Lower genital tract infections

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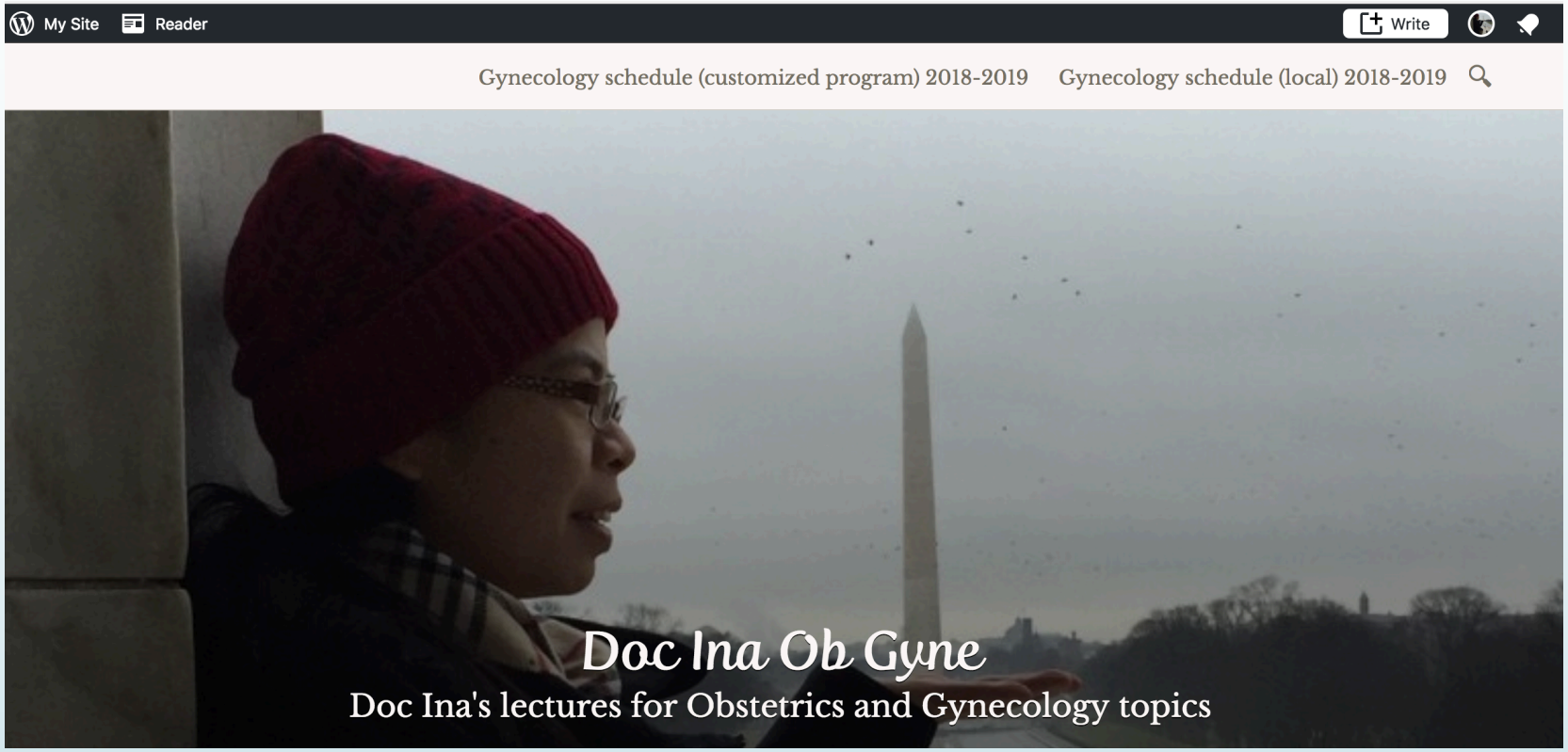

Main Reference

- Comprehensive Gynecology 7th edition, 2017 (Lobo RA, Gershenson DM, Lentz GM, Valea FA *editors);* chapter 23, Genital tract infections

Outline

- Infections of the vulva
- Infections of the vagina
- Infections of the cervix

Infections of the vulva

Cause of vulvar pruritus and irritation

Acute:

Contact Dermatitis
Allergic
Irritant

Infections
Candidiasis
Scabies
Human papilloma virus
Molluscum contagiosum
Trichomoniasis

Chronic:

Contact Dermatitis
Allergic
Irritant

Vulvar Dystrophies
Lichen planus
Lichen sclerosis
Lichen simplex chronicus
Psoriasis

Infections
Candidiasis
Human papillomavirus

Neoplasia
Paget disease
Vulvar cancer

Atrophy

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INFECTIONS OF BARTHOLIN GLANDS

- Bartholin glands are two rounded, pea-sized glands deep in the perineum that are not palpable unless enlarged.
- Bartholin glands are located at the entrance of the vagina at 5 and 7 o'clock, in the groove between the hymen and the labia minora.
- Mucinous secretions from Bartholin glands provide moisture for the epithelium of the vestibule.
- The most common cause of Bartholin gland enlargement is **cystic dilation of the Bartholin duct** → typically caused by distal obstruction secondary to non-specific inflammation or trauma.
- differential diagnosis: mesonephric cysts of the vagina and epithelial inclusion cysts.
  - Mesonephric cysts are generally more anterior and cephalad in the vagina
  - Epithelial inclusion cysts are more superficial.

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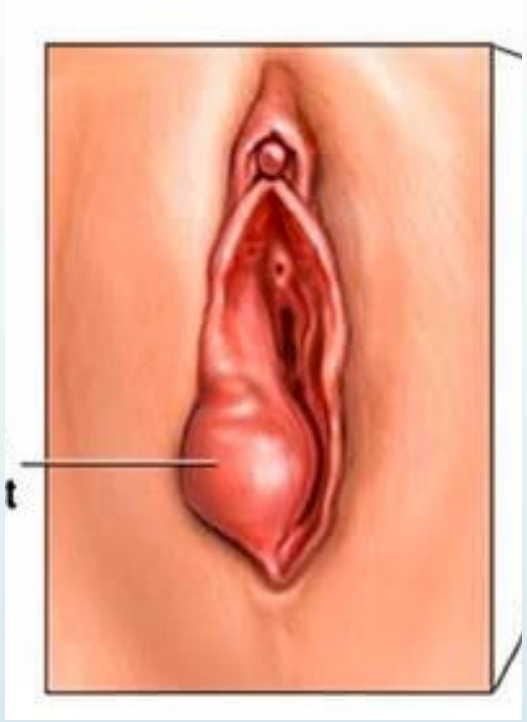
INFECTIONS OF BARTHOLIN GLANDS

- The cysts may vary from 1 to 8 cm in diameter and are usually unilateral, tense, and nonpainful.
- abscess of a Bartholin gland tends to develop rapidly over 2 to 4 days presenting with difficulty in ambulation and sitting.
  - Acute pain and tenderness can be severe, secondary to enlargement, hemorrhage, or secondary infection.
  - signs : erythema, acute tenderness, edema and, occasionally, cellulitis
  - Positive cultures from Bartholin gland abscesses are often polymicrobial and contain a wide range of bacteria similar to the normal flora of the vagina.



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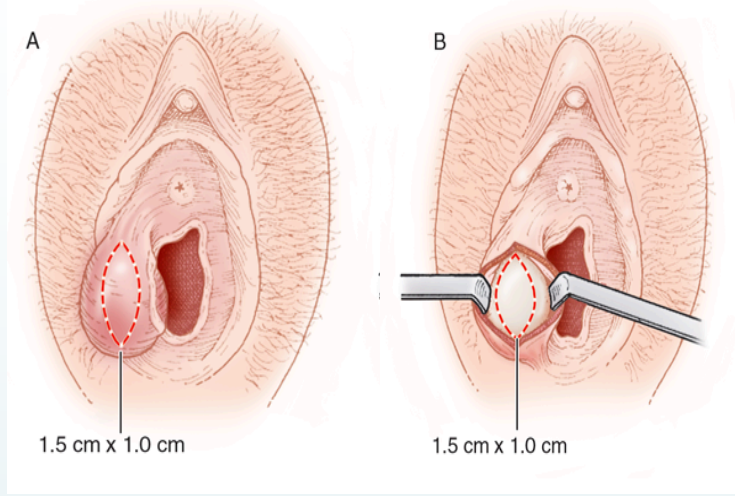
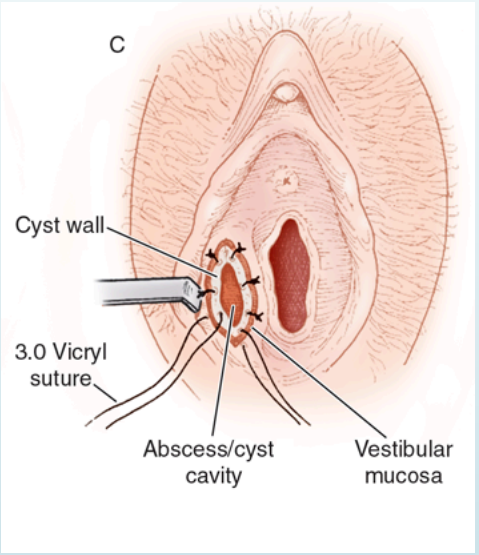
INFECTIONS OF BARTHOLIN GLANDS

- Asymptomatic cysts in women younger than 40 years do not need treatment.
- Simple incision and drainage of a Bartholin gland cyst or abscess is not recommended because recurrence after incision and drainage is frequent.
- The surgical treatment of choice is **marsupialization** to develop a fistulous tract from the dilated duct to the vestibule.
  - An elliptical wedge of tissue is excised over the cyst just proximal to the hymenal ring.
  - A cruciate incision is made into the cyst wall, and the edges of the duct or abscess are everted and sutured to the surrounding skin with interrupted absorbable sutures forming an epithelialized pouch that provides ongoing drainage for the gland.





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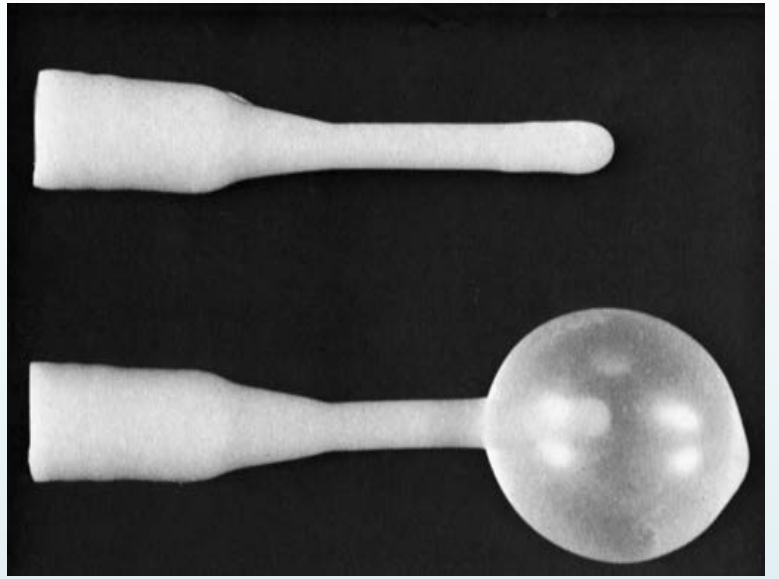
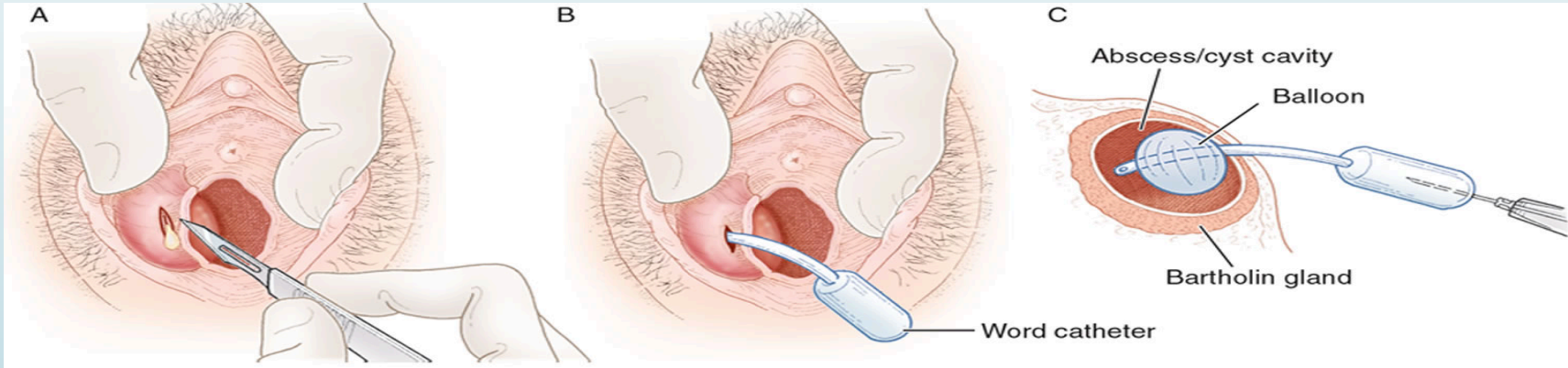
INFECTIONS OF BARTHOLIN GLANDS

An alternative surgical approach is to insert a **Word catheter**, a short catheter with an inflatable Foley balloon, through a stab incision into the abscess and leave it in place for 4 to 6 weeks

- Women older than 40 years with gland enlargement require a biopsy to exclude adenocarcinoma of the Bartholin gland.
- Excision of a Bartholin duct and gland is indicated for persistent deep infection, multiple recurrences of abscesses, or recurrent enlargement of the gland in women older than 40 years.





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PEDICULOSIS PUBIS

- the skin of the vulva is a frequent site of infestation by animal parasites, the two most common being the crab louse and the itch mite.
- Pediculosis pubis is an infestation by the crab louse, *Phthirus pubis*.
- *the* crab louse is also called the *pubic louse* and is a different species from the body or head louse.
- Lice in the pubic hair are the most contagious of all STIs, with over 90% of sexual partners becoming infected following a single exposure.
- The louse's life cycle has three stages: egg (nit), nymph, and adult. The entire life cycle is spent on the host.

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PEDICULOSIS PUBIS

- The predominant clinical symptom of louse infestation is constant pubic pruritus caused by allergic sensitization.
- Examination of the vulvar area without magnification demonstrates eggs and adult lice and pepper grain feces adjacent to the hair shafts
- For definitive diagnosis, one can make a microscopic slide by scratching the skin papule with a needle and placing the crust under a drop of mineral oil.

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SCABIES

- Scabies is a parasitic infection of the itch mite, *Sarcoptes scabiei.*
- transmitted by close contact; Unlike louse infestation, scabies is an infection that is widespread over the body, without a predilection for hairy areas.
- the adult female itch mite digs a burrow just beneath the skin → pathognomonic sign
- the predominant clinical symptom of scabies is severe but intermittent itching → more intense pruritus occurs at night when the skin is warmer and the mites are more active.
- Scabies has been termed the ***great dermatologic imitator***, and the differential diagnosis includes almost all dermatologic diseases that cause pruritus.

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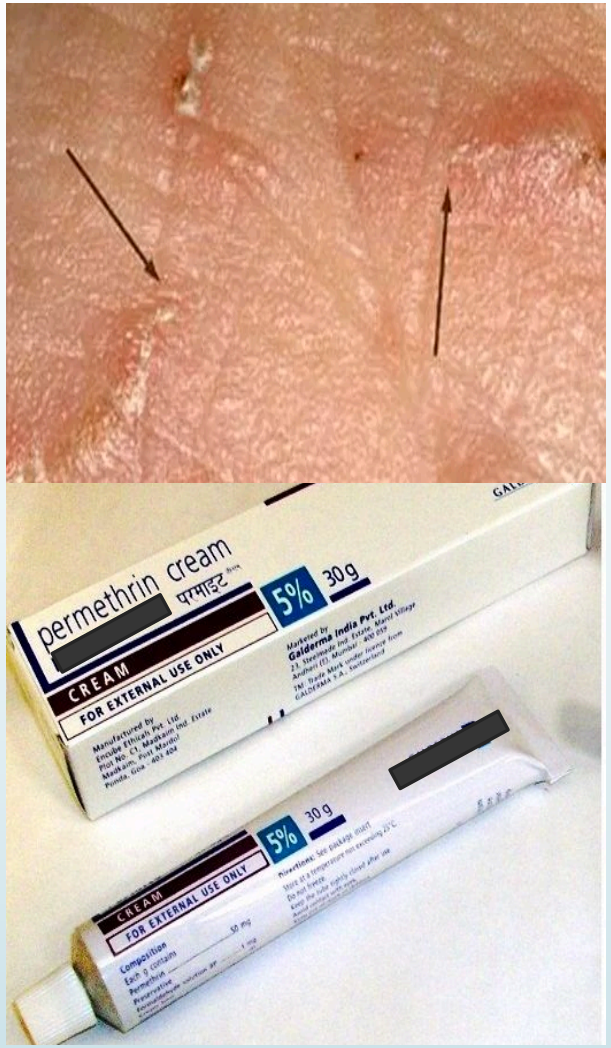
SCABIES

- therapy currently recommended is permethrin, 1% cream rinse, applied to affected areas and washed o after 10 minutes, or pyrethrins, with piperonyl butoxide applied to the affected area and washed off after 10 minutes.
- An antihistamine will help alleviate pruritus.
- To avoid reinfection by pediculosis pubis or scabies, *treatment should be prescribed for sexual contacts within the previous 6 weeks and other close household contacts.*
- Bedding and clothing should be decontaminated (i.e., machine washed, machine dried using the heat cycle, or dry cleaned) or removed from body contact for at least 72 hours.



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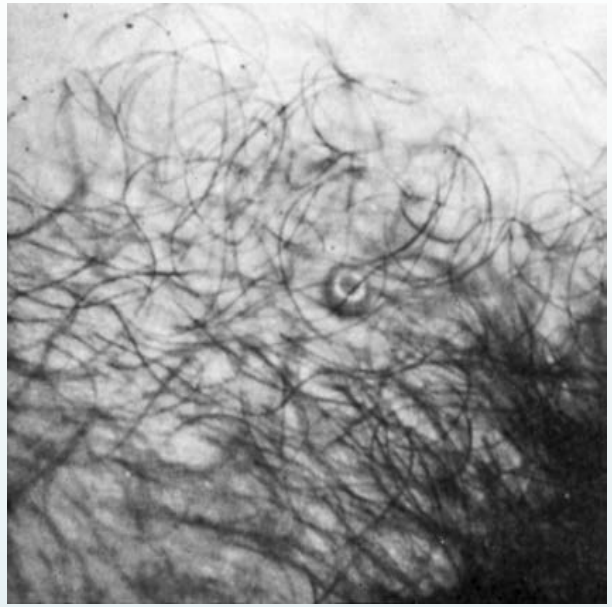
MOLLUSCUM CONTAGIOSUM

- chronic localized infection consisting of flesh-colored, dome-shaped papules with an umbilicated center.
- molluscum is spread by direct skin-to-skin contact.
- it is primarily an asymptomatic disease of the vulvar skin, and, unlike most STIs, it is only mildly contagious.
- Widespread infection in adults is most closely related to underlying cellular immunodeficiency, such as during an HIV infection, chemotherapy or corticosteroid administration.
- To confirm diagnosis → white waxy material from inside the nodule may be expressed on a microscopic slide → *intracytoplasmic molluscum bodies with Wright or Giemsa stai*n confirms the diagnosis.
- the major complication of molluscum contagiosum is bacterial superinfection
- Molluscum contagiosum is usually a self-limiting infection and spontaneously resolves after a few months in immunocompetent individuals



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Genital Ulcers

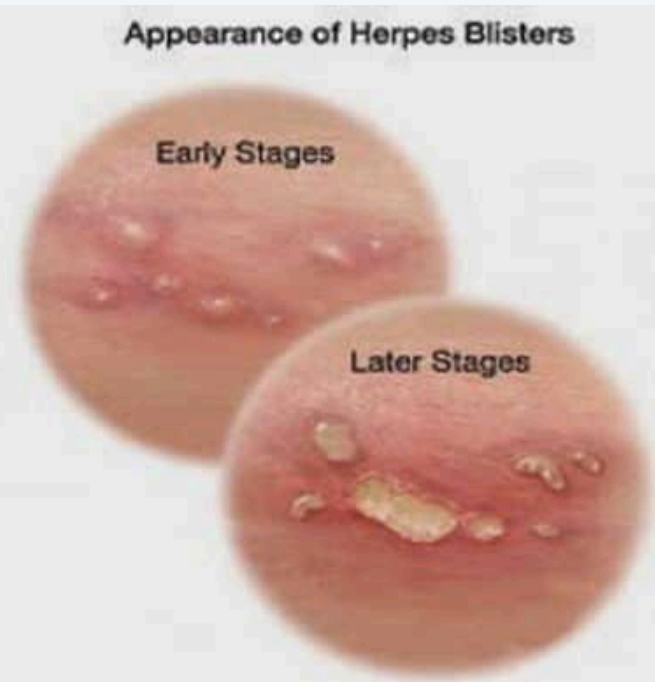
Table 23.1 Clinical Features of Genital Ulcers

	Type				
Parameter	**Syphilis**	**Herpes**	**Chancroid**	**Lymphogranuloma Venereum**	**Donovanosis**
Incubation period	2-4 wk (1-12 wk)	2-7 days	1-14 days	3 days-6 wk	1-4 wk (up to 6 mo)
Primary lesion	Papule	Vesicle	Papule or pustule	Papule, pustule, or vesicle	Papule
Number of lesions	Usually one	Multiple, may coalesce	Usually multiple, may coalesce	Usually one	Variable
Diameter (mm)	5-15	1-2	2-20	2-10	Variable
Edges	Sharply demarcated Elevated, round or oval	Erythematous	Undermined, ragged, irregular	Elevated, round or oval	Elevated, irregular
Depth	Superficial or deep	Superficial	Excavated	Superficial or deep	Elevated
Base	Smooth, nonpurulent	Serous, erythematous	Purulent	Variable	Red and rough (beefy)
Induration	Firm	None	Soft	Occasionally firm	Firm
Pain	Unusual	Common	Usually very tender	Variable	Uncommon
Lymphadenopathy	Firm, nontender Pseudoadenopathy bilateral	Firm, tender, often bilateral	Tender, may suppurate, usually unilateral	Tender, may suppurate, loculated, usually unilateral	

From Holmes KK, Mårdh PA, Sparling PF, et al, eds. *Sexually Transmitted Diseases*, 2nd ed. New York: McGraw-Hill, 1990.

Genital Herpes

- recurrent viral infection that is incurable and *highly contagious*
- herpes is transmitted during episodes of asymptomatic shedding
- two distinct types of HSV: type 1 (HSV-1) and type 2 (HSV-2).
- HSV-1 is the most commonly acquired genital herpes in women younger than 25 years and, in some series, HSV-1 may cause lower genital tract infection in 13% to 40% of patients.
- Genital HSV-1 is transmitted from orolabial lesions to the vulva during oral-genital contact or from genital to genital to genital contact with a partner with genital HSV-1.
- paresthesia of the vulvar skin followed by the eruption of multiple painful vesicles, which progress to shallow,painful superficial ulcers over a large area of the vulva.



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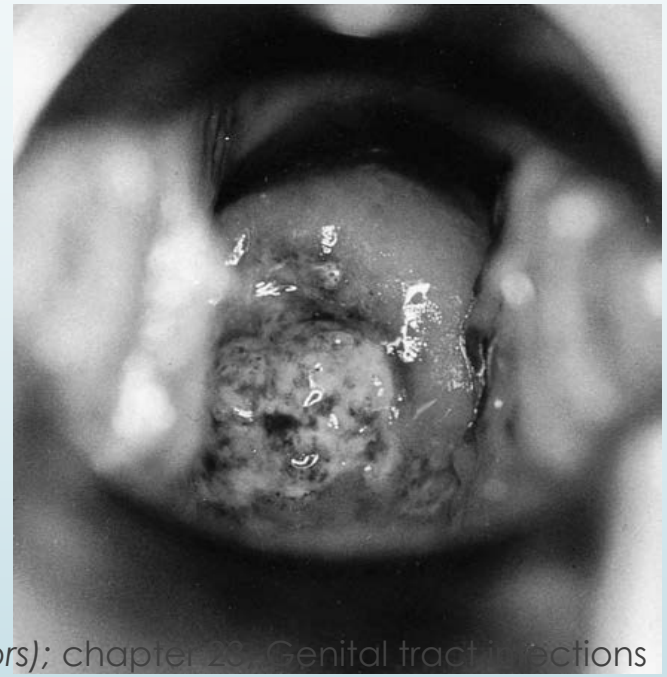
Genital Herpes

- the ulcers usually heal spontaneously without scarring
- Most symptomatic women have severe vulvar pain, tenderness, and inguinal adenopathy and simultaneous involvement of the vagina and cervix is common
- Systemic symptoms, including general malaise and fever
- symptoms of vulvar pain, pruritus, and discharge peak between days 7 and 11 of the primary infection.
- Recurrent genital herpes is a local disease with less severe symptoms. On average, a woman will have four recurrences during the first



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Genital Herpes

- the clinical diagnosis of genital herpes is often made by simple clinical inspection.
- Herpetic ulcers are painful when touched with a cotton-tipped applicator, whereas the ulcers of syphilis are painless.
- the most accurate and sensitive technique for identifying herpes virus is the polymerase chain reaction (PCR) assay.
- the Western blot assay for antibodies to herpes is the most specific method for diagnosing recurrent herpes, as well as unrecognized or subclinical infection.

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Genital Herpes

- Treatment of HSV-1 or HSV-2 may be used for three different clinical scenarios:
  - 1. Primary episode
  - 2. Recurrent episode
  - 3. Daily suppression
- Antiviral therapy is recommended for in all patients with primary episodes.
- Episodic therapy for recurrences can shorten the duration of the outbreak if started within 24 hours of prodromal symptoms or lesion appearance.
- antiviral medication should be started as early as possible during the prodrome, and definitely within 24 hours of the appearance of lesions.

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Genital Herpes

- CDC recommends that **acyclovir** or other suppressive drugs be discontinued after 12 months of suppressive therapy to determine the subsequent rate of recurrence for each individual woman

Table 23.2 Antiviral Treatment for Herpes Simplex Virus in the Nonpregnant Patient

	Antiviral Agent		
Indication	**Valacyclovir**	**Acyclovir**	**Famciclovir**
First clinical episode	1000 mg bid, 7-10 days	200 mg five times/day; or 400 mg tid, 7-10 days	250 mg tid, 7-10 days
Recurrent episodes	1000 mg daily, 5 days; or 500 mg bid, 3 days	400 mg tid, 5 days; 800 mg bid, 5 days; or 800 mg tid, 2 days	125 mg bid, 5 days 500 mg once then 250 mg bid, 2 days; 1000 mg bid, 1 day
Daily suppressive	1000 mg daily (≥10 recurrences/year) or 500 mg daily (≤9 recurrences/year)	400 mg bid	250 mg bid

Data from Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015; 64(RR-03):1-137. *bid*, Twice per day; *tid*, three times per day.

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Granuloma Inguinale (Donovanosis)

- also known as ***donovanosis***, is a chronic, ulcerative, bacterial infection of the skin and subcutaneous tissue of the vulva.
- can be spread sexually and through close nonsexual contact. However, it is not highly contagious, and chronic exposure is usually necessary to contract the disease.
- caused by an intracellular, gram-negative, nonmotile, encapsulated rod, ***Klebsiella granulomatis***.
- initial growth is a nodule that gradually progresses into a painless, slowly progressing ulcer surrounded by highly vascular granulation tissue → The ulcer has a **beefy red appearance**, and it bleeds easily when touched.
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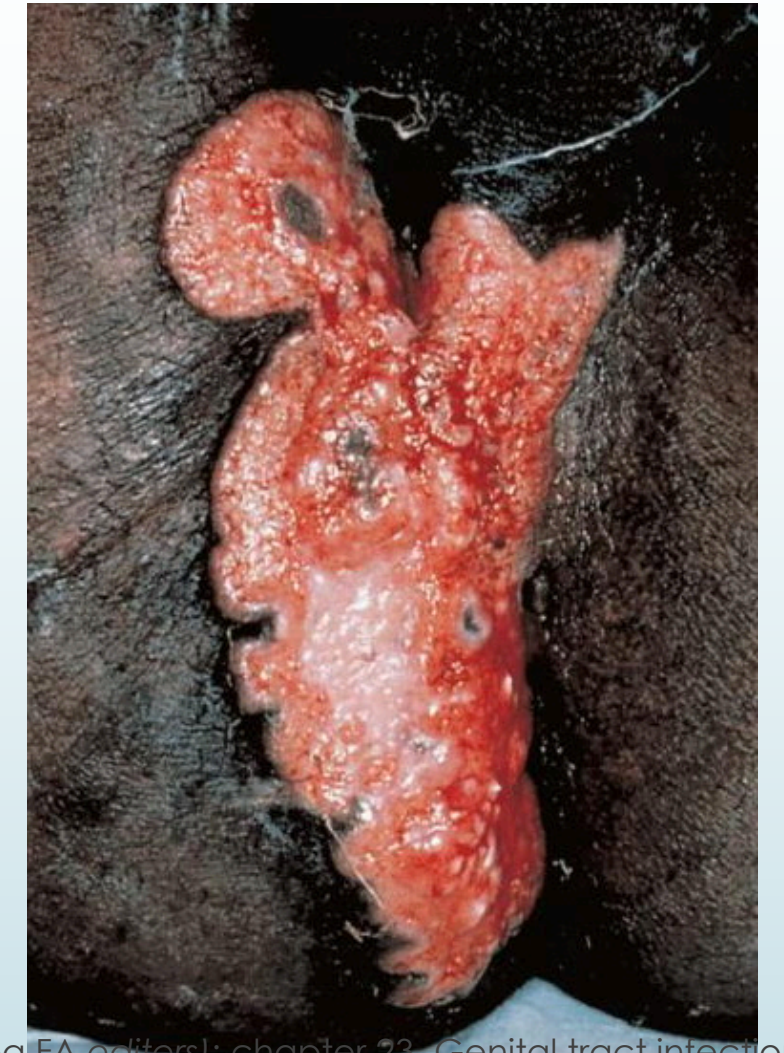

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Granuloma Inguinale (Donovanosis)

- the ulcers are painless and without regional adenopathy. Typically, multiple nodules are present, resulting in ulcers that grow and coalesce and, if untreated, will eventually destroy the normal vulvar architecture.
- diagnosis may also be established by identifying **Donovan bodies** in smears and specimens taken from the ulcers
- Donovan bodies appear as clusters of dark-staining bacteria with a bipolar (**safety pin**) appearance found in the cytoplasm of large mononuclear cells.

Donovan Bodies

Clusters of blue- or black-staining, bipolar chromatin condensations in large mononuclear cells in granulation tissue infected with Klebsiella (Calymmatobacterium granulomatis).

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Granuloma Inguinale (Donovanosis)

- CDC recommends **azithromycin** 1 g orally once a week or 500 mg daily for 3 weeks and until all lesions have healed.
- Alternative antibiotic regimens include the following:
  1. doxycycline, 100 mg orally, twice daily for a minimum of 3 weeks;
  2. ciprofloxacin, 750 mg orally twice daily;
  3. erythromycin base, 500 mg orally four times daily;
  4. trimethoprim-sulfamethoxazole (TMP-SMZ), one double-strength tablet orally twice daily.

Donovan Bodies

Clusters of blue- or black-staining, bipolar chromatin condensations in large mononuclear cells in granulation tissue infected with Klebsiella (Calymmatobacterium granulomatis).

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Lymphogranuloma Venereum

- This sexually transmitted infection is caused by serotypes L1, L2, and L3 of *C. trachomatis*.
- In women, the vulva is the most frequent site of infection, but the urethra, rectum, and cervix may also be involved.

Figure 23.10 Lymphogranuloma venereum bubo with groove sign. (From Friedrich EG. *Vulvar Disease.* 2nd ed. Philadelphia: WB Saunders; 1983.)

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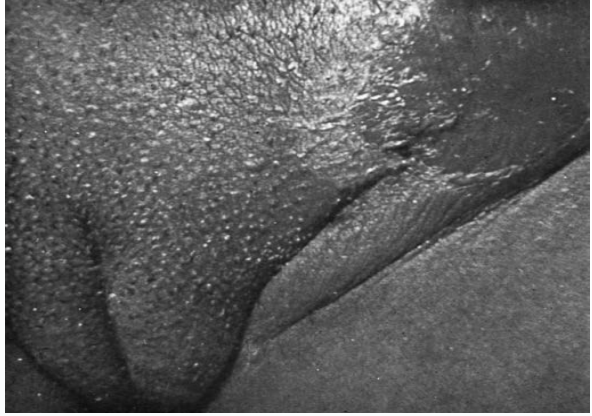
Lymphogranuloma Venereum



- *T*here are 3 distinct phases of vulvar and perirectal LGV:
  - the **primary infection:** shallow, painless ulcer that heals rapidly without therapy; typically located on the vestibule or labia
  - a **secondary phase:** painful adenopathy that develops in the inguinal and perirectal areas
    - the infected nodes become tender, enlarged, matted together, and adherent to overlying skin, forming a **bubo** (tender lymph nodes).
    - **groove sign:** double genitocrural fold → a depression between groups of inflamed nodes. → classic sign of LGV
  - **tertiary phase** : bubo ruptures spontaneously and form multiple draining sinuses and fistulas → classic signs of extensive tissue destruction of the external genitalia and anorectal region may occur during the tertiary phase.

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Lymphogranuloma Venereum

- Diagnosis is established by detecting *C. trachomatis* by culture, direct immunofluorescence, or nucleic acid detection from the pus or aspirate from a tender lymph node.
- In the absence of specific LGV diagnostic testing, patients should be treated based on the clinical presentation
- Treatment:
  - CDC recommends doxycycline, 100 mg twice daily for at least 21 days, as the preferred treatment.
  - An alternative therapy choice is erythromycin base, 500 mg four times daily orally for 21 days.

Figure 23.10 Lymphogranuloma venereum bubo with groove sign. (From Friedrich EG. *Vulvar Disease.* 2nd ed. Philadelphia: WB Saunders; 1983.)

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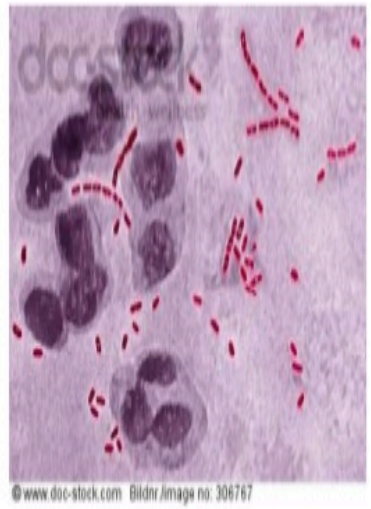
Chancroid

- Chancroid is a sexually transmitted, acute, ulcerative disease of the vulva caused by *Haemophilus ducreyi,* a highly contagious, small, nonmotile, gram-negative rod.
- the soft chancre of chancroid is always painful and tender.
- the hard chancre of syphilis is usually asymptomatic.
- Gram stain: facultative anaerobic bacterium with a classic appearance of streptobacillary chains (extracellular *school of fish*).
- Tissue trauma and excoriation of the skin must preceed initial infection because *H. ducreyi* is unable to penetrate and invade normal skin.



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Chancroid

- the initial lesion is a small papule. Within 48 to 72 hours, the papule evolves into a pustule and subsequently ulcerates.
- the extremely painful ulcers are shallow, with a characteristic ragged edge, and usually occur in the vulvar vestibule and rarely in the vagina or cervix.
- ulcers have a dirty, gray, necrotic, foul-smelling exudate and lack induration at the base (***the soft chancre***).
- approximately 50% of women develop acutely tender inguinal adenopathy (a ***bubo***) which is typically unilateral.
- Fluctuant nodes should be treated by needle aspiration to prevent rupture or by incision and drainage if larger than 5 cm.

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Chancroid

- A definitive diagnosis of chancroid requires the identification of *H. ducreyi* on special culture media that are not widely available from commercial sources;
- the clinical diagnosis is made in a woman with painful vulvar ulcers after excluding other common STIs that produce vulvar ulcers, including genital herpes, syphilis, LGV, and donovanosis.
- Treatment: CDC recommends the following:
  - azithromycin, 1 g orally in a single dose; or
  - ceftriaxone, 250 mg intramuscular (IM) in a single dose; or
  - ciprofloxacin, 500 mg orally twice daily for 3 days; or
  - erythromycin base, 500 mg orally three times daily for 7 days.

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Syphilis

- chronic, complex systemic disease produced by the spirochete *Treponema pallidum*.
- *T. pallidum* is an anaerobic, elongated, tightly wound spirochete.
- Because of its extreme thinness, T pallidum is difficult to detect by light microscopy → therefore the presence of spirochetes is diagnosed by use of specially adapted techniques, dark-field microscopy, or direct fluorescent antibody tests
- Patients are contagious during primary, secondary, and probably the first year of latent syphilis.
- Syphilis can be spread by kissing or touching a person who has an active lesion on the lips, oral cavity, breast, or genitals.

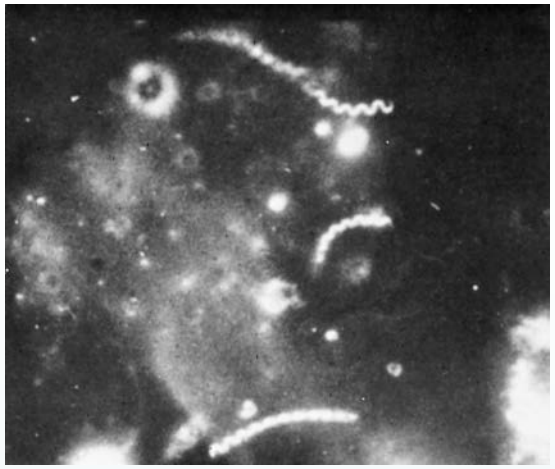
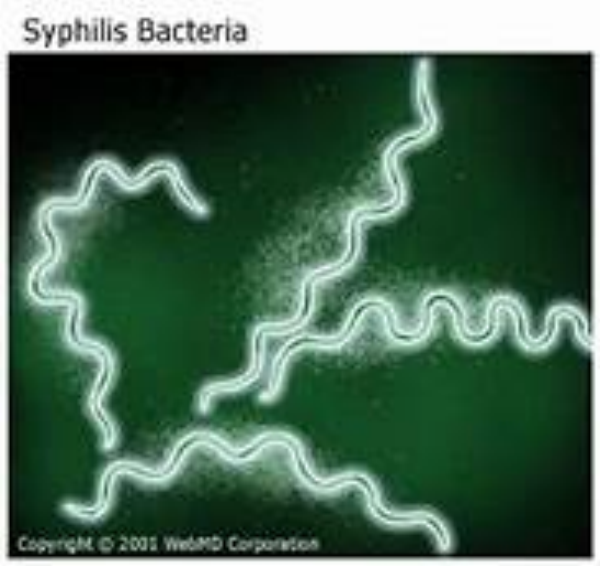


Figure 23.11 Dark-field microscopic appearance of *Treponema pallidum*. (From Larsen SA, McGrew BE, Hunter EF, et al. Syphilis serology and dark field microscopy. In: Holmes KK, Mårdh PA, Sparling PF, et al, eds. *Sexually Transmitted Diseases.* New York: McGraw-Hill; 1984.)



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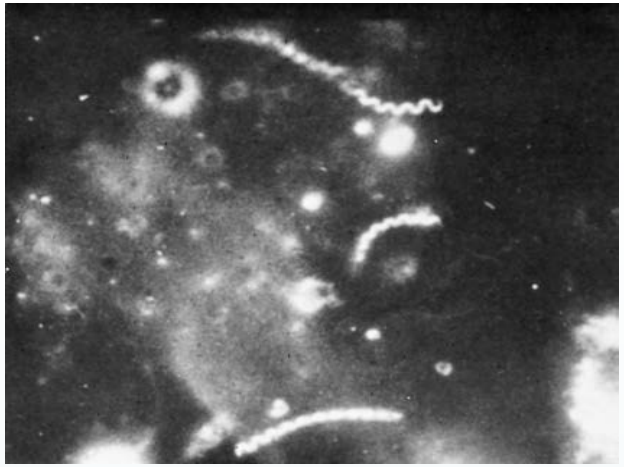
Syphilis

- Definitive diagnosis is via darkfield microscopy to detect *T. palladium* in lesion exudate or tissue.
- Presumptive diagnosis and screening rely on serologic tests:



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nonspecific nontreponemal tests: **VDRL and RPR** (used as screening tests and index of treatment response)

- false-positive results: recent febrile illness, pregnancy, immunization, chronic active hepatitis, malaria, sarcoidosis, intravenous (IV) drug use, HIV infection, advancing age, acute herpes simplex, and autoimmune diseases such as lupus erythematosus or rheumatoid arthritis.

- false-negative result: occurs in women in whom there is an excess of anticardiolipin antibody in the serum, termed the ***prozone phenomenon***.

- Women with immunocompromise also may have false-negative tests because of their inability to produce the antibodies detected by these screening tests.

Syphilis

- If a nonspecific test result is positive, the significance of this result must be confirmed by a ***specific antitreponemal tests:*** fluorescent-labeled *Treponema* antibody absorption **(FTA-ABS) test** and the micro- hemagglutination assay for antibodies to *T. pallidum* **(MHA- TP)**
- false-positive results: lupus erythematosus
- A woman with a positive reactive treponemal test usually will have this positive reaction for her lifetime, regardless of treatment or activity of the disease

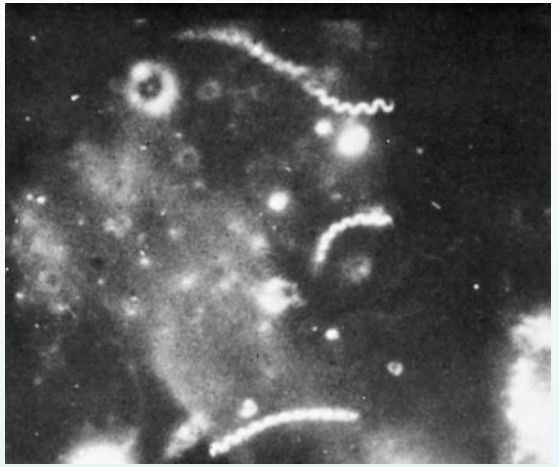

Figure 23.11 Dark-field microscopic appearance of *Treponema pallidum.* (From Larsen SA, McGrew BE, Hunter EF, et al. Syphilis serology and dark field microscopy. In: Holmes KK, Mårdh PA, Sparling PF, et al, eds. *Sexually Transmitted Diseases.* New York: McGraw-Hill; 1984.)

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Table 23.3 Potential Causes of Biologic False-Positive Results in Syphilis Serology

	Biologic False-Positive Reaction	
Cause	**Acute**	**Chronic**
Physiologic	Pregnancy	Advanced age, multiple blood transfusions
Infectious	Varicella, vaccinia, measles, mumps, infectious mononucleosis, herpes simplex, viral hepatitis, HIV seroconversion illness, cytomegalovirus, pneumococcal pneumonia, *Mycoplasma pneumoniae*, chancroid, lymphogranuloma venereum, psittacosis, bacterial endocarditis, scarlet fever, rickettsial infections, toxoplasmosis, Lyme disease, leptospirosis, relapsing fever, rat bite fever	HIV, tropical spastic paraparesis, leprosy,* tuberculosis, malaria,* lymphogranuloma venereum, trypanosomiasis,* kala-azar*
Vaccinations	Smallpox, typhoid, yellow fever	
Autoimmune disease		Systemic lupus erythematosus, discoid lupus, drug-induced lupus, autoimmune hemolytic anemia, polyarteritis nodosa, rheumatoid arthritis, Sjögren syndrome, Hashimoto thyroiditis, mixed connective tissue disease, primary biliary cirrhosis, chronic liver disease, idiopathic thrombocytopenic purpura
Other		IV drug use, advanced malignancy hypergammaglobulinemia, lymphoproliferative disease

Data from Nandwani R, Evans DTP. Are you sure it's syphilis? A review of false-positive serology. *Int J STD AIDS*. 1995;6:241; Hook EW III, Marra CM. Acquired syphilis in adults. *N Engl J Med*. 1992;326:1062.

*Biologic false-positive reaction resolves with resolution of infection.

HIV, Human immunodeficiency virus.

Syphilis

- Clinically, syphilis is divided into primary, secondary, and tertiary stages:
- **Primary syphilis**:
  - a papule, which is usually painless, appears at the site of inoculation 2 to 3 weeks after exposure. → soon ulcerates to produce the classic ***chancre*** that is a painless ulcer, with a raised indurated margin and a nonexudative base
  - the chancre is solitary, painless, and found on the vulva, vagina, or cervix
  - Nontender and firm regional adenopathy is present during the first week of clinical disease.
  - Within 2 to 6 weeks, the painless ulcer heals spontaneously→ Hence, many women do not seek treatment

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Syphilis

Secondary syphilis:

- If primary syphilis is untreated, approximately 25% of individuals develop secondary syphilis
- result from hematogenous dissemination of the spirochetes.
- systemic symptoms may occur such as rash, fever, headache, malaise, lymphadenopathy, and anorexia.
- *the classic rash of secondary syphilis is red macules and papules over the palms of the hands and the soles of the feet*
- Vulvar lesions of condyloma latum are large, raised, flattened, grayish white areas
- On wet surfaces of the vulva, soft papules often coalesce to form ulcers → larger than herpetic ulcers and are not tender unless secondarily infected.

Syphilis

- **Latent syphilis:**
  - Follows after secondary syphilis, and varies in duration from 2 to 20 years
  - characterized as positive serology without symptoms or signs of disease.
  - Women with syphilis in the primary or secondary stages and during the first year of latent syphilis are believed to be infectious.
  - Most women diagnosed with syphilis are detected via positive blood tests during the latent stage of the disease.
  - Early latent syphilis is an infection of 1 year or less.
  - All other cases are referred to as *late latent* or *latent syphilis of unknown duration*.

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Syphilis

- **Tertiary phase**
  - devastating in its potentially destructive effects on the central nervous, cardiovascular, and musculoskeletal systems.
  - manifestations of late syphilis include optic atrophy, tabes dorsalis, generalized paresis, aortic aneurysm, and gummas of the skin and bones.
  - A gumma is similar to a cold abscess, with a necrotic center and the obliteration of small vessels by endarteritis.

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Syphilis

- Treatment:
  - Parenteral penicillin G is the drug of choice for syphilis.
  - CDC recommends 2.4 million units of benzathine penicillin G IM in one dose for early syphilis (primary and early latent secondary syphilis).
  - Patients who are allergic to penicillin should receive oral tetracycline, 500 mg every 6 hours for 14 days, or
  - doxycycline, 100 mg orally twice a day for 2 weeks.
  - Approximately 60% of women develop an acute febrile reaction associated with flulike symptoms such as headache and myalgia within the first 24 hours after parenteral penicillin therapy for early syphilis ***(Jarisch-Herxheimer reaction)***

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Box 23.2 Centers for Disease Control and Prevention Recommended Treatment of Syphilis (2014)

Early Syphilis (primary, secondary, and early latent syphilis of less than 1 year in duration)

Recommended regimen: Benzathine penicillin G, 2.4 million U IM, one dose

Alternative regimen (penicillin-allergic nonpregnant patients): Doxycycline, 100 mg orally bid for 2 wk *or* tetracycline, 500 mg orally qid for 2 wk

Late Latent Syphilis (>1 year in duration, gummas, and cardiovascular syphilis)

Recommended regimen: Benzathine penicillin G, 7.2 million U total, administered as three doses of 2.4 million U IM at 1-wk intervals

Alternative regimen (penicillin-allergic nonpregnant patients): Doxycycline 100 mg orally 2 times a day for 2 wk if <1 year, otherwise, for 4 wk; *or* tetracycline, 500 mg orally qid for 2 wk if <1 year; otherwise, for 4 wk

Neurosyphilis

Recommended regimen: Aqueous crystalline penicillin G, 18-24 million U daily, administered as 3-4 million U IV every 4 hr, for 10-14 days

Alternative regimen: Procaine penicillin, 2.4 million U IM daily, for 10-14 days plus probenecid, 500 mg PO qid for 10-14 days

Syphilis in Pregnancy

Recommended regimen: Penicillin regimen appropriate for stage of syphilis. Some experts recommend additional therapy (e.g., second dose of benzathine penicillin, 2.4 million U IM) 1 wk after the initial dose for those who have primary, secondary, or early latent syphilis

Alternative regimen (penicillin allergy): Pregnant women with a history of penicillin allergy should be skin-tested and desensitized

Syphilis in HIV-Infected Patients

Primary and secondary syphilis: Benzathine penicillin G, 2.4 million U IM. Some experts recommend additional treatments, such as three weekly doses of benzathine penicillin G. Penicillin-allergic patients should be desensitized and treated with penicillin

Latent syphilis (normal CSF examination): Benzathine penicillin G, 7.2 million U as three weekly doses of 2.4 million U each

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Syphilis

- Treatment:
  - Women who have a sustained fourfold increase in nontreponemal test titers have failed treatment or become reinfected → should be retreated and evaluated for concurrent HIV infection.
  - When women are retreated, the recommendation is three weekly injections of benzathine penicillin G, 2.4 million units IM.
  - With successful treatment, the VDRL titer will become nonreactive or, at most, be reactive, with a lower titer within 1 year.
  - all women with a first attack of primary syphilis should have a negative nonspecific serology within 1 year, and women treated for secondary syphilis should have a negative serology within 2 years → if they are not, treatment failure, reinfection, and concurrent HIV infection should be investigated.

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Neurosyphilis

- Syphilis often involves the CNS.
- the diagnosis of neurosyphilis is based on a combination of clinical findings, reactive serologic tests, and abnormalities of cerebrospinal fluid, serology, cell count, or protein.
- CDC recommends aqueous crystalline penicillin G, 18 to 24 million units daily, administered as 3 to 4 million units IV every 4 hours for 10 to 14 days.
- An alternative regimen is procaine penicillin, 2.4 million units IM daily, plus probenecid, 500 mg orally four times daily for 10 to 14 days.
- It is important for all women with syphilis to be tested for HIV infection. Simultaneous syphilis and HIV infections alter the natural history of syphilis, with earlier involvement of the CNS.

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Infections of the vagina

VAGINITIS

- Vaginal discharge is the most common symptom in gynecology.
- Other symptoms associated with vaginal infection include superficial dyspareunia, dysuria, odor, and vulvar burning and pruritus.
- the three common causes of vaginitis are (1) a fungus (candidiasis), (2) a protozoon *(Trichomonas),* and (3) a disruption of the vaginal bacterial ecosystem leading to bacterial vaginosis.

Table 23.5 Typical Features of Vaginitis

Condition	Symptoms and Signs*	Findings on Examination*	pH	Wet Mount	Comment
Bacterial vaginosis†	Increased discharge (white, thin), Increased odor	Thin, whitish gray, homogeneous discharge, cocci, sometimes frothy	>4.5	Clue cells (>20%) shift in flora Amine odor after adding potassium hydroxide to wet mount	Greatly decreased lactobacilli Greatly increased cocci Small curved rods
Candidiasis	Increased discharge (white, thick)‡ Dysuria Pruritus Burning	Thick, curdy discharge Vaginal erythema	<4.5	Hyphae or spores	Can be mixed infection with bacterial vaginosis, *T. vaginalis*, or both, and have higher pH
Trichomoniasis§	Increased discharge (yellow, frothy) Increased odor Dysuria Pruritus	Yellow, frothy discharge, with or without vaginal or cervical erythema	>4.5	Motile trichomonads Increased white cells	More symptoms at higher vaginal pH

BACTERIAL VAGINOSIS

- Bacterial vaginosis is the most prevalent cause of symptomatic vaginitis
- Bacterial vaginosis reflects a shift in vaginal flora from lactobacilli-dominant to mixed flora, including genital mycoplasmas, *G. vaginalis*, and anaerobes, such as peptostreptococci, and *Prevotella* and *Mobiluncus* spp.
- Currently, bacterial vaginosis is described as a "sexually associated" infection rather than a true sexually transmitted infection.
- Histologically, there is an absence of inflammation in biopsies of the vagina—thus the term *vaginosis* rather than *vaginitis*.
- Bacterial vaginosis has been associated with upper tract infections, including endometritis, pelvic inflammatory disease, postoperative vaginal cuff cellulitis, and multiple complications of infection during pregnancy, such as preterm rupture of the membranes, endomyometritis, decreased success with in vitro fertilization, and increased pregnancy loss of less than 20 weeks' gestation.

BACTERIAL VAGINOSIS

- the most frequent symptom is an unpleasant vaginal odor, which patients describe as musty or fishy odor → often stronger following intercourse, when the alkaline semen results in a release of aromatic amines.
- vaginal discharge associated with bacterial vaginosis is thin and gray-white.
- Speculum examination reveals that the discharge is mildly adherent to the vaginal walls
- the four criteria (**AMSEL's CRITERIA**) for the diagnosis of bacterial vaginosis are
  - *(1) a homogeneous vaginal discharge is present;*
  - *(2) the vaginal discharge has a pH of 4.5 or higher;*
  - *(3) the vaginal discharge has an amine-like odor when mixed with potassium hydroxide (**whiff test**);*
  - *(4) a wet smear of the vaginal discharge demonstrates clue cells more than 20% of the number of the vaginal epithelial cells.*

For the clinician, three our of four criteria are sufficient for a presumptive diagnosis.

If available, Gram staining of vaginal secretion is an excellent diagnostic method.

BACTERIAL VAGINOSIS

- Treament:

Disease	Drug	Dose
Bacterial vaginosis*	Metronidazole (Flagyl)	500 mg PO, bid for 7 days†
	Tinidazole	2-g dose PO daily for 2 days
	Tinidazole	1-g dose PO daily for 5 days
	0.75% metronidazole gel (Metrogel)	One 5-g application intravaginally daily for 5 days‡
	2% clindamycin cream (Cleocin vaginal)	One 5-g application intravaginally every night for 7 days
	Clindamycin	300 mg PO, bid for 7 days
	Clindamycin ovules	100 mg intravaginally every night for 3 days

- Recurrent bacterial vaginosis (three or more episodes in the previous year): 10 days vaginal metronidazole, followed by twice- weekly use of 0.75% metronidazole gel for 16 weeks
- Concurrent treatment of the male partner is not recommended at this time.

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TRICHOMONAS VAGINAL INFECTION

- caused by the anaerobic flagellated protozoon, *T. vaginalis*
- thiis infection is a highly contagious STI;
- *Trichomonas* is a hardy organism and will survive for up to 24 hours on a wet towel and up to 6 hours on a moist surface.
- primary symptom of *Trichomonas* vaginal infection is profuse/copious vaginal discharge.
- the **classic discharge** of *Trichomonas* infection is termed ***frothy* (with bubbles)** and often has an unpleasant odor.
- the classic sign of a **strawberry appearance of the upper vagina and cerv**ix is rare and is noted in less than 10% of women.
- Previously, culture was considered the gold standard to detect *T. vaginalis,* and wet prep was the most commonly performed diagnostic test
- Nucleic acid amplification tests (NAATs) are 3-5x times more sensitive than wet prep. NAAT can be performed on vaginal secretions or urine.

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TRICHOMONAS VAGINAL INFECTION

- Nitroimidazoles are the only class of drugs recommended for treatment of *Trichomonas* vaginitis.
  - A single oral dose (2 g) of metronidazole or tinidazole is recommended.
  - An alternate regimen is metronidazole, 500 mg orally, twice daily for 7 days.
  - Metronidazole is safe in all trimesters of pregnancy. Patients should be warned that **nitroimidazoles inhibit ethanol metabolism**. Women should avoid alcohol for 24 hours after metronidazole and 72 hours after tinidazole therapy to avoid a **disulfiram-like reaction**.
- Topical therapy for *Trichomonas* vaginitis is not recommended because it does not eliminate disease reservoirs in Bartholin and Skene glands.

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CANDIDA VAGINITIS

- produced by a ubiquitous, airborne, gram-positive fungus.
- more than 90% of cases are caused by *Candida albicans*
- When the ecosystem of the vagina is disturbed, *C. albicans* can become an opportunistic pathogen.
- Hormonal factors, depressed cell-mediated immunity, and antibiotic use are the 3 most important factors that alter the vaginal ecosystem.
- hormonal changes associated with pregnancy and menstruation favor growth of the fungus.
- the prevalence of *Candida* vaginitis increases throughout pregnancy, probably as a result of the high estrogen levels.
- Lactobacilli inhibit the growth of fungi in the vagina. therefore when the relative concentration of lactobacilli declines, rapid overgrowth of *Candida* spp. occurs.

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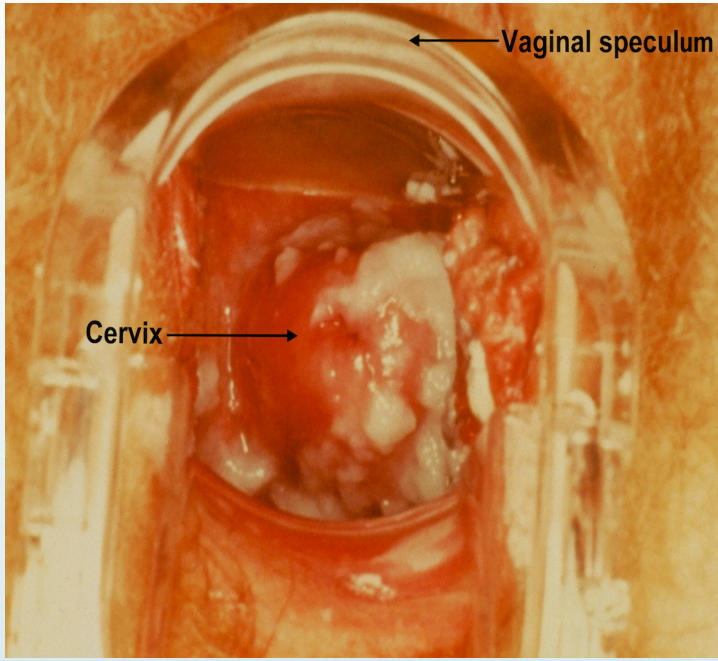
CANDIDA VAGINITIS

- Broad-spectrum antibiotics, especially those that destroy lactobacilli (e.g., penicillin, tetracycline, cephalosporins), are notorious for precipitating acute episodes of C. *albicans* vaginitis.
- the most important host factor is depressed cell-mediated immunity (Women who take exogenous corticosteroids and women with AIDS)
- the greatest enigma of this condition is the recurrence rate after an apparent cure, varying from 20% to 80%.
  - Approximately 3% to 5% of these women experience **recurrent vulvovaginal candidiasis (RVVC)** → four or more documented episodes in 1 year.



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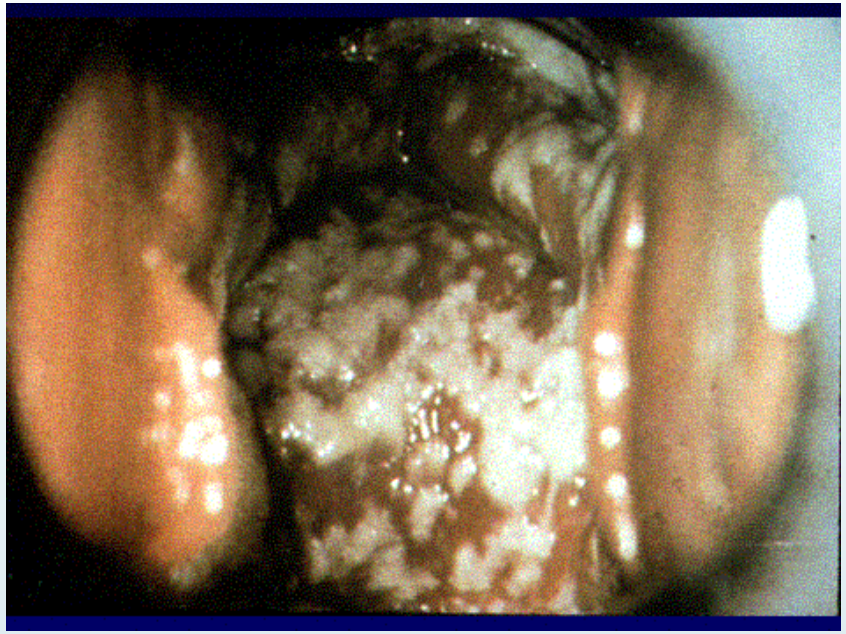
CANDIDA VAGINITIS

- Pruritus is the predominant symptom
- the vaginal discharge is white or whitish gray, highly viscous, and described as granular or occular, with no odor.
- During speculum examination, a cottage cheese–type discharge is often visualized, with adherent clumps and plaques (thrush patches) attached to the vaginal walls.
- e vaginal pH associated with this infection is below 4.5, in contrast to bacterial vaginosis and *Trichomonas* vaginitis, which are associated with an elevated pH.



Source: Loyola University Medical Education Network

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CANDIDA VAGINITIS

- diagnosis is established by obtaining a wet smear of vaginal secretion and mixing this with 10% to 20% potassium hydroxide
- alkali rapidly lyses red blood cells and inflammatory cells.
- Active disease is associated with lamentous forms, mycelia, or pseudohyphae, rather than spores.
- vaginal culture for *Candida* is particularly useful when a wet mount is negative for hyphae, but the patients have symptoms and discharge or other signs suggestive of vulvovaginal candidiasis on examination.
- Fungal culture may also be useful for women who have recently treated themselves with an antifungal agent

Figure 23.20 Microscopic appearance of vaginal smear in a case of vaginal candidiasis (potassium hydroxide preparation, yeast cells and pseudomycelia; × 320). (From Merkus JM, Bisschop MP, Stolte LA. The proper nature of vaginal candidosis and the problem of recurrence. *Obstet Gynecol Surv.* 1985;40:493-504.)

CANDIDA VAGINITIS

- Treatment: CDC recommends placing the woman into an uncomplicated or complicated category to guide treatment

Box 23.3 Classification of Vulvovaginal Candidiasis (VVC)

Uncomplicated VVC	Complicated VVC
▪ Sporadic or infrequent vulvovaginal candidiasis	▪ Recurrent vulvovaginal candidiasis
and	*or*
▪ Mild to moderate vulvovaginal candidiasis	▪ Severe vulvovaginal candidiasis
and	*or*
▪ Likely to be *C. albicans*	▪ Non-*albicans* candidiasis
and	*or*
• Nonimmunocompromised women	▪ Women with uncontrolled diabetes, debilitation, or immunosuppression

- A number of azole vaginal preparations and a single oral agent, fluconazole, are approved for treatment.
- In patients with uncomplicated vulvovaginal candidiasis, topical antifungal agents are typically used for 1 to 3 days, or a single oral dose of fluconazole.
- For patients with complicated vaginitis, topical azoles are recommended for 7 to 14 days. If using oral therapy, a second dose of fluconazole (150 mg) given 72 hours after the first dose is recommended.

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CANDIDA VAGINITIS

- In women with RVVC, the resolution of symptoms typically requires longer duration of therapy.
- 7 – 14 days of topical therapy or three doses of oral fluconazole 3 days apart (e.g., days 1, 4, and 7) are options.
- After this initial treatment, maintenance therapy will help prevent recurrence of symptoms.
- Oral fluconazole (e.g., 100-, 150-, or 200-mg dose) weekly for 6 months is typically first-line treatment.

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Table 23.6 Diagnostic Tests Available for Vaginitis

Test	Sensitivity (%)	Specificity (%)	Comments
Bacterial Vaginosis			
pH >4.5	97	64	
Amsel's criteria	92	77	Must meet three of four clinical criteria (pH >4.5, thin watery discharge, >20% clue cells, positive whiff test), but similar results achieved if two of four criteria meet Nugent criteria; Gram stain morphology score (1-10) based on lactobacilli and other morphotypes; score of 1-3 indicates normal flora, score of 7-10 bacterial vaginosis; high interobserver reproducibility
Pap smear	49	93	
Point-of-care tests			
QuickVue Advance, pH + amines	89	96	Positive if pH >4.7
QuickVue Advance, *G. vaginalis*	91	>95	Tests for proline iminopeptidase activity in vaginal fluid; if used when pH >4.5, sensitivity is 95% and specificity is 99%
OSOM BV blue	90	<95	Tests for vaginal sialidase activity
Candida			
Wet mount			
Overall	50	97	
Growth of 3-4 + on culture	85		*C. albicans* a commensal agent in 15%-20% of women
Growth of 1 + on culture	23		
pH ≤4.5	Usual		If symptoms present, pH may be elevated if mixed infection with bacterial vaginosis or *T. vaginalis* present
Pap smear	25	72	
Trichomonas vaginalis			
Wet mount	45-60	95	Increased visibility of microorganisms with a higher burden of infection
Culture	85-90	>95	
pH >4.5	56	50	
Pap smear	92	61	False-positive rate of 8% for standard Pap test and 4% for liquid-based cytologic test
Point-of-care test: OSOM	83	98.8	10 min required to perform tests for *T. vaginalis* antigens

From Eckert LO. Clinical practice: acute vulvovaginitis. *N Engl J Med*. 2006;355(12):1244-1252.

TOXIC SHOCK SYNDROME

- Toxic shock syndrome (TSS) is an acute febrile illness produced by a bacterial exotoxin, with a fulminating downhill course involving dysfunction of multiple organ systems.
- the cardinal features: abrupt onset and rapidity with which the clinical signs and symptoms may present and progress.
- A woman with TSS may develop a rapid onset of hypotension associated with multiorgan system failure.
- *S. aureus* was isolated from the vagina in more than 90% of these cases.
- Nonmenstrual TSS may be a sequelae of focal staphylococcal infection of the skin and subcutaneous tissue, often following a surgical procedure.

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TOXIC SHOCK SYNDROME

- 3 requirements for the development of classic TSS:
  - (1) the woman must be colonized or infected with *S. aureus*
  - (2) the bacteria must produce TSS toxin 1 (TSST-1) or related toxins
  - (3) the toxins must have a route of entry into the systemic circulation.
- signs and symptoms of TSS are produced by the exotoxin named ***toxin 1***.
- gynecologists should have a high index of suspicion for TSS in a woman who has an unexplained fever and a rash during or immediately fol lowing her menstrual period.
- the the patient experiences an abrupt onset of a high temperature associated with headache, myalgia, sore throat, vomiting, diarrhea, generalized skin rash, and often hypotension.

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Box 23.4 Case Definition of Toxic Shock Syndrome

1. Fever (temperature 38.9° C [102° F])
2. Rash characterized by diffuse macular erythroderma
3. Desquamation occurring 1-2 wk after onset of illness (in survivors)
4. Hypotension (systolic blood pressure ≤90 mm Hg in adults) or orthostatic syncope
5. Involvement of three or more of the following organ systems:
   a. Gastrointestinal (vomiting or diarrhea at onset of illness)
   b. Muscular (myalgia or creatine phosphokinase level twice normal)
   c. Mucous membrane (vaginal, oropharyngeal, or conjunctival hyperemia)
   d. Renal (BUN or creatinine level ≥ twice normal or ≥5 WBCs/HPF in absence of UTI)
   e. Hepatic (total bilirubin, SGOT, or SGPT twice normal level)
   f. Hematologic (platelets ≤100,000/mm^3)
   g. Central nervous system (disorientation or alteration in consciousness without focal neurologic signs when fever and hypotension are absent)
   h. Cardiopulmonary (adult respiratory distress syndrome, pulmonary edema, new onset of second- or third-degree heart block, myocarditis)
6. Negative throat and cerebrospinal fluid cultures (a positive blood culture for *Staphylococcus aureus* does not exclude a case)
7. Negative serologic test results for Rocky Mountain spotted fever, leptospirosis, rubeola

From Centers for Disease Control (CDC). Toxic-shock syndrome, United States, 1970-1982. *MMWR Morb Mortal Wkly Rep.* 1982;31:201.
BUN, Blood urea nitrogen; *HPF,* high-powered field; *SGOT,* serum glutamic-oxaloacetic transaminase; *SGPT,* serum glutamic-pyruvic transaminase; *UTI,* urinary tract infection; *WBC,* white blood cell count.

TOXIC SHOCK SYNDROME

- the most characteristic manifestations of TSS are the skin changes.
  - During the first 48 hours, the skin rash appears similar to intense sunburn.
  - During the next few days, the erythema will become more macular and resemble a drug-related rash.
  - From days 12 to 15 of the illness, there is a fine, flaky desquamation of skin over the face and trunk, with sloughing of the entire skin thickness of the palms and soles.

- During pelvic examination, patients complain of tenderness of the external genitalia and vagina.

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Box 23.5 Laboratory Abnormalities in Early Toxic Shock Syndrome

Present in >85% of patients
Coagulase-positive staphylococci in cervix or vagina
Immature and mature polymorphonuclear cells >90% of WBCs
Total lymphocyte count <650/mm^3
Total serum protein level <5.6 mg/dL
Serum albumin level <3.1 g/dL
Serum calcium level <7.8 mg/dL
Serum creatinine clearance >1 mg/dL
Serum bilirubin level >1.5 mg/dL
Serum cholesterol level ≤120 mg/dL
Prothrombin time >12 seconds
Present in >70% of patients
Platelet count <150,000/mm^3
Pyuria >5 WBCs/HPF
Proteinuria ≥2+
BUN >20 mg/dL
Aspartate aminotransferase (formerly SGOT) >41 U/L

From Chesney PJ, Davis JP, Purdy WK, et al. Clinical manifestations of toxic shock syndrome. *JAMA.* 1981;246:746.
BUN, Blood urea nitrogen; *HPF,* high-powered field; *SGOT,* serum glutamic-oxaloacetic transaminase; *WBCs,* white blood cells.
Results were available for at least 18 patients per category with the following exceptions: cervicovaginal cultures (12 patients), cholesterol level (15 patients), and prothrombin time (14 patients).

TOXIC SHOCK SYNDROME

- the management of a classic case of severe TSS demands an intensive care unit and the skills of an expert in critical care medicine.
- the first priority is to eliminate the hypotension produced by the exotoxin.
- Copious amounts of IV fluids are given while pressure and volume dynamics are centrally monitored.
- Mechanical ventilation is required for women who develop adult respiratory distress syndrome.
- When the woman is initially admitted to the hospital, it is important to obtain cervical, vaginal, and blood cultures for *S. aureus*.
- it is prudent to wash out the vagina with saline or dilute iodine solution to diminish the amount of exotoxin that may be absorbed into the systemic circulation.

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TOXIC SHOCK SYNDROME

- Treatment:
- Women with TSS caused by methicillin-susceptible *S. aureus* should be treated with clindamycin, 600 mg IV every 8 hours, plus nafcillin or oxacillin, 2 g IV every 4 hours.
- Most experts recommend a 1- to 2-week course of therapy with an antistaphylococcal agent such as clindamycin or dicloxacillin even in the absence of a positive *S. aureus* culture.
- In patients with TSS caused by methicillin-resistant *S. aureus* (MRSA): clindamycin plus vancomycin (30 mg/kg/day IV in two divided doses) or linezolid (600 mg oral or IV every 12 hours) is used.
- the infected site should be drained and débrided. Treatment with mupirocin to decrease colonization is recommended, applying half of the ointment from a single-use tube into one nostril and the other half into the other nostril twice daily for 5 days.

Comprehensive Gynecology 7th edition, 2017 (Lobo RA, Gershenson DM, Lentz GM, Valea FA *editors);* chapter 23, Genital tract infections

CERVICITIS

CERVICITIS

- can be associated with trauma, inflammatory systemic disease, neoplasia, and infection.
- the cervix (and cervical mucus) acts as a barrier between the abundant bacterial flora of the vagina and the bacteriologically sterile endometrial cavity and oviducts.
- Cervical infection can be ectocervicitis or endocervicitis. Ectocervicitis can be viral (HSV) or from a severe vaginitis (e.g., strawberry cervix associated with *T. vaginalis* infection) or *C. albicans*.
- Endocervicitis may be secondary to infection with *C. trachomatis* or *N. gonorrhoeae*.
- Infection of the endocervix becomes a major reservoir for sexual and perinatal transmission of pathogenic microorganisms.
- Primary endocervical infection may result in secondary ascending infections, including pelvic inflammatory disease and perinatal infections of the membranes, amniotic fluid, and parametria.

MUCOPURULENT CERVICITIS

- 2 simple, definitive, objective criteria have been developed to establish mucopurulent cervicitis:
  - 1. gross visualization of yellow mucopurulent material on a white cotton swab (
  - 2. presence of 10 or more PMN leukocytes per microscopic field (magnification, × 1000) on Gram-stained smears obtained from the endocervix. A
- Symptoms that suggest cervical infection include vaginal discharge, deep dyspareunia, and postcoital bleeding.
- the physical sign of a cervical infection is a cervix that is hypertrophic and edematous.
- *C. trachomatis and N. gonorrhea are* the most common cause of cervical infection in many women with mucopurulent cervicitis

Figure 23.21 Mucopurulent cervicitis demonstrated by a cotton swab test.

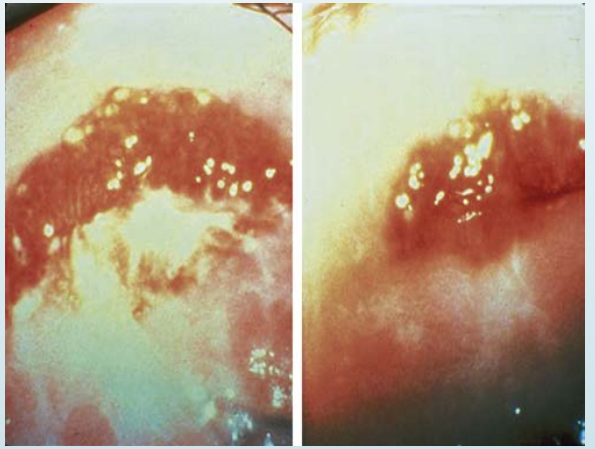

Figure 23.22 Patient with *C. trachomatis* mucopurulent cervicitis with resolution post treatment.

MUCOPURULENT CERVICITIS

- Gold standard for diagnosis: NAAT
- When mucopurulent cervicitis is clinically diagnosed, empirical therapy for *C. trachomatis* is recommended for women at increased risk of this common STI (age <25 years, new or multiple sex partners, unprotected sex).
- Recommended regimens for presumptive cervicitis therapy include:
  - azithromycin, 1 g orally in a single dose
  - doxycycline, 100 mg orally twice daily for 7 days
  - *Add gonococcal treatment if the prevalence is over 5% in the population assessed.*
- Women treated for chlamydia should be instructed to abstain from sexual intercourse for 7 days after single-dose therapy or until completion of the 7-day regimen

Figure 23.21 Mucopurulent cervicitis demonstrated by a cotton swab test.

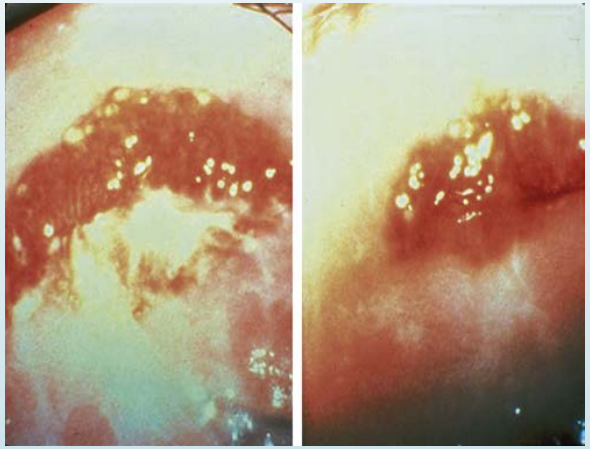

Figure 23.22 Patient with *C. trachomatis* mucopurulent cervicitis with resolution post treatment.

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Box 23.6 Centers for Disease Control and Prevention Recommended Dual Treatment of Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum in Adults (2014)

Ceftriaxone, 250 mg IM, single dose
or, if not an option
Cefixime, 400 mg PO, single dose
plus
Azithromycin 1 g orally in a single doses, preferably under direct observation

Modified from Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep.* 2015;64(RR-03):1-137.

Box 23.7 Recommended Regimens for Treatment of Chlamydial Infection

Azithromycin, 1 g PO, single dose*
or
Doxycycline, 100 mg PO bid for 7 days

Alternative Regimens

Erythromycin base, 500 mg PO qid for 7 days
or
Erythromycin ethylsuccinate, 800 mg PO qid for 7 days
or
Ofloxacin, 300 mg PO bid for 7 days
or
Levofloxacin, 500 mg PO once daily for 7 days

Modified from Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep.* 2015;64(RR-03):1-137. *bid*, Twice per day; *qid*, four times per day.
*Consider concurrent treatment for gonococcal infection if prevalence of gonorrhea is high in the patient population under assessment.

Outline

- Infections of the vulva
- Infections of the vagina
- Infections of the cervix

Thank you!

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