associated with resistance to other antibiotics, spectinomycin can be reserved for use against multidrug-resistant strains of *N. gonorrhoeae*. Nevertheless, outbreaks caused by strains resistant to spectinomycin have been documented in Korea and England when the drug has been used for primary treatment of gonorrhea.

Third-generation cephalosporins have remained highly effective as single-dose therapy for gonorrhea, but the recent isolation of strains highly resistant to ceftriaxone (minimal inhibitory concentrations [MICs], 2 μg/mL) in Japan and some European countries is cause for concern. Even though the MICs of ceftriaxone against certain strains may reach 0.015–0.125 μg/mL (higher than the MICs of 0.0001–0.008 μg/mL for fully susceptible strains), these levels are greatly exceeded in the blood, the urethra, and the cervix when the routinely recommended parenteral dose of ceftriaxone is administered. The rising MICs of oral cefixime (the previously recommended alternative oral third-generation cephalosporin) against *N. gonorrhoeae*, combined with this drug's limited capacity to reach levels sufficiently higher than MICs in the blood, the urethra, the cervix, and especially the pharynx, have resulted in the removal of cefixime from the list of first-line agents for treatment of uncomplicated gonorrhea. All *N. gonorrhoeae* strains with reduced susceptibility to ceftriaxone and cefixime (i.e., cephalosporin-intermediate/resistant strains) contain (1) a mosaic *penA* allele, which is the principal resistance determinant and encodes a penicillin-binding protein (PBP2) whose sequence differs in 60 amino acids from that of wild-type PBP2, and (2) additional genetic resistance determinants that are also required for high-level penicillin resistance.

CLINICAL MANIFESTATIONS

Gonococcal Infections in Men Acute urethritis is the most common clinical manifestation of gonorrhea in male patients. The usual incubation period after exposure is 2–7 days, although the interval can be longer and some men remain asymptomatic. Strains of the PorB.1A serotype tend to cause a greater proportion of cases of mild and asymptomatic urethritis than do PorB.1B strains. Urethral discharge and dysuria, usually without urinary frequency or urgency, are the major symptoms. The discharge initially is scant and mucoid but becomes profuse and purulent within a day or two. Gram's staining of the urethral discharge may reveal PMNs and gram-negative intracellular monococci and diplococci (Fig. 181-1). The clinical manifestations of gonococcal urethritis are usually more severe and overt than those of nongonococcal urethritis, including urethritis caused by *Chlamydia trachomatis* (Chap. 213); however, exceptions are common, and it is often impossible to differentiate the causes of urethritis on clinical grounds alone. The majority of cases of urethritis seen in the United States today are not caused by *N. gonorrhoeae* and/or *C. trachomatis*. Although a number of other organisms may be responsible, many cases do not have a specific etiologic agent identified.

Most symptomatic men with gonorrhea seek treatment and cease to be infectious. The remaining men, who are largely asymptomatic, accumulate in number over time and constitute about two-thirds of all infected men at any point in time; together with men incubating the organism (who shed the organism but are asymptomatic), they serve as the source of spread of infection. Before the antibiotic era, symptoms of urethritis persisted for ~8 weeks. Epididymitis is now an uncommon complication, and gonococcal prostatitis occurs rarely, if at all. Other unusual local complications of gonococcal urethritis include edema of the penis due to dorsal lymphangitis or thrombophlebitis, submucous inflammatory "soft" infiltration of the urethral wall, periurethral abscess or fistula, inflammation or abscess of Cowper's gland, and seminal vesiculitis. Balanitis may develop in uncircumcised men.

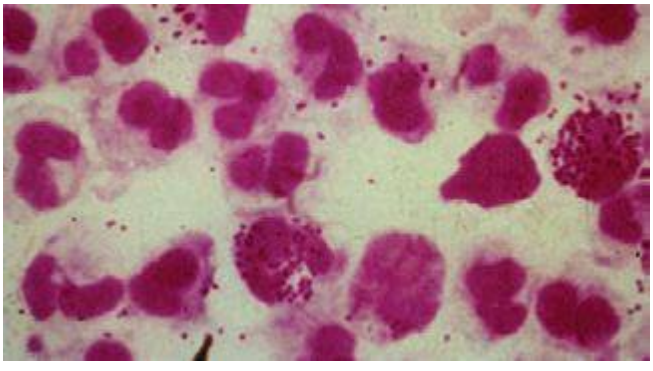

FIGURE 181-1 Gram's stain of urethral discharge from a male patient with gonorrhea shows gram-negative intracellular monococci and diplococci. *(From the Public Health Agency of Canada.)*

Gonococcal Infections in Women • ***GONOCOCCAL CERVICITIS*** Mucopurulent cervicitis is a common STI diagnosis in American women and may be caused by *N. gonorrhoeae, C. trachomatis*, and other organisms, including *Mycoplasma genitalium* (Chap. 212). Cervicitis may coexist with candidal or trichomonal vaginitis. *N. gonorrhoeae* primarily infects the columnar epithelium of the cervical os. Bartholin's glands occasionally become infected.

Women infected with *N. gonorrhoeae* usually develop symptoms. However, the women who either remain asymptomatic or have only minor symptoms may delay in seeking medical attention. These minor symptoms may include scant vaginal discharge issuing from the inflamed cervix (without vaginitis or vaginosis per se) and dysuria (often without urgency or frequency) that may be associated with gonococcal urethritis. Although the incubation period of gonorrhea is less well defined in women than in men, symptoms usually develop within 10 days of infection and are more acute and intense than those of chlamydial cervicitis.

The physical examination may reveal a mucopurulent discharge (mucopus) issuing from the cervical os. Because Gram's stain is not sensitive for the diagnosis of gonorrhea in women, specimens should be submitted for culture or a nonculture assay (see "Laboratory Diagnosis," below). Edematous and friable cervical ectopy and endocervical bleeding induced by gentle swabbing are more often seen in chlamydial infection. Gonococcal infection may extend deep enough to produce dyspareunia and lower abdominal or back pain. In such cases, it is imperative to consider a diagnosis of pelvic inflammatory disease (PID) and to administer treatment for that disease (Chaps. 163 and 213).

N. gonorrhoeae may also be recovered from the urethra and rectum of women with cervicitis, but these are rarely the only infected sites. Urethritis in women may produce symptoms of internal dysuria, which is often attributed to "cystitis." Pyuria in the absence of bacteriuria seen on Gram's stain of unspun urine, accompanied by urine cultures that fail to yield $>10^2$ colonies of bacteria usually associated with urinary tract infection, signifies the possibility of urethritis due to *C. trachomatis*. Urethral infection with *N. gonorrhoeae* may also occur in this context, but in this instance urethral cultures are usually positive.

GONOCOCCAL VAGINITIS The vaginal mucosa of healthy women is lined by stratified squamous epithelium and is rarely infected by *N. gonorrhoeae*. However, gonococcal vaginitis can occur in anestrogenic women (e.g., prepubertal girls and postmenopausal women), in whom the vaginal stratified squamous epithelium is often thinned down to the basilar layer, which can be infected by *N. gonorrhoeae*. The intense inflammation of the vagina makes the physical (speculum and bimanual) examination extremely painful. The vaginal mucosa is red and edematous, and an abundant purulent discharge is often present. Infection in the urethra and in Skene's and Bartholin's glands often accompanies gonococcal vaginitis. Inflamed cervical erosion or abscesses in nabothian cysts may also occur. Coexisting cervicitis may result in pus in the cervical os.

Anorectal Gonorrhea Because the female anatomy permits the spread of cervical exudate to the rectum, *N. gonorrhoeae* is sometimes recovered from the rectum of women with uncomplicated gonococcal cervicitis. The rectum is the sole site of infection in only 5% of women with gonorrhea. Such women are usually asymptomatic but occasionally have acute proctitis manifested by anorectal pain or pruritus, tenesmus, purulent rectal discharge, and rectal bleeding. Among men