

Testing for the presence of HPV DNA in the cervical scrape is a molecular method of cervical cancer screening. HPV testing has a higher sensitivity but lower specificity, as compared to Pap test. HPV DNA testing may be added to cervical cytology for screening in women aged 30 years or older. HPV testing of women younger than 30 is not recommended because of the high incidence of infection, and thus the particularly low specificity of HPV test results in this age group.

- Cervical cancer screening and preventive measures are carried out in a step wise fashion. Recommendations for the frequency of Pap screening vary, but in general the first smear should be at age 21 years or within 3 years of onset of sexual activity, and thereafter every 3 years. After age 30, women who have had normal cytology results and are negative for HPV may be screened every 5 years. Women with a normal cytology result, but test positive for high-risk HPV DNA, should have cervical cytology repeated every 6 to 12 months.
- When the result of a Pap test is abnormal, a colposcopic examination of the cervix and vagina is performed to identify the lesion. The mucosa is examined with a magnifying glass following application of acetic acid, which highlights abnormal epithelium as white spots (*acetowhite areas*). Abnormal appearing areas are biopsied. Women with biopsy confirmed LSIL can be followed in a conservative fashion. Some gynecologists will perform local ablation (e.g., cryotherapy) of LSIL, particularly if there is concern about the reliability of patient follow-up. HSILs are treated with cervical conization (superficial excision).

- **A new aspect of cervical cancer prevention is vaccination against high-risk oncogenic HPVs, which is now recommended for all girls and boys by age 11 to 12 years, as well as young men and women up to age 26 years.** Two HPV vaccines are now FDA-licensed. Both provide nearly complete protection against high-risk oncogenic HPV types 16 and 18 (together accounting for approximately 70% of cervical cancers), and one also provides protection against HPV types 6 and 11, which are responsible for genital warts. Vaccination is now recommended for boys as well as girls due to the role of that males play in the spread of HPV to women and the toll that HPV-related anal and oropharyngeal cancers take in men. The vaccines offer protection for up to 10 years; longer follow-up studies are still pending. Since the HPV vaccine does not protect against all high-risk HPV types, current guidelines recommend that cervical cancer screening be continued as in the past.

### KEY CONCEPTS

- Cervical low-grade squamous intraepithelial lesions (LSILs) are productive HPV infections that usually regress spontaneously, but occasionally progress to high-grade squamous intraepithelial lesions (HSILs).
- HSILs are characterized by progressive deregulation of the cell cycle and increasing cellular atypia. HSILs may progress to invasive carcinoma.
- Almost all cervical precursor lesions and cervical carcinomas are caused by high-risk HPV types, most commonly HPV-16.

## BODY OF UTERUS AND ENDOMETRIUM

The uterus has two major components: the myometrium and the endometrium. The myometrium is composed of tightly interwoven bundles of smooth muscle that form the wall of the uterus. The internal cavity of the uterus is lined by the endometrium, which is composed of glands embedded in a cellular stroma. The uterus is affected by a variety of disorders, the most common of which results from endocrine imbalances, complications of pregnancy, and neoplastic proliferation.

### Endometrial Histology in the Menstrual Cycle

**The endometrium undergoes dynamic physiologic and morphologic changes during the menstrual cycle in response to sex steroid hormones coordinately produced in the ovary.** The ovary is influenced by hormones produced by the pituitary due to signals from the hypothalamus. Together the hypothalamic, pituitary, and ovarian factors and their interactions regulate maturation of ovarian follicles, ovulation, and menstruation.

“Dating” the endometrium by its histologic appearance may be used to assess hormonal status, document ovulation, and determine causes of endometrial bleeding and

infertility (Fig. 22-19). Progression through a normal menstrual cycle is correlated with the following histologic features:

- The cycle commences with *menses*, during which the superficial portion of the endometrium, referred to as the functionalis, is shed.
- The *proliferative phase* is marked by rapid growth of glands and stroma arising from the deeper portion of the endometrium (basalis). During the proliferative phase the glands are straight, tubular structures lined by regular, tall, pseudostratified columnar cells. Mitotic figures are numerous, and there is no evidence of mucus secretion or vacuolation. The endometrial stroma is composed of spindle cells with scant cytoplasm that are also actively proliferating (Fig. 22-19A).
- At *ovulation*, endometrial proliferation ceases and differentiation commences in response to the effects of progesterone made by the corpus luteum in the ovary.
- *Postovulation* is initially marked by the appearance of *secretory vacuoles* beneath the nuclei in the glandular epithelium (Fig. 22-19B). Secretory activity is most prominent during the third week of the menstrual cycle, when the basal vacuoles progressively move to the apical surface. When secretion is maximal, between 18 and 24 days, the glands are dilated. By the fourth week