biopsy or curettage is part of a comprehensive workup of the patient in the operating room that includes laparoscopy, hysteroscopy, or hysterosalpingography to assess the presence or absence of uterine or tubal lesions that contribute to infertility. In these cases, the endometrial sampling may not be timed as precisely for the mid- to late luteal phase. Nonetheless, histologic evaluation provides the gynecologist with information regarding the response of the endometrium to hormonal stimulation, including indirect evidence of ovulatory function.

The secretory phase is constant in the normal cycle, lasting 14 days from the time of ovulation to the onset of menstruation. Variations in cycle length occur because the proliferative phase of the cycle varies, both between cycles and between women. Accordingly, the gynecologist correlates the cycle date by histology with the woman’s cycle date based on the time of onset of the upcoming menstrual period, not the last menstrual period. Ovulation with secretory endometrial changes ceases in most women by age 53, although rarely ovulation with secretory endometrium and a confirmed corpus luteum of the ovary has been seen up to at least age 56 (personal observation).

The biopsy findings help confirm that ovulation occurred, and indicate whether there was sufficient secretory effect, mediated by progesterone, during the luteal phase. To utilize fully the morphologic interpretation, the gynecologist compares the histologic date to the clinical data, including the date of the rise in the basal body temperature, the time of the serum
luteinizing hormone (LH) surge, transvaginal ultrasound evaluation of follicular or corpus luteum development, serum progesterone level, or subtraction of 14 days from the onset of menses. Consequently, the biopsy typically is timed to coincide with the luteal (secretory) phase of the cycle. In addition to defining the precise histologic date, an endometrial biopsy is part of the infertility workup to exclude other organic uterine abnormalities.

This chapter reviews the morphologic variations caused by ovarian hormonal stimulation that provide a background for the interpretation of endometrial biopsies in infertility patients. These patterns include changes resulting from normal hormonal fluctuations during the menstrual cycle and variations in normal development that are caused by abnormalities in the endogenous ovarian hormonal levels during the reproductive years. The latter represent the so-called dysfunctional abnormalities that are, for the most part, due to abnormalities in ovarian follicular development or in hormone production by the corpus luteum. Ovarian dysfunction also can result in abnormal bleeding, and Chapter 5 reviews dysfunctional uterine bleeding caused by ovulatory abnormalities. During gestation the endometrium undergoes other “normal,” that is, physiologic, alterations as discussed in Chapter 3.

General Considerations in Histologic Evaluation

Histologic evaluation begins with identification of surface epithelium, a prerequisite for orienting the underlying glands and stroma. The surface epithelium is less responsive to sex steroid hormones than the underlying glands, but it often shows alteration in pathologic conditions, especially when the abnormalities are subtle or focal. For example, during the proliferative phase, estrogenic stimulation induces development of ciliated cells along the surface. In contrast, ciliated surface epithelial cells are far more frequent in pathologic conditions, particularly those associated with unopposed estrogen stimulation, such as hyperplasia and metaplasia.

The subsurface endometrium is divided into two regions, the functionalis (stratum spongiosum) and the basalis (stratum basale) (Fig. 2.1). The functionalis, situated between the surface epithelium and the basalis, is important to evaluate because it shows the greatest degree of hormonal responsiveness. The size and distribution of glands as well as the cytologic features of the glandular epithelial cells are important features in the histologic evaluation. Under normal conditions, the glands should be regularly spaced and have a perpendicular arrangement from the basalis to the surface epithelium. In the secretory phase, the endometrium also shows a stratum compactum, a thin region beneath the surface epithelium. In the stratum compactum the stroma is dense and the glands are straight and narrow, even when the glands in the functionalis are tortuous. The basalis adjoins the myometrium, serving to regenerate the functionalis and surface epithelium following shedding during menses. The endometrium of the basalis is less responsive to steroid hormones, and typically shows irregularly shaped, inactive appearing glands, dense stroma, and aggregates of spiral arteries. The spiral arteries of the basalis (basal arteries) have thicker muscular walls than those in the functionalis. In biopsies, tissue fragments that contain basalis often do not have surface epithelium. The glands and stroma of the basalis cannot be dated, as they are unresponsive to steroid hormones. A specimen consisting solely of endometrium from the basalis is therefore inadequate for dating.

Tissue from the lower uterine segment or isthmus is another region of the endometrium that is less responsive to steroid hormones. In the lower uterine segment the endometrium has shorter, poorly developed, inactive glands dispersed in a distinctive stroma (Fig. 2.2). The columnar cells lining the glands resemble those of the corpus. Some glands near the junction with the endocervix show a transition to mucinous endocervical-type epithelium. The stromal cells in the lower uterine segment are elongate and resemble fibroblasts with more abundant eosinophilic cytoplasm, in contrast to the oval to rounded stromal cells with minimum cytoplasm seen in the corpus.