Benign Changes of the Female Genital Tract

Portio and Vagina

Physiological Changes

Cytolysis

Due to the activity of vaginal lactobacilli (Döderlein bacilli), the cytoplasm of intermediate cells lysed and glycogen is liberated. The sugar molecules derived from the glycogen are then metabolized into lactic acid. This creates an acidic environment and serves as a protective mechanism against potentially pathogenic microbes.

The physiological disintegration of squamous epithelial cells is called cytolysis. As the process requires glycogen-containing cells, it can only take place when the vaginal epithelium has developed at least the upper intermediate cell layer (Fig. 3.1) (411). No cytolysis is observed in an atrophic smear because parabasal cells do not contain glycogen (410). Superficial cells are protected from cytolysis because of their keratin-like cytoplasmic scaffold; hence, there is no cytolysis even when estrogen activity is high and the eosinophilia index is also high. (409).

Physiological cytolysis affects only the cytoplasm, not the nucleus (379). It is brought about by Döderlein bacilli, lactobacilli that exist only in the vagina. These bacilli are immobile rods of various lengths—though they exhibit a relatively uniform length within the same smear (227). Long piliform variants occasionally occur (Fig. 3.2). The bacilli completely or partially dissolve the cytoplasm of glycogen-containing intermediate cells, thus creating a fine granular protein precipitate that is sometimes misinterpreted as “coccal flora” by inexperienced examiners (Fig. 3.3). The bacilli then ferment the released glycogen to lactic acid. The resulting acidic environment (approximately pH 4) protects the epithelium against infections as it creates unfavorable growth conditions for foreign bacteria (410). Cytolysis therefore largely excludes the presence of pathogens from the vagina, although fungal infections are not affected by colonization of the vagina with lactobacilli.

If cytolysis is pronounced, most of the nuclei exist as naked nuclei and often show edematous swelling, although the chromatinit structure is still well preserved and the nuclear envelope smooth. The enlarged nuclei pose a problem when cytolysis needs to be differentiated from dysplastic processes (Fig. 3.4). Topical application of an antibiotic will prevent cytolysis and may thus be advantageous when establishing the diagnosis (368).

The presence of a lactobacillus flora is not necessarily associated with the image of cytolysis in the vaginal smear. This is particularly true when the cells have been collected with a spatula, since this procedure predominately sets free cells derived from the superficial tissue layer where cytolysis caused by bacteria is not possible. By contrast, collecting the cells with a cotton swab yields cells from the vaginal secretion covering the portio vaginalis, and this essentially consists of defoliated cells that are in the process of undergoing cytolysis (322).

Degeneration

Unlike cytolysis, the degeneration of cells found in the cytological smear affects both cytoplasm and nucleus.

Nuclear changes:
- Nuclear swelling
- Karyolysis
- Karyorrhexis
- Karyopyknosis
- Hyperchromatic nuclear envelope

Cytoplasmic changes:
- Perinuclear halo
- Pseudoeosinophilia
- Vacuolation
- Hyalinization
- Structural changes
- Heterolysis
- Changes in cell shape
- Condensation of mucus
- Disturbed cell maturation
Benign Changes of the Female Genital Tract

Fig. 3.1 **Image of cytolysis.** In addition to well-preserved and partly basophilic, partly eosinophilic superficial cells with pyknotic nuclei, there are large intermediate cells undergoing lysis. Their nuclei are vesicular and often naked (→). There are numerous rod-shaped bacteria, representing vaginal lactobacilli (Döderlein bacilli). ×400.

Fig. 3.2 **Lactobacilli.** A piliform, elongated morphological variant of these bacilli and vesicular cell nuclei are visible between the superficial cells. ×630.

Fig. 3.3 **Cytolysis by lactobacilli.** Vesicular, naked nuclei (→) and cytoplasmic debris, accompanied by a dust-like protein precipitate. ×630.
Whereas cytolysis by lactobacilli is a sign of vitality of the squamous epithelium with well-preserved nuclei, degeneration is a process of cell death (necrosis) that is largely induced by the unfavorable environment of exfoliated cells. The absence of lactobacilli causes the pH to rise, thus leading almost instantly to the appearance of foreign bacteria (185). Even without a visible inflammatory reaction, this causes rapid cell death, with the loss of a normal chromatin structure being observed particularly in the less resistant parabasal and endocervical cells, but also in the more highly differentiated squamous epithelial cells and nonepithelial cells (93).

**Nuclear Changes**

- **Nuclear swelling:** Osmotic cell regulation ceases, causing water influx and nuclear swelling (Figs. 3.5-3.7). This may cause problems in distinguishing degeneration from dysplastic processes (160).
- **Karyolysis:** The formation of unstructured, hypochromatic, and enlarged nuclei is called karyolysis (Fig. 3.5).
- **Karyopyknosis:** Loss of water then causes the dead nuclei to shrink and become hyperchromatic; this is called nuclear condensation or karyopyknosis (Fig. 3.5) (178, 425).
- **Karyorrhexis:** The rupture of the nucleus into fragments is called karyorrhexis. The chromatin structure first becomes very

---

Fig. 3.4 **Cytolysis by lactobacilli.** The swelling of individual nuclei, yielding nuclei with several times their normal size (→). Their chromatin structure remains evenly distributed, and the nuclear envelope is smooth. ×630.

Fig. 3.5 **Karyopyknosis.** Nuclear degeneration of parabasal cells by both karyolysis and karyopyknosis, resulting in an increased (→) or decreased (⇐) nuclear size. The cytoplasm is often pale and pseudoeosinophilic, or it shows hyaline degeneration (⇓). ×400.
Fig. 3.6 **Karyorrhexis.** Nuclear degeneration by karyorrhexis, while the cytoplasm is still intact. The nuclei are hyperchromatic; they show a perforated nuclear envelope and a fragmented chromatin pattern (→). At the terminal stage, only some nuclear debris remains (→→). ×630.

Fig. 3.7 **Hyperchromatic nuclear envelopes.** The smear shows atrophic vaginitis with partial activation and enlargement of the nuclei, and also formation of nucleoli. Also visible are degenerative changes of nuclei and cytoplasm, such as cytoplasmic signs of cytolysis and pseudoeosinophilia and distinct hyperchromatic nuclear envelopes (→→). The background of the preparation indicates inflammation. ×400.

Fig. 3.8 **Perinuclear halo.** Cytoplasmic degeneration of a parabasal cell (→). The nucleus is already condensed, and the cytoplasm is amphophilic and shows a perinuclear halo. A still intact parabasal cell (on the right) and several superficial cells lie nearby. ×630.
coarse and then disintegrates, while gaps in the nuclear envelope result in a fragmented chromatin pattern (Fig. 3.6). The entire chromatin scaffold finally breaks up into many condensed and hyperchromatic fragments.

- **Hyperchromatic nuclear envelope**: Chromatin particles adhering to the inner nuclear membrane create the appearance of a hyperchromatic nuclear envelope (Fig. 3.7) (93).

**Cytoplasmic changes**

- **Perinuclear halo**: Shrinking of the nuclei leads to the formation of perinuclear halos (Fig. 3.8) (160).
- **Pseudoeosinophilia**: The degenerative changes eventually affect the cytoplasm as well; it becomes pseudoeosinophilic as a result of denaturation (Fig. 3.9) (368).
- **Vacuolation**: Water uptake leads to cell enlargement and formation of vacuoles (Fig. 3.10).
- **Hyalinization**: Condensation of the cytoplasm causes intense red staining, which is called hyalinization (Fig. 3.11) (356).
- **Structural changes**: Disintegration (or partial lysis) of the cytoplasm is often the result
of structural changes. In some areas of the cell, the cytoplasm may exhibit complete chromophobia, although some rudimentary structures are still stained. The stained structures may appear as dots (“polka dot cells,” Fig. 3.12) or as ridges that form window-like gaps between them (“fenestrated cells,” Fig. 3.13) (212).

**Heterolysis:** Lysis of the cytoplasm due to enzymes derived from bacteria other than Döderlein bacilli is called heterolysis (Fig. 3.14). Especially with atrophic cells, this may lead to confluence of several cells and formation of pseudosyncytial cells, known as **cell cohesion** (Fig. 3.15) (358). When the cytoplasm lyses completely, naked nuclei remain and often dominate the entire cell image.

**Changes in shape:** Cell degeneration naturally affects atrophic smears, in particular, because parabasal cells are very sensitive to environmental factors. Elongation of the cytoplasm, possibly due to forces acting on the cell surface, leads to the formation of **spindle-shaped** cells (Fig. 3.16).

**Condensation of mucus:** Chemotactic effects cause condensation of the mucus that covers the cells. This is probably responsible for the presence of blue blobs in the smears; these may be easily confused with enlarged naked nuclei with nucleoli (Fig. 3.17) (1).

**Disturbed cell maturation:** Severely degenerated smears occasionally exhibit signs of a disturbance of squamous epithelial maturation, showing cells with hugely
Fig. 3.13 **Fenestrated cells.** Cytoplasmic degeneration of superficial cells with partial disintegration resulting in ridges. The cells are overlaid by leukocytes. A normal intermediate cell is visible on the lower right. ×630.

Fig. 3.14 **Image of heterolysis.** Infection with *Gardnerella* causes the cytoplasm of intermediate cells to disintegrate without simultaneously inducing an inflammatory reaction. ×250.

Fig. 3.15 **Atrophic cell cohesion.** Pseudosyncytial cell sheet formed by parabasal cells. ×630.