However, repeated anovulation may result in bleeding that, in certain clinical situations, may prompt an endometrial biopsy. In this setting biopsies reveal stromal condensation and eosinophilic epithelial metaplasia similar to those seen in menstrual endometrium. However, unlike menstrual endometrium, the endometrium of women with anovulatory cycles lacks progesterone-dependent morphologic features (e.g., glandular secretory changes and stromal pre-decidualization), since the source of progesterone, the corpus luteum, does not develop without ovulation. Most commonly the endometrium is comprised of pseudostratified glands and contains scattered mitotic figures (Fig. 22-20*A*). More severe consequences of repeated anovulation are discussed under "Endometrial Hyperplasia."

Inadequate Luteal Phase

This term refers to a condition that manifests clinically as infertility associated with either increased bleeding or amenorrhea. The cause is believed to be inadequate progesterone production during the post-ovulatory period. Endometrial biopsy performed at an estimated postovulatory date shows secretory endometrium with features that lag behind those expected for the estimated date.

Inflammatory Disorders

The endometrium and myometrium are relatively resistant to infections, primarily because the endocervix forms a barrier to ascending infection. Thus, although chronic inflammation in the cervix is an expected and frequently insignificant finding, it is of concern in the endometrium, excluding the menstrual phase.

Acute Endometritis

Acute endometritis is uncommon and limited to bacterial infections that arise after delivery or miscarriage. Retained products of conception are the usual predisposing influence; the causative agents include group A hemolytic streptococci, staphylococci, and other bacteria. The inflammatory response is chiefly limited to the stroma and is entirely nonspecific. Removal of the retained gestational fragments by curettage, accompanied by antibiotic therapy, promptly clears the infection.

Chronic Endometritis

Chronic endometritis occurs in association with the following disorders:

- Chronic pelvic inflammatory disease (PID)
- Retained gestational tissue, postpartum or post-abortion
- Intrauterine contraceptive devices
- Tuberculosis, either from miliary spread or, more often, from drainage of tuberculous salpingitis. Both are rare in Western countries.

The diagnosis of chronic endometritis rests on the identification of plasma cells in the stroma, which are not seen in normal endometrium (Fig. 22-20*B*). In about 15% of cases no cause is apparent. Some women with this so-called "nonspecific" chronic endometritis have gynecologic complaints such as abnormal bleeding, pain, discharge, and infertility. *Chlamydia* may be involved and is commonly associated with both acute (e.g., neutrophils) and chronic (e.g., lymphocytes, plasma cells) inflammatory cell infiltrates. The responsible organisms may or may not be detected by culture. If infection is suspected on clinical grounds, antibiotic therapy is indicated even in the face of negative cultures, as it may prevent other sequelae (e.g., salpingitis).

Endometriosis and Adenomyosis

Endometriosis is defined by the presence of "ectopic" endometrial tissue at a site outside of the uterus. The abnormal tissue most commonly includes both endometrial glands and stroma, but may consist only of stroma in some cases. It occurs in the following sites, in descending order of frequency: (1) ovaries, (2) uterine ligaments, (3) rectovaginal septum, (4) cul de sac, (5) pelvic peritoneum, (6) large and small bowel and appendix, (7) mucosa of the cervix, vagina, and fallopian tubes, and (8) laparotomy scars.

Endometriosis takes a significant toll on the afflicted; it often causes *infertility, dysmenorrhea* (painful menstruation), *pelvic pain*, and other problems. The disorder is principally a disease of women in active reproductive life, most often in the third and fourth decades, and affects approximately 6% to 10% of women. Uncommonly endometriosis may "invade" and "spread," behaviors that often contribute to significant complications. For example, involvement of the muscular wall of the bowel by endometriosis can result in intestinal symptoms (Fig. 22-21).

Pathogenesis. The pathogenesis of endometriosis remains elusive. Proposed origins of endometriotic lesions fall into two main categories: (1) those that propose an origin from the uterine endometrium and (2) those that propose an origin from cells outside the uterus that have the capacity to give rise to endometrial tissue. The leading theories are as follows:

- *The regurgitation theory* proposes that endometrial tissue implants at ectopic sites via retrograde flow of menstrual endometrium. Retrograde menstruation through the fallopian tubes occurs regularly even in normal women and can explain the distribution of endometriosis within the peritoneal cavity.
- *The benign metastases theory* holds that endometrial tissue from the uterus can "spread" to distant sites (e.g., bone, lung, and brain) via blood vessels and lymphatic channels.
- *The metaplastic theory* suggests that endometrium arises directly from coelomic epithelium (mesothelium of pelvis or abdomen), from which the müllerian ducts and ultimately the endometrium itself originate during embryonic development. In addition, mesonephric remnants may undergo endometrial differentiation and give rise to ectopic endometrial tissue.
- *The extrauterine stem/progenitor cell theory* is a recent idea that proposes that stem/progenitor cells from the bone marrow differentiate into endometrial tissue.