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Normal Endometrium

During the reproductive years, normal endometrium comprises glands, stroma, and vascular elements that synchronously proliferate, differentiate, and then disintegrate at roughly 28-day intervals. During a menstrual cycle, the epithelium lining the glands, stroma, and vasculature of the functional layer of the endometrium undergoes well-defined morphological changes. At the same time, the glands and stroma of the basal portion of the corpus endometrium and the lower uterine segment endometrium show no significant morphological changes. Our descriptions of normal endometrium are based on 1,012 contemporaneously gathered hysterectomy-controlled cases and 1,690 office-based samplings (Table 5.1).

Proliferative Endometrium

During its proliferative phase, the endometrium responds to increasing estrogen levels by the synchronous proliferation of glands, stroma, and blood vessels. Based on an average 28-day menstrual cycle, proliferative endometrial changes may be divided into early (days 4–7), mid (days 8–10), and late (days 11–13) intervals. Because of persisting estrogens, perimenopausal endometrium is generally indistinguishable from proliferative endometrium. During the early proliferative phase, the growth of all three endometrial components is coordinated. Later, both gland and blood vessel

TABLE 5.1. Normal endometrium.

Diagnosis	Hysterectomy	Average Age (years)	Office Biopsy (% with cell block)	Average Age (years)
Proliferative	347	46	500 (90%)	42
Interval	25	41	61 (97%)	41
Secretory	310	42	481 (97%)	42
Menstrual	47	41	76 (97%)	41
Mixed function			29 (87%)	48
Inactive/atrophic	235	55	433 (51%)	58
Benign NOS	48	45	110 (71%)	45
Total	1,012		1,690	

NOS, not otherwise specified.

development outpace the development of the stroma, and, as a result, glands and blood vessels become coiled.

The epithelium of early proliferative endometrium typically shows narrow, straight glands (Fig. 5.1) and cohesive, flat sheets (Fig. 5.2) that exhibit mild nuclear crowding and overlapping which reflects nuclear pseudostratification. Although the epithelial cell layer of early proliferative endometrium is only one cell thick, its pseudostratification results from and reflects resting nuclei occupying a basal position within the cell's apical-to-base axis and actively dividing nuclei occupying an apical position (Fig. 5.3). Epithelial cell nuclei are oval to cigar shaped, with smooth contours, evenly dispersed chromatin, and small, conspicuous nucleoli. The nuclear-to-cytoplasmic ratio is relatively high. Mitotic figures, although present, are less conspicuous in early than in mid and late proliferative periods. The background of cytology preparations is clean. Because of persisting endometrial breakdown and remodeling, some stromal/epithelial exodus-like structures, similar to the stromal-epithelial aggregates seen in contemporaneously collected cervicovaginal smears, are seen. This finding does not indicate noncyclical endometrial breakdown and bleeding.

Mid and late proliferative endometrium resembles early proliferative endometrium except that glandular cells show slightly more prominent small nucleoli and more frequent mitoses. The nuclear size of dividing cells varies (anisonucleosis) because dividing cells have 2N or 4N chromatin in addition to mitotic figures. The cells' nuclei may resemble those of a benign hyperplasia and, rarely,

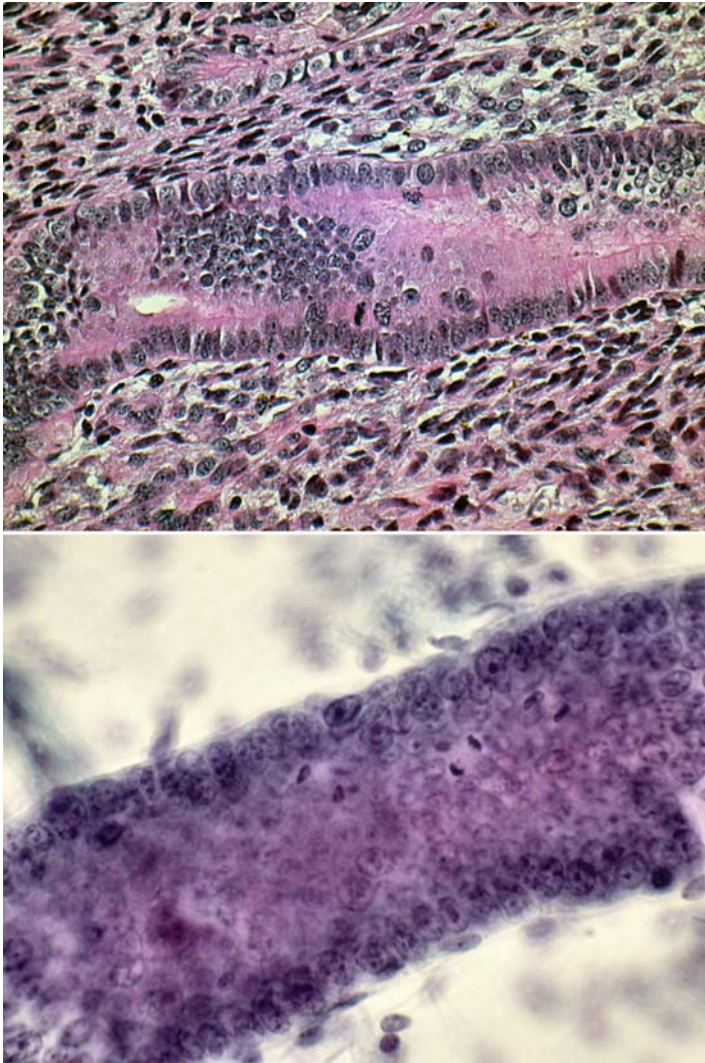


FIG. 5.1. A cell block (*top*) and brush cytology preparation (*bottom*) show the organization of the proliferative endometrial gland. The nuclei are tightly packed and pseudostratified. Apical mitoses are seen. The glands of proliferative endometrium replicate one another in size and in proliferative activity in that they are regularly regular. One of the subtlest keys to the cytological recognition of disordered proliferative states is up to threefold size variability between otherwise architecturally preserved glands.

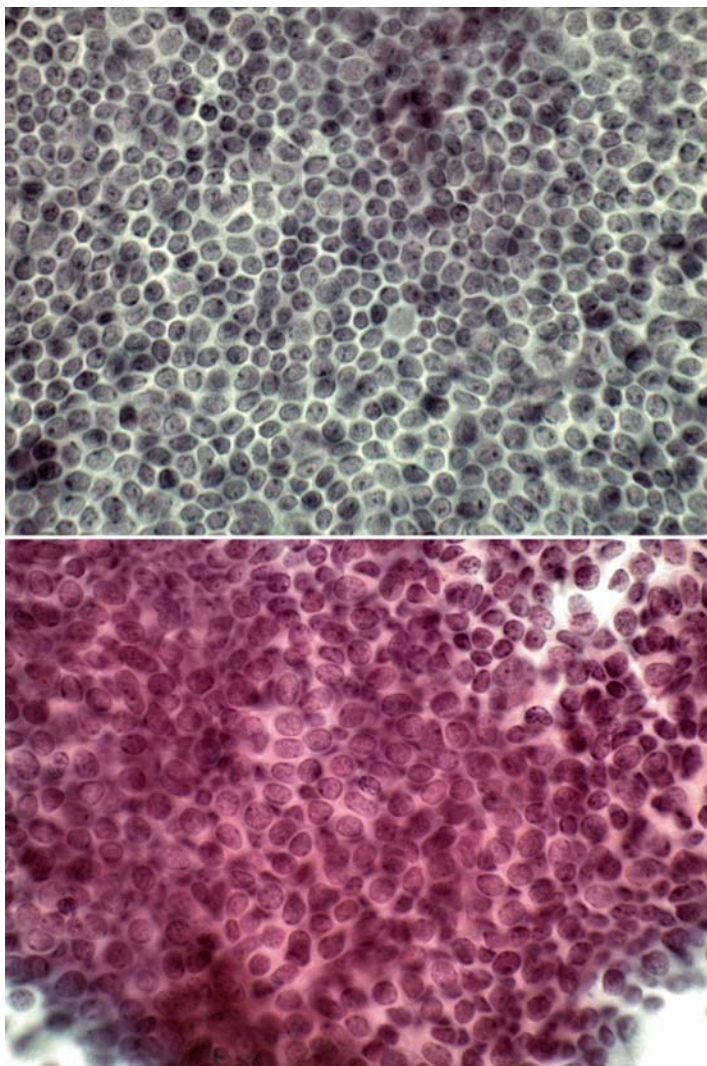


FIG. 5.2. An en face view of surface proliferative endometrium is not unlike that seen in surface epithelium of the early postmenopausal years. Nuclei appear crowded because of pseudostratification. The *top image* shows occasional interspersed ciliated cells that appear larger with more voluminous nucleoplasm. The *bottom image* shows how cell crowding with pseudostratification causes nuclei to appear as if they are mounted one over another. Pseudostratification should not be misinterpreted as loss of polarity; rather, it reflects the functional status of the epithelial sheet.

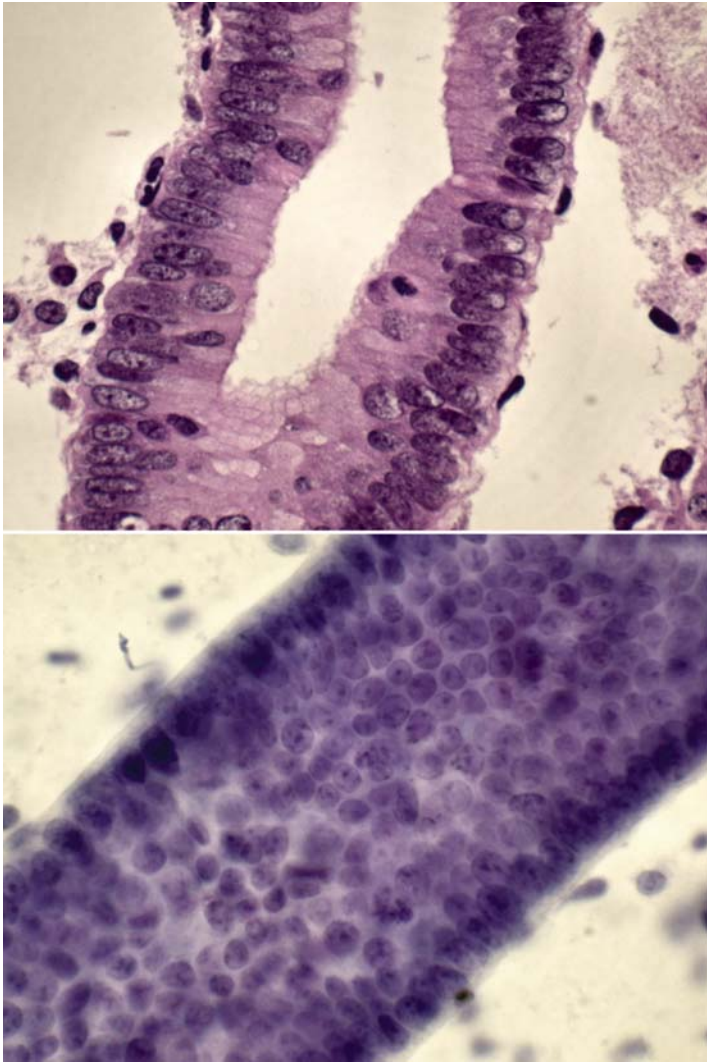


FIG. 5.3. A cell block (*top*) and brush cytology preparation (*bottom*) show the organization of the proliferative endometrial gland. The nuclei are tightly packed and pseudostratified. Apical mitoses are seen. Pseudostratification results from and reflects resting nuclei occupying the basal position within the cell's apical-to-base axis and actively dividing nuclei occupying the apical position. The rather tight but orderly nuclear packing of proliferative endometrium reflects the functional nuclear-dominant metabolism enjoyed by these cells. More mitotic figures may be seen among the glands of proliferative endometrium than in endometrial cancer.

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