Gynecologic Infections

Jamil D. Bayram and Mamta Malik

Not all gynecologic infections, including pelvic inflammatory disease, are sexually transmitted, although many are. They are often asymptomatic in women and their sex partners.

Sexually transmitted diseases are common, particularly in young, sexually active women with multiple sex partners.

A careful history, physical examination, and diagnostic tests are important to differentiate gynecologic infections because modalities of treatments vary.

Microscopic diagnosis of yeast infections has a sensitivity of only 50% and fails to diagnose the disorder in a large percentage of patients with symptomatic vulvovaginal candidiasis.

Most young, sexually active patients with genital ulcers have a genital herpes infection; syphilis or chancroid disease should be considered as well.

Treatment should be instituted for most gynecologic infections based on the presumed diagnosis because many patients with genital infections will not have a laboratory-confirmed diagnosis.

Gonorrhea is becoming increasingly resistant to antibiotics; the clinician should check local susceptibilities before treatment.

Diseases Characterized by Genital Ulcers

Genital ulcers may also be caused by chancroid, granuloma inguinale, herpes simplex virus (HSV), lymphogranuloma venereum (LGV), and syphilis.

CHANCROID

Epidemiology

The number of reported cases of chancroid in the United States has varied for the past 10 years but remains very low. Only 28 cases were reported domestically in 2009.¹

Pathophysiology

Chancroid, a sexually transmitted disease caused by the short gram-negative bacillus Haemophilus ducreyi, is characterized by painful genital ulcers and painful lymphadenopathy.² The incubation period is 4 to 7 days.

H. ducreyi infection occurs through loss of integrity of the epithelial layer of the skin, most commonly following minor trauma such as sexual intercourse. Once the bacteria have breached the integument, secretion of a cytologically lethal toxin causes apoptosis and necrosis of cells, which results in the characteristic ulcer formation seen with chancroid.

Presenting Signs and Symptoms

H. ducreyi forms a vesicopustule that progresses to a painful ulcer with a necrotic base and surrounding erythema. Because of autoinoculation, multiple lesions may develop.
The adenitis is generally unilateral and tender with overlying erythema. The lesions may become fluctuant and rupture spontaneously. Fever, chills, and malaise may accompany the lymphadenitis. Women may have adenitis without external ulcerative lesions.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

Chancroid must be differentiated from other genital ulcers based on clinical findings. The chancre of syphilis, for example, is clean and painless with a hard base. The diagnosis of chancroid is established by culturing a swab of the lesion onto a specific medium.

The presence of more than one sexually transmitted disease is very common (including syphilis, HSV infection, and human immunodeficiency virus [HIV] infection), as is infection of the ulcer with fusiforms, spirochetes, and other organisms.

**TREATMENT**

Several treatment regimens have been recommended and are listed in Box 126.1.

**FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION**

Follow-up within 1 week to reevaluate the ulceration is recommended. Safe sex practices, such as condom use, as well as regular genital self-examination, should be discussed. Sexual partners should be informed.

**GRANULOMA INGUINALE (DONOVANOSIS)**

**EPIDEMIOLOGY**

The incidence of granuloma inguinale is low, with less than 100 cases reported in the United States per year. The peak demographic of occurrence is in people between the ages of 20 and 40 years who are sexually active.

**PATHOPHYSIOLOGY**

Granuloma inguinale is a chronic granulomatous anogenital infection caused by *Calymmatobacterium granulomatis*. Granuloma inguinale is primarily a sexually transmitted disease, but gastrointestinal transmission is possible. Its onset is insidious, with a median incubation period of about 50 days.

**PRESENTING SIGNS AND SYMPTOMS**

The lesions, which can occur on the skin and mucous membranes of the genitalia or perineal area, are relatively painless nodules that transform into shallow, sharply demarcated ulcers with a red base. The lesions spread by contiguity, and the ulcer then becomes purulent, painful, and foul smelling.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

*C. granulomatis* is difficult to culture because it is an intracellular parasite. Identification is usually made from scraped material or a biopsy specimen obtained from the periphery of the lesion. Bipolar-staining bacteria are best identified within mononuclear cells (Donovan bodies) by Wright or Giemsa staining. Note that genital ulcers are also caused by syphilis, chancroid, and LGV.

**TREATMENT**

See Box 126.2 for treatment.

**FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION**

Risk for relapse remains a concern for up to 18 months after treatment. Carcinoma (squamous and basal cell variants) is

**BOX 126.1 Recommended Treatment Regimens for Chancroid**

<table>
<thead>
<tr>
<th>Treatment Regimen</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin, 1 g orally once</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone, 250 mg intramuscularly once</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin, 500 mg orally twice per day for 3 days*</td>
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<td></td>
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<tr>
<td>Erythromycin base, 500 mg orally three times per day for 7 days</td>
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</table>

*Ciprofloxacin is contraindicated in pregnant and lactating women.

**BOX 126.2 Treatment Regimens for Donovanosis**

A. **Recommended regimen:**
   - Doxycycline, 100 mg orally twice per day for at least 3 weeks and until all lesions have healed completely*

B. **Alternative regimens** (all given orally for a duration of at least 3 weeks and until all lesions have healed completely):
   - Azithromycin, 1 g/wk
   - Ciprofloxacin, 750 mg twice per day*
   - Erythromycin base, 500 mg four times per day
   - Trimethoprim-sulfamethoxazole, 160 mg/800 mg (1 tablet) twice per day*

*Doxycycline and ciprofloxacin are contraindicated in pregnant and lactating women. Sulfonamides are relatively contraindicated.
begin with painful lesions that are often described as burning (Fig. 126.1). These lesions begin as vesicles and then rupture to expose an ulcerated base that persists for 1 to 2 weeks before crusting over and healing without scars. The vesicles and ulcers contain many highly infectious virus particles, and viral shedding occurs until the lesions disappear. Vulvar lesions may last for 3 or more weeks before complete healing. The cervix and vagina may also be involved, with a gray, necrotic cervix and profuse leukorrhea. External dysuria is common, and bilateral inguinal lymphadenopathy is usual.

The primary episode, defined as genital herpes without antibodies to HSV-1 and HSV-2, is typically associated with systemic symptoms, including headache, fever, malaise, and other flulike symptoms in about two thirds of the cases. Following primary infection, latent HSV usually localizes in the sacral ganglion and perhaps the dermis. Recurrent attacks tend to be more subtle and are the most frequently seen outbreaks in the emergency department (ED). Recurrence can be precipitated by immunodeficiency, trauma, fever, or sexual intercourse.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

A significant number of patients with the typical signs and symptoms of herpesvirus infection are later found to have syphilis; therefore, screening for treponemal antibodies is an important part of the ED evaluation. The diagnosis of HSV infection can be made clinically if the typical, painful, shallow multiple vulvar ulcers are present. Laboratory confirmation is best attained by polymerase chain reaction (PCR) testing.
LYMPHOGRANULOMA VENEREUM

EPIDEMIOLOGY

LGV is rarely reported in developed countries—perhaps in part because of the lack of a standardized diagnostic test or surveillance requirements. However, outbreaks have been reported in populations of homosexual men in Western Europe and North America since 2003, with the largest cluster of case reports occurring in the United Kingdom and New York City.

PATHOPHYSIOLOGY

LGV is an acute or chronic sexually transmitted disease caused by Chlamydia trachomatis types L1, L2, and L3. The disease is acquired during intercourse or through contact with contaminated exudates from active lesions. C. trachomatis enters the system through loss of skin integrity (breaks and abrasions) or by crossing the epithelial cells of mucous membranes and multiplies in regional lymph nodes after lymphatic dissemination. The primary mode of transmission is sexual; however, spread by fomites, nonsexual personal contact, and laboratory accidents has been documented.

PRESENTING SIGNS AND SYMPTOMS

The most common clinical manifestation of LGV in heterosexuals is tender inguinal or femoral lymphadenopathy (or both), which is typically unilateral. The initial vesicular or ulcerative lesion is transient and often goes unnoticed. Inguinal buboes appear 1 to 4 weeks after exposure and have a tendency to fuse, soften, and break down to form multiple draining sinuses with extensive scarring. In women, genital lymph drainage is to the perirectal glands. Early anorectal manifestations include proctitis with tenesmus and bloody purulent discharge; late manifestations are chronic inflammation of rectal and perirectal tissue. These changes can lead to obstruction, rectal stricture, and occasionally, rectovaginal and perianal fistulas.

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

The early lesion of LGV must be differentiated from the lesions of syphilis, genital herpes simplex, chancroid, and granuloma inguinale; lymph node involvement must be distinguished from that caused by tularemia, tuberculosis, plague, neoplasm, or pyogenic infection; and rectal stricture must be distinguished from that secondary to neoplasm and ulcerative colitis.

The complement fixation test may be positive, but cross-reaction with other chlamydiae occurs. Although a positive reaction may reflect remote infection, high titers usually indicate active disease. Specific immunofluorescence tests for immunoglobulin M are more specific for acute infection.
ARTHRALGIA, PHARYNGITIS, AND LYMPHADENOPATHY. THIS STAGE IS TYPICALLY SEEN 4 TO 10 WEEKS AFTER THE INITIAL APPEARANCE OF A CHANCER. INFECTIVITY CAN OCCUR IN THE FIRST TWO STAGES (UP TO 2 TO 4 YEARS FOLLOWING INFECTION).

The third stage—the asymptomatic latent phase—may last many years. It is defined as syphilis characterized by seroreactivity without other evidence of disease.

The fourth stage—tertiary syphilis—has numerous neurologic, cardiovascular, and other systemic effects and develops in about 25% of untreated patients.

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

The diagnosis of syphilis should be considered in any patient with an ulcerative lesion in the genital area, as well as in patients with unexplained rashes, arthralgia, and neurologic or systemic complaints.

Screening includes the rapid plasma reagin and Venereal Disease Research Laboratory tests, which must be followed by confirmatory testing when positive. If the serologic results are nonreactive and spirochetes cannot be demonstrated by darkfield examination, the serologic tests should be repeated in 1 month.

TREATMENT

Penicillin remains the mainstay of treatment across the board (Box 126.5). According to the CDC guidelines, parenteral penicillin is considered to be the only treatment documented to be efficacious in pregnancy. Treatment with penicillin is the same as for the corresponding stage of syphilis in non-pregnant women. For pregnant patients who are allergic to penicillin, tetracycline and doxycycline are contraindicated. Pregnant patients who are allergic to penicillin should be skin-tested and desensitized.
The Jarisch-Herxheimer reaction, caused by massive release of treponemal antigens and manifested by fever, headache, and myalgias, can occur in any patient in the first 24 hours following initiation of therapy and is observed most often in patients with early syphilis (frequently in those with secondary syphilis). Because this reaction in pregnant women may precipitate early labor or cause fetal distress, these patients should be hospitalized for monitoring. Concern for this reaction should not prevent or delay therapy. Systemic glucocorticoids administered 12 hours before or concurrent with antibiotics may minimize the effects, and antipyretics have been used for supportive care.

**FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION**

Quantitative serologic tests should be performed in patients with syphilis to monitor the results of treatment. Sexual contacts must be notified and evaluated for possible infection. All patients with syphilis should be tested for HIV to assess for possible coinfection. Delay in diagnosis during pregnancy past 20 weeks’ gestation should prompt fetal ultrasound to rule out congenital syphilis.

**Diseases Characterized by Vaginal Discharge**

**BACTERIAL VAGINOSIS**

**EPIDEMIOLOGY**

Although the range is wide, depending on the population, prevalence rates for bacterial vaginosis (BV) have been estimated to be 4% to 40%. However, because *Gardnerella vaginalis* is present in 50% to 70% of asymptomatic women, the exact incidence of BV is difficult to estimate.

**PATHOPHYSIOLOGY**

BV is a polymicrobial infection that results from replacement of the normal *Lactobacillus* species in the vagina by high concentrations of the anaerobic *G. vaginalis*, *Mycoplasma hominis*, and *Mobiluncus curtisi*. It can be a precursor infection to upper genital tract extension, including cervicitis and pelvic inflammatory disease (PID). Infection is related to the *Lactobacillus* concentration and changes in pH within the vaginal vault but remains primarily multifactorial.

**PRESENTING SIGNS AND SYMPTOMS**

Clinical signs include a thick, homogeneous, milky vaginal discharge sometimes with a fishy odor. Usually, no other symptoms are present.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

BV can be diagnosed with the use of clinical criteria (see Amsel’s diagnostic criteria below) or Gram stain, with the
latter considered to be the “gold standard” laboratory method for diagnosis.

Clinical diagnosis requires three of the following four criteria:

- Homogeneous, thin vaginal fluid that adheres to the vaginal walls
- Presence of vaginal epithelial cells with borders obscured by adherent small bacteria (clue cells)
- Vaginal fluid pH higher than 4.5
- Release of an amine “fishy” odor with alkalinization (adding 10% KOH) of the vaginal fluid (“whiff test”)

**PATHOPHYSIOLOGY**

Trichomoniasis is caused by *Trichomonas vaginalis*, an anaerobic protozoan that is transmitted primarily through sexual activity. *T. vaginalis* measures 10 μm in diameter and structurally has a flagellum that allows it to move around vaginal and urethral tissues. The incubation period for infection ranges from 4 to 28 days.

**PRESENTING SIGNS AND SYMPTOMS**

Many women infected with *T. vaginalis* are asymptomatic. Typical symptoms, if present, include vulvar irritation, dyspareunia, dysuria, urinary frequency, and a malodorous, profuse, purulent vaginal discharge. Physical examination may reveal an erythematous vaginal mucosa or punctate hemorrhages on the cervix.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

Although candidiasis and BV are included in the differential diagnosis of vaginitis, trichomonal infections are less typically associated with pruritus or malodor. The diagnosis is made by identification of motile trichomonads on a saline wet preparation but are seen in only 60% to 70% of confirmed cases when cultures are performed.

**TREATMENT**

Treatment regimens are listed in Box 126.7. Patients with allergy to a nitroimidazole may undergo metronidazole desensitization. Because of adverse pregnancy outcomes with *Trichomonas* infection, such as premature rupture of membranes, preterm delivery, and low birth weight, women can be treated with 2 g metronidazole in a single dose at any stage of pregnancy.

**TRICHOMONIASIS**

**EPIDEMIOLOGY**

Trichomoniasis affects 2 to 3 million women in the United States per year. A total of 216,000 visits to physician offices were reported in women 15 to 44 years of age for this issue in 2009 alone.¹

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Patients in whom trichomoniasis is diagnosed should be advised to notify sex partners to seek treatment because of the known exposure. Investigation for persistent trichomoniasis versus an alternative diagnosis such as candidiasis or gonorrhea should be pursued on follow-up via repeated examination if vaginal discharge is still present.

Vulvovaginal candidiasis (VVC) is exceedingly common, with 75% of women expected to have at least one episode during their lifetime. However, only 10% to 20% of women will have symptoms to the extent that diagnostic and therapeutic considerations are warranted.\(^2\)

**PATHOPHYSIOLOGY**

*Candida albicans* is a normal vaginal flora that is the primary cause of 25% of cases of vaginitis and approximately 90% of vaginal yeast infections (noncandidal species cause the remaining infections). These saprophytic fungi are isolated from the vagina in 20% to 40% of asymptomatic women. Infection should especially be suspected in women who have recently been taking antibiotics or high-dose estrogen oral contraceptives and in women who are immunosuppressed (e.g., due to diabetes or corticosteroid therapy). The pH of vaginal secretions is maintained by the normal vaginal flora (lactobacilli, diphtheroids, and *Staphylococcus epidermidis*) and should be 4.0 to 4.5. Several factors such as age, phase of the menstrual cycle, hormonal contraception, and sexual activity may change the vaginal milieu by causing an increase in vaginal pH and hence may result in vulvovaginitis.

**PRESENTING SIGNS AND SYMPTOMS**

Common symptoms include vulvovaginal pruritus, dyspareunia, external dysuria, and a white, thick, curdlike vaginal discharge. Physical examination typically reveals erythematous or edematous mucosa in addition to the classic discharge described previously.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

Several infections may mimic VVC; however, the diagnosis is based on the characteristic clinical findings along with microscopy. Microscopic evaluation reveals a normal pH (4 to 4.5) with hyphae, pseudohyphae, or budding yeast on a saline wet preparation or 10% potassium hydroxide preparation. Fifty percent of women with candidiasis have a negative wet mount but a positive *Candida* culture. Recurrent VVC, defined as four or more episodes of symptomatic VVC in 1 year, affects 5% of women. Vaginal cultures should be performed for patients with recurrent VVC to confirm the clinical diagnosis and to identify unusual species (including non-*albicans* species), particularly *Candida glabrata*.\(^3\)

**TREATMENT**

Treatment regimens are listed in Box 126.8. For recurrent VVC caused by *C. albicans*, some specialists recommend a longer duration of initial therapy (e.g., 7 to 14 days of topical therapy or a 100-mg, 150-mg, or 200-mg oral dose of fluconazole every third day for a total of three doses [days 1, 4, and 7]) before initiating a maintenance antifungal regimen. Maintenance regimens include oral fluconazole (i.e., 100-mg, 150-mg, or 200-mg dose) weekly for 6 months, which is the first line of treatment. If this regimen is not feasible, topical treatments used intermittently as a maintenance regimen can be considered. For severe VVC (i.e., extensive vulvar erythema, edema, excoriations, and fissure formation), either 7 to 14 days of topical azole or 150 mg of fluconazole in two

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**BOX 126.8 Treatment Regimens for Uncomplicated Vulvovaginal Candidiasis**

<table>
<thead>
<tr>
<th>Over-the-Counter Intravaginal Agents</th>
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</thead>
<tbody>
<tr>
<td>• Butoconazole 2% cream, 5 g intravaginally for 3 days</td>
</tr>
<tr>
<td>or</td>
</tr>
<tr>
<td>• Clotrimazole 1% cream, 5 g intravaginally for 7 to 14 days, or 2% cream, 5 g intravaginally for 3 days</td>
</tr>
<tr>
<td>or</td>
</tr>
<tr>
<td>• Miconazole 2% cream, 5 g intravaginally for 7 days, or 4% cream, 5 g intravaginally for 3 days, or 100-mg vaginal suppository for 7 days, or 200-mg vaginal suppository for 3 days, or 1200-mg vaginal suppository for 1 day</td>
</tr>
<tr>
<td>or</td>
</tr>
<tr>
<td>• Tioconazole 6.5% ointment, 5 g intravaginally in a single application</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Prescription Intravaginal Agents</th>
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</thead>
<tbody>
<tr>
<td>• Butoconazole 2% cream (single-dose bioadhesive product), 5 g intravaginally for 1 day</td>
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<tr>
<td>or</td>
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<tr>
<td>• Nystatin 100,000-unit vaginal tablet, one tablet for 14 days</td>
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<tr>
<td>or</td>
</tr>
<tr>
<td>• Terconazole 0.4% cream, 5 g intravaginally for 7 days, or 0.8% cream, 5 g intravaginally for 3 days, or 80-mg vaginal suppository, one suppository for 3 days</td>
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<table>
<thead>
<tr>
<th>Oral Agent</th>
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</thead>
<tbody>
<tr>
<td>• Fluconazole, 150-mg oral tablet, one tablet in a single dose</td>
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</tbody>
</table>

sequential doses (second dose 72 hours after the initial dose) should be used.3

Options for the treatment of non-albicans VVC include a longer duration of therapy (7 to 14 days) with an azole drug other than fluconazole (oral or topical) as first-line therapy. If VVC recurs, 600 mg of boric acid in a gelatin capsule administered vaginally once daily for 2 weeks is recommended.5

Azole drugs are not absorbed to any degree from the vagina, and these local regimens applied for 7 days are the only ones recommended to be used safely in pregnancy.

FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION

Patients in whom VVC is diagnosed should be advised to have their sex partners evaluated as well given that males with symptomatic balanitis should be identified and treated to prevent recurrent female infection. Avoidance of vaginal douching is encouraged to minimize disruption of the normal vaginal milieu.

Diseases Characterized by Cervicitis and Urethritis

CHLAMYDIA

EPIDEMIOLOGY

C. trachomatis infection is the most commonly reported notifiable disease in the United States. C. trachomatis and Neisseria gonorrhoeae are isolated in combination in about 20% to 40% of women with purulent cervicitis,10 but accurate disease rates are limited by the fact that 80% of women infected with these pathogens are asymptomatic. During the period 2005 to 2009, the chlamydial infection rate in women increased by 20.3% (from 492.2 to 592.2 cases per 100,000 females).1

PATHOPHYSIOLOGY

C. trachomatis is an obligate intracellular bacterium that is transmitted sexually. Chlamydial infections in women are usually asymptomatic and may lead to PID, which is a major cause of infertility and ectopic pregnancy. Women are most commonly seen with infection of the genital tract, typically 1 to 3 weeks after exposure.

PRESENTING SIGNS AND SYMPTOMS

Chlamydial infection is usually asymptomatic and frequently not identified until overt infection develops. It causes a variety of clinical signs and symptoms, including intermenstrual or postcoital bleeding, lower abdominal pain, and even fever. Chlamydia can cause cervicitis, PID, and Fitz-Hugh–Curtis syndrome (FHCS).

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

Chlamydial infections can be diagnosed by culture. However, newer DNA methods using ligase chain reaction or PCR offer both sensitivity and specificity not achieved with the older tests. For DNA tests, samples should be taken from the cervix or from urine.

TREATMENT

Treatment regimens are listed in Box 126.9. In pregnant women, treatment with doxycycline, ofloxacin, and levofloxacin are contraindicated. Therefore, the recommended regimen is azithromycin, 1 g orally in a single dose, or amoxicillin, 500 mg orally three times per day for 7 days, with erythromycins being the alternative regimen.

FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION

Repeated testing 3 to 4 weeks after completion of therapy (test of cure) is recommended only in pregnant women, patients with persistent symptoms, and those with suspected reinfection. Testing for coinfection with HIV or syphilis (or both) should be performed. Patients should be advised to notify sex partners to undergo evaluation, testing, and treatment.

BOX 126.9 Treatment Regimens for Uncomplicated Genital Chlamydia Infections

<table>
<thead>
<tr>
<th>Recommended Regimens</th>
<th>Alternative Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azithromycin, 1 g orally in a single dose</td>
<td>Erythromycin base, 500 mg orally four times per day for 7 days</td>
</tr>
<tr>
<td>or Doxycycline, 100 mg orally twice per day for 7 days</td>
<td>or Erythromycin ethylsuccinate, 800 mg orally four times per day for 7 days</td>
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<tr>
<td></td>
<td>or Levofloxacin, 500 mg orally once daily for 7 days</td>
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<tr>
<td></td>
<td>or Ofloxacin, 300 mg orally twice per day for 7 days</td>
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GONORRHEA

EPIDEMIOLOGY

The highest incidence of infection is found in the 15- to 24-year-old age group, and transmission occurs via sexual contact. In 2009, the gonorrhea rate was 105.5 cases per 100,000 population in women.1

PATHOPHYSIOLOGY

*N. gonorrhoeae*, a gram-negative diplococcus typically found inside polymorphonuclear cells, is the causative agent in gonorrhea infections. Incubation times for gonorrhea range from 3 to 5 days. Infection is usually asymptomatic, but if present, the most common clinical sign is endocervicitis. The virulence and pathophysiology of *N. gonorrhoeae* subtypes depend on the antigenic characteristics of the organism.

PRESENTING SIGNS AND SYMPTOMS

As mentioned in the previous section, infection is often asymptomatic, but if manifestations do develop, they often occur during menses and have a clinical picture similar to that of *Chlamydia* infection. Patients may have dysuria, urinary frequency, and urgency with a purulent urethral discharge. Vaginitis and cervicitis with inflammation of the Bartholin glands are common findings. Infection may be asymptomatic with only slightly increased vaginal discharge and moderate cervicitis on physical examination. Infection may remain as a chronic cervicitis—an important reservoir of gonococci. Systemic complications follow dissemination of gonococci from the primary site via the bloodstream and include meningitis, endocarditis, and arthritis.

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

Gonococcal urethritis or cervicitis must be differentiated from nongonococcal urethritis; from cervicitis or vaginitis secondary to *C. trachomatis*, *G. vaginalis, T. vaginalis*, or *C. albicans*; and from many other pathogens associated with sexually transmitted disease. Gram stains are often negative.

In the past, culture has been the gold standard for diagnosis; however, nucleic acid amplification tests that detect both *N. gonorrhoeae* and *C. trachomatis* in cervical and urethral swab specimens and urine have become more widely used.

TREATMENT

Therapy is typically administered before antimicrobial susceptibilities are known (Box 126.10). The decision to treat can be based on laboratory confirmation; however, in patients with high clinical suspicion for the disease or in those likely to be lost to follow-up, empiric therapy should not be delayed. Specific antibiotic regimens are recommended for patients with complicated gonococcal infections such as bacteremia, endocarditis, arthritis, meningitis, and conjunctivitis. Because antibiotic resistance is becoming an increasing problem, the physician should check local sensitivities before treating.

<table>
<thead>
<tr>
<th>Recommended Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone, 250 mg intramuscularly (IM) in a single dose (treatment of choice)</td>
</tr>
<tr>
<td>Cefixime, 400 mg orally in a single dose</td>
</tr>
<tr>
<td>Ceftizoxime, 500 mg IM and Azithromycin 1 gm orally in a single dose</td>
</tr>
<tr>
<td>Doxycycline 100 mg orally twice daily for 7 days</td>
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<table>
<thead>
<tr>
<th>Alternative Regimens (less desirable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefpodoxime, 400 mg orally</td>
</tr>
<tr>
<td>Cefuroxime axetil, 1 g orally</td>
</tr>
<tr>
<td>Azithromycin, 2 g orally (use in limited circumstances)</td>
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</tbody>
</table>


*Because coexistent chlamydial infection is common, it is recommended that doxycycline (100 mg twice daily orally for 7 days) be added if Chlamydia trachomatis has not been excluded.*

Patients should be advised to notify sex partners to be treated based on exposure regardless of the presence or absence of symptoms. Unprotected sexual intercourse should be avoided until 7 days after completion of the treatment regimen. Uncomplicated cases should be referred to follow-up with a primary care or public health provider within 72 hours for reevaluation. Use of condoms should be recommended with the understanding that they offer partial protection. Serologic testing for syphilis should be performed in all patients with gonorrhea.

URETHRITIS

EPIDEMIOLOGY

Causative agents of nongonococcal urethritis include *Ureaplasma urealyticum* (40% to 60% of cases), *C. trachomatis*
(15% to 55% of cases), *M. hominis* (5% to 10% of cases), and *T. vaginalis* (<5% of cases).

**PATHOPHYSIOLOGY**

Urethritis can result from infectious and noninfectious conditions. Infectious urethritis is usually transmitted sexually and is categorized as gonococcal urethritis (*N. gonorrhoeae*) or nongonococcal urethritis (i.e., *C. trachomatis*, *U. urealyticum*, *M. hominis*, *Mycoplasma genitalium*, *T. vaginalis*). Asymptomatic infections are common. Rare infectious causes of urethritis most commonly include LGV, herpes genitalis, syphilis, and adenovirus.

**PRESENTING SIGNS AND SYMPTOMS**

Symptoms, if present, include discharge of mucopurulent or purulent material, dysuria, and urethral pruritus.

**DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING**

Gram stain is the preferred rapid diagnostic test for evaluating urethritis. The presence of gram-negative intracellular diplococci on a urethral smear is indicative of gonorrhea infection, which is frequently accompanied by chlamydial infection. If Gram stain microscopy is not available, patients should be treated with drug regimens effective against both gonorrhea and chlamydia.

Urethritis can be documented on the basis of any of the following signs or laboratory tests:

- Mucopurulent or purulent discharge on examination
- Microscopy of urethral secretions demonstrating five or more white blood cells (WBCs) per oil immersion field
- Positive leukocyte esterase test on first-void urine or microscopic examination of first-void urine sediment demonstrating 10 or more WBCs per high-power field

**TREATMENT**

For gonococcal urethritis, refer to the treatment of uncomplicated gonorrhea infections. Because of possibility of concomitant infection, *Chlamydia* infection should be presumed and also treated unless it is ruled out. See Box 126.11 for the treatment of nongonococcal urethritis.

**FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION**

Reevaluation is recommended if the symptoms persist or recur following completion of therapy. Alternative causes (*T. vaginalis*, HSV, adenovirus, *Mycoplasma*, and *Ureaplasma* species) should be pursued when nongonococcal urethritis does not improve with the recommended treatment.

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**BOX 126.11 Treatment Regimens for Nongonococcal Urethritis**

**Recommended Regimens**
- Azithromycin, 1 g orally in a single dose
- Doxycycline, 100 mg orally twice per day for 7 days

**Alternative Regimens**
- Erythromycin base, 500 mg orally four times per day for 7 days
- Erythromycin ethylsuccinate, 800 mg orally four times per day for 7 days
- Levofloxacin, 500 mg orally once daily for 7 days
- Ofloxacin, 300 mg orally twice per day for 7 days

**Recurrent or Persistent Urethritis**
- Metronidazole, 2 g orally in a single dose
- Tinidazole, 2 g orally in a single dose, plus azithromycin, 1 g orally in a single dose (if not used for the initial episode)

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**PELVIC INFLAMMATORY DISEASE**

**EPIDEMIOLOGY**

PID is diagnosed in more than 1 million women each year. Infertility as a result of tubal involvement after PID is the second most common cause of female infertility in the United States. Following PID, infertility occurs in 12% of women; the risk for ectopic pregnancy increases 7- to 10-fold, and chronic pelvic pain develops in approximately 20% of women.

**PATHOPHYSIOLOGY**

PID is a polymicrobial infection of the upper genital tract (endometrium, fallopian tubes, ovaries) that is associated most commonly with *N. gonorrhoeae* and *C. trachomatis* and, to a lesser extent, with some endogenous organisms, including anaerobes, *Haemophilus influenzae*, and enteric gram-negative...
rods. Retrograde spread of the organisms occurs in as many as 20% of women with cervicitis and often results in PID with salpingitis, endometritis, or tuboovarian abscesses (TOA). PID is most common in young, nulliparous, sexually active women with multiple sex partners.

The specific mechanism of infection in PID is unknown. However, numerous risk factors have been identified, including previous sexually transmitted disease, high number of sexual partners, inconsistent or no regular use of condoms, sexual intercourse at an early age, and intrauterine devices. Pregnancy can be a protective factor because of the mucous plug, which helps prevent upward transmission of infection.

PRESENTING SIGNS AND SYMPTOMS

Symptoms suggesting PID include bilateral lower abdominal pain, dyspareunia, vaginal discharge (75% of patients), abnormal vaginal bleeding, low back pain, nausea and vomiting, and fever. Mucopurulent discharge or leukorrhea in the vaginal vault has good sensitivity but low specificity for PID.

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

Diagnosis of PID is usually based on the clinical findings of lower abdominal tenderness, cervical motion tenderness, or adnexal tenderness for which another cause is not likely (Box 126.12). Women with PID may have subtle or mild symptoms, thus complicating the diagnosis.

The differential diagnosis includes appendicitis, ectopic pregnancy, septic abortion, hemorrhagic or ruptured ovarian cysts or tumors, degeneration of a myoma, and acute enteritis (Fig. 126.3).

TREATMENT

Antimicrobial coverage should include N. gonorrhoeae, C. trachomatis, gram-negative facultative bacteria, anaerobes, and streptococci. No single therapeutic regimen has been established (Box 126.13). Outpatient management is appropriate for most patients with mild to moderate PID who do not meet the criteria for admission.

As a result of the emergence of quinolone-resistant N. gonorrhoeae, regimens that include a quinolone agent are no longer recommended for the treatment of PID.13

Parenteral therapy may be discontinued 24 hours after the patient improves clinically, and oral therapy with doxycycline, 100 mg orally twice daily, should be continued for a total of 14 days.

BOX 126.12 CDC Suggested Criteria for Diagnosis, Empiric Treatment, and Hospitalization for Patients with PID

A. Minimum diagnostic criteria (for diagnosis and empiric treatment of PID in sexually active young women experiencing pelvic or lower abdominal pain if no other cause is identified):

- Cervical motion tenderness
- Adnexal tenderness
- Uterine tenderness

B. Additional diagnostic criteria (used to enhance specificity of the diagnosis of PID once any of the minimum criteria listed above is met):

- Oral temperature higher than 101° F (>38.3° C)
- Abnormal cervical or vaginal mucopurulent discharge
- Presence of abundant numbers of WBCs on saline microscopy of vaginal fluid
- Elevated erythrocyte sedimentation rate
- Elevated C-reactive protein
- Laboratory documentation of cervical infection with Neisseria gonorrhoeae or Chlamydia trachomatis

C. Additional diagnosis criteria (most specific criteria for the diagnosis of PID):

- Histopathologic evidence of endometritis on an endometrial biopsy specimen
- Transvaginal ultrasonography, computed tomography12 (see Fig. 126.3), or magnetic resonance imaging showing thickened, fluid-filled tubes with or without free pelvic fluid and a tuboovarian complex
- Laparoscopic abnormalities consistent with PID

D. Criteria for hospitalization (recommended criteria for hospitalization of patients with PID):

- Unable to exclude surgical emergencies such as appendicitis in the diagnosis
- Pregnancy
- Presence of tuboovarian abscess
- Severe illness such as intractable nausea and vomiting, high fever, or leukocytosis
- Inability to follow or tolerate an outpatient oral regimen
- Failure to respond clinically to oral antimicrobial therapy

Fig. 126.3 Computed tomography scan of a patient with pelvic inflammatory disease showing bilateral adnexal masses. A, Tuboovarian abscesses; U, uterus.


CDC, Centers for Disease Control and Prevention; PID, pelvic inflammatory disease; WBCs, white blood cells.
CHAPTER 126  GYNECOLOGIC INFECTIONS

TUBOOVARIAN ABSCESS

EPIDEMIOLOGY

TOA is the most common intraabdominal abscess in premenopausal women and develops in up to one third of patients hospitalized with PID. Rupture is categorized as a surgical emergency with rates of occurrence as high as 15%.

PATHOPHYSIOLOGY

TOA is usually a complication of PID, although cases can infrequently occur without the preexisting presence of PID. TOAs typically result from salpingitis that progresses to oophoritis. Ovarian infection occurs after contamination with purulent material from the fallopian tube. Adherence of tubal fimbriae to the ovary forms a large, cylinder-shaped TOA. Most TOAs consist of polymicrobial anaerobic bacteria.

PRESENTING SIGNS AND SYMPTOMS

Patients with TOA typically have abdominal pain and severe, asymmetric tenderness, often with peritoneal signs on palpation. Fever and leukocytosis are usually but not always present as well. TOA can be bilateral, although unilateral disease is more common and accounts for 60% of such abscesses.

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

Definitive diagnosis is made by direct visualization or use of an imaging study. Pelvic ultrasonography has a reported sensitivity of 93% and specificity of 98%. Computed tomography may be used to define the abscess better or may be appropriate if the ultrasound evaluation is inconclusive. Appendicitis, PID, and ovarian torsion are common entities in the differential diagnosis.

TREATMENT

All patients with suspected TOA should be hospitalized. Initial parenteral therapy options are the same as those listed for PID, but continued oral therapy should include clindamycin (or metronidazole) for 14 days in addition to doxycycline.

TOAs may require transcutaneous or transvaginal aspiration. Surgical excision is also an option. Unless rupture is suspected, high-dose antibiotic therapy should be instituted, and the efficacy of therapy should be monitored with ultrasonography. Ruptured TOA is a life-threatening condition that requires immediate medical therapy associated with surgery.

Unilateral adnexitomy is acceptable for unilateral abscesses. Hysterectomy and bilateral salpingo-oophorectomy may be necessary for overwhelming infection or in cases of chronic disease with intractable pelvic pain.

BOX 126.13 Treatment Regimens for Pelvic Inflammatory Disease

Outpatient Treatment Regimens

Recommended regimen:
- Ceftriaxone, 250 mg intramuscularly (IM) once, plus doxycycline, 100 mg orally (PO) twice daily for 14 days, with or without metronidazole, 500 mg PO twice daily for 14 days
  - or
- Cefoxitin, 2 g IM in a single dose, and probenecid, 1 g PO, administered concurrently in a single dose, plus doxycycline, 100 mg PO twice daily for 14 days, with or without metronidazole, 500 mg PO twice daily for 14 days
  - or
- Cefotaxime, 500 mg (or ceftriaxone, 500 mg) IM once, plus doxycycline, 100 mg PO twice daily for 14 days, with or without metronidazole, 500 mg PO twice daily for 14 days

Alternative regimen:
- If parenteral cephalosporin therapy is not available: Fluoroquinolones (levofloxacin, 500 mg PO once daily, or ofloxacin, 400 mg twice daily for 14 days) with or without metronidazole (500 mg PO twice daily for 14 days)

Inpatient Treatment Regimens (Parenteral)

Recommended regimen:
- Cefotetan 2, g intravenously (IV) every 12 hours (or cefoxitin, 2 g IV every 6 hours), plus doxycycline, 100 mg PO or IV every 12 hours
  - or
- Clindamycin, 900 mg IV every 8 hours, plus a gentamicin loading dose IV or IM (2 mg/kg of body weight), followed by a maintenance dose (1.5 mg/kg) every 8 hours. Single daily dosing (3 to 5 mg/kg) can be substituted

Alternative regimen:
- Ampicillin-sulbactam, 3 g IV every 6 hours, plus doxycycline, 100 mg PO or IV every 12 hours


FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION

Compliance with the full 2-week course of oral antibiotic therapy should be encouraged. Advise against sexual activity pending resolution of the disease process. Patients should be referred for follow-up in 72 hours for reevaluation. Patients should be advised to notify any sex partners who were active with the patient during the 60 days before the onset of symptom to receive treatment as per CDC recommendations.
FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION

Compliance with the full 2-week course of oral antibiotics should be encouraged. Patients should be referred for follow-up in 72 hours for reevaluation. Advise against sexual activity pending resolution of the disease process.

FITZ-HUGH–CURTIS SYNDROME

EPIDEMIOLOGY

The incidence of FHCS is lower in adult women (4% to 14%) than in adolescent girls (27%).

PATHOPHYSIOLOGY

FHCS is described as inflammation of the liver capsule (perihepatitis) without damage to the liver parenchyma. A purulent or fibrinous exudate appears on the capsular surface, and swelling of the liver capsule produces pleuritic right upper quadrant pain. This syndrome is an extrapelvic manifestation of PID.

PRESENTING SIGNS AND SYMPTOMS

Illness consists of two phases. The acute phase is characterized by sharp, right upper quadrant, pleuritic abdominal pain that can radiate to the shoulder; the chronic phase results from the formation of peritoneal adhesions, which cause persistent, typically right upper quadrant abdominal pain. Tubal infections may or may not be present concurrently.

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

Perihepatitis was formerly believed to be caused solely by N. gonorrhoeae, but C. trachomatis is now known to more often be the causative agent. Salpingitis is invariably the source, but the syndrome occasionally follows appendicitis and other causes of peritonitis. FHCS is frequently misdiagnosed as cholecystitis, pneumonia, perforated peptic ulcer, or renal colic. Liver enzyme levels may be mildly elevated.

Diagnosis is difficult and based on clinical features. A high index of suspicion should be maintained in women seen in the ED with upper abdominal pain and normal routine results on gallbladder and liver function tests. FHCS is a more likely cause of upper quadrant pleuritic pain than cholecystitis is and should be suspected in any woman with pleuritic upper quadrant pain and physical signs of salpingitis. Associated signs and symptoms of fever, leukocytosis, abdominal pain, cervicitis, or PID may be present, but their absence does not exclude the diagnosis.

TREATMENT

The goal of treatment is bacterial eradication with antibiotics to prevent chronic abdominal pain and adhesions. Complications are uncommon but can include subdiaphragmatic abscess and small bowel obstruction.

Although no formal antibiotic recommendations exist, patients with FHCS usually require admission for observation and parenteral antibiotic therapy. Initial options are the same as those listed for inpatient treatment of PID. Like TOA, continued outpatient oral therapy should include clindamycin (or metronidazole) for 14 days in addition to doxycycline.

FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION

Compliance with the full 2-week course of oral antibiotic therapy should be encouraged. Advise against sexual activity pending resolution of the disease process. Patients should be referred for follow-up in 72 hours for reevaluation. Patients should be advised to notify any sex partners who were active with the patient during the 60 days before the onset of symptom to receive treatment as per CDC recommendations.
CHAPTER 126  GYNECOLOGIC INFECTIONS

Diseases Characterized by Genital Warts or Mucosal Abscess

HUMAN PAPILLOMAVIRUS

EPIDEMIOLOGY

HPV is the most common sexually transmitted virus in the United States. Its prevalence corresponds inversely with age (highest in younger age groups, 50% in females 20 to 24 years of age) and declines substantially after the age of 24 years. However, the gross clinical prevalence of HPV is less than 1%.11

PATHOPHYSIOLOGY

HPV is a double-stranded DNA virus that infects the epithelial cells of skin and mucosa and can cause cellular changes leading to formation of warts. HPV infection is a sexually transmitted illness that is most commonly asymptomatic but has been associated with various disease processes such as benign anogenital warts, as well as with invasive cancer. Of the greater than 100 types of HPV, more than 40 can infect the genital area. A quadrivalent HPV vaccine that provides protection against types 6, 11, 16, and 18 was licensed for use in the United States in June 2006. HPV subtypes 6 and 11 most commonly cause genital warts (condylomata acuminata),3 which can occur on the vulva, perianal area, urethra, vaginal walls, or cervix. These subtypes have also been identified as the causative agent of laryngeal or respiratory papillomatosis in infants and children, but the route of transmission is not completely understood.

PRESENTING SIGNS AND SYMPTOMS

The average incubation period for visible warts is about 3 months. Genital warts may be asymptomatic but can be pruritic. On clinical examination the lesions are generally papillary, verrucous (wartlike), or macular in character (Fig. 126.5). Lesions usually first appear individually, but large confluent growths can develop. Vaginal and cervical warts are more common than labial warts, although most of them are flat lesions visible only with colposcopy.

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

Several laboratory methods such as PCR have been developed for confirmation of genital HPV infection, but the ED diagnosis remains primarily clinical.

TREATMENT

Subclinical genital HPV infection usually clears spontaneously. Treatment is indicated for those with genital warts or precancerous lesions and not for subclinical HPV infection (Box 126.14).

Extensive warts may require CO2 laser treatment under local or general anesthesia. Intravesical interferon, photodynamic therapy, and topical cidofovir are associated with more side effects and are no more effective than other therapies.

In women who have exophytic cervical warts, biopsy evaluation to exclude high-grade squamous intraepithelial lesions must be performed before treatment is initiated. Management of exophytic cervical warts should include consultation with a specialist.

FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION

Curative measures to prevent transmission once infected are not available, and therefore routine examination of sex...
BOX 126.14 Treatment Regimens Recommended for External Genital Warts Caused by Human Papillomavirus

Patient Applied

- Podofilox 0.5% solution or gel, twice per day for 3 days, followed by 4 days of no therapy. This cycle can be repeated, as necessary, for up to four cycles
- Imiquimod 5% cream, once daily at bedtime three times per week for up to 16 weeks
- Sinecatechin 15% ointment, three times daily for up to 16 weeks

Provider Administered

- Cryotherapy with liquid nitrogen or cryoprobe. Applications repeated every 1 to 2 weeks
- Podophyllin resin, 10% to 25% in a compound tincture of benzoin
- Trichloroacetic acid or dichloroacetic acid, 80% to 90%
- Surgical removal by either tangential scissors excision, tangential shave excision, curettage, or electrosurgery

Swelling of the Bartholin glands occurs in 2% of women of reproductive age, most commonly between the ages of 20 and 30. Development of this disease process in patients older than 40 years is atypical and should lead to assessment for possible malignancy as part of the diagnostic and treatment plan.

PATHOPHYSIOLOGY

The Bartholin glands are bilateral vulvovaginal secretory structures located in the labia minora on the posterolateral aspect of the vestibule. Normally pea sized, these glands drain fluid through a 2.5-cm duct into a fold between the hymeneal ring and the labium that serves to maintain moisture of the vaginal mucosa. Duct occlusion can result in cyst and subsequently abscess formation. Isolates from cultures of abscesses are most commonly anaerobic organisms (*Bacteroides fragilis*, *Peptostreptococcus*), aerobic *N. gonorrhoeae* is the causative agent in approximately 10% to 15% of cases, and *C. trachomatis* is found even less frequently.

PRESENTING SIGNS AND SYMPTOMS

Onset of disease can occur rapidly over a period of several hours or may progress more gradually over several days. The initial symptoms are pain, dyspareunia, and sometimes fever. Findings on physical examination are a unilateral labial mass with tenderness, redness, and swelling in the Bartholin gland area. Elevated temperature is observed in approximately one third of patients.

Microscopically, acute inflammation is present within the Bartholin duct, as well as within the gland stroma about the duct. The abscess, when fully developed, contains purulent exudate.

DIFFERENTIAL DIAGNOSIS AND MEDICAL DECISION MAKING

Cultures and Gram staining of material expressed from the duct may identify gonococci. Cervical gonococcal and chlamydial cultures should be performed and the organisms treated if present.

TREATMENT

Management of the abscess consists of simple incision and drainage. After sterile preparation of the area, a scalpel stab incision, ideally no longer than 1.5 cm (longer incisions will make it difficult to keep the Word catheter in place), should be made deep into the abscess from the inside of the labium. An outside incision can cause permanent fistula formation. Loculations should be broken manually followed by placement of a Word catheter with its balloon tip inserted into the abscess before inflation with water or lubricating gel (Fig. 126.6). Simple incision and drainage without Word catheter placement may be inadequate and result in recurrence. After successful drainage, routine antibiotic therapy is not recommended for uncomplicated Bartholin gland abscesses in otherwise healthy women. Treatment of *N. gonorrhoeae* and *C. trachomatis* should be initiated only in patients with confirmed disease.

FOLLOW-UP, NEXT STEPS IN CARE, AND PATIENT EDUCATION

Follow-up in 72 hours for reevaluation should be arranged. Refer the patient to gynecology for removal of the catheter in 2 to 4 weeks.
SUGGESTED READINGS


REFERENCES

References can be found on Expert Consult @ www.expertconsult.com.
REFERENCES


