

SLIDE DESCRIPTIONS

THE NORMAL UTERINE CERVIX

Histology Of The Ectocervix

1. The normal epithelium of the ectocervix in the cyclic woman is a nonkeratinizing stratified squamous epithelium within which the complete life cycle of the squamous cell occurs beginning in the basal or germinal layer and is completed through senescence and cell death at the surface. In contrast to the epidermis, the normal ectocervical mucosa is composed of four layers: the germinal layer, deep and superficial spinus layers, and the superficial layer, lacking a granular cell layer and stratum corneum. In the routine cytologic sample, cells from the superficial and superficial spinus layers only are observed. In the child or postmenopausal adult, cells more reminiscent of the superficial and deep spinus layers predominate.

2. The normal, mature nonkeratinizing stratified squamous epithelium of the uterine cervix retains the potential for further differentiation. This is a protective mechanism on the part of the epithelium in response to a variety of external stimuli and is commonly observed in uterine prolapse or descensus. Further differentiation is usually manifested by the development of a granular cell layer and stratum corneum as depicted here. Within the normal epithelium, it is unusual to observe kerato-hyalin pearl formation or individual cell keratinization. This process of "hyperdifferentiation" in the uterine cervix is often referred to as hyperkeratosis.

Cytology Of The Squamous Mucosa

3. Cells derived from the superficial layer of the cervical mucosa are usually polygonal in configuration with small, pyknotic nuclei. Superficial squamous cells possess a cell area of approximately $1600 \mu^2$. The nuclei occupy 2 to 3 percent of the total cell area and possess a calculated area of approximately $20-30 \mu^2$. The cytoplasmic staining reaction is usually eosinophilic although cyanophilic superficial squamous cells are observed.

4. Depicted here are four superficial squamous cells and portion of an intermediate squamous cell. Note the pyknotic nuclei, polygonal configurations and eosinophilic staining reactions of the superficial squamous cells. Compare the nucleus of the intermediate squamous cell with those of the superficial squamous cells. The former has two to three times the area ($30-40 \mu^2$), a finely granular chromatin pattern, and, frequently, a longitudinal fold.

5. While the cell in the upper left hand portion of this slide contains a pyknotic nucleus, the other three cells depicted represent intermediate squamous cells. Like the superficial squamous cell, intermediate squamous cells possess a polygonal configuration and similar cytoplasmic area. Their cytoplasmic staining reaction varies from a predominant cyanophilia to eosinophilia.

6. Depicted in this slide are two intermediate squamous cells and two superficial squamous cells. Note that the main distinction between them is the size and morphology of the nucleus. Cytoplasmic staining reaction and area (size), are not constant distinguishing features.

7. Under dominant progesterone stimulation, as in pregnancy or luteal phase of the menstrual cycle, the stratified squamous mucosa of the uterine cervix does not reach full maturation. In this situation there is a dominance of cells of the intermediate squamous type. Also, resulting from progesterone stimulation, glycogen accumulates in the cytoplasm of the intermediate squamous cells. Depicted here are intermediate squamous cells with prominent perinuclear glycogen deposition. In the center of the field are several intermediate squamous cells with a boat-shaped or navicular configuration. This configuration is most often observed in cellular samples derived from the pregnant patient.

8. In the presence of hyperkeratosis of the uterine cervical epithelium, mature squamous cells reflecting this alteration in maturation are frequently observed in the cellular sample. Anucleate squames, illustrated in the lower portion of this field, are the characteristic cell type observed in the presence of

hyperkeratosis. Less frequently, cells originating from the granular cell layer may be present. The granular cell is characterized by the presence of brown cytoplasmic granules of varying size, illustrated here by the upper orangeophilic squamous cell and cyanophilic intermediate type squamous cell on the right. The eosinophilic superficial squamous cell in the upper-left portion of the field contains uniform pale granules which probably represent an artifact of incomplete dehydration or drying during cover-slipping. Such granules should not be confused with the coarser brown granules of the true granular cell.

9. Again depicted are anucleate squames characteristically associated with hyperkeratosis of the uterine cervix. Note that the squames in the upper portion of the field contain "nuclear ghosts." The intermediate squamous cell in the lower right contains a number of large brown granules suggesting that this cell originated in the underlying granular cell layer of the altered cervical epithelium.

Histology Of The Endocervix

10. The endocervical canal is lined by simple columnar mucous-secreting epithelium. Under the influence of estrogen and progesterone, the endocervical mucosa undergoes cyclic morphologic alterations such as variation in secretory activity, nuclear location, and cell blight. Three cell types may be identified within the endocervical epithelium and include the non-ciliated, mucous-secreting cells, ciliated columnar cell, and, rarely, intercalated or peg cell. A well defined basement membrane is not present beneath the columnar lining epithelium by light microscopy.

11. A study of 140 normal cervixes has demonstrated that an abrupt transition between stratified squamous epithelium of the ectocervix and simple columnar epithelium of the endocervix occurs in approximately one-third of cyclic women. Such an abrupt transition at the squamo-columnar junction is depicted here. Also illustrated is a slight inflammatory infiltrate in the cervical stroma.

12. In approximately two-thirds of normal cervixes, the junction between mature ectocervical mucosa and simple columnar endocervical epithelium is gradual and characterized histologically by a zone of squamous metaplasia and/or reserve cell hyperplasia. The area occupied by other than mature stratified squamous or simple columnar epithelium had been referred to as the "transition zone" and includes part of the "transformation zone" described by the colposcopist. Depicted here is a short transition zone of immature squamous metaplasia.

13. This graph represents a plot of the anatomical distribution of stratified squamous and simple columnar epithelia in 140 normal cervixes. For practical purposes, the normal location of the anatomical external cervical os is located 5 mm to the right of the vertical dotted line. In 75 percent of the normal cervixes examined, the squamo-columnar junction occurred within a zone extending from 1 mm to 10 mm to the right of the reference point represented here by the vertical dotted line. In order to present a working hypothesis of the stages of cervical carcinogenesis, it is important to establish distribution patterns for the normal epithelia covering the uterine cervix. The predominant location of specific abnormal reactions then can be related to this pattern, permitting attempts at correlation between the specific abnormality and anatomical distribution.

Cytology Of The Endocervical Cell

14. In the cellular sample, cells originating from endocervical columnar epithelium occur singly, in sheets, or in strips. The shape of the endocervical columnar cell is dependent on the method by which the sample is collected and the prospective from which the cell is viewed. When observed in samples collected by physical force, the isolated endocervical cell retains its columnar form. In contrast, spontaneously desquamated cells tend to be round or oval as depicted here. Isolated cells in a fluid environment tend to round up. Contrast the size of the isolated endocervical cell with normal superficial and intermediate cells in the field.

15. A sheet of normal endocervical cells is depicted here. Note the regularity of arrangement and more or less well defined cell boundaries providing what is frequently termed a "honeycomb" arrangement. In contrast with the nucleus of the intermediate squamous cell in the field which has a nuclear area of approximately $35 \mu^2$, the mean nuclear area of the endocervical cell is approximately $54 \mu^2$.

16. This slide depicts an arrangement of endocervical cells more familiar to the pathologist - a strip of endocervical mucosa with a side-by-side arrangement of the cells. Such an arrangement emphasizes the columnar configuration and frequent basal location of the nucleus in cells actively secreting mucus in the apical portion. The cytoplasmic staining reaction of the endocervical cell will vary with the variation of the Papanicolaou technique utilized. With EA-65 counterstain, an eosinophilic cytoplasmic staining reaction will predominate. When based on columnar forms, the reported mean cell area of the endocervical cell is $188 \mu^2$.

17. Depicted here are normal endocervical cells with delicate cilia. These eosinophilic structures appear to extend from more densely stained zones at the apical ends of the cells. Such zones represent a row of anchoring granules for the cilia and morphologically resemble the terminal bars of ciliated columnar cells arising in respiratory tract. The nuclei of endocervical cells vary little in shape but considerable variation in size may occur between one cell and the next. This is particularly pronounced in the presence of inflammation or regeneration. The nuclear chromatin is generally in the form of delicate granules which are irregularly dispersed. Again, in the presence of inflammation, the chromatin material may become reticulated or irregularly clumped. In contrast to most normal squamous cells, the endocervical cell nucleus usually contains one or more small, distinct eosinophilic nucleoli or cyanophilic chromocenters.

HISTOPATHOLOGY OF INFLAMMATION OF THE UTERINE CERVIX

Histopathology Of Herpes Simplex Reaction

18. This slide depicts the margin of the epithelial reaction to Herpes simplex genitalis in stratified squamous epithelium. The adjacent normal epithelium is to the left and the reactive epithelium is to the right. Note multinucleation, nuclear molding and translucent nature of the affected nuclei. Compare with the cells depicted in slide 49.

19. This is another example of the histological reaction of stratified squamous epithelium to Herpes simplex infection. Again, note the multinucleation and large, eosinophilic intranuclear Cowdry Type-A inclusions. Compare with the cellular changes in slides 50 and 51.

20. This slide represents early vesicle formation in stratified squamous epithelium of the uterine cervix of a pregnant woman near term whose baby subsequently died approximately two weeks after delivery due to a disseminated Herpes virus infection. Several nuclei in the vesicle on the far right of the slide contain eosinophilic, intranuclear inclusions.

Chronic Follicular Cervicitis

21. Illustrated here is a microscopic section of uterine cervix with a dense inflammatory infiltrate composed primarily of lymphocytes. Note the development of lymphoid nodules in the deeper aspects of the inflammatory process. The epithelium overlying chronic follicular cervicitis is often compressed or ulcerated.

CYTOPATHOLOGIC MANIFESTATIONS OF INFLAMMATION

Acute Inflammation

22. A dense inflammatory exudate originating in severe acute or chronic cervicitis may obscure epithelial cell morphology to the extent that satisfactory cytologic examination is precluded. Here the inflammatory infiltrate is composed principally of polymorphonuclear leukocytes. If an inflammatory exudate sufficiently excludes adequate epithelial cell recognition, the specimen should be reported as "unsatisfactory for cytologic examination."

Chronic Follicular Cervicitis

23. Due to compression and ulceration of the ectocervical or endocervical mucosa secondary to chronic follicular cervicitis, a routine cellular sample may reflect this underlying inflammatory process. Characteristically, cells of both mature and immature lymphocytic origin are present as well as histiocytes

