Normal Serviks Kolposkopisi

'Normal Colposcopy of Cervix'

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Kadın Hastalıkları ve Doğum Anabilim Dalı

Gross Anatomy

- The term cervix is derived from the latin for *neck*.
  - The lower portion (portio, or vaginal cervix) extend into the vagina.
  - The upper or supravaginal cervix extends from the vaginal attachment to the lower uterine segment.

- Topographic areas on the cervical surface are conventially identified using the numbers on a clock face
  - A lesion site is by the nearest clock-face number

- In the nulliparaous patient, the cylindrical cervix comprises 50% of the total uterine size
  - 3 cm in length, 2 cm in diameter

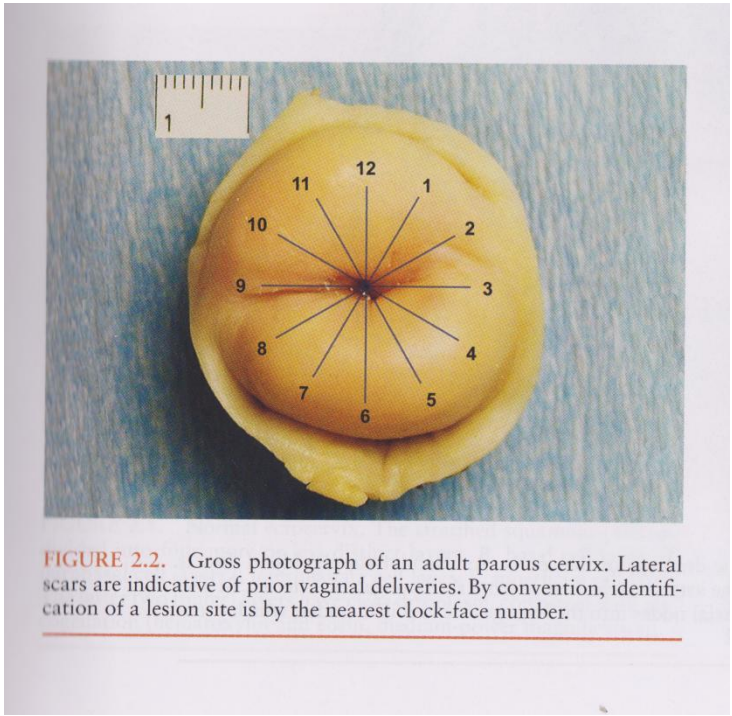
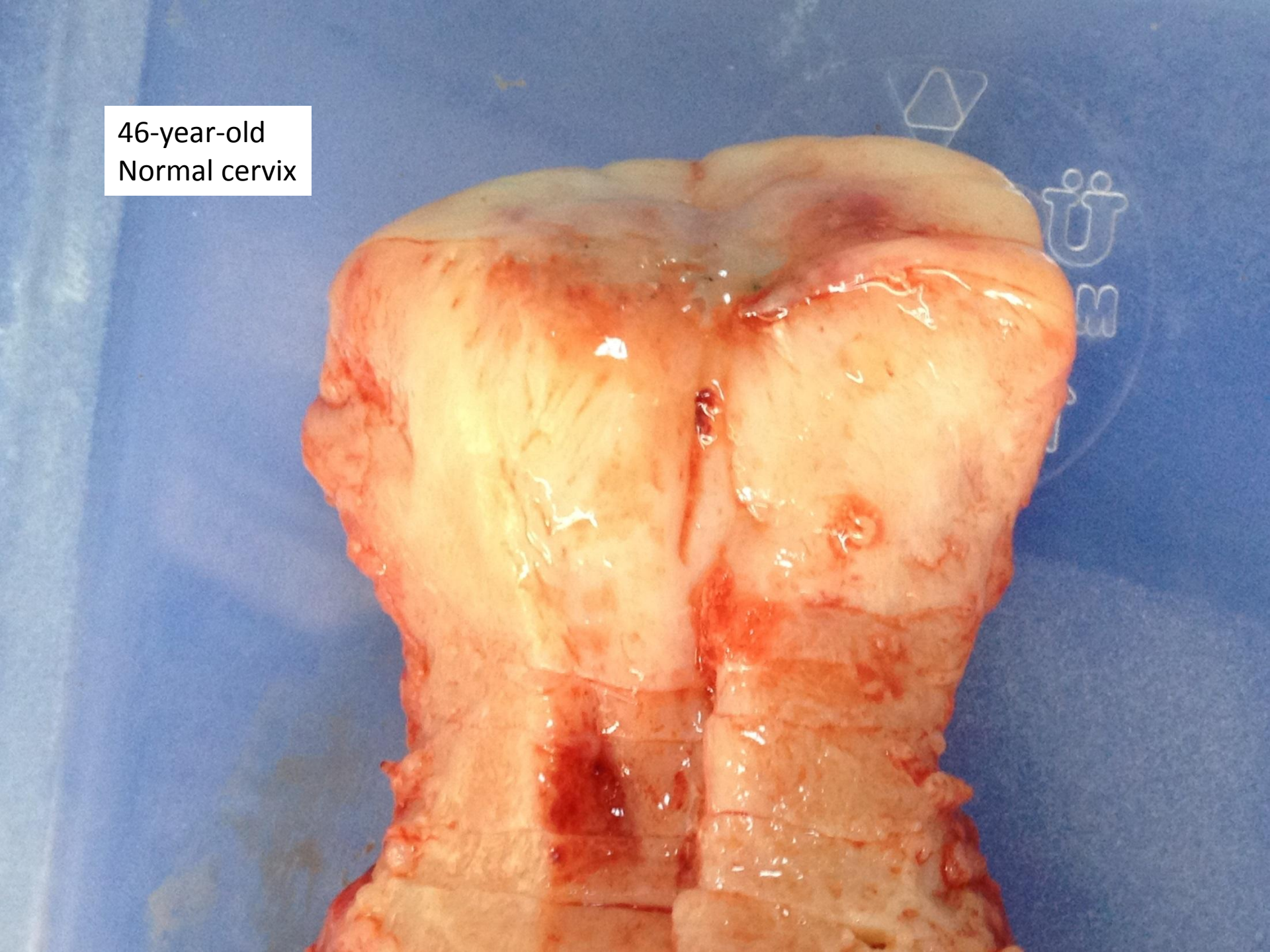


FIGURE 2.2. Gross photograph of an adult parous cervix. Lateral scars are indicative of prior vaginal deliveries. By convention, identification of a lesion site is by the nearest clock-face number.


46-year-old
Normal cervix

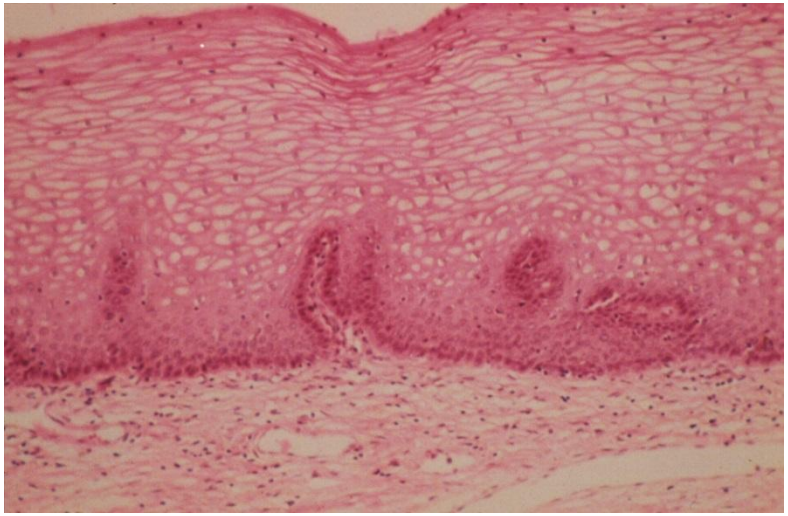
Cervical Canal

- 3 cm in length and extends from the external os to the lower uterine segment or isthmus.
- It has a fusiform shape and the diameter varies
  - 8 mm at its widest point
- At the cervicouterine junction it narrows and becomes rounded
  - Internal cervical os
- It contains ridges that disappear after vaginal delivery
  - *Plicae palmatae* or *arbor vitae*

FIGURE 2.3. Gross photograph of a lower uterine segment and endocervix. The parallel plicae palmatae ridges are best seen near the external os. The remaining canal is covered by glistening, clear mucus.

Squamous Epithelium

- The majority of cervix portio is covered by stratified squamous epithelium.
- As the squamous cells mature, they enlarge and increase in overall volume, while the amount of nuclear material decreases.
  - Basket-weave pattern
- Cervical squamous cells are arbitrarily divided into four distinct layers:
  - Basal or germinal layer
  - Parabasal or prickle cell layer
  - Intermediate or navicular cell layer
  - Superficial or stratum corneum layer



Squamous Epithelium

- Basal layer
  - One or two layers of small cuboidal cells that contain large dark staining nuclei.
- Parabasal layer
  - Irregular polyhedral cells with large, dark oval nuclei.
  - Tonofilaments and desmosomes are present
- Intermediate layer
  - Flattened cells with glycogen-rich clear cytoplasm
  - Comprises the majority of squamous cells
  - The nuclei are small, dark and round
- Superficial layer
  - Flat, elongated cells with small pyknotic nuclei
  - Collagen and keratin filament are present

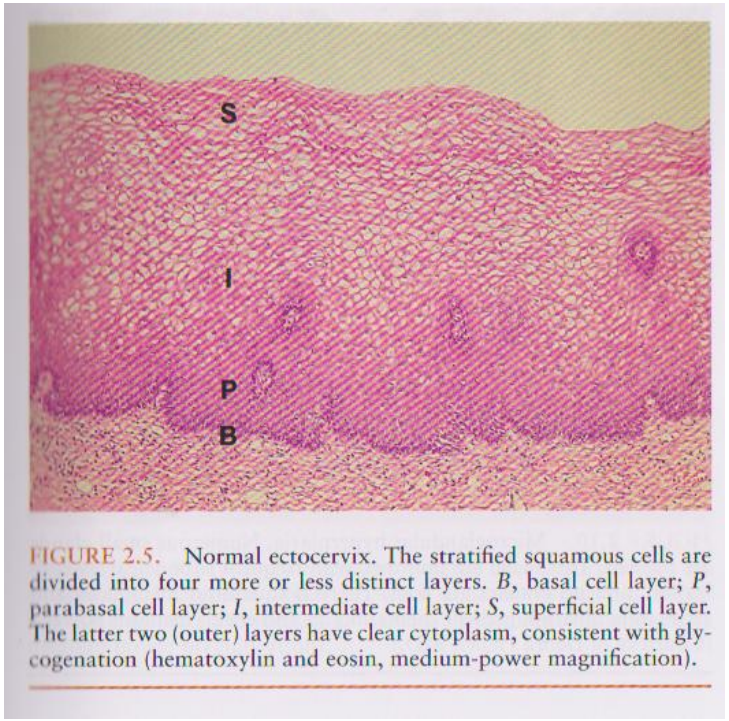


FIGURE 2.5. Normal ectocervix. The stratified squamous cells are divided into four more or less distinct layers. *B*, basal cell layer; *P*, parabasal cell layer; *I*, intermediate cell layer; *S*, superficial cell layer. The latter two (outer) layers have clear cytoplasm, consistent with glycogenation (hematoxylin and eosin, medium-power magnification).

Squamous Epithelium

- Maturation of squmous cells is estrogen dependent and can take as little as 4 days.
  - Estrogen stimulates DNA synthesis and shortens the cell cycle

- In the premenopausal and postmenopausal state, the less mature squamous cells (basal and parabasal) predominate.

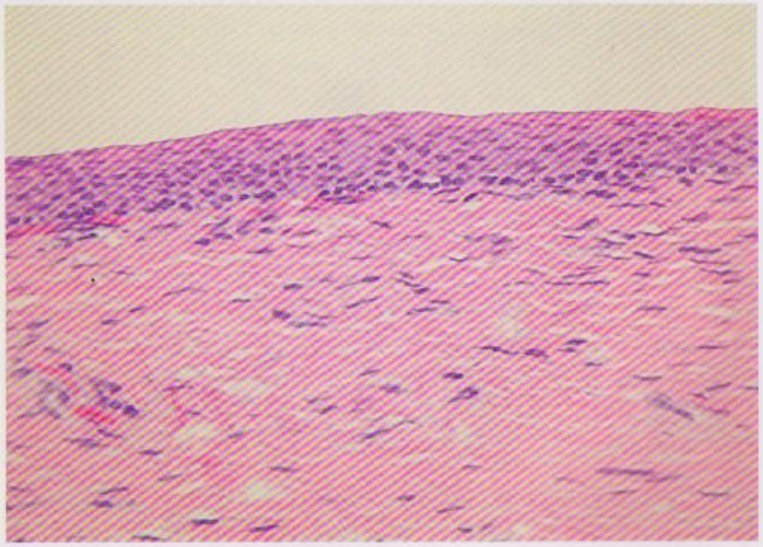
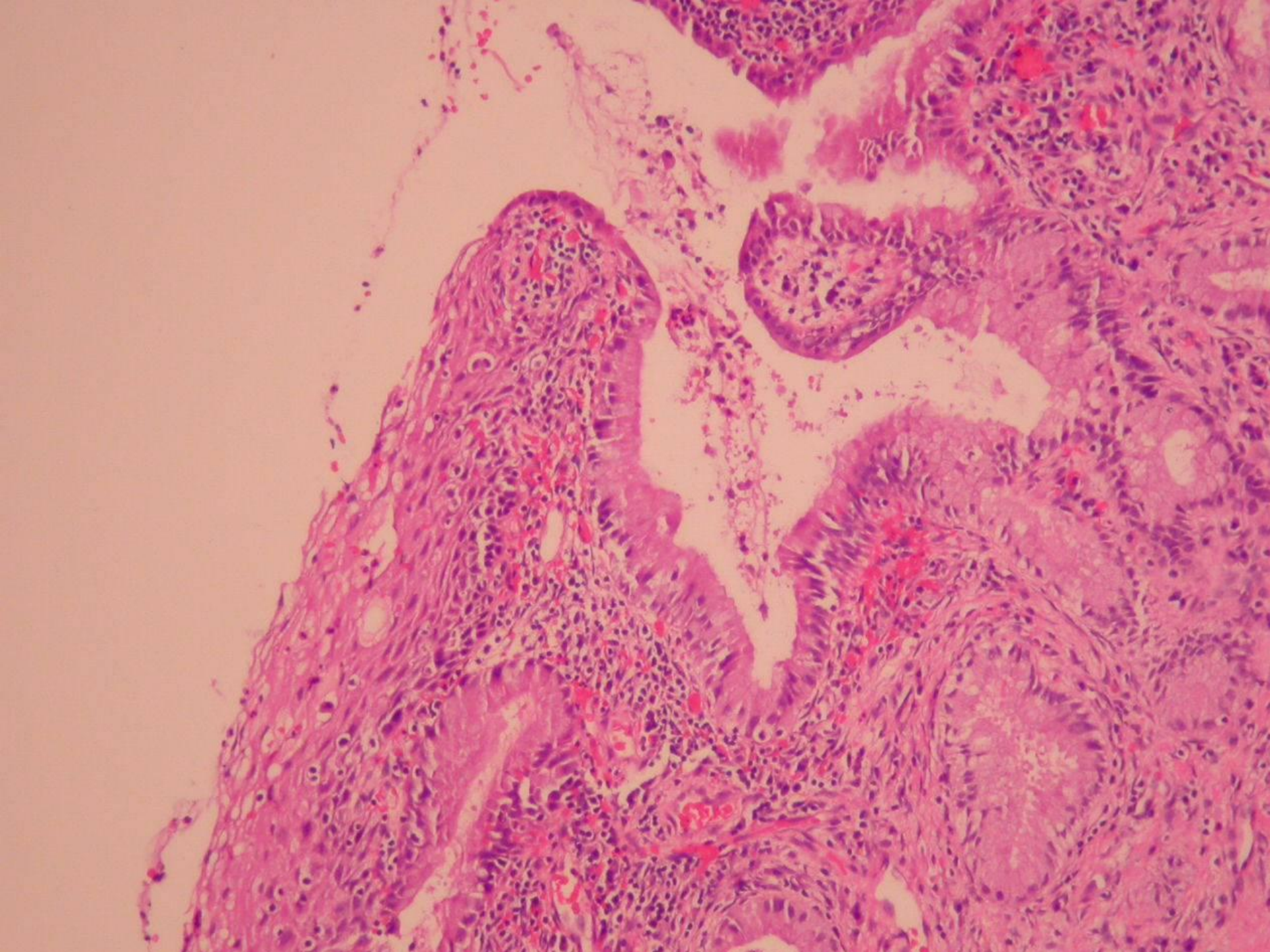
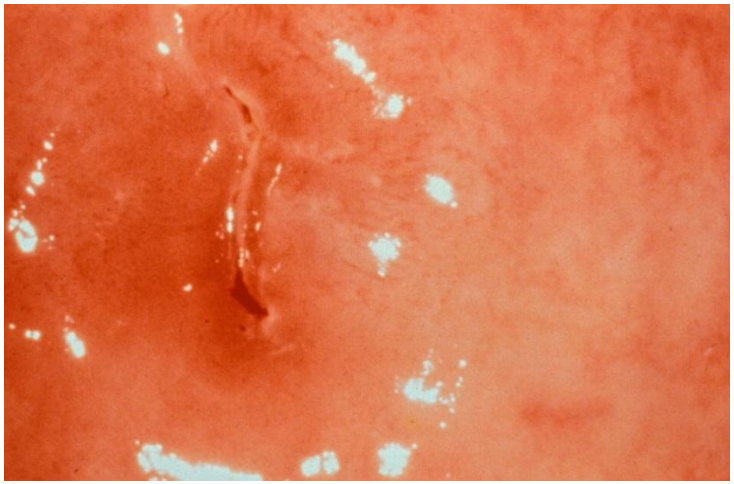


FIGURE 2.6. Atrophic ectocervix. The number of squamous cell layers is decreased and parabasal cells predominate (hematoxylin and eosin, high-power magnification).



Colposcopy of Squamous Epithelium

- Smooth featureless surface
- Orange or dark pink color
- Distinctive oblique capillaries
- Not modified by acetic acid
- Stains mahony brown with iodine



Columnar Epithelium

- A single layer of tall columnar cells lines the endocervical canal
- The majority of these cells secrete mucus.
- Endocervical cells invaginate into the cervical stroma to a depth of 5 to 8 mm
  - Since there are no ductal or acinar structures, this process technically represent crypt formation, but by convention they are called endocervical glands.

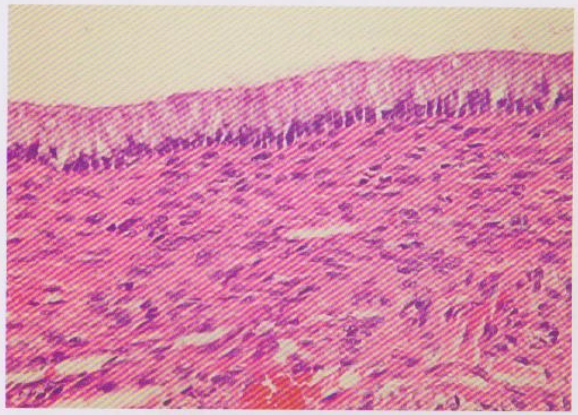


FIGURE 2.7. Normal endocervix. A single layer of columnar cells with basal nuclei covers the surface (hematoxylin and eosin, high-power magnification).

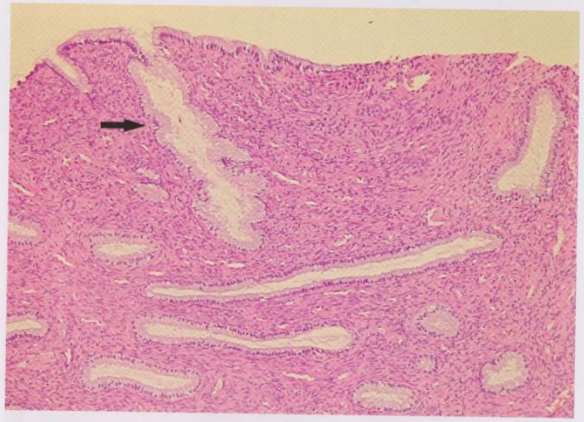
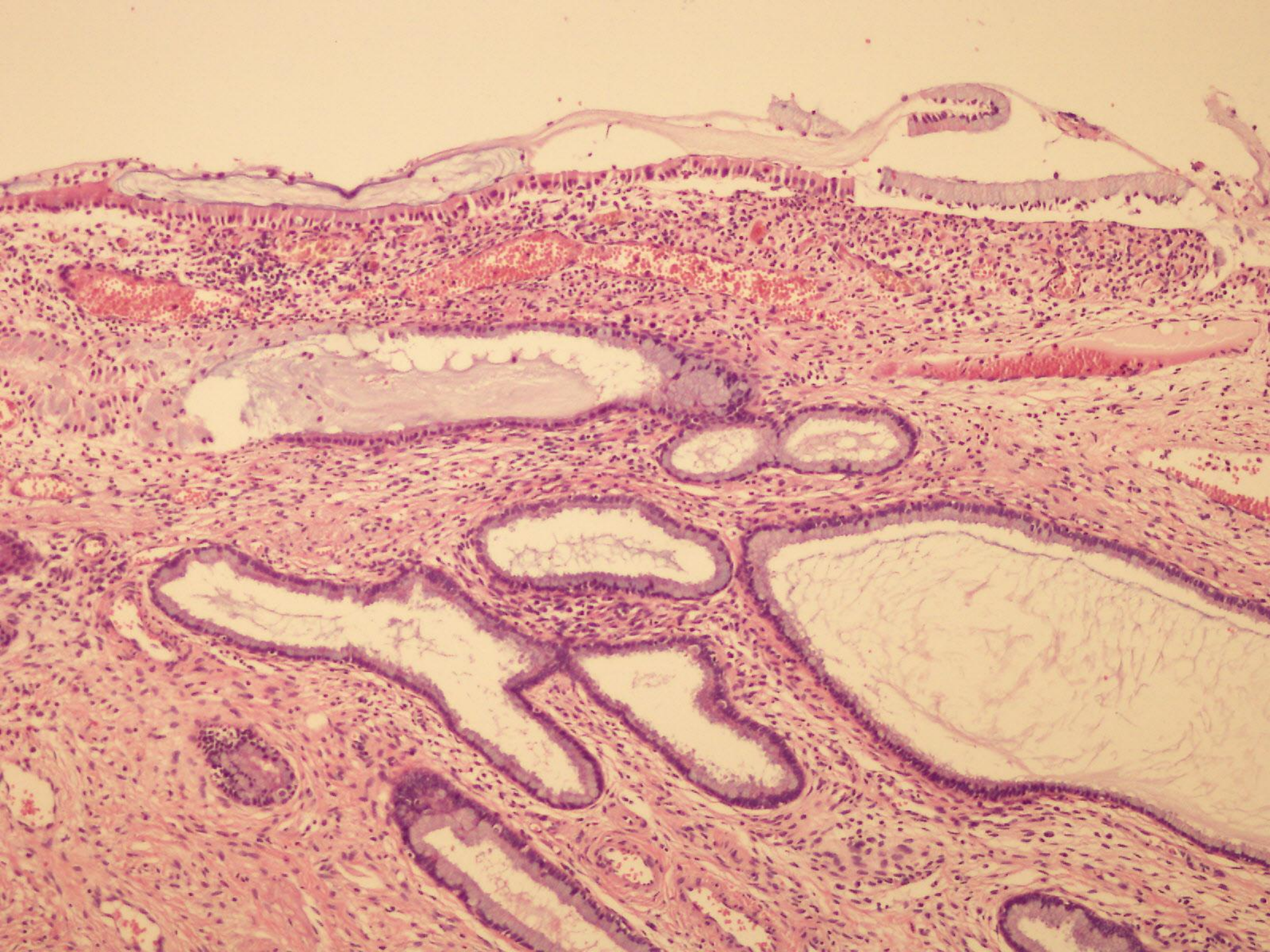
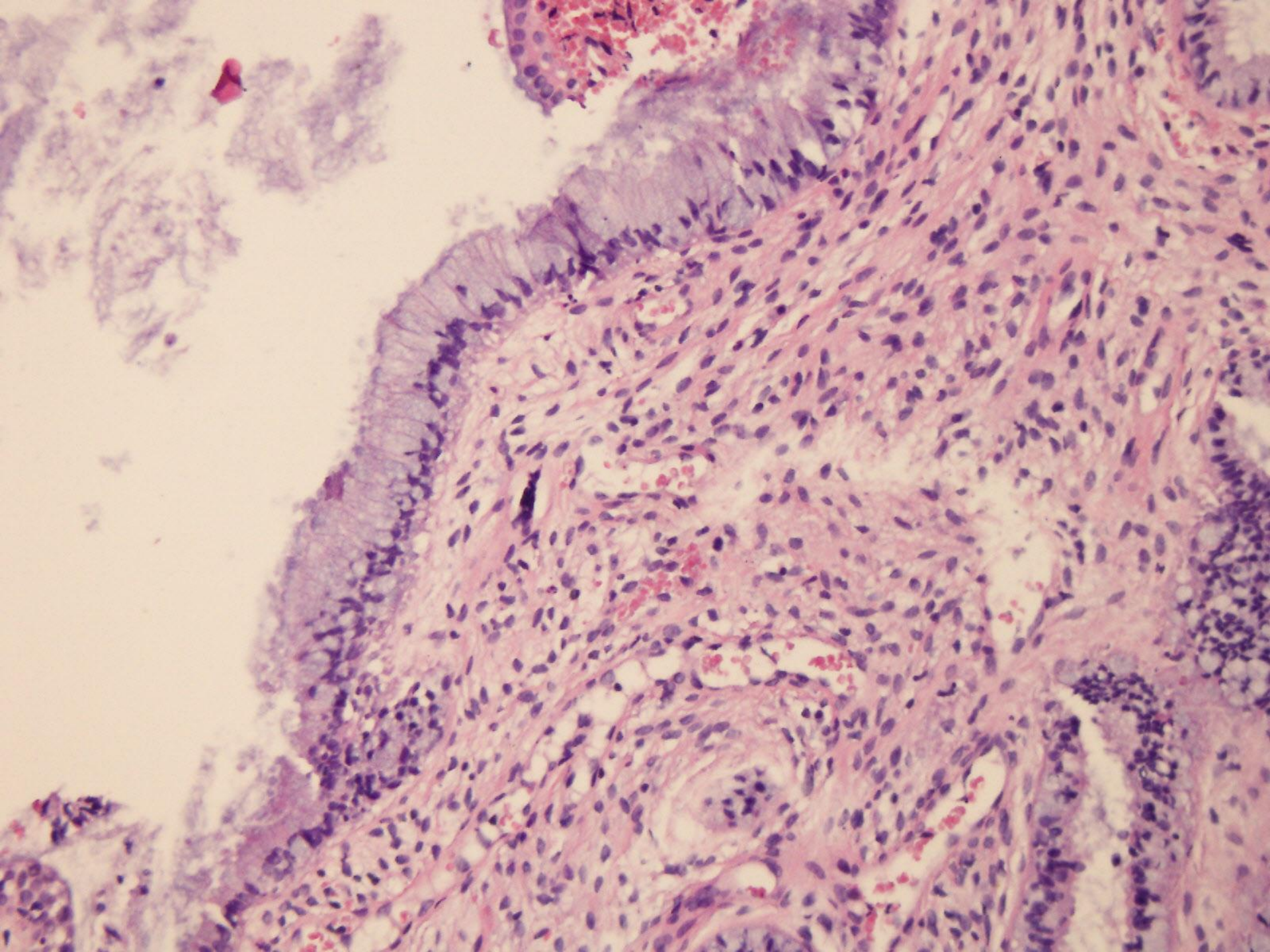


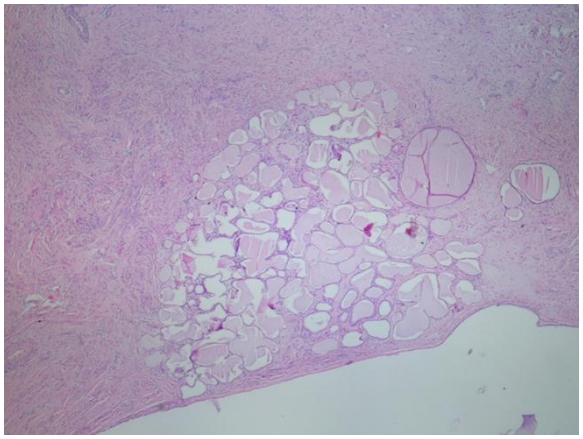
FIGURE 2.8. Endocervical glands. Although they are called glands because of their appearance in cross section, the structures should be considered crypts (*arrow*) (hematoxylin and eosin, medium-power magnification).

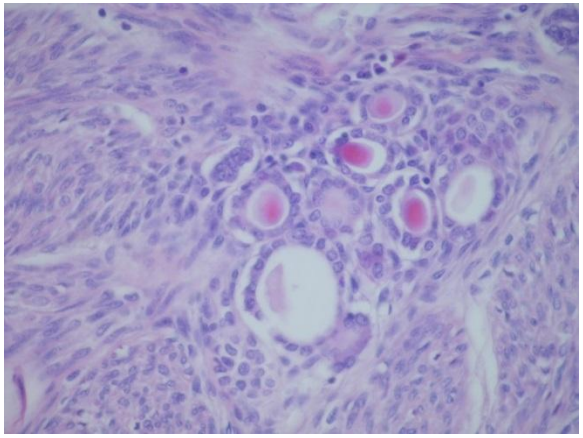


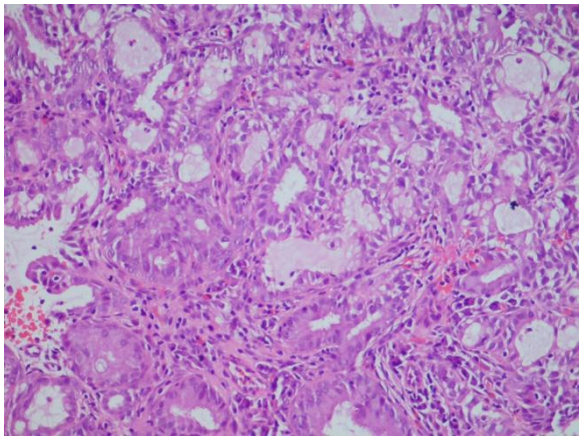


Columnar Epithelium

- Compression of a group of arborizing glands can result in the formation of *tunnel clusters*
- *Mesonephric remnants* in cervical stroma
- *Microglandular hyperplasia* is another form of benign gland proliferation.

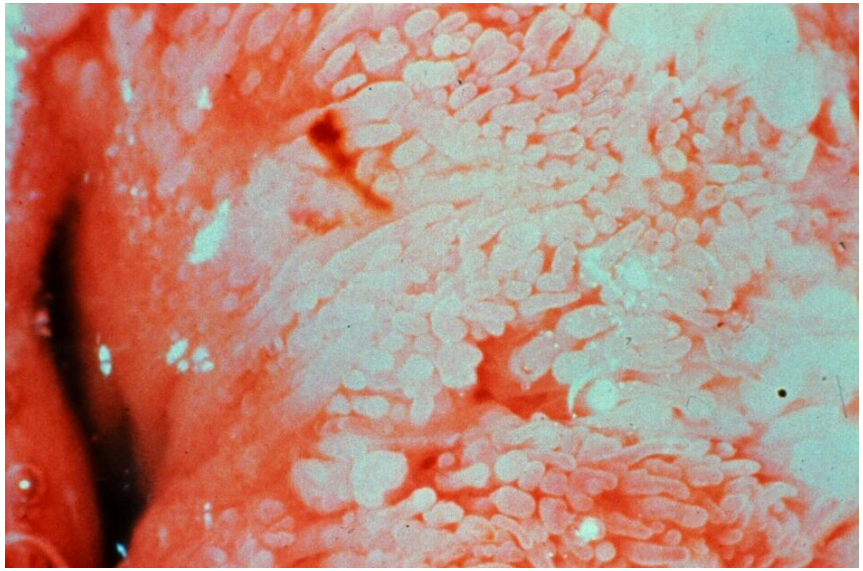






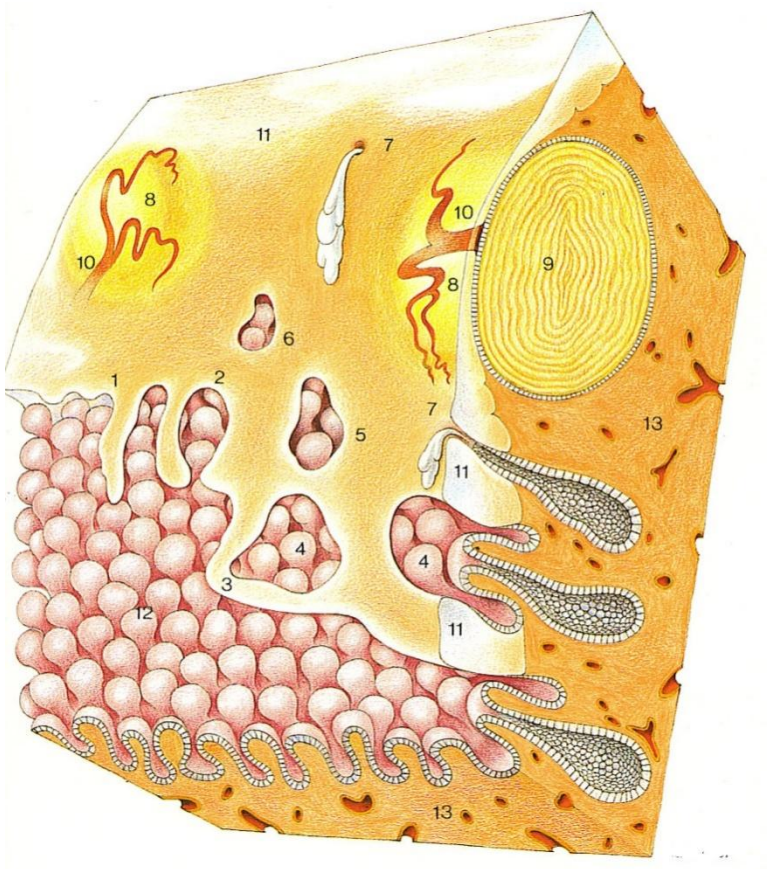
Colposcopy of Columnar Epithelium

- Distinctive contour
- Dark red before acetic acid



The Normal Transformation Zone

- Nonkeratinized stratified squamous epithelium extends from Hart's line (the embryologic junction between the vagina and vulva) to the SCJ on the cervix at the woman's birth.
- Columnar epithelium is a single cell layer of tall mucus secreting cells.
- Columnar epithelium covers villi, small polypoid projections that contain central loop capillaries.



The Normal Transformation Zone

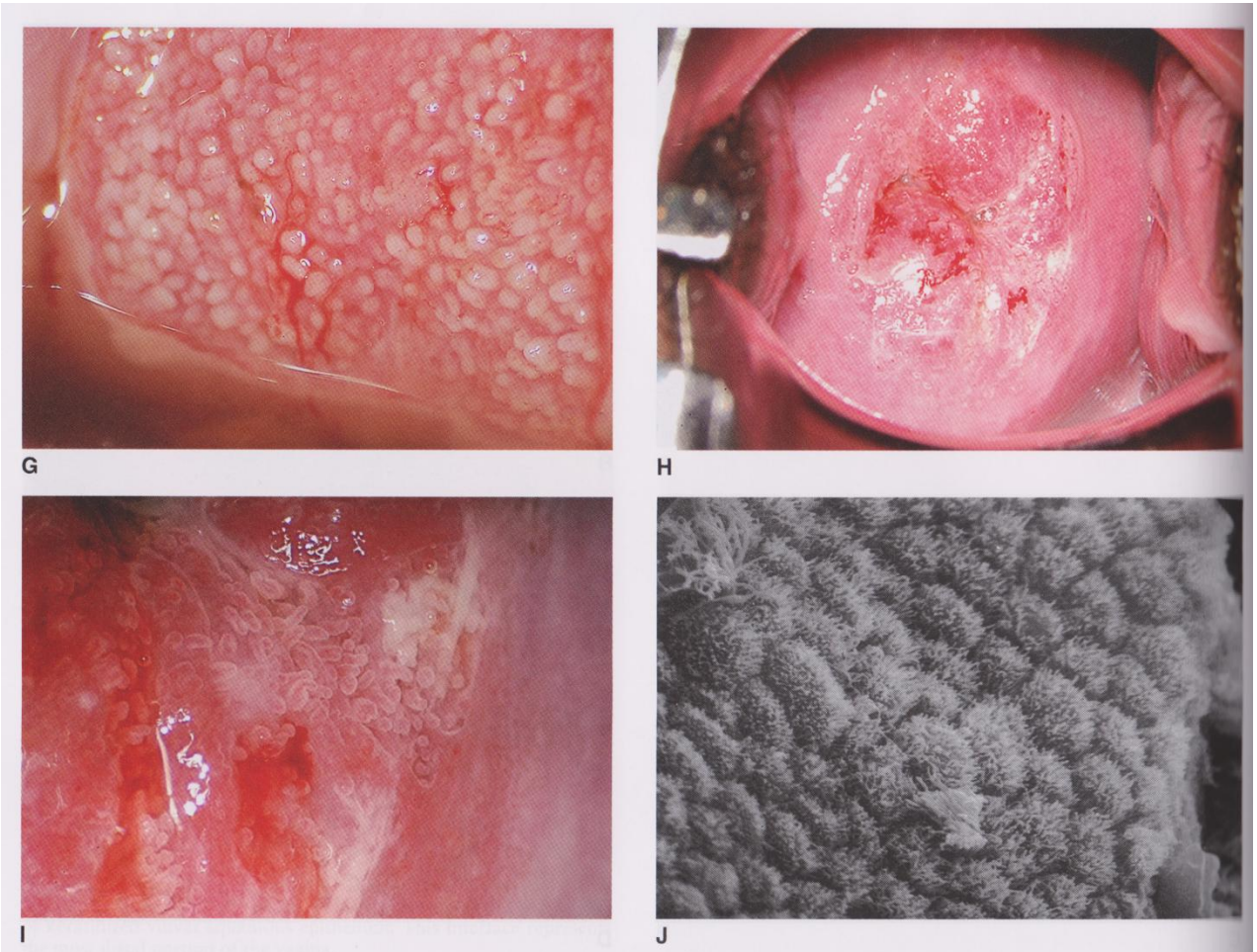


FIGURE 8.5. (*Continued*) **J:** Surface electron micrograph of columnar epithelium. Notice the microvilli projecting from the cell's surfaces. (Courtesy of, and approved for reproduction by, the International Cervical Cancer (INCCA) foundation.)

The Normal Transformation Zone

- In reproductive age women, the SCJ is variably positioned on the ectocervix or may be slightly within the endocervical canal.

- Later in life, the SCJ may not be easily identified colposcopically since the cellular interface may be hidden deeply within the endocervical canal.

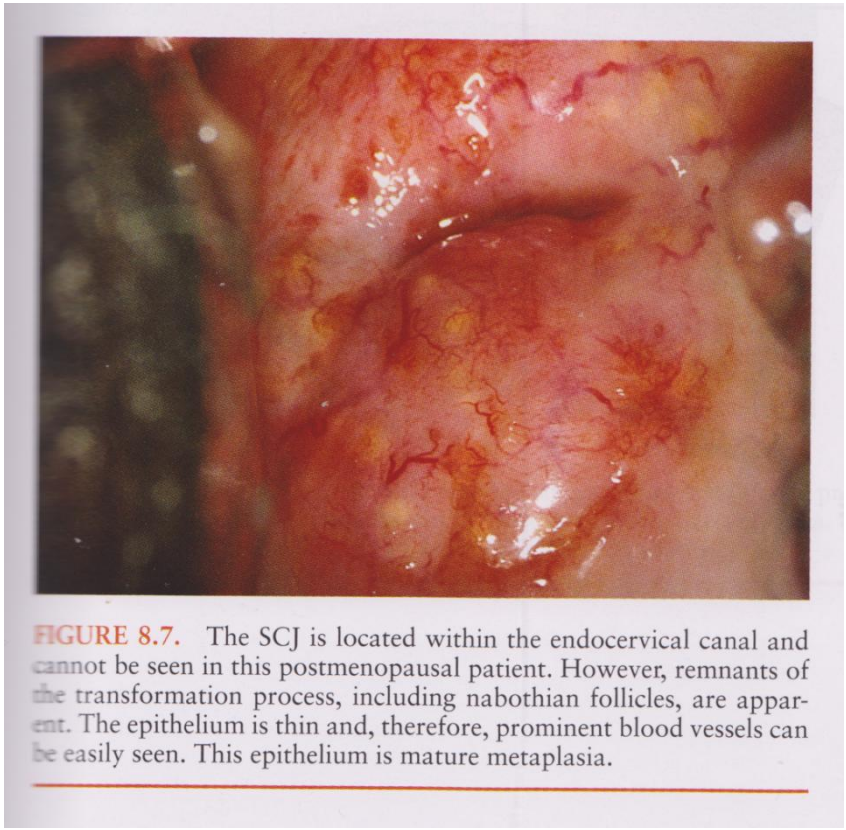
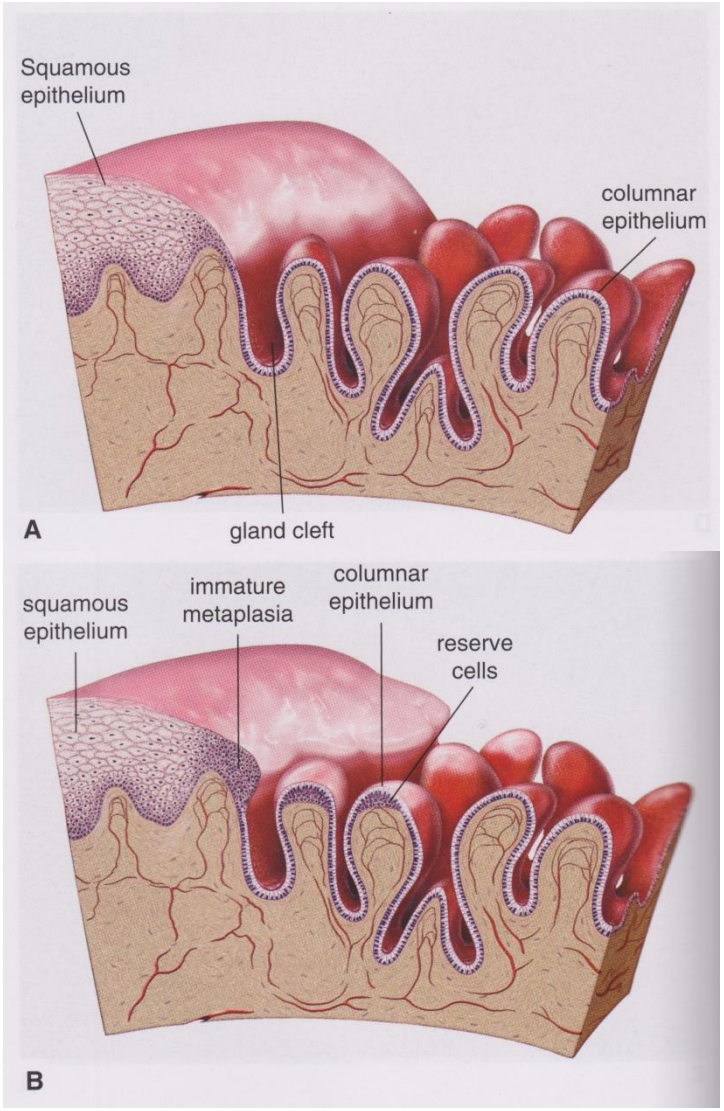


FIGURE 8.7. The SCJ is located within the endocervical canal and cannot be seen in this postmenopausal patient. However, remnants of the transformation process, including nabothian follicles, are apparent. The epithelium is thin and, therefore, prominent blood vessels can be easily seen. This epithelium is mature metaplasia.

The Normal Transformation Zone

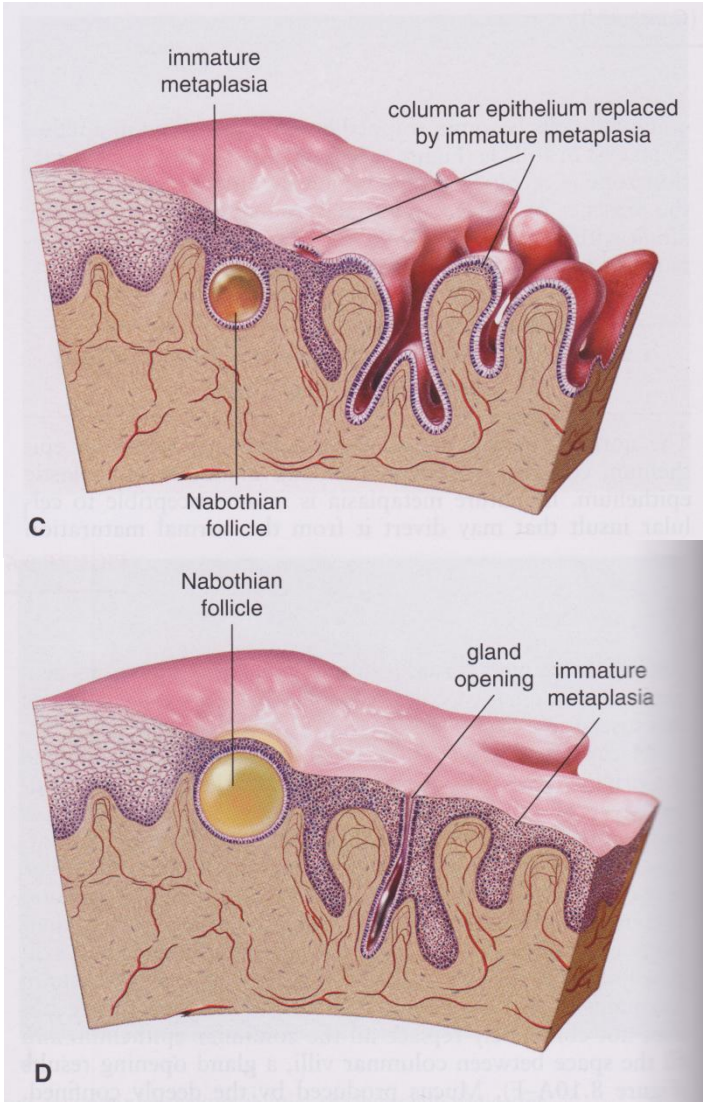
- The traumatized acid-irritated columnar epithelium is replaced by small, round, nuclear dense reserve cells positioned beneath the columnar epithelium.
- These cells eventually proliferate and differentiate to form a thin replacement layer of immature metaplastic epithelium, then a multicell layer of mature metaplastic epithelium.
- Initially, this metaplastic cellular change appears on the exposed tips of columnar villi
  - Blanching of villi tip

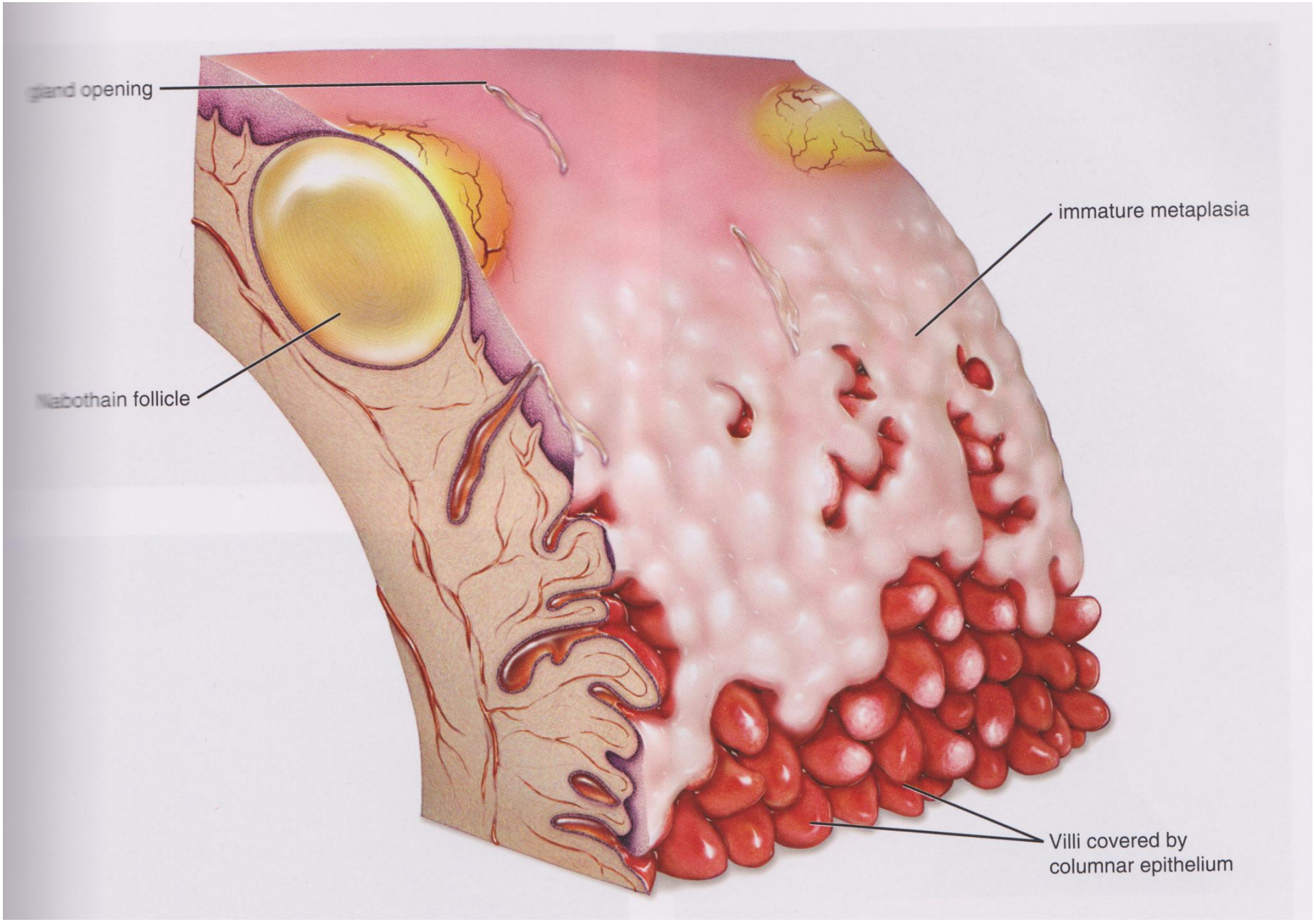


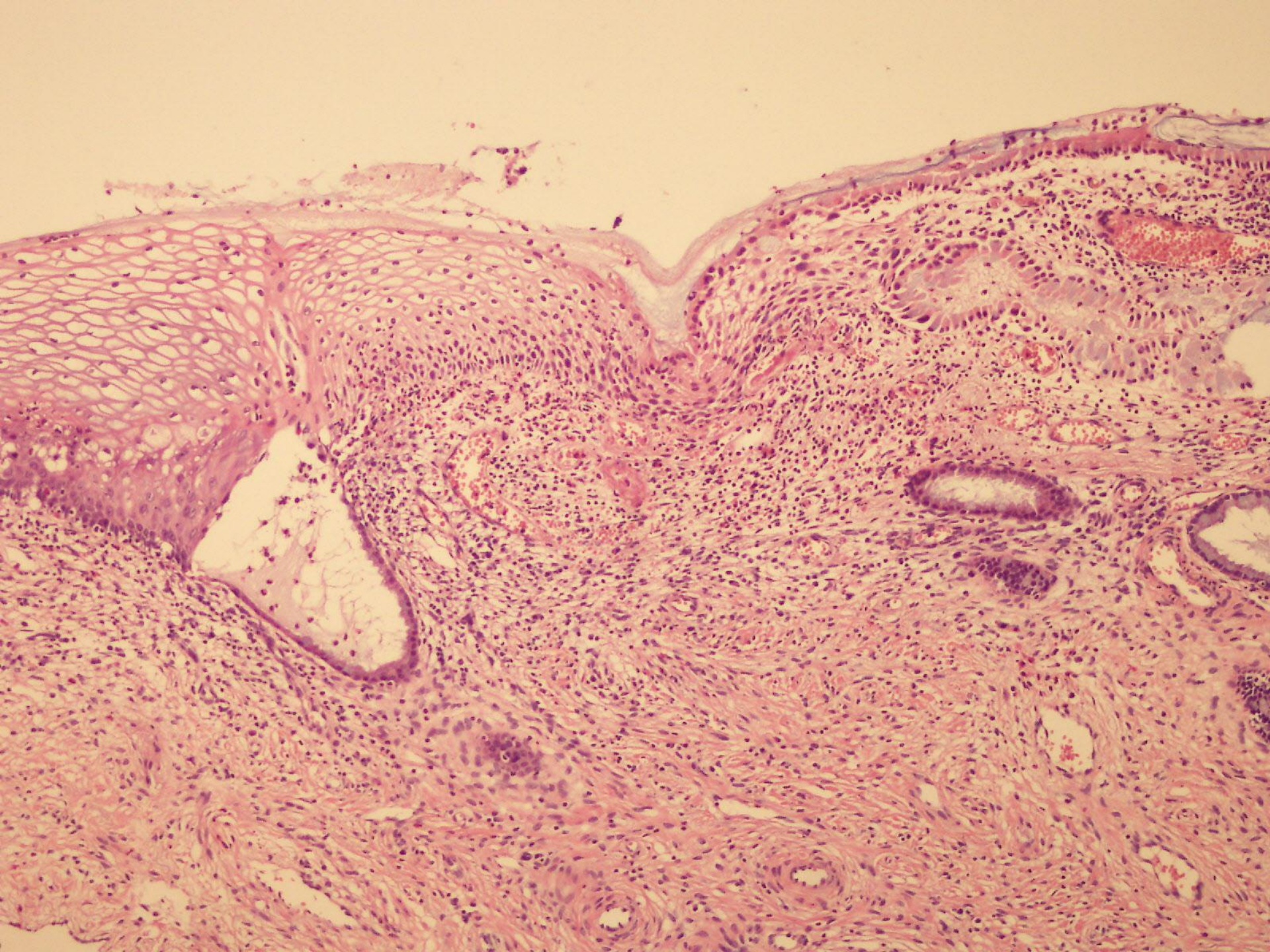
The Normal Transformation Zone

- The immature metaplastic epithelium fuses or bridges with immature metaplastic epithelium on adjoining villi.

- Finally, opalascent sheets of immature metaplasia are formed that extend as tongue-like projections toward the os.




gland opening
Nabothain follicle
immature metaplasia
Villi covered by
columnar epithelium



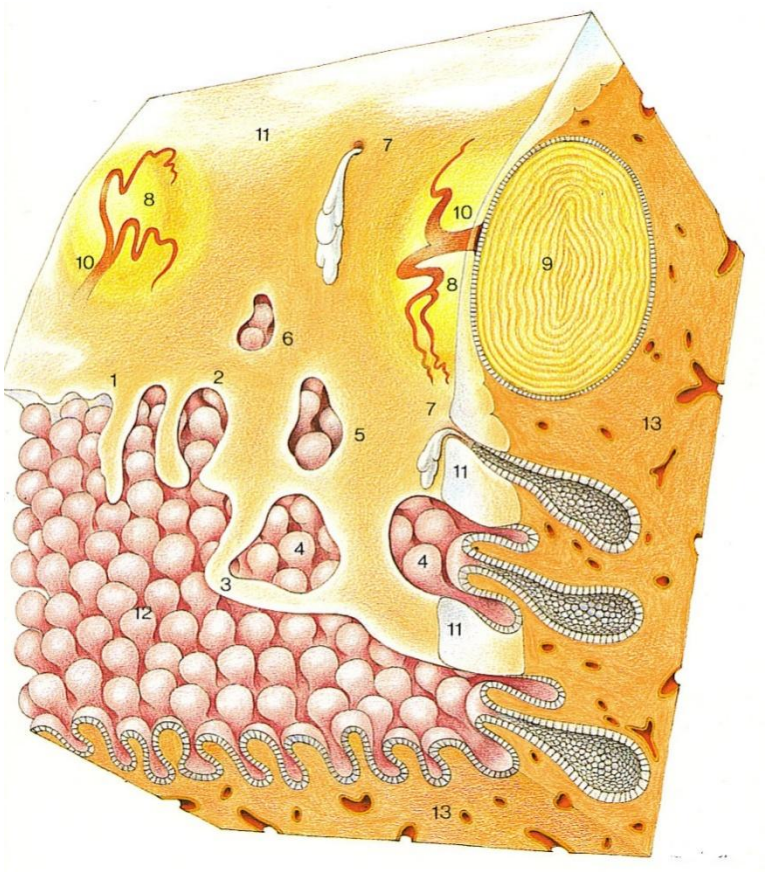
The Normal Transformation Zone

- The epithelial transfomation process is episodic but progressive, starting in the periphery of the transformation zone and advancing concentrically toward the os and extending up the canal in later life.
- Noncontiguous islands of immature metaplasia may be seen proximal to the advancing SCJ that eventually coalasce.
- Maximal TZ activity is seen in late fetal life, at the onset of estogen surge at menarche, during the first pregnancy, an in women using combined oral contraceptives.

Mature Metaplasia

- Multi-cell layer of fully differentiated squamous epithelium that lies between immature metaplasia and the original SCJ
  - İmmature metaplasia contains only a few layers of undifferentiated cells

- Mature metaplasia has two unique features not found in original squamous epithelium
  - Gland openings
  - Nabothian cysts

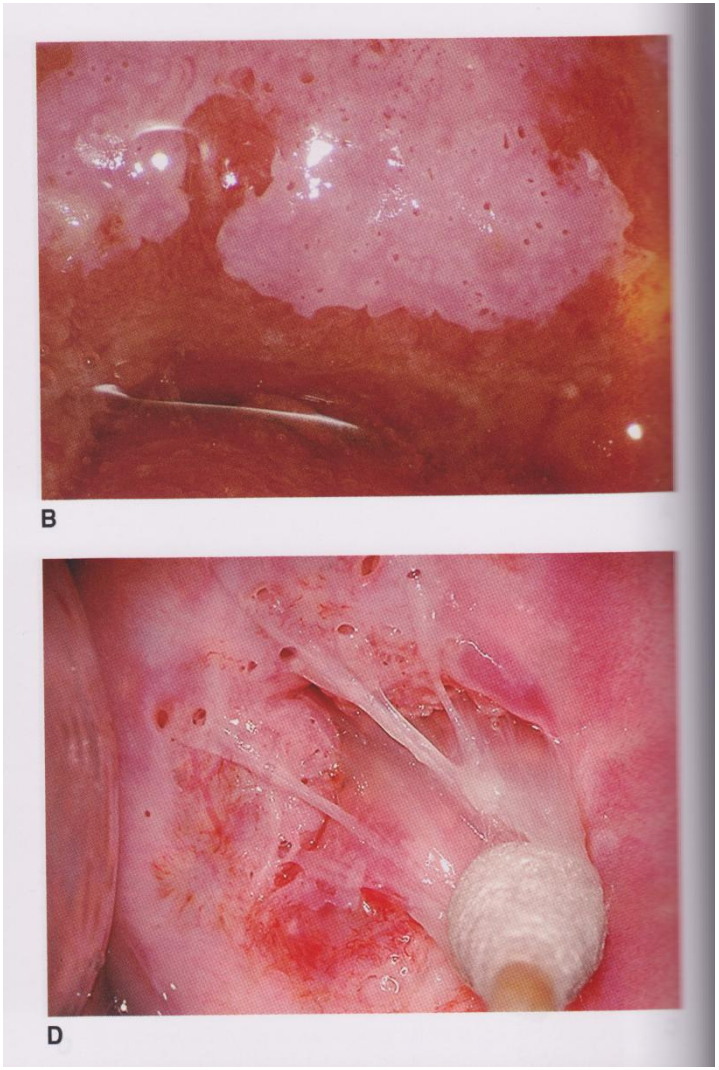


Mature Metaplasia

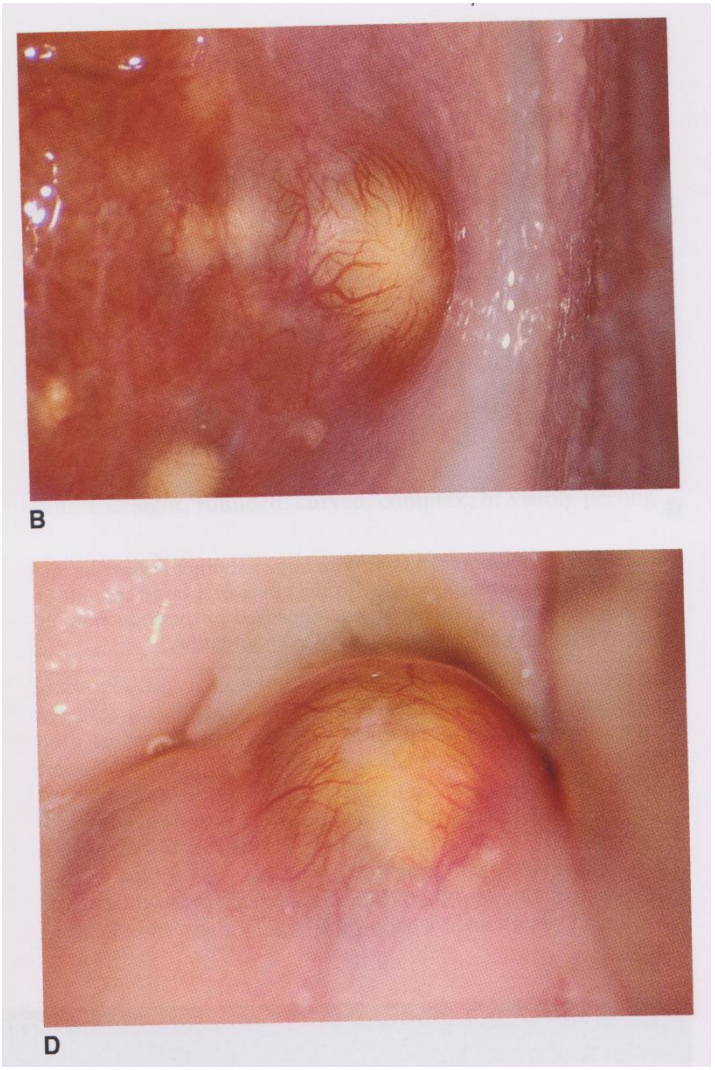
- Gland openings
  - Advancing metaplastic epithelium surrounds a cleft between columnar villi on the surface but does not completely replace all the columnar epithelium and fill the space between columnar villi
  - Mucus produced by the deeply confined, remaining columnar cells protrudes to the surface through this opening.

- Nabothian cysts
  - The cleft becomes occluded by metaplastic epithelium at the surface and the mucus produced by the retained columnar cells becomes trapped beneath.

Mature Metaplasia



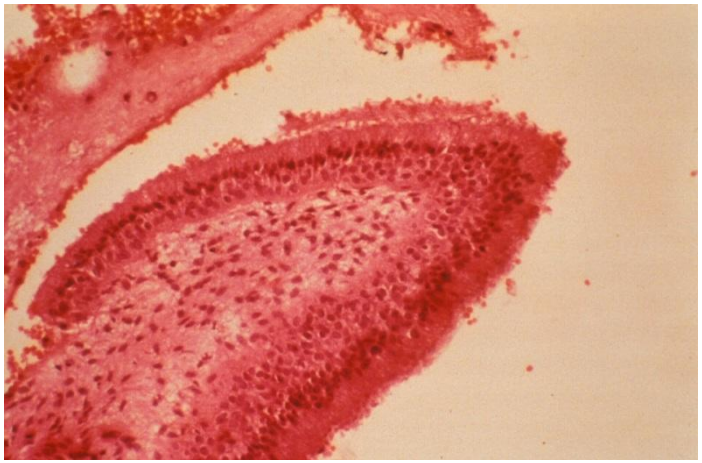
Gland openings

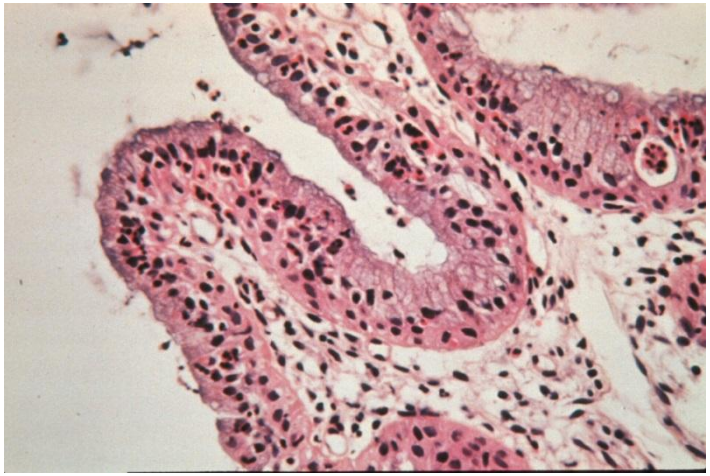


Nabothian cysts

Histology of Immature Metaplasia

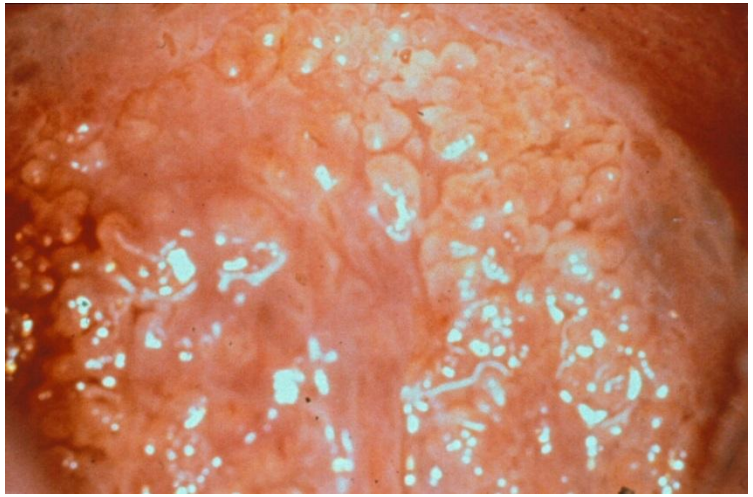
- Undifferentiated squamous epithelium
- Variable villous remnants
- Dense immature cells, often stellate in shape
- Intense inflammatory cell infiltrate

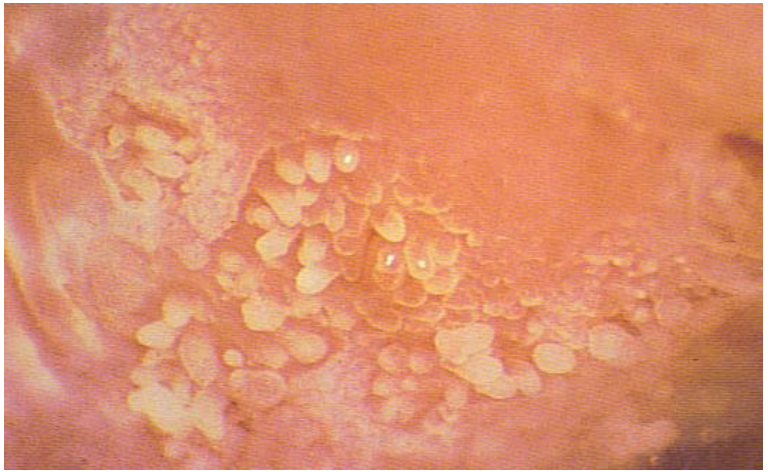


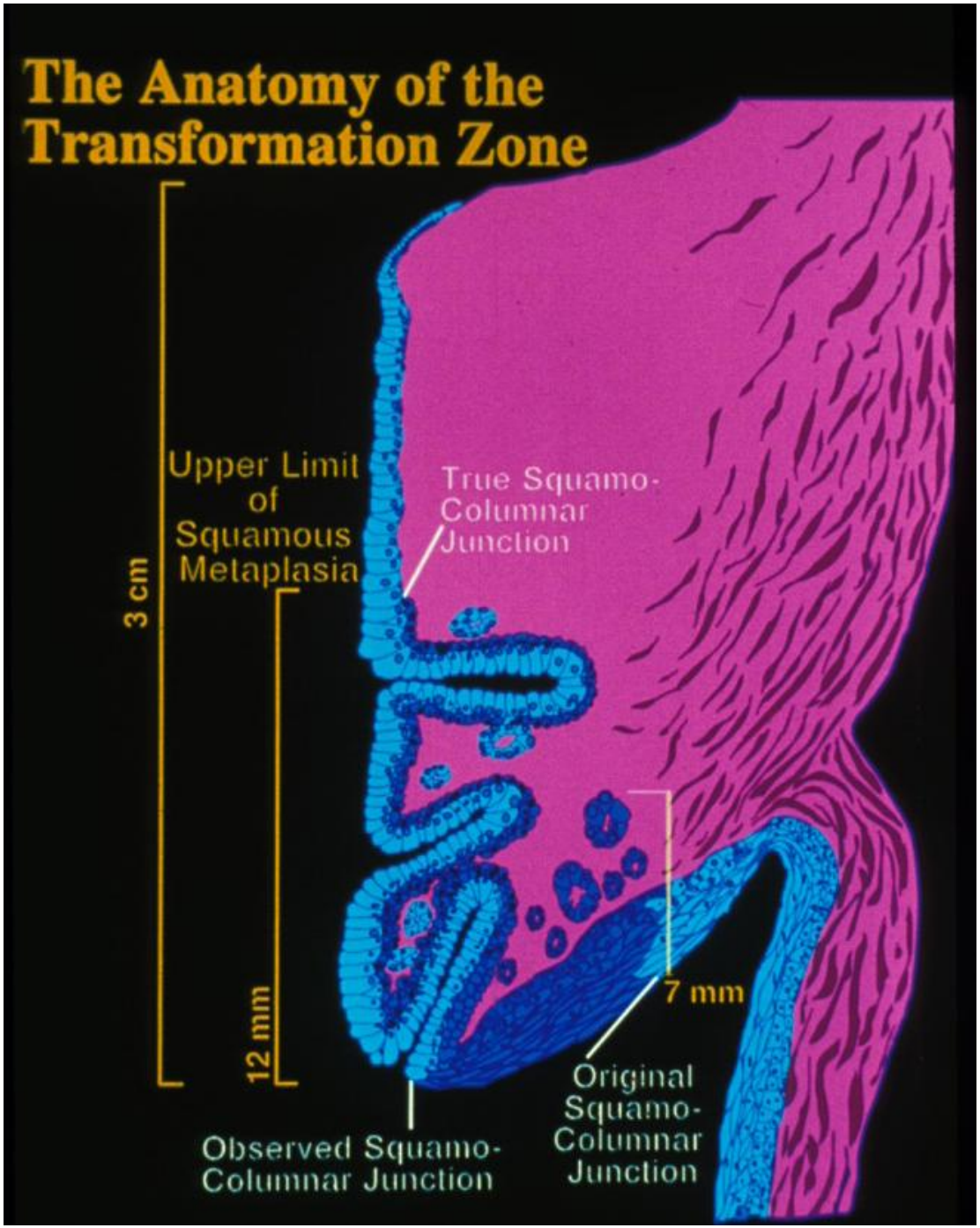


Colposcopy of Immature Metaplasia

- Stage 1: Glazed villi: faintly acetowhite
- Stage 2: Fused denser aectowhite villi
- Stage 3: Flat amorphous sheet with absent vessels






The Anatomy of the Transformation Zone
3 cm
Upper Limit of Squamous Metaplasia
12 mm
True Squamo-Columnar Junction
7 mm
Original Squamo-Columnar Junction
Observed Squamo-Columnar Junction

Colposcopic Features

Epithelial color

Before and after application of 3%-5% acetic acid or Lugol's iodine

Vasculature

Type of vessel, vessel patern, vessel caliber, intercapillary distance

Surface topography

Flat, ulcerated, raised surfaces

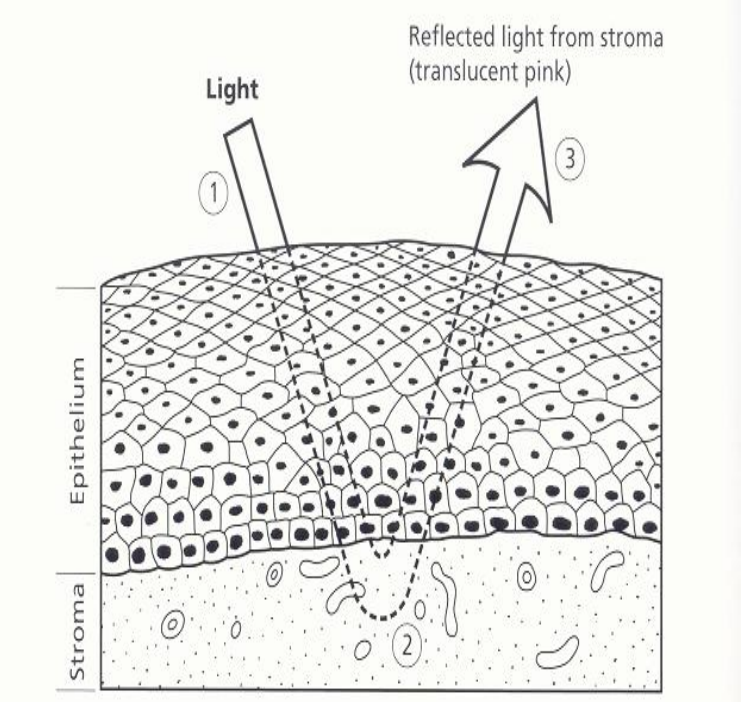
Margin characteristics

Colposcopic Signs

Type of tissue	Colposcopic sign	Etiology
Epithelial	Acetowhite epithelium	Increased cellular and nuclear density Increased protein agglutination
	Leukoplakia	Traumatically induced, thickened superficial epithelium
	Ulceration	Absence of epithelium caused by trauma, infection, medications
Vascular	Punctation and mosaic	Alterations in epithelial capillaries due to proliferative effect of the normal immature metaplastic process
	Atypical blood vessels	Very immature metaplastic epithelium Postradiation angiogenesis Granulation tissue

Epithelial Color

- Color is derived by the interaction of transmitted colposcopic light with the epithelium and stroma.
- The nuclear-to-cytoplasmic ratio of epithelial cells and epithelial thickness affect the intensity of reflected white light.
  - As each increases, the amount of white light returned to the colposcopist increases, and the amount of red color emitted from transilluminated blood vessels decreases
- Healthy mature nonkeratinized stratified squamous epithelium (whether original squamous epithelium or mature metaplastic epithelium) has a pink color.
  - A network of capillaries underlies stratified squamous epithelium, 10 to 15 cell layers thick



Epithelial Color

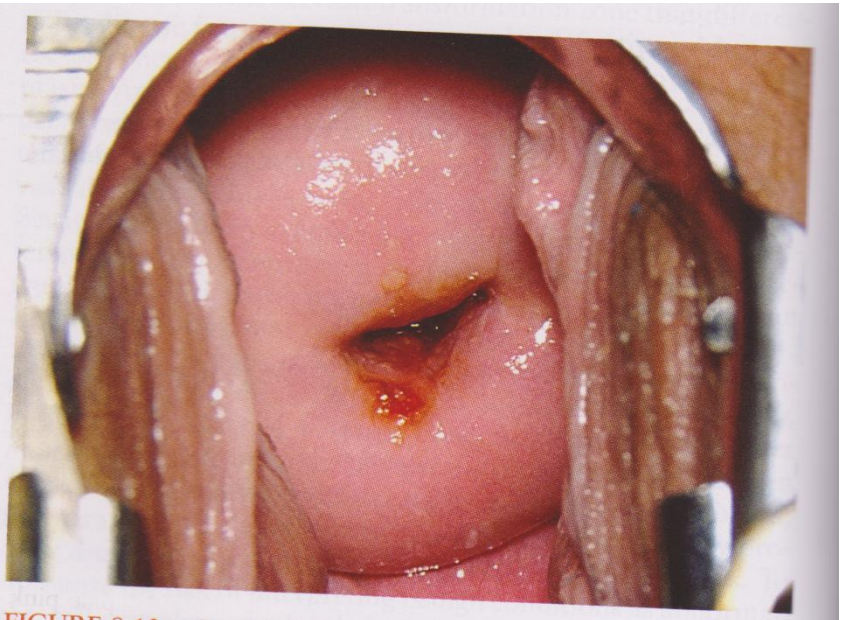


FIGURE 8.13. Stratified squamous epithelium of the cervix, demonstrating a pink color.

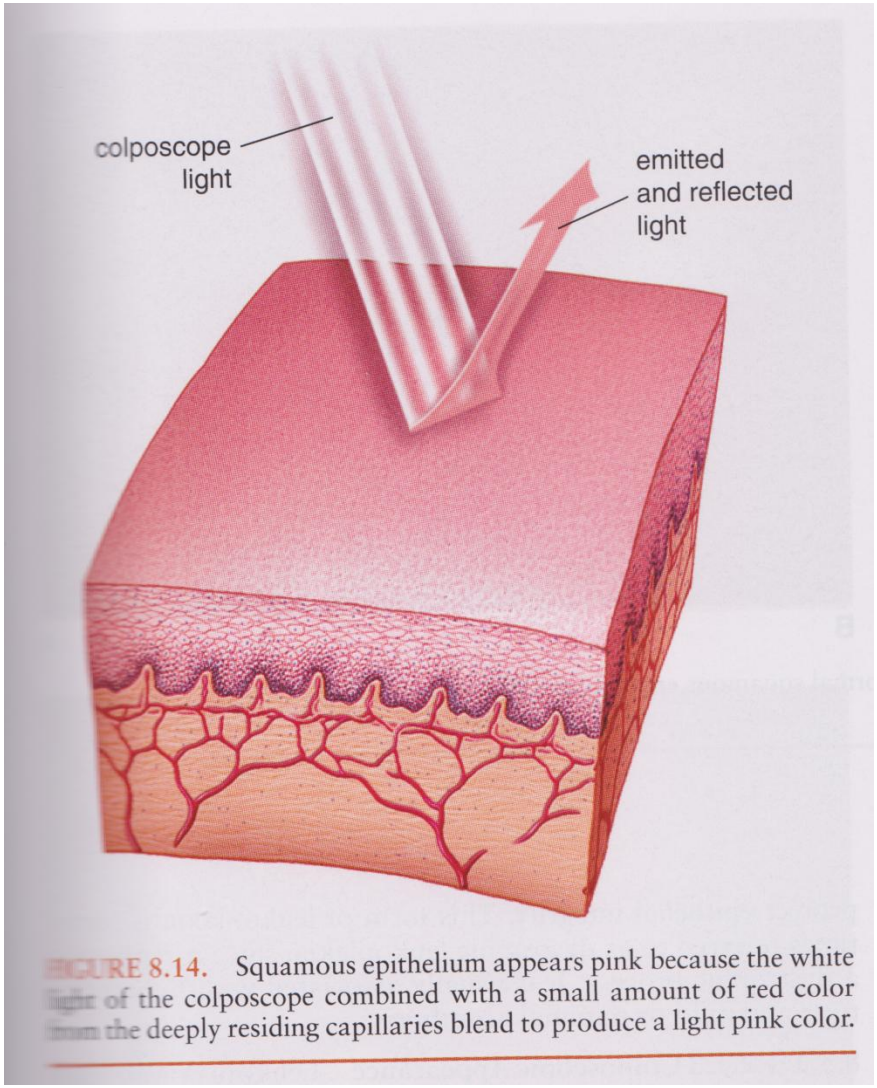


FIGURE 8.14. Squamous epithelium appears pink because the white light of the colposcope combined with a small amount of red color from the deeply residing capillaries blend to produce a light pink color.

Epithelial Color

- At high-power magnification, tiny, superficially located dark red blood vessels can be detected (network capillaries)
- These loop capillaries in stromal papillae penetrate into the lower one-third of the squamous epithelium to nourish the maturing cells.

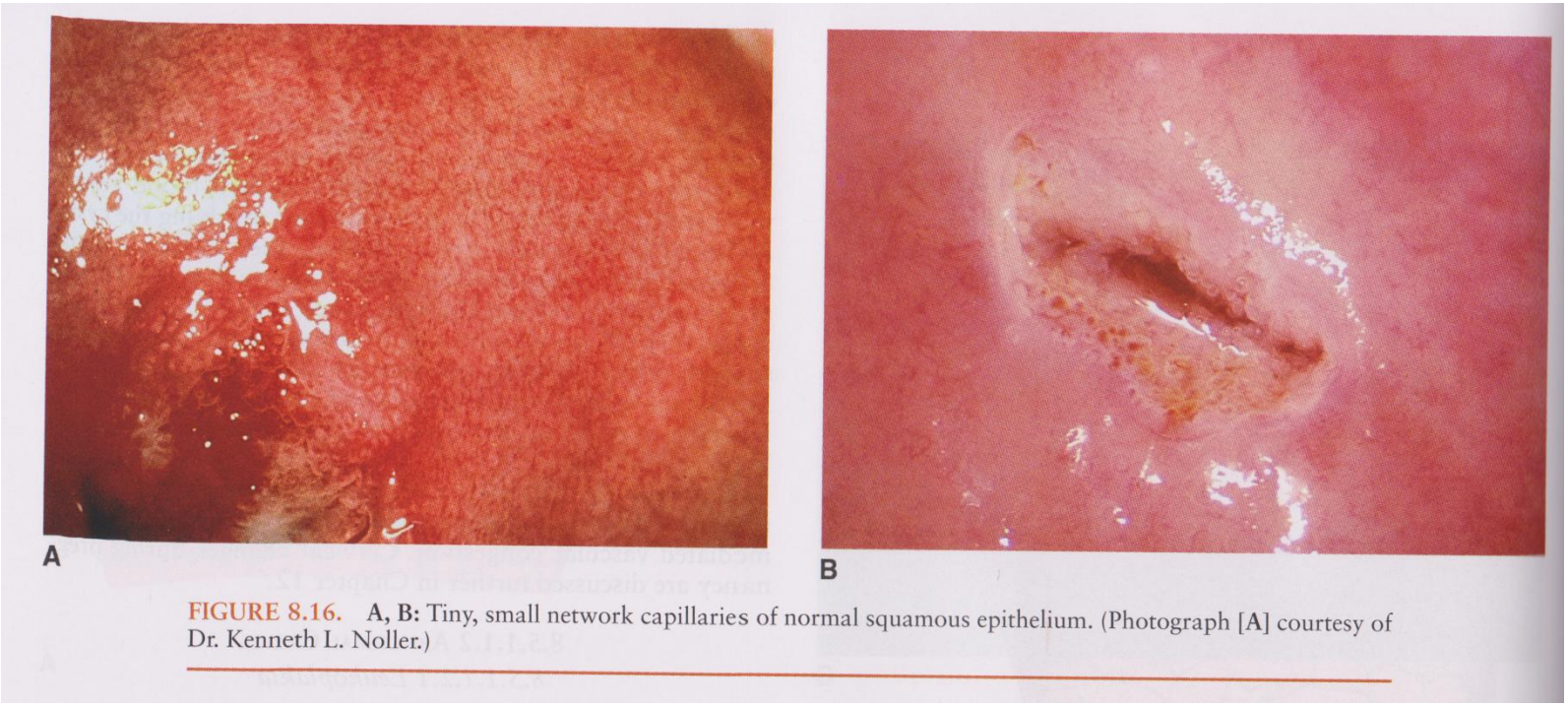


FIGURE 8.16. A, B: Tiny, small network capillaries of normal squamous epithelium. (Photograph [A] courtesy of Dr. Kenneth L. Noller.)

Epithelial Color

- Both columnar epithelium and immature metaplastic epithelium appear red.
- The close proximity of the underlying loop capillaries, which are covered by only a single cell layer of columnar epithelium, emits a predominant red hue from the transilluminated light.
- The color of immature metaplastic epithelium varies depending on its stage of maturation.
- Amber yellow, round nabothian cysts may be observed in metaplastic epithelium.
  - Normal arboreal branching dilated vessels

Leukoplakia

- Epithelium that appers white prior to the application of acetic acid.
- Most commonly associated with an increase in amount of keratin
- Etiology includes chronic trauma due to pessary, diaphragm, retained tampon.
- Leukoplakia noted outside the TZ is not likely associated with neoplastic process.
- It may cover and obscure underlying neoplastic lesions.

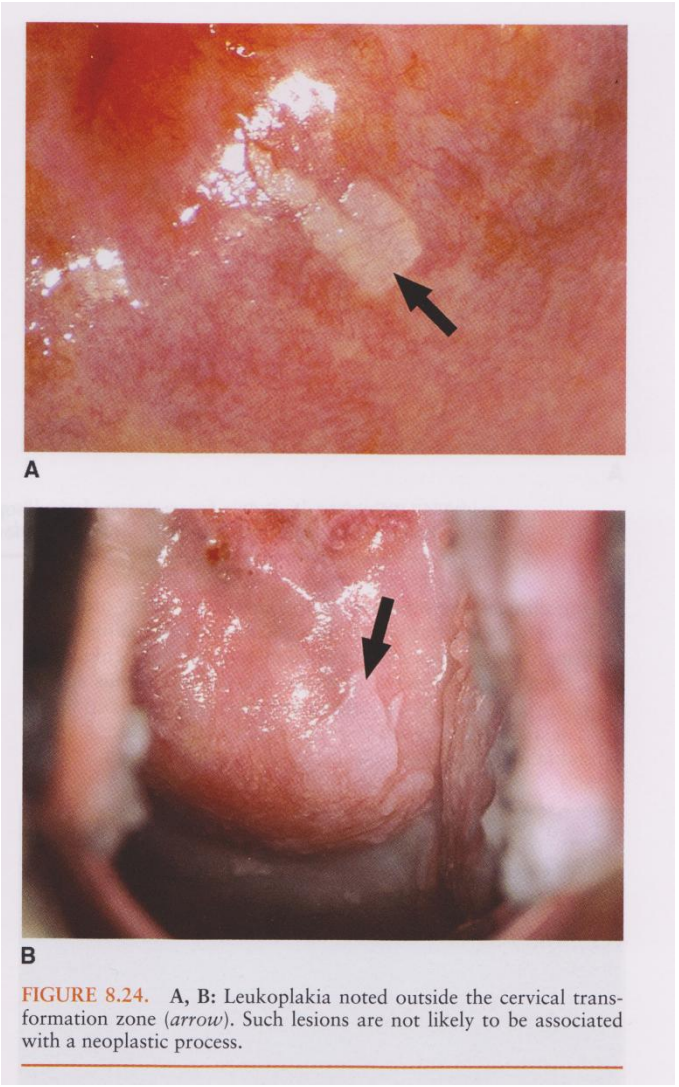


FIGURE 8.24. **A, B:** Leukoplakia noted outside the cervical transformation zone (*arrow*). Such lesions are not likely to be associated with a neoplastic process.

Leukoplakia

- It varies in color, size, distribution and contour.

- Tiny pinpoint white elevations are commonly noted in women who have had previous ablative or excisional procedures of cervix
  - Micropapular projections may assume an intermittent linear pattern, radiating from the the os.

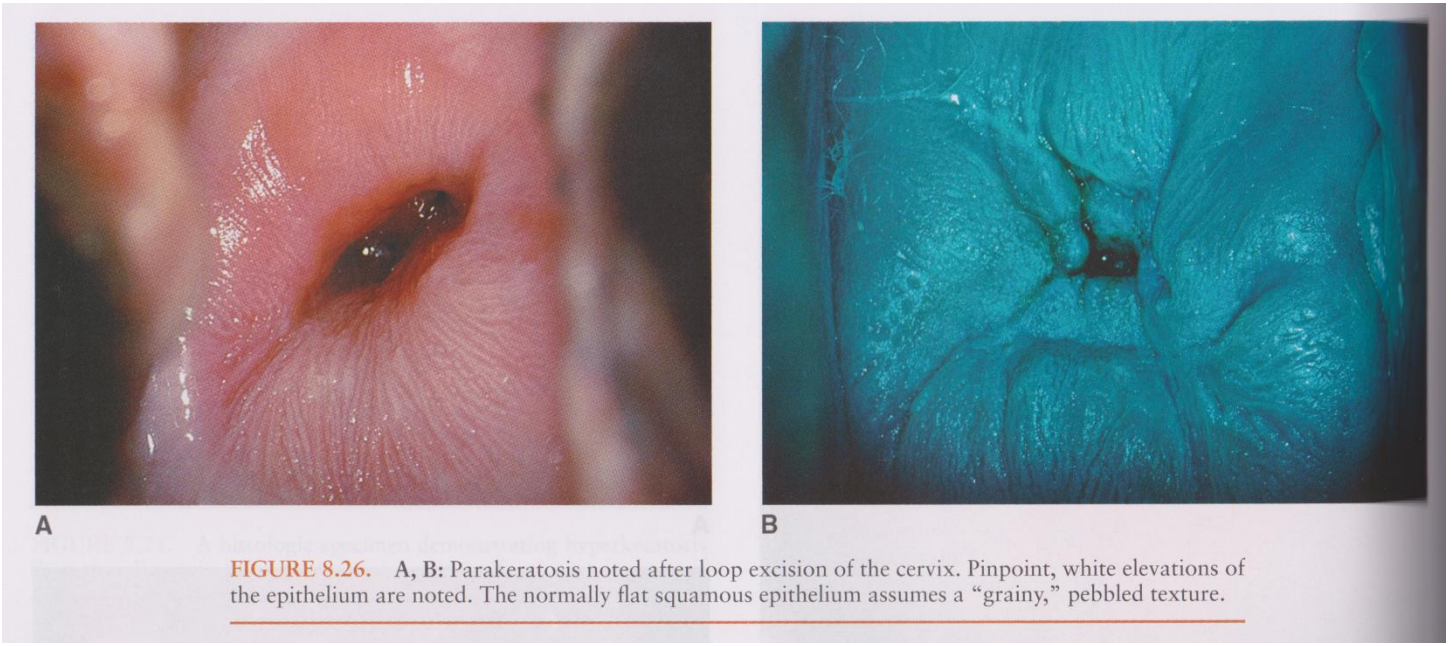


FIGURE 8.26. A, B: Parakeratosis noted after loop excision of the cervix. Pinpoint, white elevations of the epithelium are noted. The normally flat squamous epithelium assumes a "grainy," pebbled texture.

Application of 3%-5% Acetic Acid

- Healthy, mature stratified epithelium whether it is original squamous epithelium or mature metaplastic epithelium retains its pink-tan color.

- The dark red color of columnar epithelium becomes blanched assuming a transient, translucent white color.
  - Each villus assumes a more distinct outline, appearing as grape-like or narrow polypoid structures
  - The transient white color persists for only several minutes, then returning to the original red color.
  - Any persisting acetowhite color after this time represents immature metaplasia or neoplasia

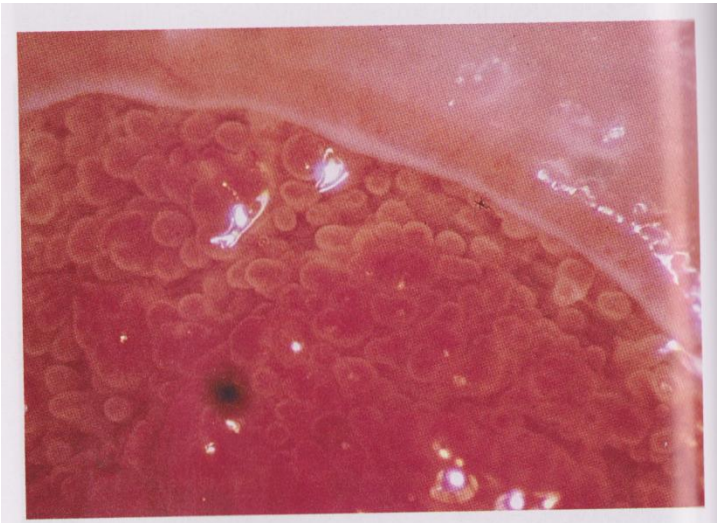
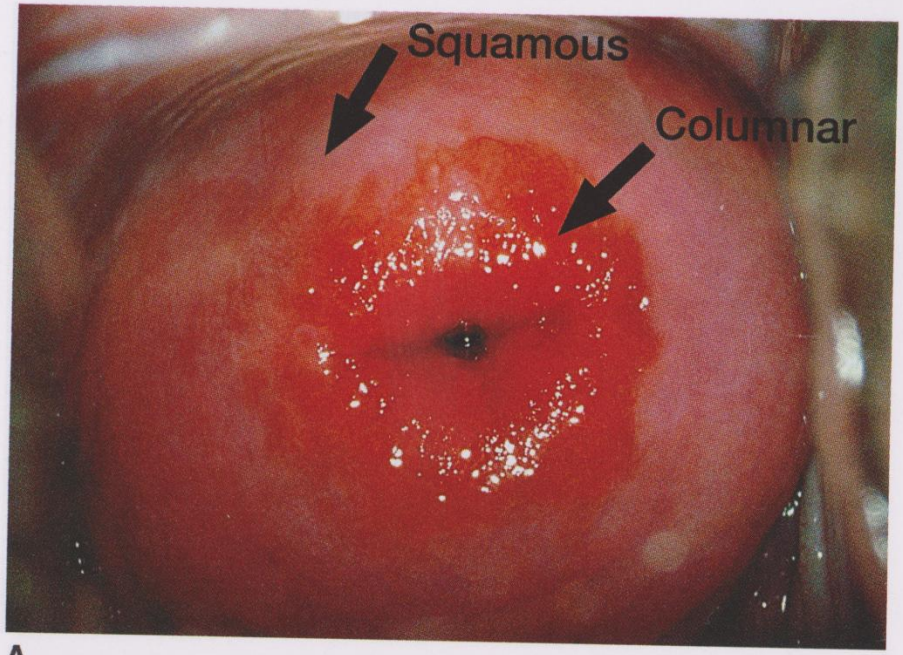


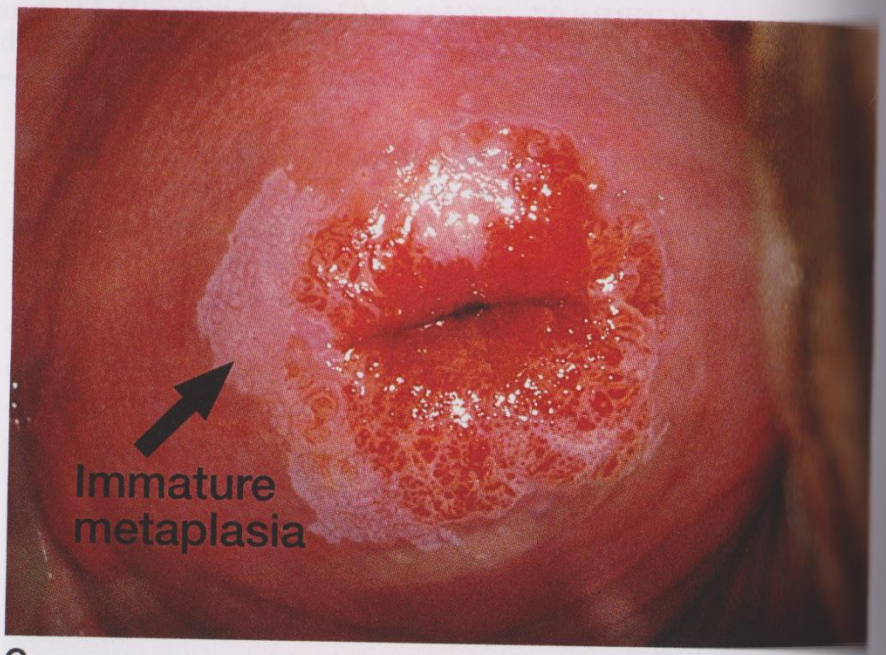
FIGURE 8.31. A high-magnification colpophotograph of columnar epithelium demonstrating grape-like villous structures covered by columnar epithelium. The acetic acid application makes the villi appear more distinct.



A

B

FIGURE 8.30. **A:** Before acetic acid application, the squamous epithelium is pink (*arrow*), and columnar and immature metaplasia are red (*arrow*). **B:** Immediately following acetic acid application, squamous epithelium remains pink, columnar epithelium blanches a faint white color, and immature metaplasia becomes translucent white. **C:** The columnar epithelium returns quickly to a red color, while the area of immature metaplasia remains white (*arrow*).

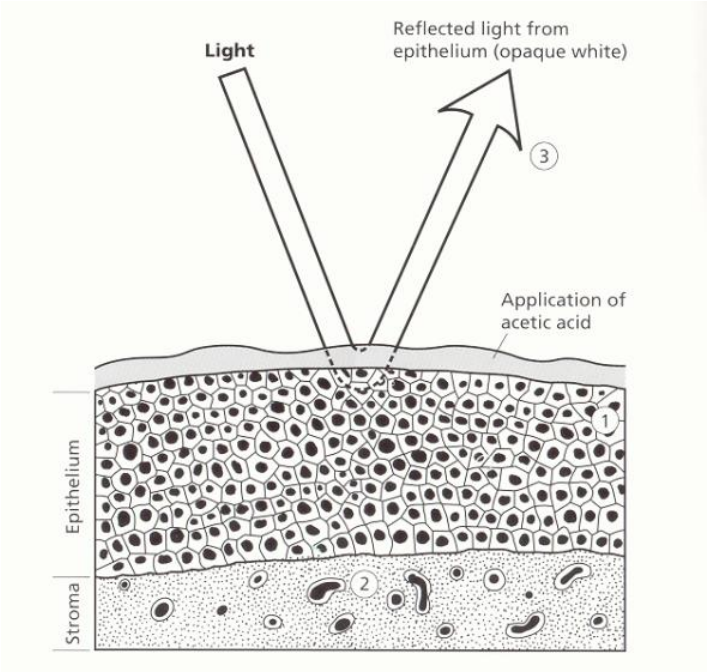


C

Acetowhite Epithelium

- Eptihelium that transiently changes color form pink or red to white after the application of acetic acid.
  - Acetic acid may produce osmotic changes in the tissue that cause a diffusion of intracellular fluid to the extracellular space
  - This causes tissue to assume a greater nuclear-to-cytoplasmic ratio

- The temporary reaction is noted in immature metaplastic, reperative and neoplastic epithelium.
  - It is seen in 57% of normal cervices.



Acetowhite Epithelium

- The acetowhite color of normal immature metaplastic epithelium develops rapidly and fades rapidly.
  - ‘snow-white’ or faintly white appearance
- It may be difficult to reestablish the same level of acetowhitening by reapplying more acetic acid once the initial acetowhite color has faded.
- The white color appears translucent especially in regions of very immature metaplasia.

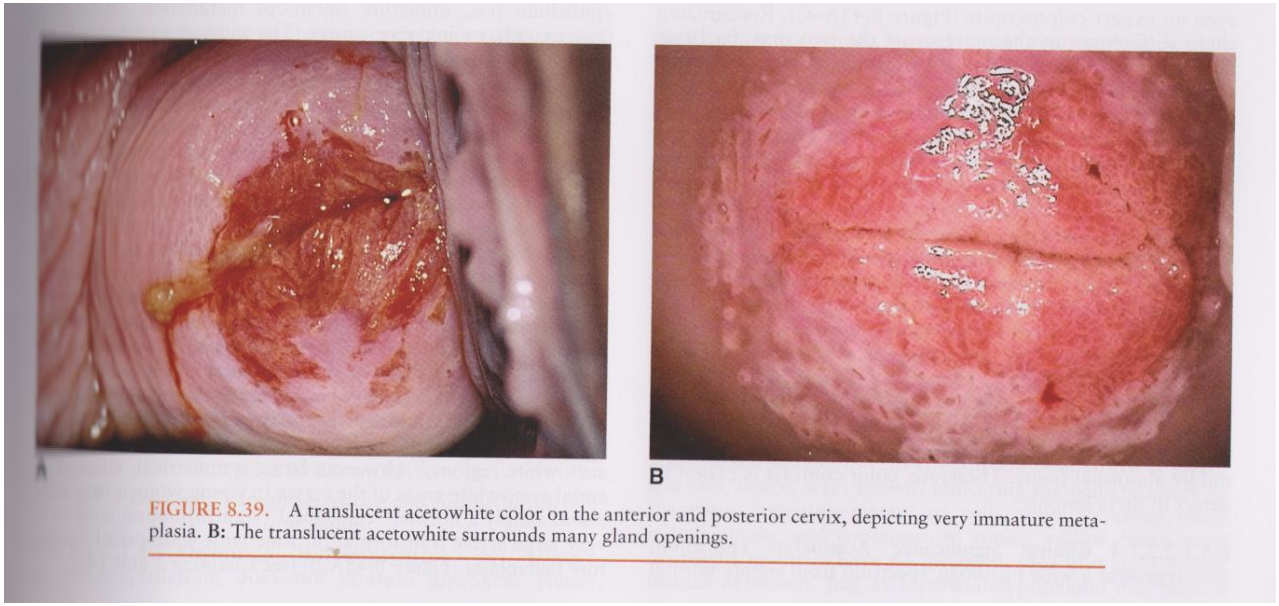
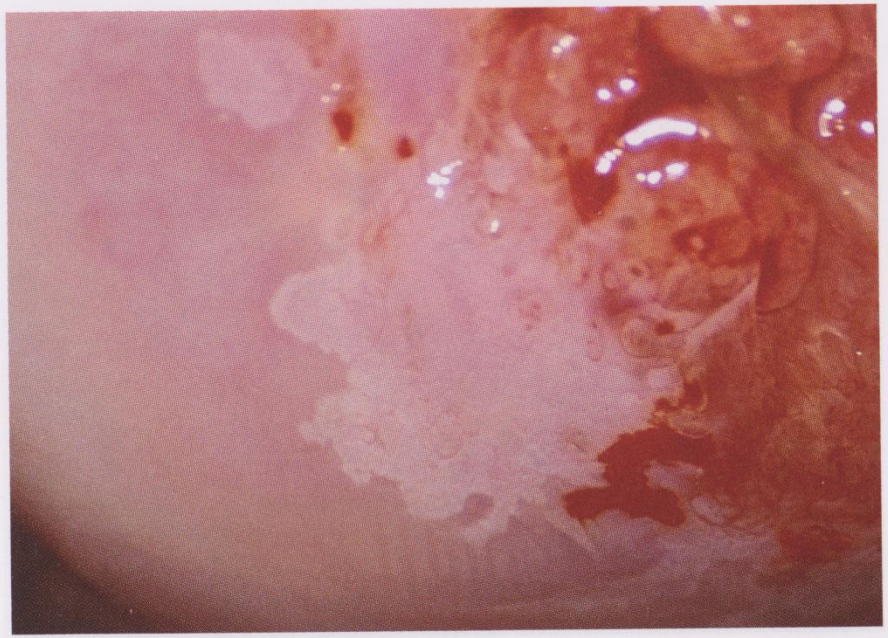


FIGURE 8.39. A translucent acetowhite color on the anterior and posterior cervix, depicting very immature metaplasia. **B:** The translucent acetowhite surrounds many gland openings.

Acetowhite Epithelium

- An easily visualized active, normal, immature TZ in a young women may be confused with a low-grade neoplasia, especially witha ASC or LSIL cytology

- Large, symmetrical, circumferential acetowhite areas of the cervix in young women may represent simply a normal ‘congenital’ transformation zone or a very large active TZ with widespread immature neoplasia.



A

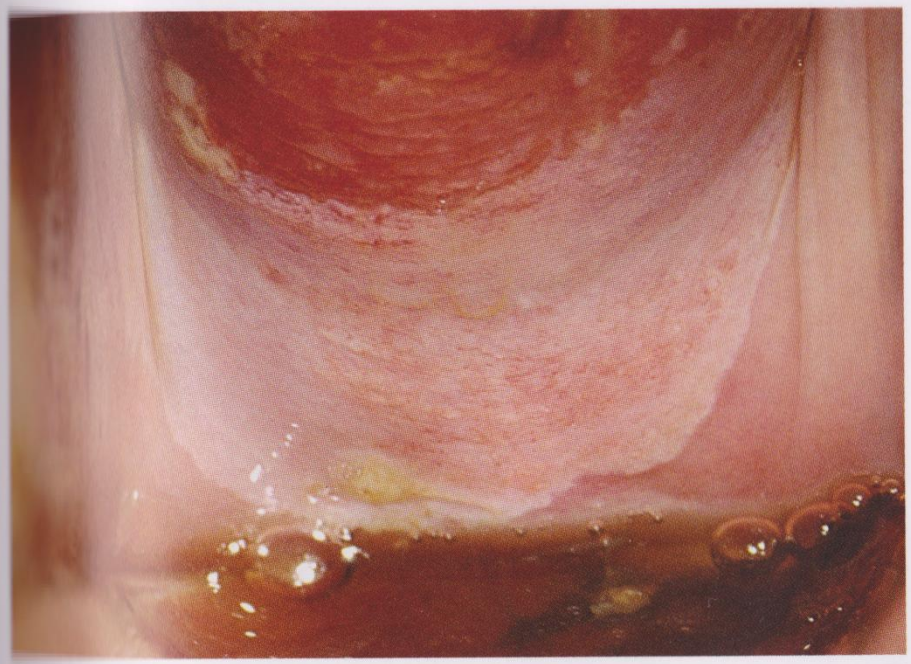
B

FIGURE 8.42. **A:** A low-grade lesion with an irregular "geographic" margin. **B:** A low-grade lesion with an irregular margin is seen in this cervix at the SCJ at 12 to 2 o'clock. **C:** An area of immature metaplasia with a straighter margin and more translucent acetowhitening is seen on the same cervix from 6 to 8 o'clock.

C

immature metaplasia

Transformation zone in posterior fornix



A

B

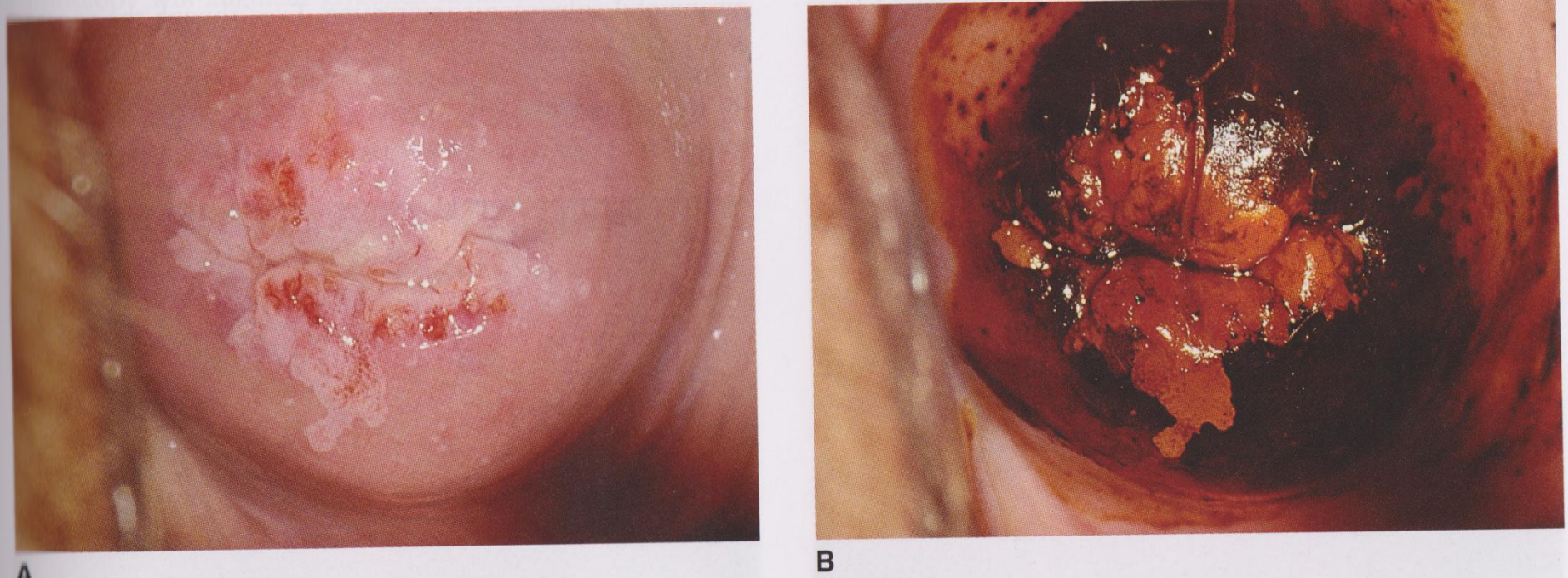
FIGURE 8.45. **A:** A congenital transformation zone extends into the posterior vaginal fornix. This area may mimic a LSIL or areas of immature metaplasia. **B:** The same area as noted in (**A**) is also seen following the application of Lugol's iodine solution.

Application of Lugol's Iodine Solution

- Lugol's iodine solution is a stain for glycogen.
  - Iodine has an affinity for glycogen
- Iodine-negative epithelium does not contain glycogen
- Non-glycogen containing normal immature metaplasia appears yellow and normal columnar epithelium appears pink.
- Normal original vaginal and cervical mucosal squamous epithelium and mature metaplastic epithelium assume a transient mahogany-brown color.
  - Iodine uptake denotes an invariably benign epithelium.

3%-5% acetic acid

Lugol's Iodine Solution



A

B

FIGURE 8.46. **A:** Mature metaplastic epithelium appears pink following 3% to 5% acetic acid application, and a very active transformation zone with numerous shades of acetowhite is seen. **B:** Since it contains glycogen, it stains a rich mahogany brown color. The iodine-negative areas that are yellow represent immature metaplastic epithelium following Lugol's iodine solution application. However, without histologic evaluation it would be difficult to accurately predict whether this is all an entirely normal process or has one or more areas of neoplastic change.

Vasculature

- The spesific vessel pattern, vessel caliber, and intercapillary distance between these vessels help differentiate normal from abnormal vessels.

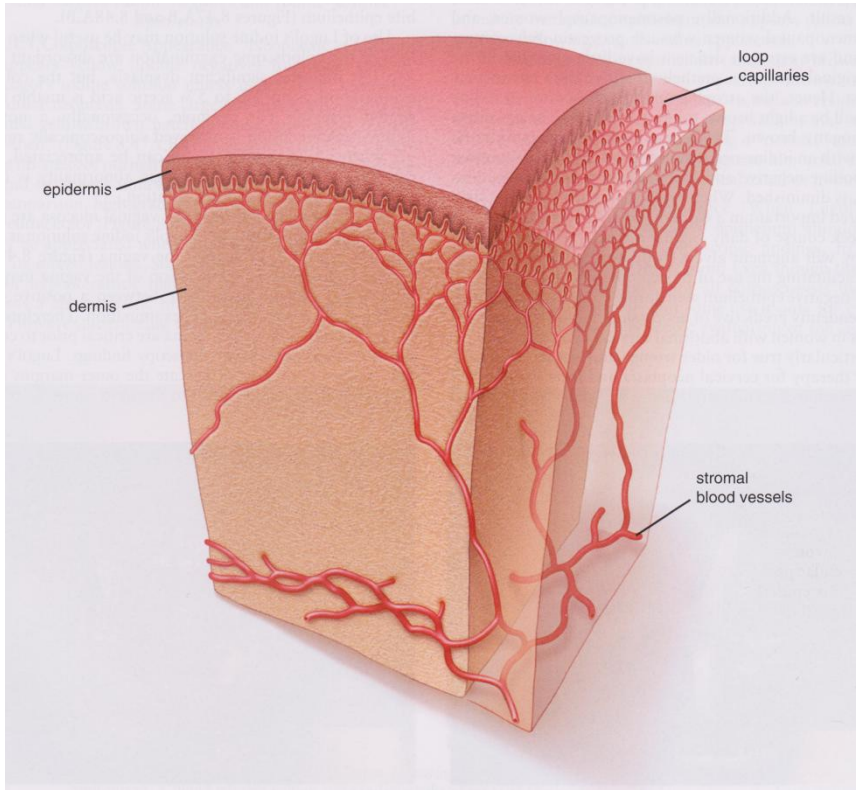
- Acetic acid has vasoconstrictive effect, vessels are best studied after the application of normal saline.
  - Green filter causes red vessels to appear black.

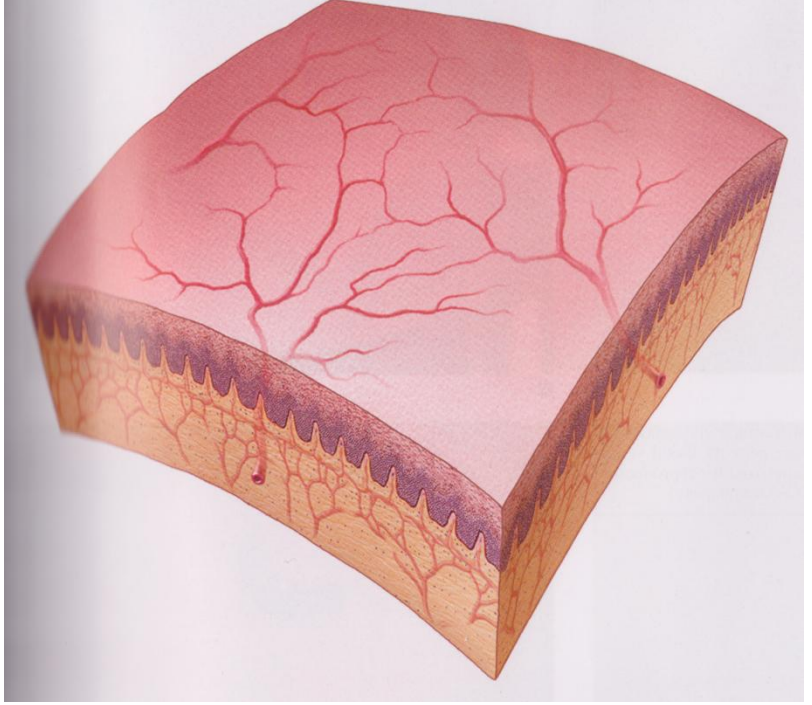
Vasculature of Normal Cervix

- Original squamous epithelium has two types of blood vessels:
  - Network vessels
  - Hairpin capillaries

- Network vessels form a vascular plexus that lies in the submucosal stroma.
  - More prominent in during pregnancy, infections, postmenopusal period, oral contraceptive use

- Hairpin terminal vessels extends toward the epithelial surface in the connective tissue papillae.
  - They have afferent (arterial) and efferent (venous) branches
  - İntercapillary distance 100 (50-250) micrometer

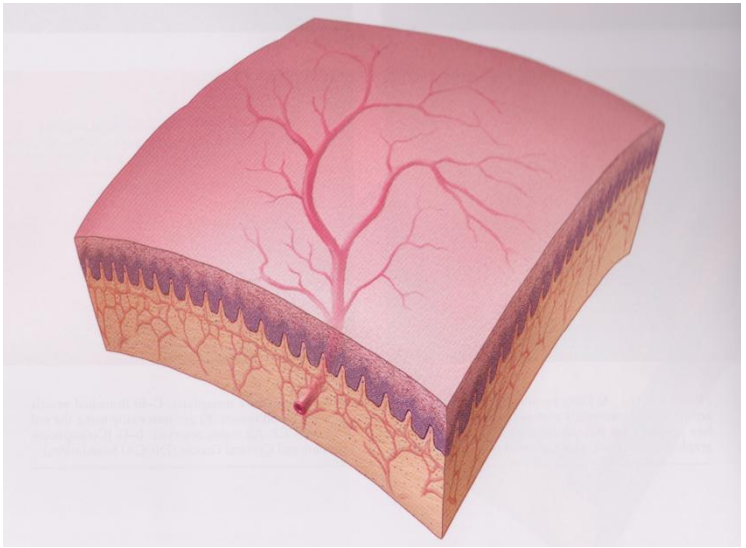

loop
capillaries
epidermis
dermis
stromal
blood vessels



Vasculature of Normal Cervix

- Branched vessels taper along their coarse and have a regular or orderly appearance

- Branches from the long terminal vessels usually emerge at an acute angle, much like branches projecting from a tree trunk.
  - Branches have a smaller diameter than the parent vessel




30-year-old
Cycle day 17

Punctation

- Appearance of single-looped terminal capillaries within stromal papillae.

- It is a nondiagnostic colposcopic finding since it may represent either a normal vascular pattern or an abnormal modification of existing vascular architecture.

Punctation

- During the transformation process, the clefts or folds between the villi become filled by immature metaplastic epithelium.
- Initially, the original afferent and efferent capillary loop remains central within each villus.
- As the clefts fill with metaplastic epithelium, the vessels and encompassing stroma develop into stromal papillae similar to those of the original squamous epithelium.
- The vessels in the stromal papillae adjacent to the block of immature metaplastic squamous epithelium can appear as fine vascular punctation pattern.

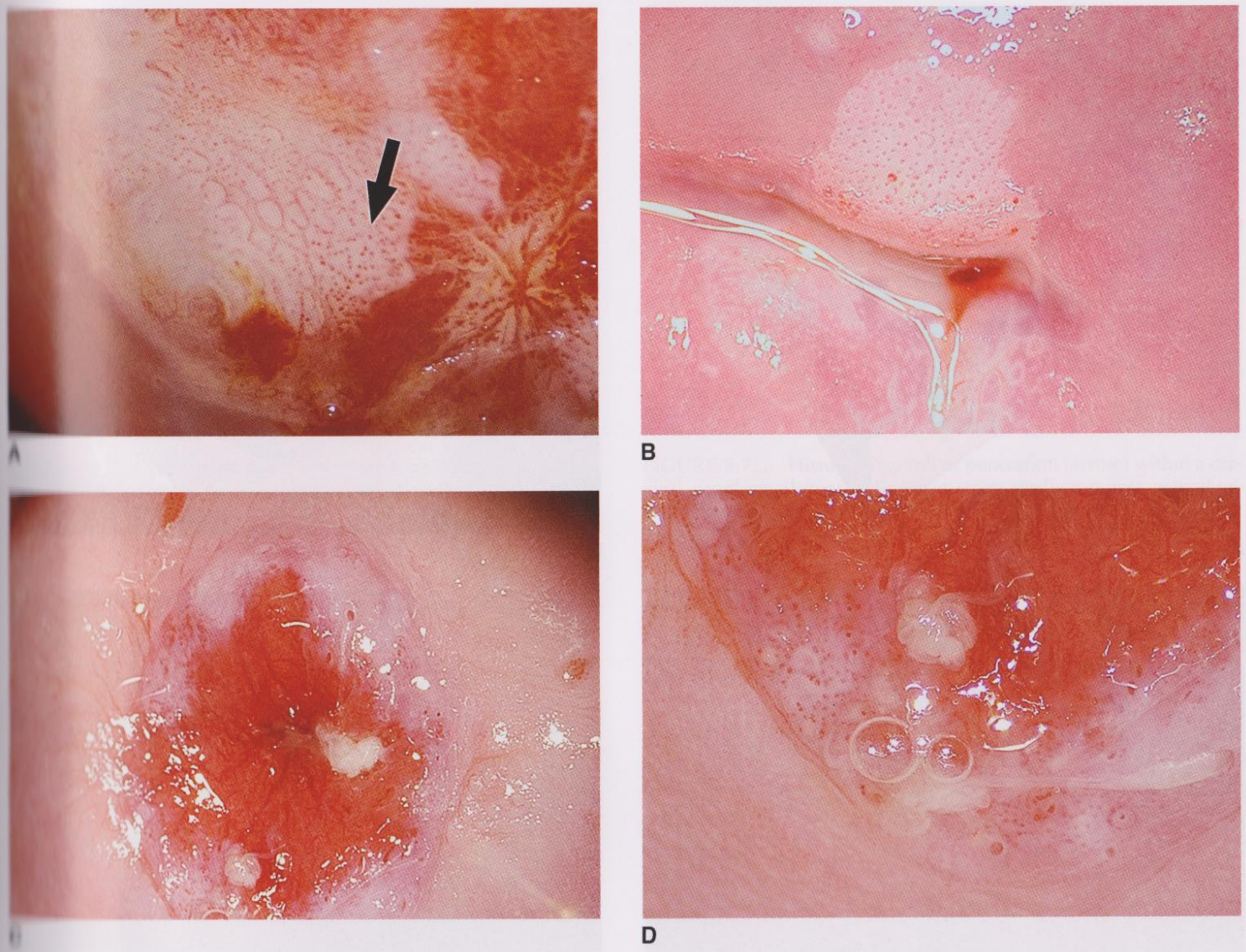


FIGURE 8.66. **A:** Fine punctation (*arrow*) of the cervix following acetic acid application. In some areas, a mosaic pattern is forming. **B:** Acetowhite epithelium makes a good background to contrast the vessel changes. **C, D:** Fine punctation in a cervix following an excisional procedure. Also note the globular acetowhite columnar epithelial finding. (Courtesy of, and approved for reproduction by, the International Cervical Cancer (INCCA) foundation.)

Mosaic

- Vascular pattern produced when capillaries in stromal papillae are arranged parallel to the epithelial surface and form a basket-like structure around blocks or pegs of epithelium.

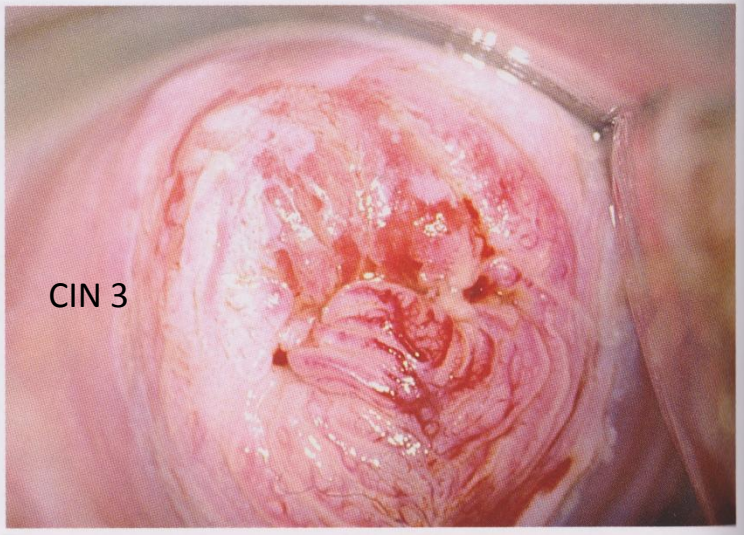
- It may be seen in normal immature squamous metaplastic epithelium.
  - Uniformly consistent small intercapillary distance

Atypical Vessels

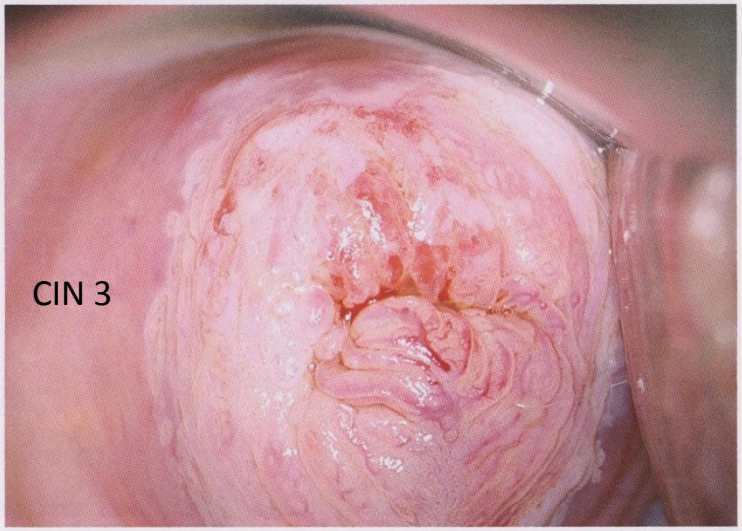
- It may be observed in areas of very early normal immature metaplasia.
  - These vessels are covered by a thin layer of very translucent epithelium.
- In women who previously received local radiation therapy of the lower genital tract.
- Decidual tissue associated with pregnancy.
- Granulation tissue in the proximal vaginal cuff following hysterectomy

A

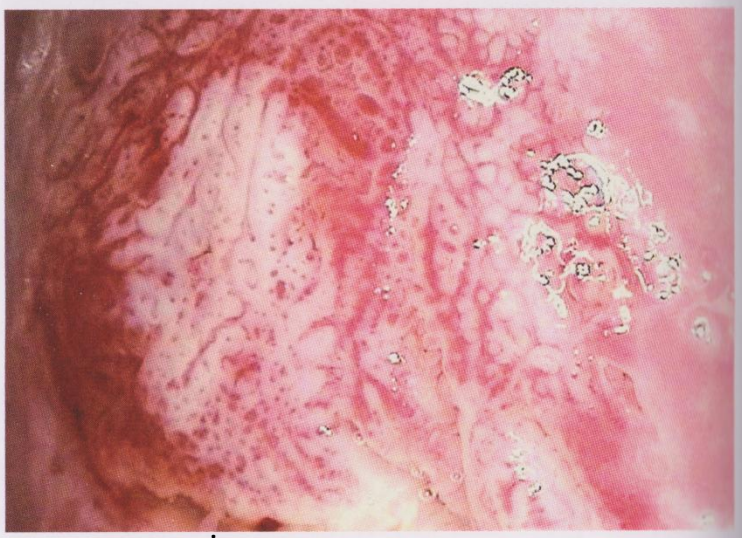
Atypical vessels



B



C



D

İmmature metaplasia

FIGURE 8.92. **A:** Very dilated nonbranching blood vessels are seen on the posterior lip of the cervix during the saline examination. These appear to be atypical vessels. **B, C:** Following 3% to 5% acetic acid application, a large area of acetowhite epithelium is noted. The epithelium of the posterior cervix is translucent white especially in the area of the large vessels. This represents immature metaplasia. It is easy to overlook the opaque acetowhite epithelium at 9 o'clock with coarse punctation that represents CIN 3. **D:** A prominent straight vessel in a young woman within extensive mosaic and punctation in a large area of immature metaplasia.

Conclusion

- There is no single colposcopic sign or anatomical feature detected within the cervical transformation zone that differentiates disease from normality or provides definitive evidence of the presence or degree of premalignant or early invasive neoplasia.

- Any condition that causes increased cellular division, decreased cellular maturation, increased or decreased thickness of epithelium, abnormal cellular metabolism or increased vascularization can produce atypical colposcopic findings.

- Benign conditions such as squamous metaplasia, regeneration, repair, inflammation and infection may produce dramatic epithelial and vascular colposcopic changes.