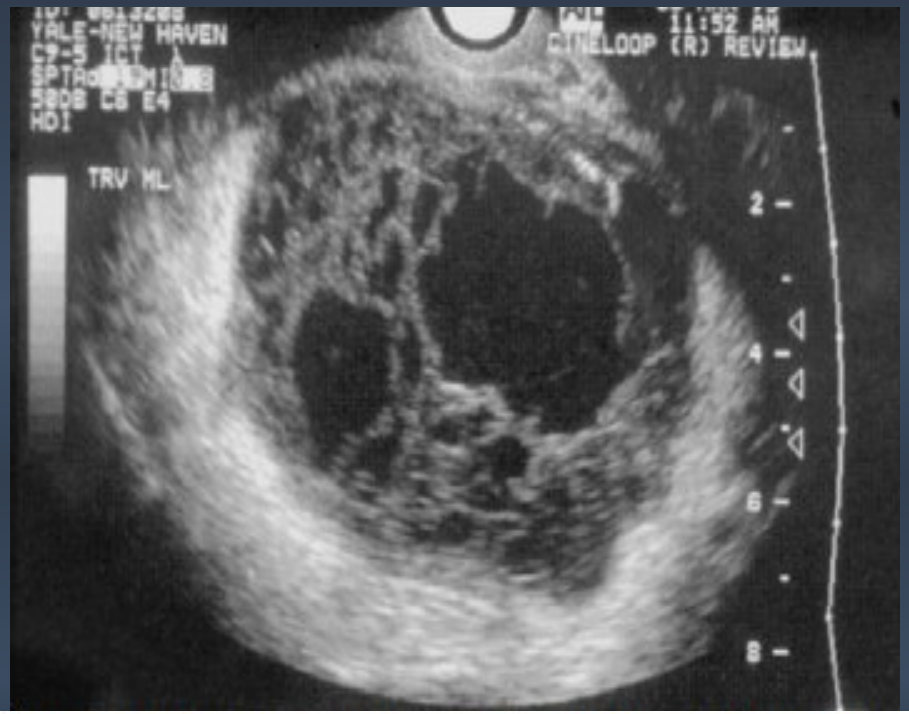


FIGURE 22-9 Pelvic magnetic resonance imaging of a patient with tubo-ovarian abscesses.

LESS COMMON SEXUALLY TRANSMITTED INFECTIONS AND INFESTATION



- √ Chancroid is caused by Haemophilus ducreyi. The lesions, called soft chancres, are painful and are usually accompanied by pelvic adenopathy. Diagnosis is made clinically and confirmed with cultures. Treatment is with azithromycin, 1 g orally in a single dose, or ceftriaxone, 250 mg intramuscularly in a single dose.

- √ Granuloma inguinale (donovanosis) is caused by Calymmatobacterium granulomatis. The lesions are red and raised. Treatment is with doxycycline, 100 mg twice a day for a minimum of 3 weeks.

- √ Lymphogranuloma venereum is caused by C. trachomatis. Vesicles progress to bubo formation. A complement fixation test is available for diagnosis. Treatment is with doxycycline, 100 mg twice a day for at least 3 weeks.

✓ Molluscum contagiosum is caused by Poxviridae.

The raised papules with waxy cores are desiccated or treated with cryotherapy or topical imiquimod.

✓ Syphilis is relatively uncommon in the United States. It is particularly important, however, for the obstetrician to recognize this infection in the pregnant patient or in the patient who may become pregnant. Syphilis is caused by Treponema pallidum.

Treatment is with parenteral (intramuscular) benzathine penicillin G.

✓ Pediculosis pubis is caused by the crab louse Phthirus pediculosis, a millimeter-sized insect that infests the pubic area.

Treatment is with permethrin 1% crème rinse.

✓ Scabies is caused by a microscopic mite, Sarcoptes scabiei. Infestation is common and found worldwide.

Treatment is with permethrin 5% crème or ivermectin.



Reproductive tract infections part II

Prepared and lectured by

Oday Hamad , MD

Teaching assistant , AUG

TREPONEMA



- Treponema pallidum
- Disease
- Treponema pallidum causes syphilis

Important Properties

- Treponema pallidum has not been grown on bacteriologic media or in cell culture.
- Nonpathogenic treponemes, which are part of the normal flora of human mucous membranes, can be cultured.
- Treponema pallidum grows very slowly. The medical importance of that fact is that antibiotics must be present at an effective level for several weeks to kill the organisms and cure the disease.
- For example, benzathine penicillin is the form of penicillin used to treat primary and secondary syphilis because the penicillin is released very slowly from this depot preparation, and bactericidal concentrations are present for weeks after administration of the antibiotic.

- The antigens of T. pallidum induce specific antibodies, which can be detected by immunofluorescence or hemagglutination tests in the clinical laboratory.

- They also induce nonspecific antibodies (reagin), which can be detected by the flocculation of lipids (cardiolipin) extracted from normal mammalian tissues (e.g., beef heart).

- Both specific antitreponemal antibody and nonspecific reagin are used in the serologic diagnosis of syphilis.

Transmission & Epidemiology

Treponema pallidum is transmitted from spirochete containing lesions of skin or mucous membranes (e.g., genitalia, mouth, and anus) of an infected person to other persons by intimate contact. It can also be transmitted from pregnant women to their fetuses.

Rarely, blood for transfusions collected during early syphilis is also infectious.

Treponema pallidum is a human organism only.

There is no animal reservoir.

Syphilis occurs worldwide, and its incidence is increasing.

Pathogenesis & Clinical Findings

- Treponema pallidum produces no important toxins or enzymes. The organism often infects the endothelium of small blood vessels, causing endarteritis. This occurs during all stages of syphilis but is particularly important in the pathogenesis of the brain and cardiovascular lesions seen in tertiary syphilis.

- In primary syphilis, the spirochetes multiply at the site of inoculation, and a local, nontender ulcer (chancre) usually forms in 2 to 10 weeks . The ulcer heals spontaneously, but spirochetes spread widely via the bloodstream (bacteremia) to many organs.

- One to 3 months later, the lesions of secondary syphilis may occur. These often appear as a maculopapular rash, notably on the palms and soles , or as moist papules on skin and mucous membranes (mucous patches).

- Moist lesions on the genitals are called condylomata lata . These lesions are rich in spirochetes and are highly infectious, but they also heal spontaneously. Patchy alopecia also occurs. Constitutional symptoms of secondary syphilis include low-grade fever, malaise, anorexia, weight loss, headache, myalgias, and generalized lymphadenopathy.

- Pharyngitis, meningitis, nephritis, and hepatitis may also occur. In some individuals, the symptoms of the primary and secondary stages may not occur, and yet the disease may progress.

About one-third of these early (primary and secondary) syphilis cases will "cure" themselves, without treatment.

Another third remain latent (i.e., no lesions appear, but positive serologic tests indicate continuing infection).

The latent period can be divided into early and late stages. In the early latent period, which can last for 1 or 2 years after the secondary stage, the symptoms of secondary syphilis can reappear and patients can infect others. In the late latent period, which can last for many years, no symptoms occur and patients are not infectious.

In the remaining one third of people, the disease progresses to the tertiary stage .

Tertiary syphilis may show granulomas (gummas), especially of skin and bones; central nervous system involvement, also known as neurosyphilis (e.g., tabes, paresis); or cardiovascular lesions (e.g., aortitis, aneurysm of the ascending aorta).

Treponema pallidum also causes congenital syphilis .

The organism is transmitted across the placenta, typically after the third month of pregnancy, and fetal infection can occur. In the infected neonates, skin and bone lesions, such as Hutchinson's teeth, mulberry molars, saber shins, saddle nose, snuffles, and frontal bossing, are common.

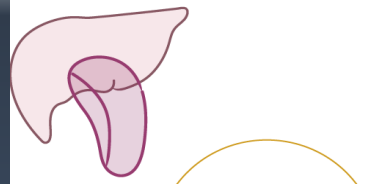
Other findings, such as hepatosplenomegaly, interstitial keratitis, and eighth nerve deafness, also occur. Fetal infection can also result in stillbirth.

Immunity to syphilis is incomplete. Antibodies to the organism are produced but do not stop the progression of the disease. Patients with early syphilis who have been treated can contract syphilis again. Patients with late syphilis are relatively resistant to reinfection.

Congenital Syphillis

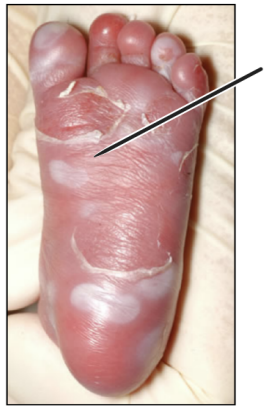
Early (First 2 years)

Hepatosplenomegaly



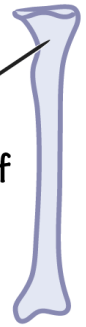


"Snuffles" (syphilitic rhinitis)



Vesicular & bullous eruptions

Bilateral destruction of medial tibial metaphyses.

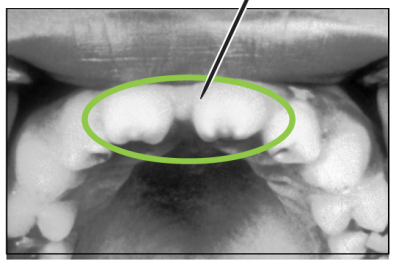


Wimberger sign

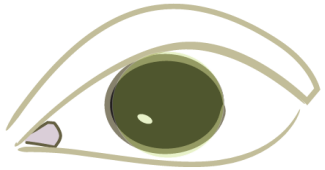
Late

Hutchinson's Triad:

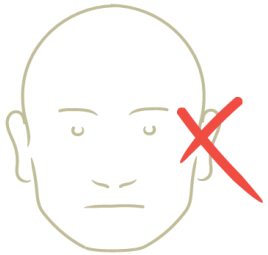
Hutchinson incisors

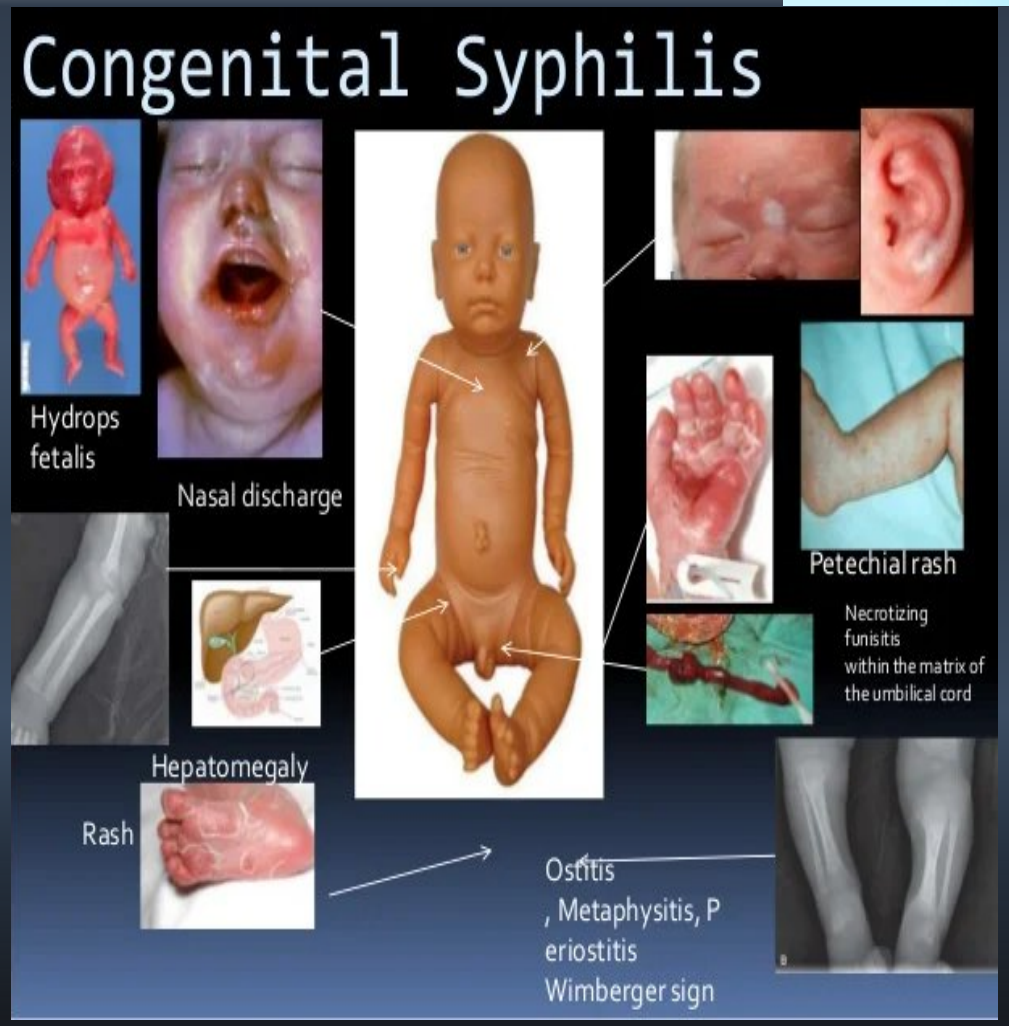


Interstitial keratinitis



Sensorineural deafness





Laboratory Diagnosis

There are three important approaches.

Microscopy Spirochetes are demonstrated in the lesions of primary or secondary syphilis, such as chancres or condylomata lata, by dark field microscopy or by direct fluorescent antibody (DFA) test.

They are not seen on a Gram-stained smear. In biopsy specimens, such as those obtained from the gummas seen in tertiary syphilis, histologic stains such as



FIGURE 24–1 *Treponema pallidum*—dark field microscopy. The coiled form of this spirochete is in the center of the field. (Source: Dr. Schwartz, Centers for Disease Control and Prevention.)

Nonspecific Serologic Tests

These tests involve the use of nontreponemal antigens.

Extracts of normal mammalian tissues (e.g., cardiolipin from beef heart) react with antibodies in serum samples from patients with syphilis. These antibodies, which are a mixture of IgG and IgM, are called “reagin” antibodies.

Flocculation tests (e.g., Venereal Disease Research Laboratory [VDRL] and rapid plasma reagin [RPR] tests) detect the presence of these antibodies. These tests are positive in most cases of primary syphilis and are almost always positive in secondary syphilis.

The titer of these nonspecific antibodies decreases with effective treatment, in contrast to the specific antibodies, which are positive for life.

False-positive reactions occur in infections such as leprosy, hepatitis B, and infectious mononucleosis and in various autoimmune diseases. Therefore, positive results have to be confirmed by specific tests .

Results of nonspecific tests usually become negative after treatment and should be used to determine the response to treatment.

These tests can also be falsely negative as a result of the prozone phenomenon. In the prozone phenomenon, the titer of antibody is too high (antibody excess), and no flocculation will occur. On dilution of the serum, however, the test result becomes positive . These tests are inexpensive and easy to perform and therefore are used as a method of screening the population for infection

Nontreponemal test

- False negative

- Early primary S
- Latent acquired S
- Late CS
- *Prozone* phenomenon

- False Positive
  - Viral infection (EBV, Hepatitis, Varicela, Measles)
  - Lymphoma
  - TB
  - Malaria
  - Endocarditis
  - CT diseases
  - Pregnancy
  - IV drugs
  - Wharton Jelly contamination in cord samples

The laboratory diagnosis of congenital syphilis is based on the finding that the infant has a higher titer of antibody in the VDRL test than has the mother.

Furthermore, if a positive VDRL test result in the infant is a false-positive one because maternal antibody has crossed the placenta, the titer will decline with time.

If the infant is truly infected, the titer will remain high.

However, irrespective of the VDRL test results, any infant whose mother has syphilis should be treated.

Specific Serologic Tests

- These tests involve the use of treponemal antigens and therefore are more specific than those described earlier. In these tests, T. pallidum reacts in immunofluorescence (FTA-ABS)2 or hemagglutination (TPHA, MHA-TP)3 assays with specific treponemal antibodies in the patient's serum.
- These antibodies arise within 2 to 3 weeks of infection; therefore, the test results are positive in most patients with primary syphilis.
- These tests remain positive for life after effective treatment and cannot be used to determine the response to treatment or reinfection. They are more expensive and more difficult to perform than the nonspecific tests and therefore are not used as screening procedures.

Treatment

- Penicillin G is effective in the treatment of all stages of syphilis.
- A single injection of benzathine penicillin G (2.4 million units) can eradicate T. pallidum and cure early (primary and secondary) syphilis.
- Note that benzathine penicillin is used because the penicillin is released very slowly from this depot preparation.
- Treponema pallidum grows very slowly, which requires that the penicillin be present in bactericidal concentration for weeks.
- If the patient is allergic to penicillin, doxycycline can be used but must be given for prolonged periods to effect a cure.
- In neurosyphilis, high doses of aqueous penicillin G are administered because benzathine penicillin penetrates poorly into the central nervous system. No resistance to penicillin has been observed.
- However, strains resistant to azithromycin have emerged.

- Pregnant women with syphilis should be treated promptly with the type of penicillin used for the stage of their disease. Neonates with a positive serological test should also be treated. Although it is possible that the positive test is caused by maternal antibody rather than infection of the neonate, it is prudent to treat without waiting several months to determine whether the titer of antibody declines.
- More than half of patients with secondary syphilis who are treated with penicillin experience fever, chills, myalgias, and other influenza like symptoms a few hours after receiving the antibiotic.
- This response, called the Jarisch- Herxheimer reaction, is attributed to the lysis of the treponemes and the release of endotoxin-like substances. Patients should be alerted to this possibility, advised that it may last for up to 24 hours, and told that symptomatic relief can be obtained with aspirin.
- The Jarisch-Herxheimer reaction also occurs after treatment of other spirochetal diseases such as Lyme disease, leptospirosis, and relapsing fever.
- Tumor necrosis factor (TNF) is an important mediator of this reaction because passive immunization with antibody against TNF can prevent its symptoms.

Hx: A 33-year-old woman returns for follow-up after treatment of a syphilitic chancre on her labia 15 months ago. Her RPR at that time was (+) at a titer of 1:64, and her FTA-ABS was also (+). She was treated with 2.4 mU of benzathine penicillin IM × 1. She has had 3 male sexual partners since then. She has no other medical problems.

PE: Exam normal

Lab: RPR (+) at a titer of 1:32

What should be done next?

A. Retreat with benzathine penicillin 2.4 mU IM × 1.

B. Retreat with benzathine penicillin 2.4 mU IM q week × 3.

C. Perform a lumbar puncture prior to treatment.

D. Have her return in 6 months for repeat RPR.

Seroreversion of RPR in Treated Syphilis

- Time to seroreversion
  - Primary = 1 year
  - Secondary = 2 years
  - Late latent = 5 years
- Failure to serorevert
  - Reinfection
  - Biological false (+)
  - Inadequate therapy
    - Neurosyphilis does not respond to benzathine pen

Syphilis - CSF Exam in Syphilis



- Indications

  Neurologic or ophthalmologic signs/S

  - Signs of active tertiary syphilis
    - Aortitis
    - Gumma

  Treatment failure

- Diagnostic of neurosyphilis (any of):-

-VDRL (+)

-Protein > 45 mg/Dl

- Lymphocytes > 5 cells/μL

Syphilis - Screening



- •Test at-risk groups
- - MSM, HIV infection
- - Incarceration, sex worker
- - Men 20-29 years of age
- Frequency of testing

  MSM, HIV infection: q 3 months

- Others: Unclear

HUMAN IMMUNODEFICIENCY VIRUS AND ACQUIRED IMMUNODEFICIENCY SYNDROME

Epidemiology

Since the first description of AIDS in 1981 and the identification of the causative organism, HIV, in 1983, more than 78 million people are estimated to have been infected and 39 million people have died. At least 35million people worldwide are living with HIV infection.

Highly active anti-retroviral therapy {ART) has dramatically reduced mortality for those who are able to access care, transforming HIV from a universally fatal infection into a long-term manageable condition, with a consequent rise in global prevalence

HIV-associated indicator conditions

Respiratory

- Tuberculosis, pneumocystis[a], bacterial pneumonia, aspergillosis

Neurology

- Cerebral toxoplasmosis[a], primary cerebral lymphoma[a], cryptococcal meningitis[a], progressive multifocal leucoencephalopathy[a], aseptic meningitis/encephalitis, cerebral abscess, space-occupying lesion of unknown cause, Guillain–Barré syndrome, transverse myelitis, peripheral neuropathy, dementia

Dermatology

- Kaposi's sarcoma[a], severe/recalcitrant seborrhoeic dermatitis, severe/recalcitrant psoriasis, multidermatomal/recurrent herpes zoster

Gastroenterology

- Persistent cryptosporidiosis[a], oral candidiasis, oral hairy leukoplakia, chronic diarrhoea of unknown cause, weight loss of unknown cause, *Salmonella*, *Shigella*, *Campylobacter*, hepatitis B infection, hepatitis C infection

Oncology

- Non-Hodgkin's lymphoma[a], anal cancer, anal intraepithelial dysplasia, lung cancer, seminoma, head and neck cancer, Hodgkin's lymphoma, Castleman's disease

Gynaecology

- Cervical cancer[a], vaginal intraepithelial neoplasia, cervical intraepithelial neoplasia, grade 2 or above

Haematology

- Any unexplained blood dyscrasia, including thrombocytopenia, neutropenia and lymphopenia

Ophthalmology

- Cytomegalovirus retinitis, infective retinal diseases including herpesviruses and toxoplasma, any unexplained retinopathy

ENT

- Lymphadenopathy of unknown cause, chronic parotitis, lymphoepithelial parotid cysts

Other

- Mononucleosis-like syndrome (primary HIV infection), pyrexia of unknown origin, any lymphadenopathy of unknown cause, any sexually transmitted infection

Mother-to-child transmission (transplacental, perinatal, breast-feeding)



- Vertical transmission is the most common route of HIV infection in children. European studies suggest that, without intervention, 15% of babies born to HIV-positive mothers are likely to be infected, although rates of up to 40% have been reported from Africa and the USA.

- Increased vertical transmission is associated with advanced disease in the mother, maternal viral load, prolonged and premature rupture of membranes, and chorioamnionitis. Transmission can occur in utero, although the majority of infections take place perinatally. Breast-feeding has been shown to double the risk of vertical transmission.

In the developed world, interventions to reduce vertical transmission, including screening for infection in pregnancy, the use of anti-retroviral agents (ARVs) and the avoidance of breast-feeding, have led to a dramatic fall in the numbers of infected children. In the UK, the risk of vertically transmitted infection is 1 : 1000. The lack of access to these interventions in resource-poor countries in which 90% of infections occur is a major global issue.

Contaminated blood, blood products and organ donations

Screening of blood and blood products was introduced in 1985 in Europe and North America. Prior to this, HIV infection was associated with the use of clotting factors (for hemophilia) and with blood transfusions.

In some parts of the world where blood products may not be screened and in areas where the rate of new HIV infections is very high, transfusion-associated transmission continues to occur.

Contaminated needles (intravenous drug misuse, injections and needle-stick injuries)

- The practice of sharing needles and syringes for intravenous drug use continues to be a major route of transmission of HIV in parts of South-east Asia, Latin America and Eastern Europe. In some areas, including the UK, successful education and needle exchange .
- schemes have reduced the rate of transmission by this route. Iatrogenic transmission from needles and syringes used in developing countries is reported. Healthcare workers have a risk of approximately 0.3% following a single needle-stick injury with known HIV positive blood.

CLINICAL APPROACH TO THE PATIENT WITH HIV



Diagnosis and natural history

- HIV is now a manageable chronic condition with a life expectancy that can match that of the general population, in those who start effective ART early enough .
- Starting treatment when disease is more advanced compromises clinical outcomes.

Investigation of HIV

HIV infection is diagnosed either by detection of virus-specific antibodies (anti-HIV) or by direct identification of viral material.

Detection of IgG antibody to envelope components

This is the most commonly used marker of infection. The routine tests used for screening are based on enzyme-linked immunosorbent assay (ELISA) techniques, which may be confirmed with Western blot assays. Up to 3months (mean 6weeks) may elapse from initial infection to antibody detection (serological latency, or window period).

These antibodies to HIV have no protective function and persist for life. As with all IgG antibodies, anti-HIV will cross the placenta. All babies born to HIV-positive women will thus have the antibody at birth. In this situation, anti-HIV antibody is not a reliable marker of active infection, and in uninfected babies will be gradually lost over the first 18 months of life.

- Simple and rapid HIV antibody assays are increasingly available, giving results within minutes. Assays that can utilize alternative body fluids to serum/plasma, such as oral fluid, whole blood and urine, are now available and home testing kits are being developed.

- These tests are extremely sensitive and may give false-positive results, making it necessary to perform a confirmatory test.

- A serologic testing algorithm for recent HIV seroconversions (STARHS) can be used to identify recently acquired infection.

- A highly sensitive ELISA that is able to detect HIV antibodies 6-8 weeks after infection is used on blood in patients with a positive oral fluid test, in parallel with a less sensitive (detuned) test that identifies later HIV antibodies within 130days.

- A positive result on the sensitive test and a negative 'detuned' test are indicative of recent infection, while positive results on both tests point to an infection that is more than 130days old.

- The major application of this is in epidemiological surveillance and monitoring.

Box 12.9 Summary of the Centers for Disease Control (CDC) classification of HIV infection

Absolute CD4 count (/mm^3)	A *Asymptomatic or persistent generalized lymphadenopathy or acute seroconversion illness*	B *HIV-related conditions,*[a] *not A or C*	C *Clinical conditions listed in AIDS surveillance case definition (see Box 12.10)*
>500	A1	B1	C1
200–499	A2	B2	C2
<200	A3	B3	C3

[a]Examples of category B conditions include: bacillary angiomatosis, candidiasis (oropharyngeal), constitutional symptoms, oral hairy leukoplakia, herpes zoster involving more than one dermatome, idiopathic thrombocytopenic purpura, listeriosis, pelvic inflammatory disease, especially if complicated by tubo-ovarian abscess, peripheral neuropathy.

Box 12.10 AIDS-defining conditions

- Candidiasis of bronchi, trachea or lungs
- Candidiasis, oesophageal
- Cervical carcinoma, invasive
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (1-month duration)
- Cytomegalovirus (CMV) disease (other than liver, spleen or nodes)
- CMV retinitis (with loss of vision)
- Encephalopathy, HIV-related
- Herpes simplex, chronic ulcers (1-month duration), or bronchitis, pneumonitis or oesophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (1-month duration)
- Kaposi's sarcoma
- Lymphoma, Burkitt's
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma (primary) of brain
- *Mycobacterium avium-intracellulare* complex or *M. kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis*, any site
- *Mycobacterium*, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis jiroveci* pneumonia
- Pneumonia, recurrent
- Progressive multifocal leucoencephalopathy
- *Salmonella* septicaemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome, due to HIV

End-organ effects of HIV



Neurological disease

- Infection of the nervous tissue occurs at an early stage but clinical neurological involvement increases as HIV advances. This includes AIDS dementia complex (ADC), sensory polyneuropathy and aseptic meningitis .

- These conditions are much less common since the introduction of ART. The pathogenesis is thought to be due both to the release of neurotoxic products by HIV itself and to cytokine abnormalities secondary to immune dysregulation.

- Sensory polyneuropathy is seen in advanced HIV infection, mainly in the legs and feet, although hands may be affected. Severe forms cause intense pain, usually in the feet, which disrupts sleep, impairs mobility and generally reduces the quality of life
- Autonomic neuropathy may also occur with postural hypotension and diarrhoea. Autonomic nerve damage is found in the small bowel

Box 12.11 Some mucocutaneous manifestations of HIV infection[a]

Skin

- Dry skin and scalp
- Onychomycosis
- Seborrhoeic dermatitis
- Tinea: cruris, pedis
- Pityriasis: versicolor, rosea
- Folliculitis
- Acne
- Molluscum contagiosum
- Warts
- Herpes zoster: multi-dermatomal disseminated
- Papular pruritic eruption
- Scabies
- Ichthyosis
- Kaposi's sarcoma

Mucous membranes

- Candidiasis: oral, vulvovaginal
- Oral hairy leukoplakia
- Aphthous ulcers
- Herpes simplex: genital, oral, labial
- Periodontal disease
- Warts: oral, genital

[a]*See also pages 1384–1385.*

Hematological complications

These are common in advanced HIV infection.

- Lymphopenia progresses as the CD4 count falls.
- Anaemia of chronic HIV infection is usually mild, normochromic and normocytic.
- Neutropenia is common and usually mild.
- Isolated thrombocytopenia may occur early in infection and be the only manifestation of HIV for some time