Chapter 1

Endometrium

Histology of the endometrium
  Superficial functional layer
  Basal layer
Endometrial cells
  Luminal epithelial cells
  Glandular epithelial cells
Endometrial cycle
The menstrual cycle
  The menstrual phase
  The proliferative phase (estrogenic or follicular)
  The secretory phase (luteal or progesterational)
Molecular biology of the endometrial cycle
Objectives

The lining of the uterus is comprised of elements essential to the pregnancy process. As the endometrium continuously changes, the maternal milieu that surrounds the embryo also changes. During this process the embryo and endometrium are in constant communication.

The purpose of this chapter is to:

1) Review the normal histology of the endometrium.
2) Review the morphologic and functional differences between luminal and glandular endometrial epithelia.
3) Review the morphology and molecular aspects of the endometrial and ovarian cycles.
4) Concentrate on the changes that occur in preparation for implantation.

Histology of the endometrium

The endometrium consists of columnar epithelium with or without cilia (depending on the phase of the menstruation cycle) and its basal lamina, glands, and a specialized, cellular stroma rich with blood vessels (Fig. 1-1) (PATTEN, 1953; AREY, 1954; RHODIN, 1974). The circulation consists of end branches of the uterine arteries called spiral arteries as well as a venous outflow system (BARASH, ET AL., 1992; BROSENS, ET AL., 2002).

Functionally, the endometrium consists of two layers:

1) Superficial functional layer
2) Basal layer

SUPERFICIAL FUNCTIONAL LAYER

This layer is lost during menstruation and regenerates during the proliferative phase of the menstrual cycle from the basal layer. The morphological features of the functional layer change during the menstrual cycle, which usually lasts 28 days.

BASAL LAYER

This layer is retained as the source of regeneration of a new functional layer following the menstrual flow. Its morphological appearance does not change with the menstrual cycle.
FIGURE 1-1. Histology of the endometrium.
The endometrium consists of a single layered columnar surface epithelium, penetrating into the underlying connective tissue and thus forming tubular glands. The epithelium has different types of cells. The surface (luminal) cells have microvilli and cilia. They also form uterodomes. The number of ciliated cells change with the menstrual cycle. The secretory epithelium forms tubular glands and secretes glycogen and other substances during the secretory phase. The stromal cells are mesenchymal in origin but they are mixed with an abundance of bone marrow derived immunocompetent cells. The endometrium goes through cyclic alterations that involve the uterine glands and blood vessels as preparation for blastocyst implantation and placental development.
**Endometrial cells**

Two main cell types that constitute the endometrial lining, the *luminal epithelial cells* (LE) and the *glandular epithelial cells* (GE), both originate from the same progenitor cells in the basal glands during postmenstrual regeneration (*Fig. 1-1*) (*FERENCZY, ET AL., 1974A, 1974B, 1995*).

**LUMINAL EPITHELIAL CELLS (LE)**

Luminal epithelial cells (LE) are distinct from the glandular epithelium. They are cuboidal, show less cyclic secretory changes and at the mid-secretory phase develop apical cell swellings called *uterodomes* or *pinopodes* (*Figs. 1-1, 2, 3*). These structures have been associated with a high level of receptivity of the endometrium (*FERENCZY, ET AL., 1974A, 1974B; LUDWIG, ET AL., 1991; BENTIN-LEY, ET AL., 1999, 2002; DEVELIOGLU, ET AL., 1999; NIKAS, ET AL., 1999, 2002; STAVREUS-EVERS, ET AL., 2001, 2002; ADAMS, ET AL., 2002*). Some luminal cells have cilia but their numbers change with the phase of the cycle. These ciliated cells are distributed in small groups or singly among large populations of luminal cells. They also have numerous microvilli. Occasionally cells have relatively few cilia and a few microvilli but contain apical protrusions of varying heights (*Figs. 1-1, 2, 3A and 3B*).

**GLANDULAR EPITHELIAL CELLS (GE)**

The uterine glands are simple glands with slight branching. The epithelial cells lining these glands are responsible for the changes in the secretory phase. They are columnar, and have pronounced secretory organelles during this phase.

Ultrastructurally the luminal epithelial cells are characterized by a moderate number of microvilli and occasional small protrusions (*Figs. 1-3A, 3B*). *FERENCZY ET AL., 1974A, 1974B; BENTIN-LEY, ET AL., 1999; 2002*). Although the microvilli are usually relatively short (approximately 0.2 µm in length), microvilli on secretory cells adjacent to the endometrial glands are often much taller (0.5-1 µm in length). Secretory cells also possess one and occasionally two central cilia, which are slightly thinner and considerably shorter than the cilia on ciliated cells. During the secretory phase, the morphology of the endometrial lining changes dramatically. The formation of uterodomes is accompanied by a loss of free surface microvilli. When uterodomes are pinched off and separate from the cell body, crater-like invaginations form. This is a typical pattern seen in the secretory phase.
**FIGURE 1-2.** Close up diagram of the endometrial epithelium.
1) Surface (luminal) epithelium with cilia. 2) Luminal epithelium with microvilli. 3) Epithelial cell with an uterodome. 4) Basal lamina. 5) Stromal cells.