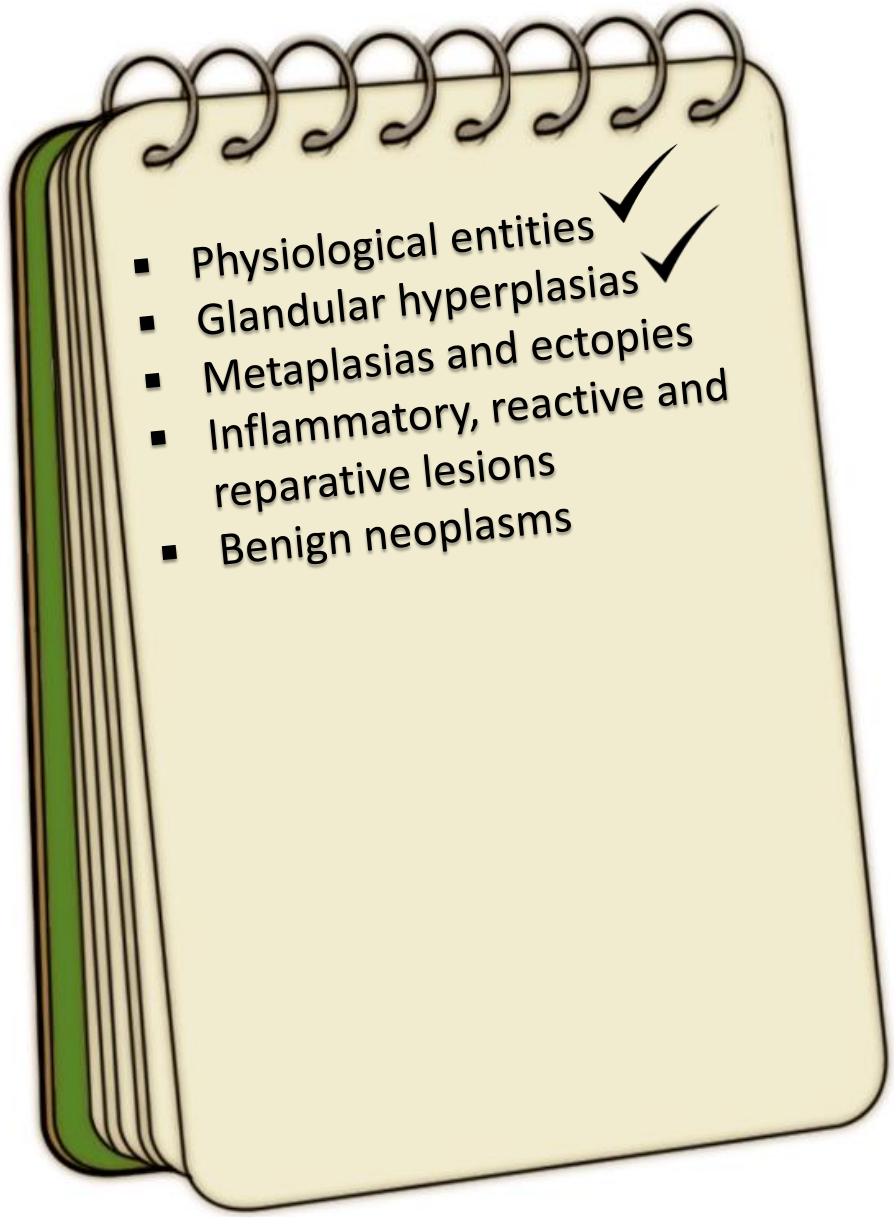
საშვილოსნოს ყელის კეთილთვისებიანი დაზიანებები, რომლებიც ახდენენ სიმსივნის მიმიკრიას

Benign mimics of cervical cancer

მანანა ჯიქურაშვილი, MD

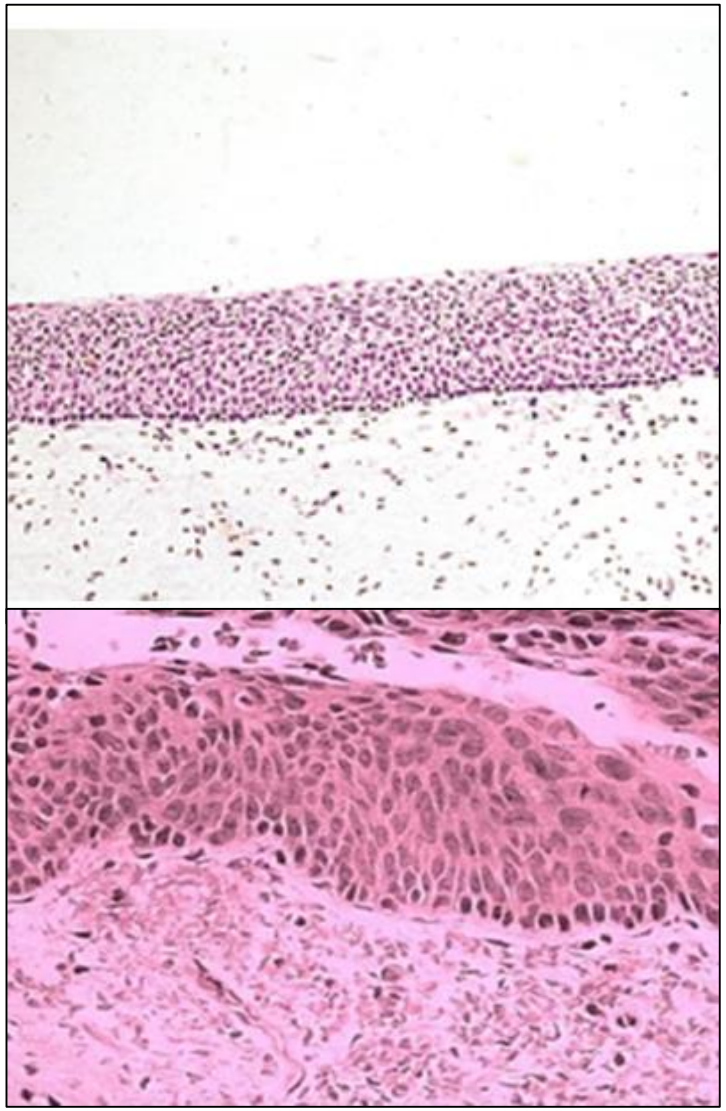
2017

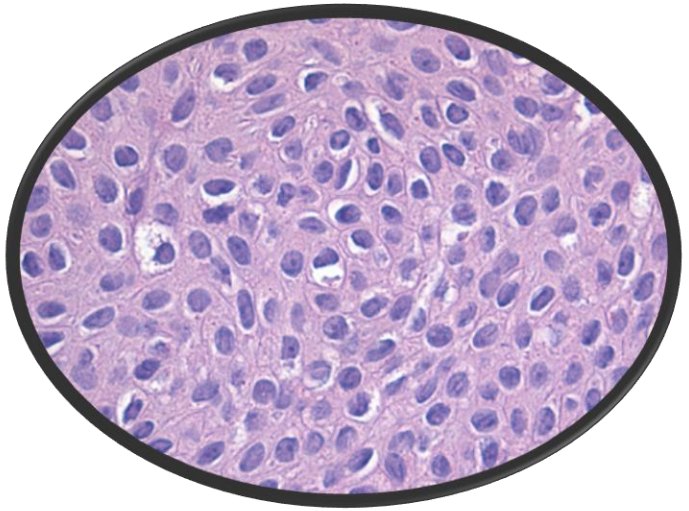

Physiological entities
Glandular hyperplasias
Metaplasias and ectopies
Inflammatory, reactive and reparative lesions
Benign neoplasms

Metaplasias and ectopies

Transitional cell metaplasia (TCM)

- Occurs mostly in postmenopausal women
- Related to alterations in the hormonal microenvironment
- Comprises epithelium which is up to and sometimes greater than 10 cells thick
- Composed by cells similar with parabasal and basal cells, present in all the thickness of the exocervical mucosa
- Vertically aligned elongated nuclei, fine and powdery, uniform chromatin, and indistinct nucleoli
- Some of these cells contain moderate amounts of pale-staining cytoplasm, resembling umbrella cells of the urothelium
- Nuclei may contain grooves and halos
- Without cellular atypia & cellular pleomorphism
- Inactive mitotically/Low mitotic activity

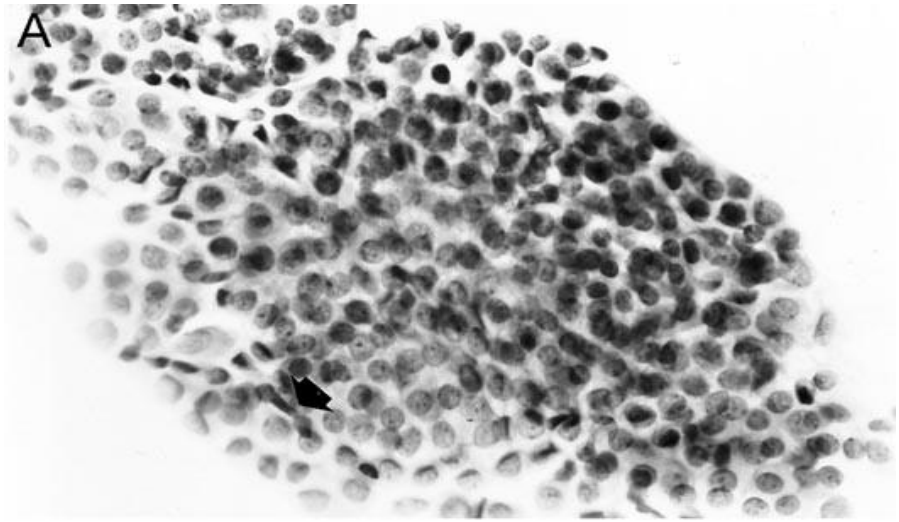


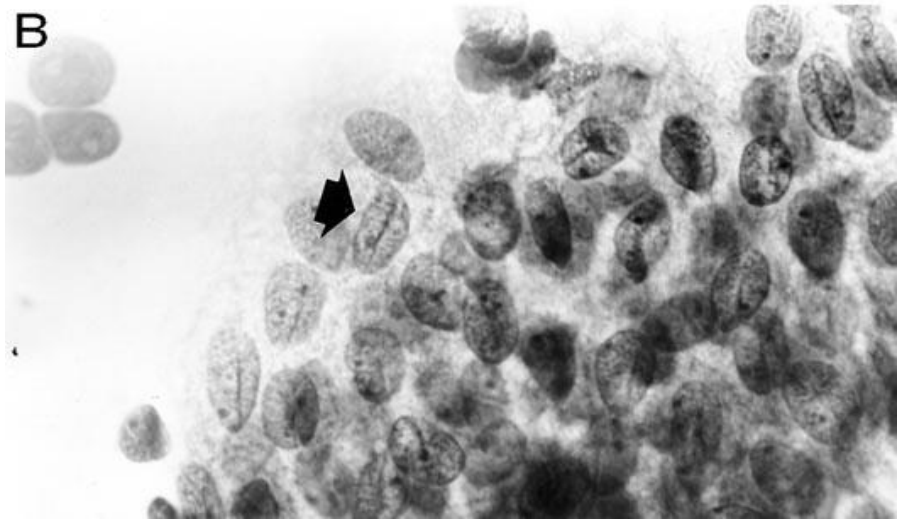


CK13+
CK17+
CK18+
CK20 -

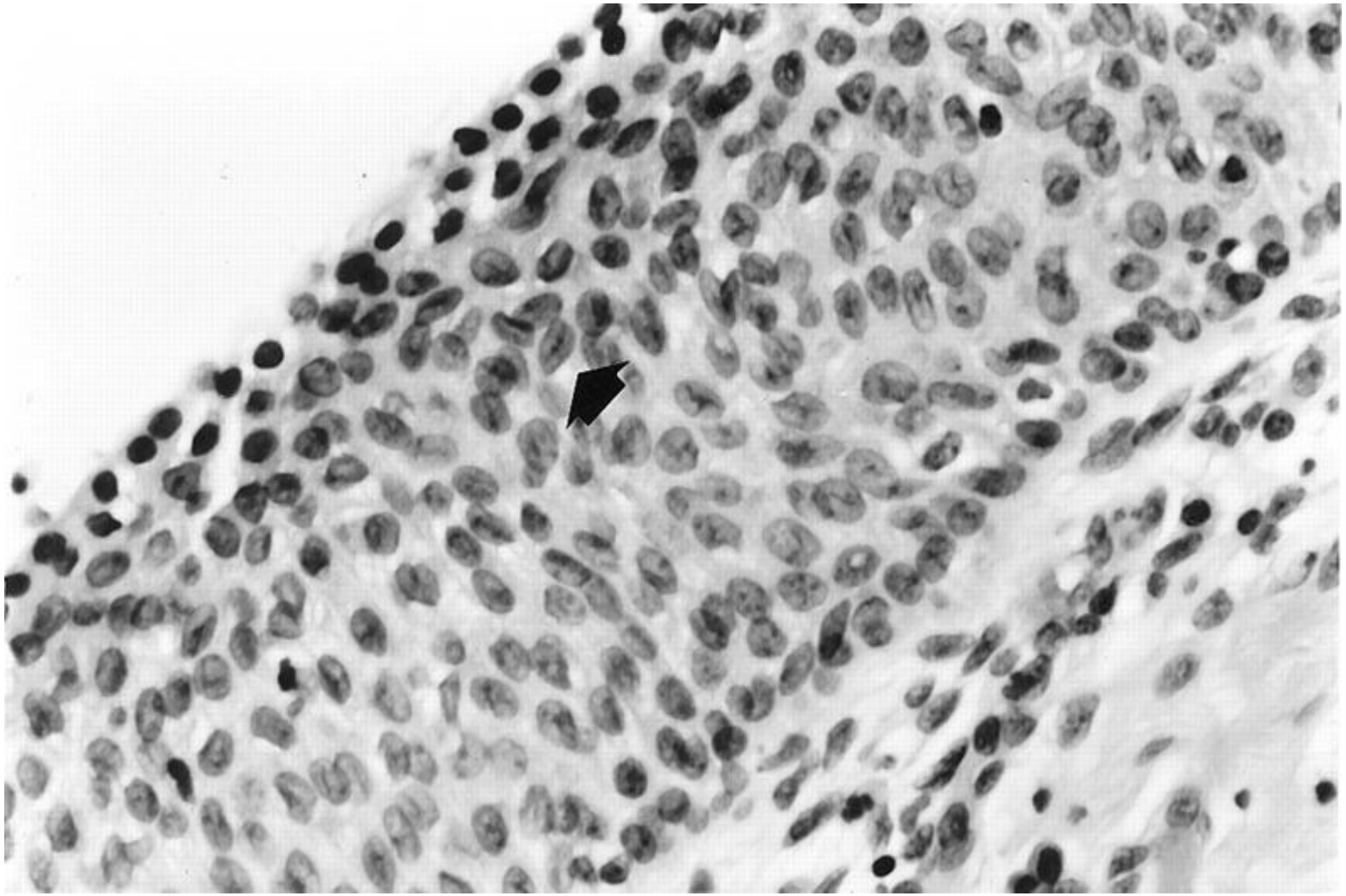
Metaplasias and ectopies

Transitional cell metaplasia (TCM)





A, a sheet of overlapping cells with round uniform nuclei includes rows of umbrellalike cells (arrow)
B, note the nuclear grooves (arrow)



There is a surface layer of umbrellalike cells and a streaming proliferation of elongated nuclei. Note the nuclear grooves (arrow)

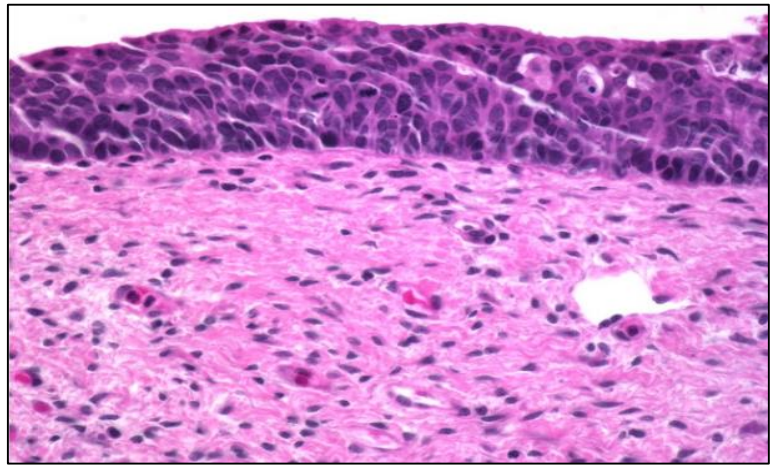
Metaplasias and ectopies

Transitional cell metaplasia (TCM)

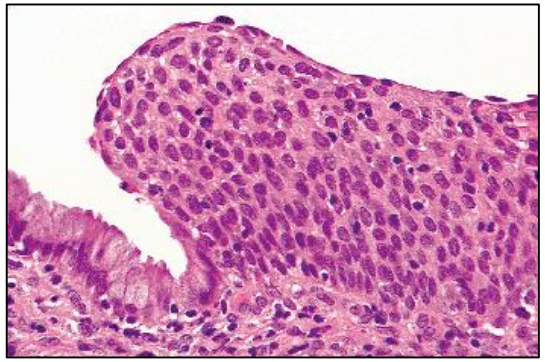
DDX:

- High-grade CIN
- Immature squamous metaplasia
- Atrophy

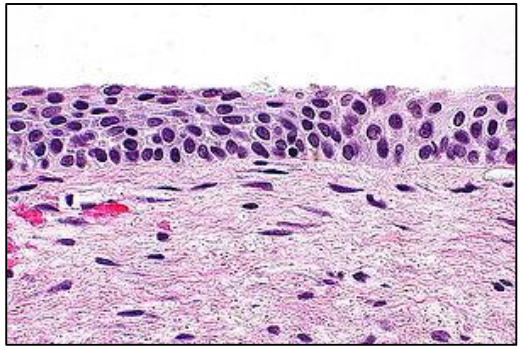
- Mitotically active lesion
- Atypical mitotic figures, nuclear hyperchromatism, and pleomorphism
- Loss of nuclear polarity with disorganized alignment and nuclear overlapping



- The cytoplasm is usually more abundant in squamous metaplasia
- Cells have a more squamoid appearance
- Nuclear grooves are not conspicuous



- The numbers of cell layers often are much lower
- The affected parabasal cells do not have the urothelial morphology



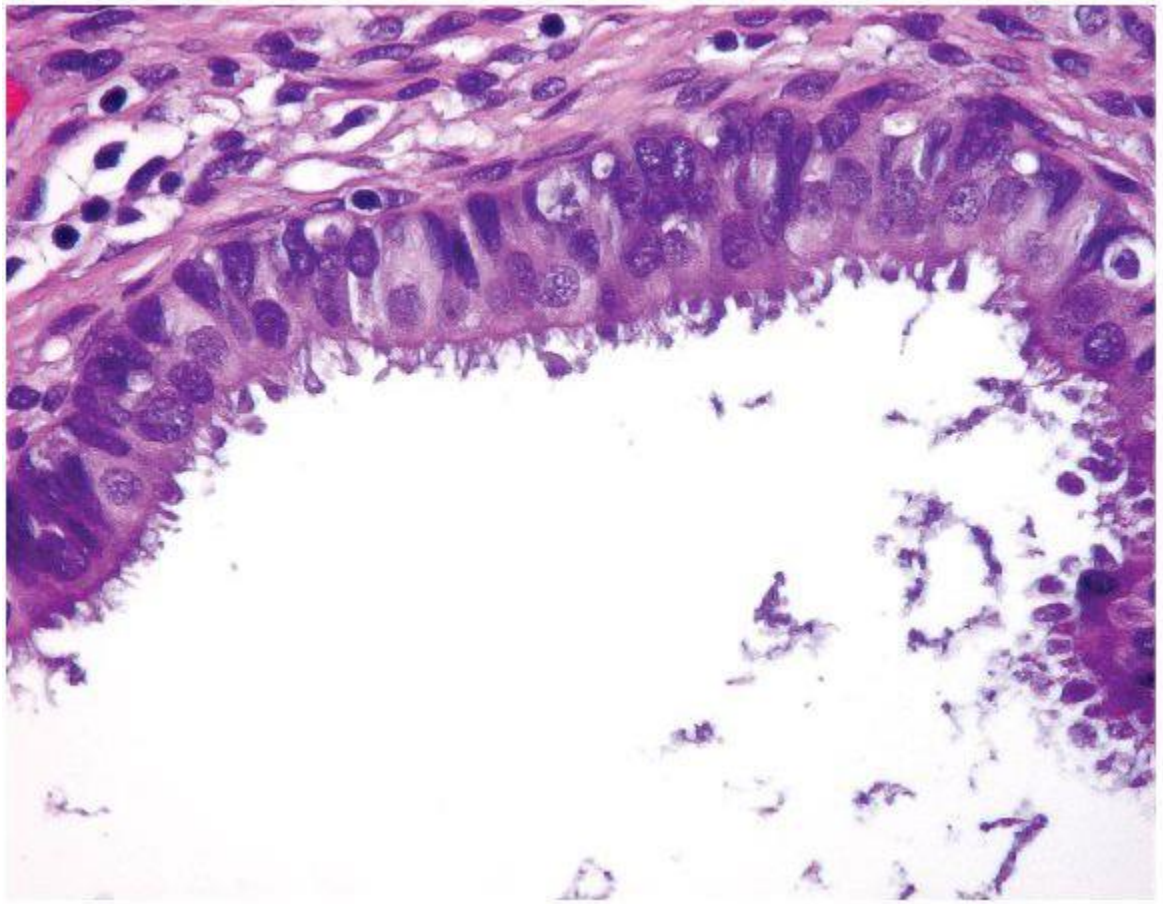
Feature	TCM	HSIL
Epithelial thickness	>10 layers	8–12 layers
Growth pattern	Cell streaming	Cell disorganization
Mitosis	Rare/normal	Many/abnormal
n:c Ratio	Low	High
Chromatin	Fine	Hyperchromatic
Halos and grooves	+	-

Metaplasias and ectopies

Tubal metaplasia (TM)

- Commonly seen in premenopausal women, incidentally
- Tends to occur in the upper endocervix, mainly in deep glands
- Can be extensive and can mimic cervical glandular intraepithelial neoplasm (CGIN)
- The mitotic activity is low
- The glands can show abnormal architecture and elicit a hypercellular stromal reaction (should not lead to confusion with adenocarcinoma)
- It can mimic ciliated CGIN as well as usual CGIN
- Atypical tubal metaplasia has been described and this comprises enlarged and crowded nuclei, stratification and increased mitotic activity

- CEA and p16 – negative (including the atypical form)
- There is a pseudo-infiltrative version which can mimic MDA
- MDA is ER/PR negative while tubal metaplasia is positive



Metaplasias and ectopies

Tubal metaplasia (TM)

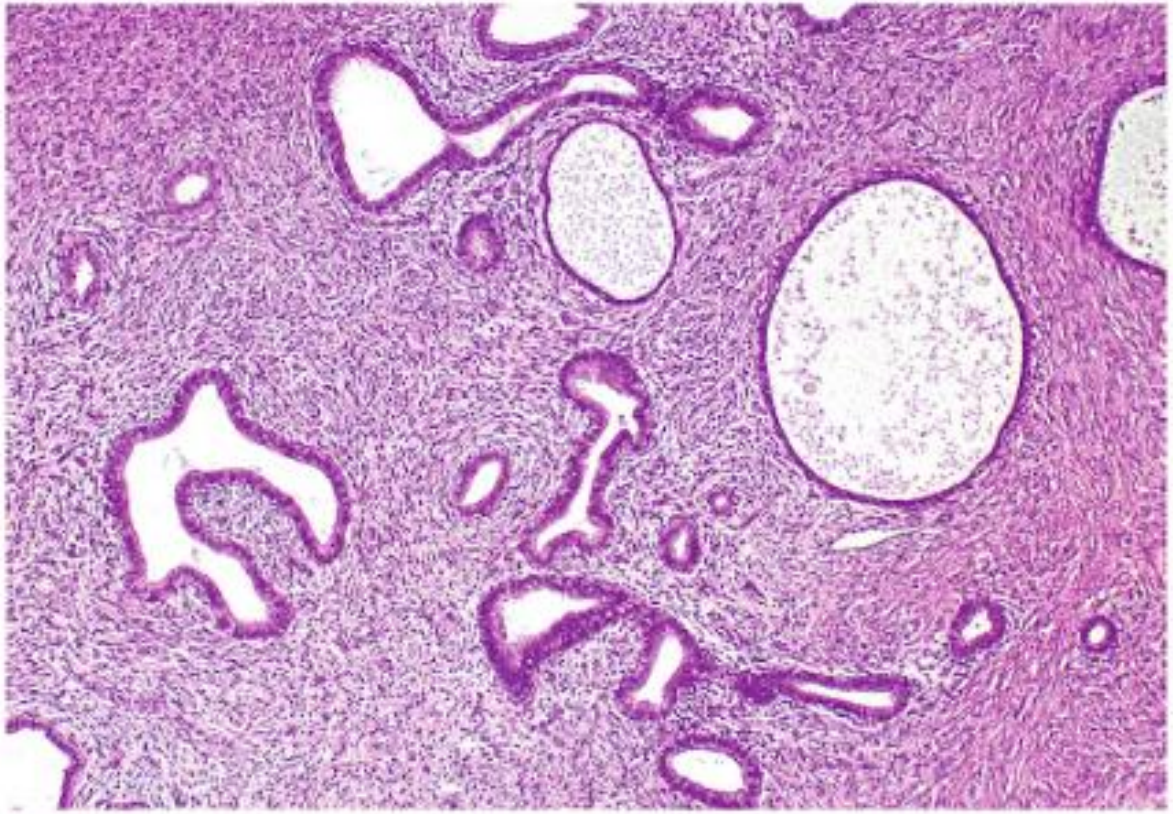


Fig. 4.4 Tubal metaplasia. The glands vary in size and shape, and some are cystic. The periglandular stroma is more cellular than normal

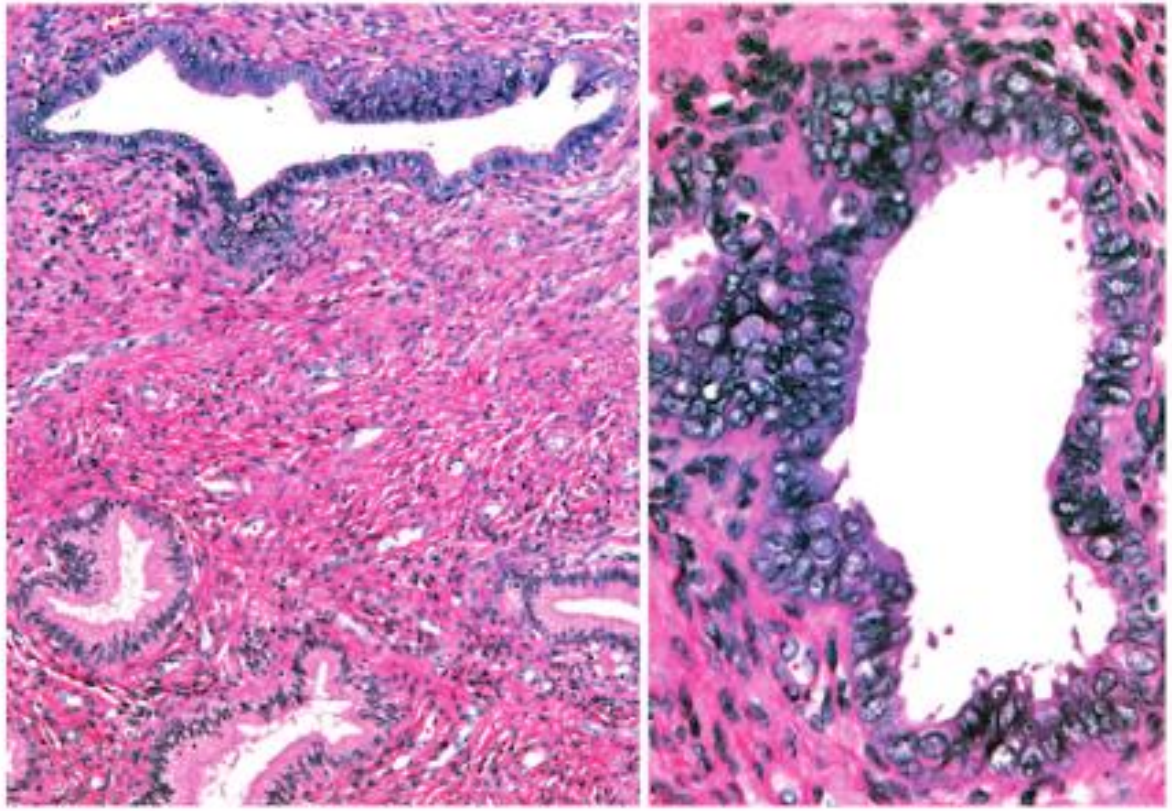


Fig. 4.6 Tubo-endometrioid metaplasia within a previous cone biopsy site. Left: The tuboendometrioid glands (top) contrast with the normal

Metaplasias and ectopies

Tubal metaplasia (TM)

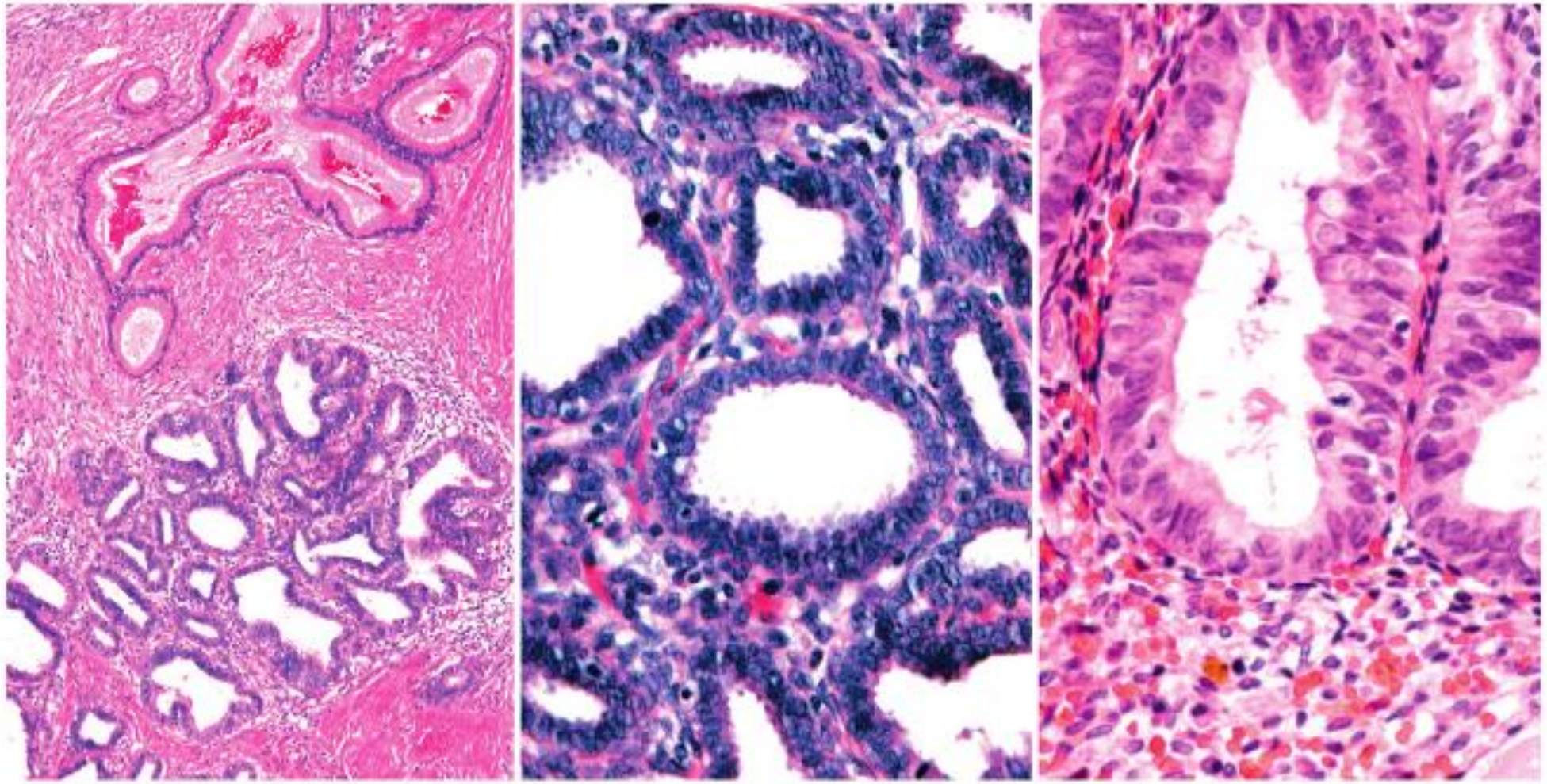
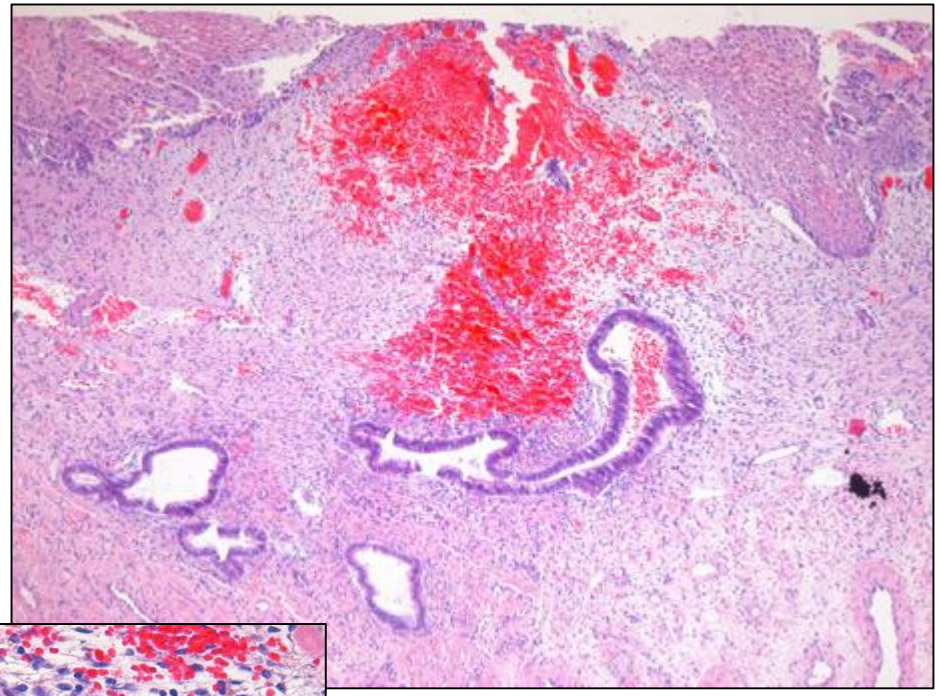


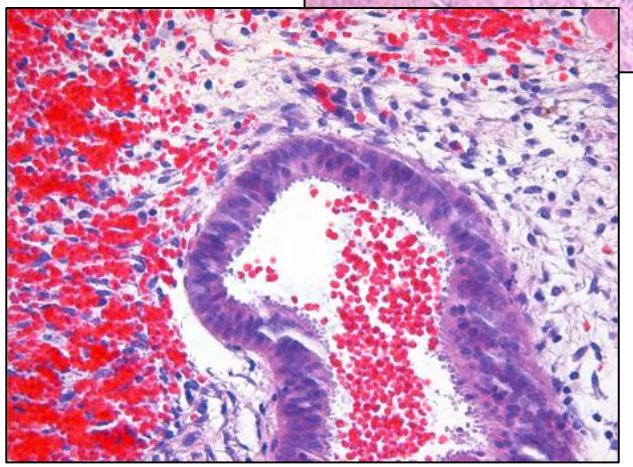
Fig. 4.7 Superficial cervical endometriosis. Left: A focus of endometriosis subtending normal endocervical glands could be misinterpreted as a tunnel cluster, but note endometriotic stroma within the focus. Center: Higher power view showing hyperchromatic mucin-poor cells that could suggest endocervical glandular dysplasia or adenocarcinoma in situ. Right: A different focus of endocervical endometriosis. Note endometriotic

Metaplasias and ectopies

Endometriosis

- This comprises ectopic endometrial glands and stroma anywhere in the cervix but usually in the superficial one third of the wall
- Deep endometriosis in pts with pelvic endometriosis
- It can be cystic or may even form a circumscribed mass
- Stromal endometriosis – glands are sparse or absent
- During pregnancy or with progesterone therapy, decidual change in the stroma may be noted
- The pathogenesis of cervical endometriosis is either by implantation at surgery or trauma or true metaplasia like tubal and tubo-endometrioid metaplasia





- It can mimic CGIN although the presence of stroma together with haemorrhage in endometriosis helps to distinguish it from the neoplastic process

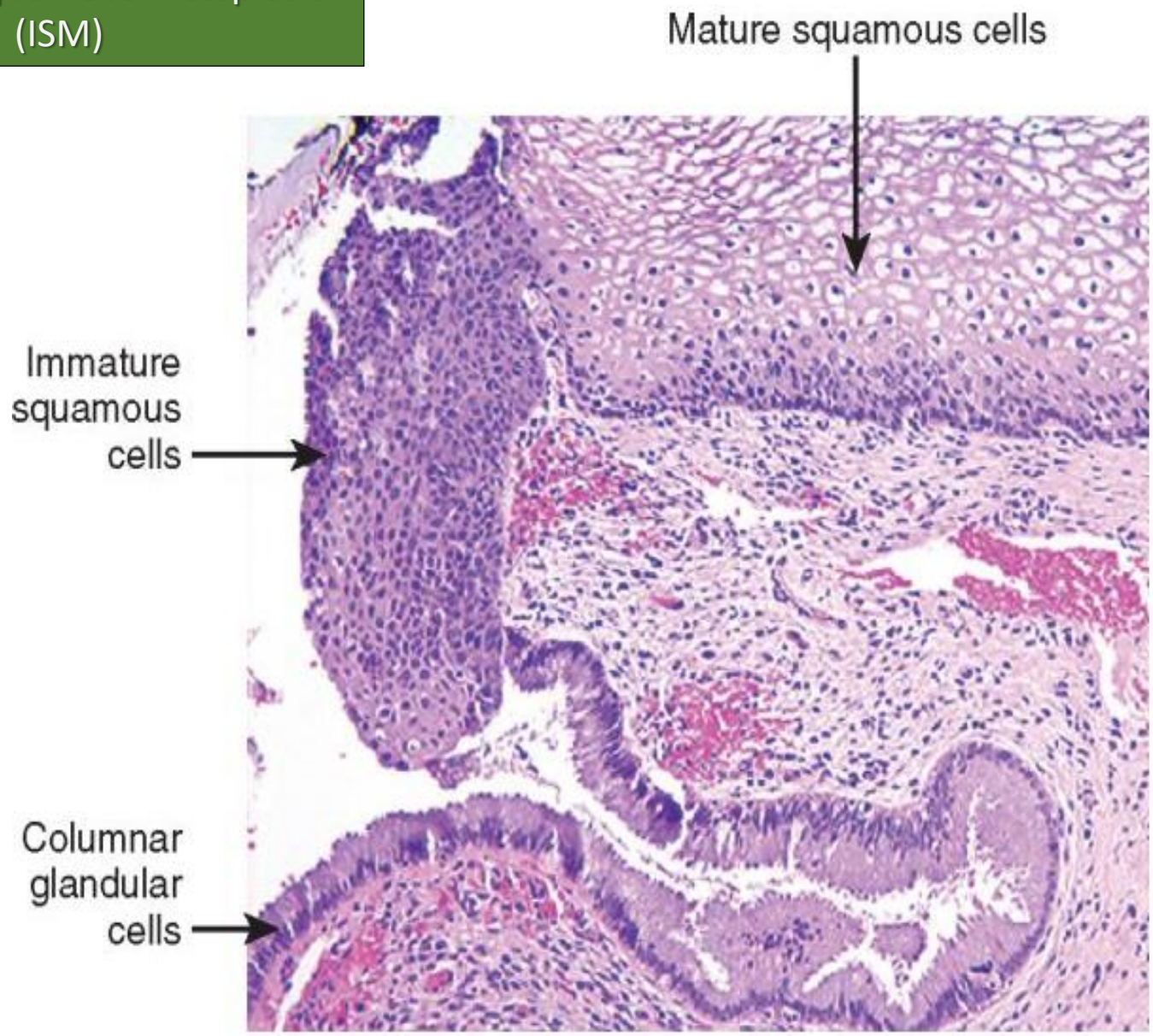
Metaplasias and ectopies

Immature squamous metaplasia (ISM)

- Common during puberty, pregnancy and postpartum
- Often sharply demarcated from mature squamous epithelium by a perpendicular line
- The metaplastic epithelium can extend to the endocervical glandular structures
- There is cell organisation and cohesion and no atypia
- Mitoses are rare, and confined to the lower third of the epithelium

- A small percentage can show mild atypia (so-called atypical immature squamous metaplasia or AIM)

- Typical IM and mature squamous metaplasia is consistently negative for p16, in contrast to CIN



Metaplasias and ectopies

Immature squamous metaplasia (ISM)

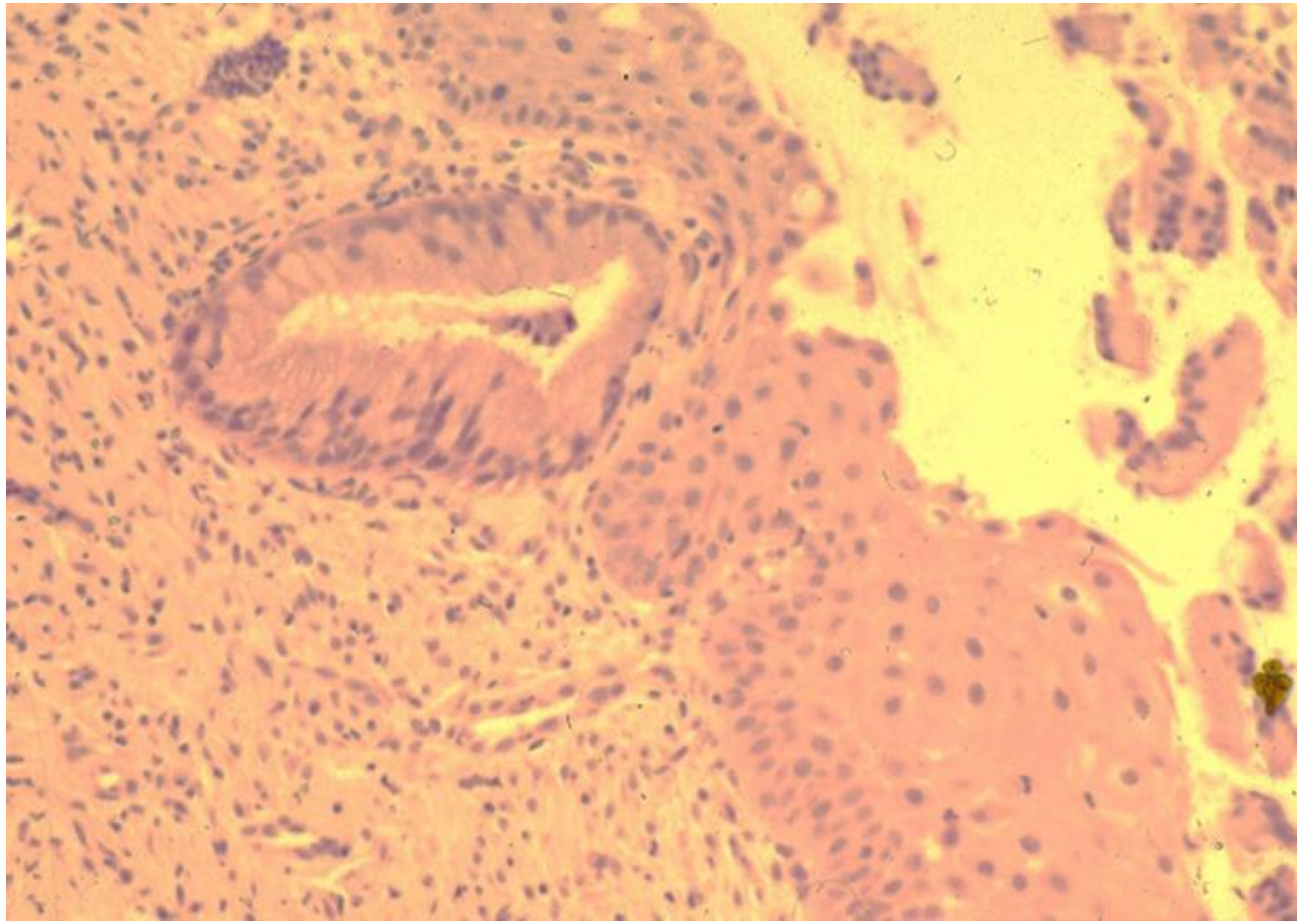
Hyperplasia of the reserve, under-columnar cells, that are more numerous, the cytoplasm being increasingly eosinophilic since the cell is maturating to squamous cell

↓

The phase of immature squamous metaplasia
relative uniform aspect of the metaplastic squamous cells, resembling with the native parabasal cells, with preserved polarity, uniform nuclei and reduced cytoplasm

↓

The cellular maturation occurs to the surface; finally, the mature squamous metaplasia is difficult to differentiate from the native squamous epithelium

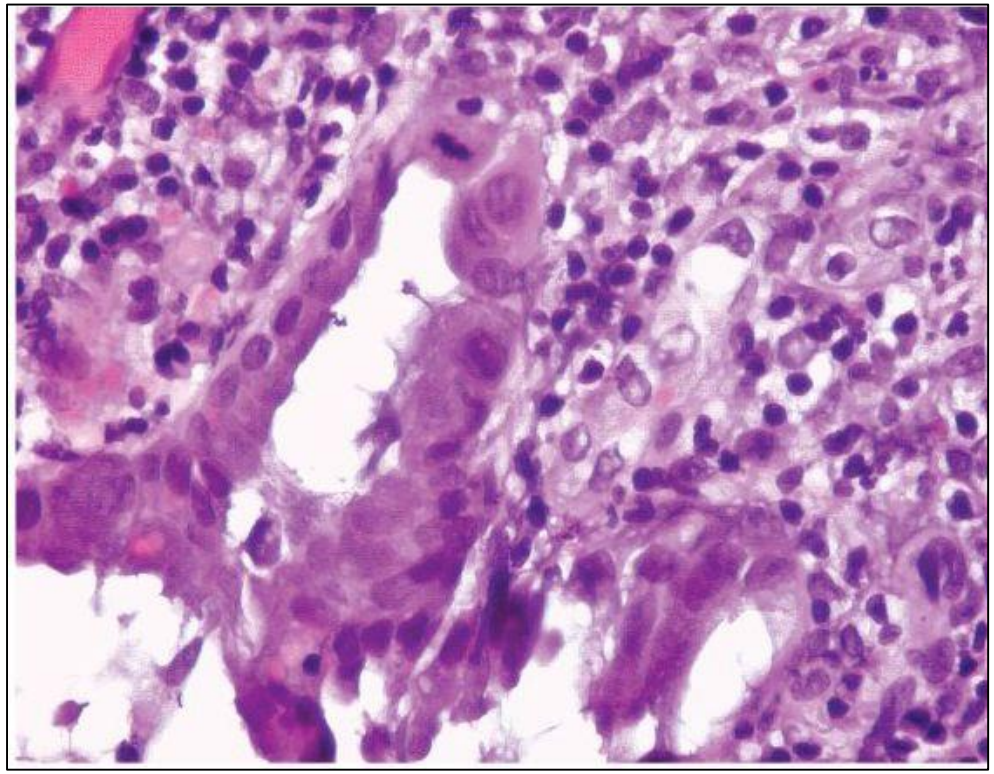


Immature squamous metaplasia with underlying endocervical crypt

Metaplasias and ectopies

Oxyphilic metaplasia

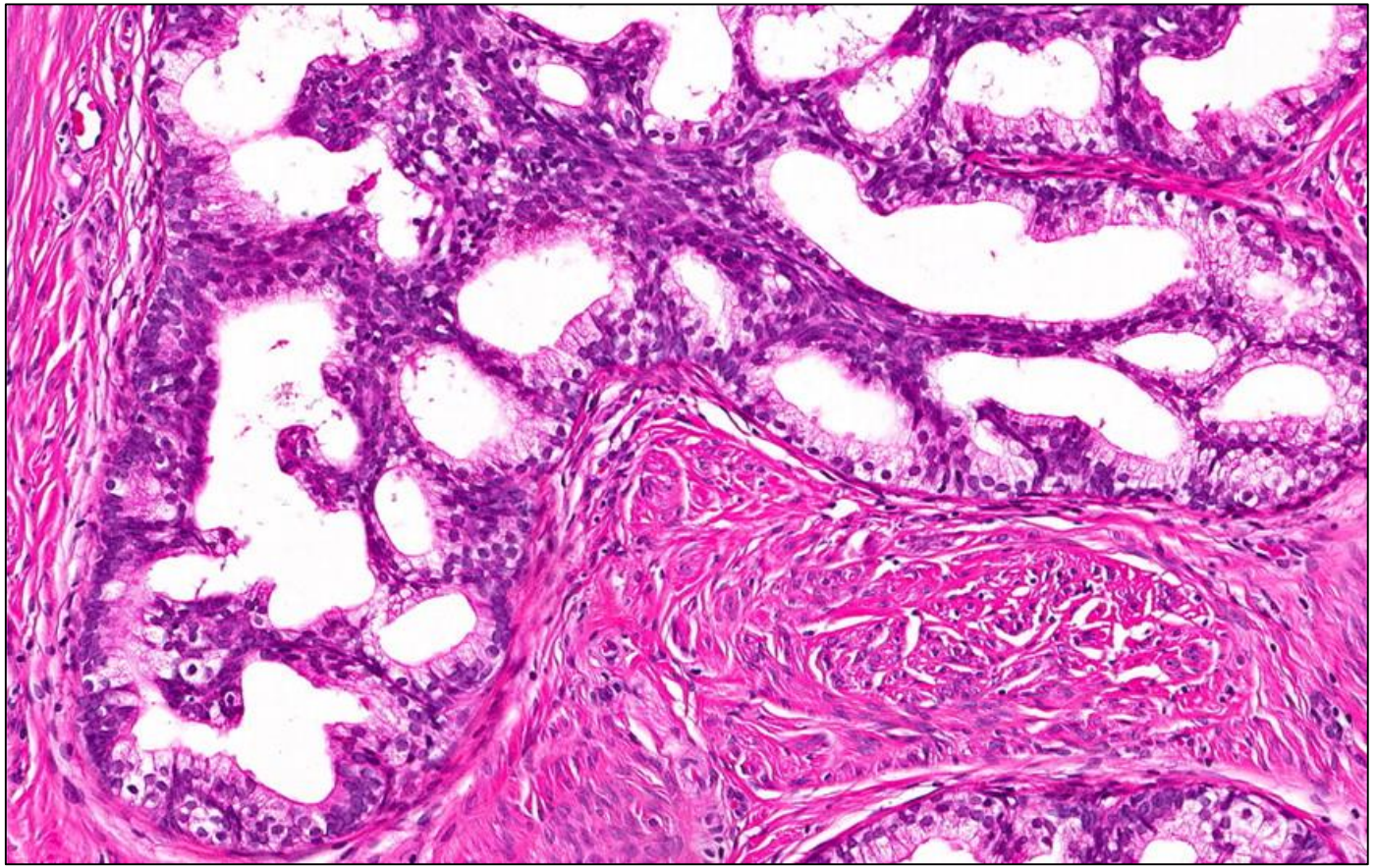
- Similar to eosinophilic metaplasia in the endometrium
- It generally does not cause any problems with regard to mimics of neoplasia
- Usually focal, alternating with normal mucinous columnar cells
- Confined to areas with inflammation and mucosal injury
- Deep cytoplasmic eosinophilia + absence of abnormal mitosis



Metaplasias and ectopies

Ectopic prostatic tissue

- These are considered to derive from paraurethral Skene's glands and the ectopic tissue is usually on the ectocervix
- It comprises of a glandular component encircling squamous elements
- They are usually PSA & PAP positive
- They do not generally mimic any neoplasia



Metaplasias and ectopies

Ectopic prostatic tissue

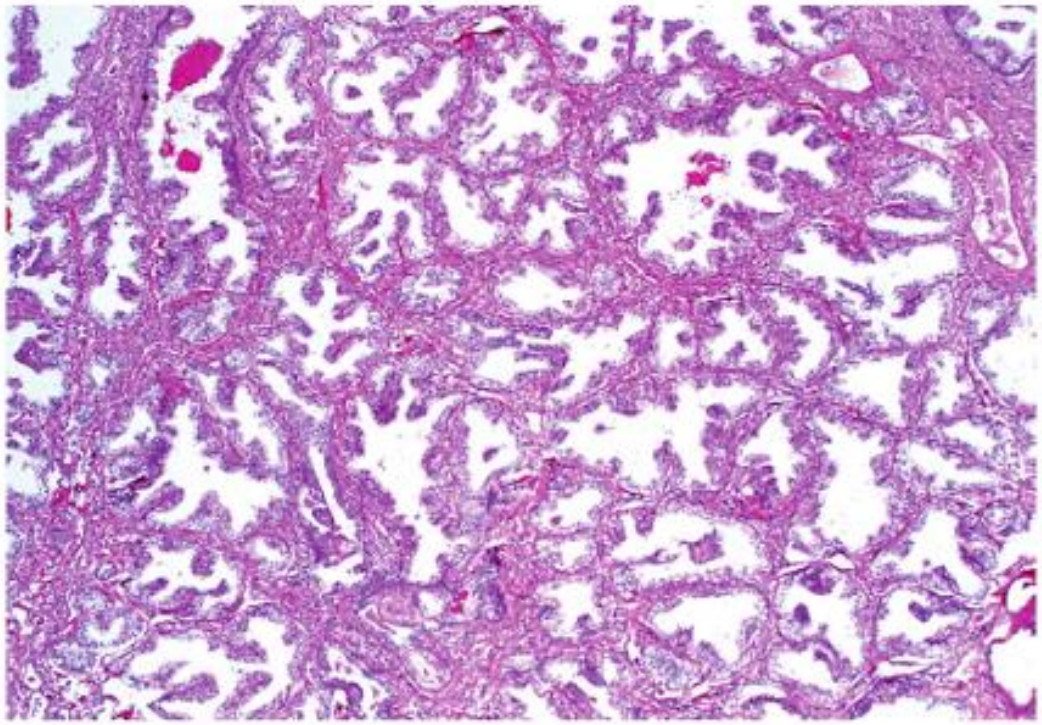


Fig. 4.15 Ectopic prostatic tissue.

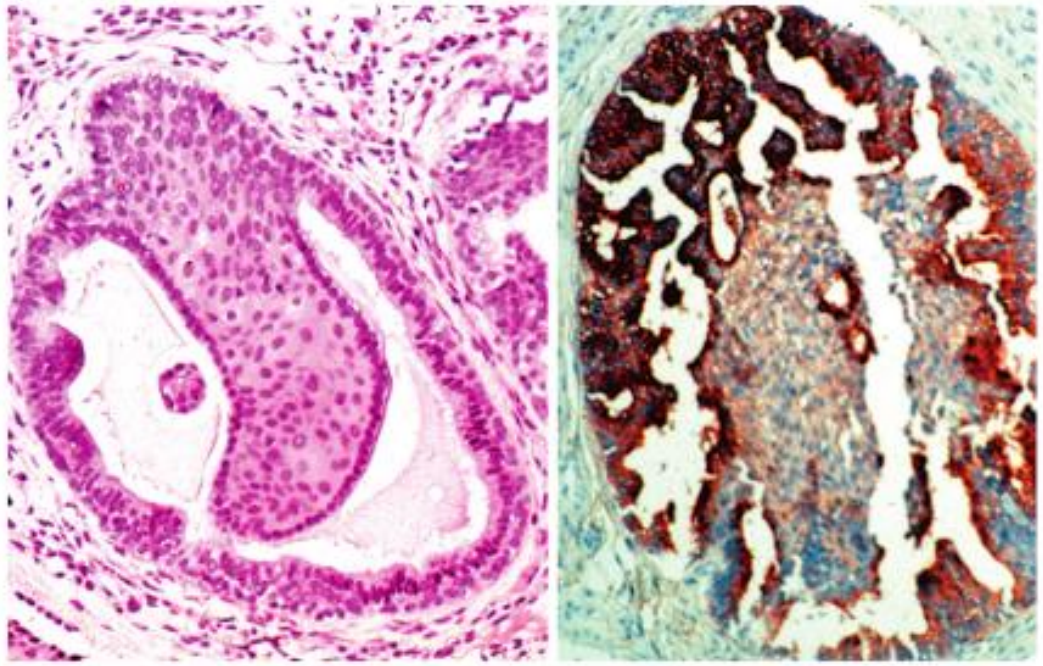
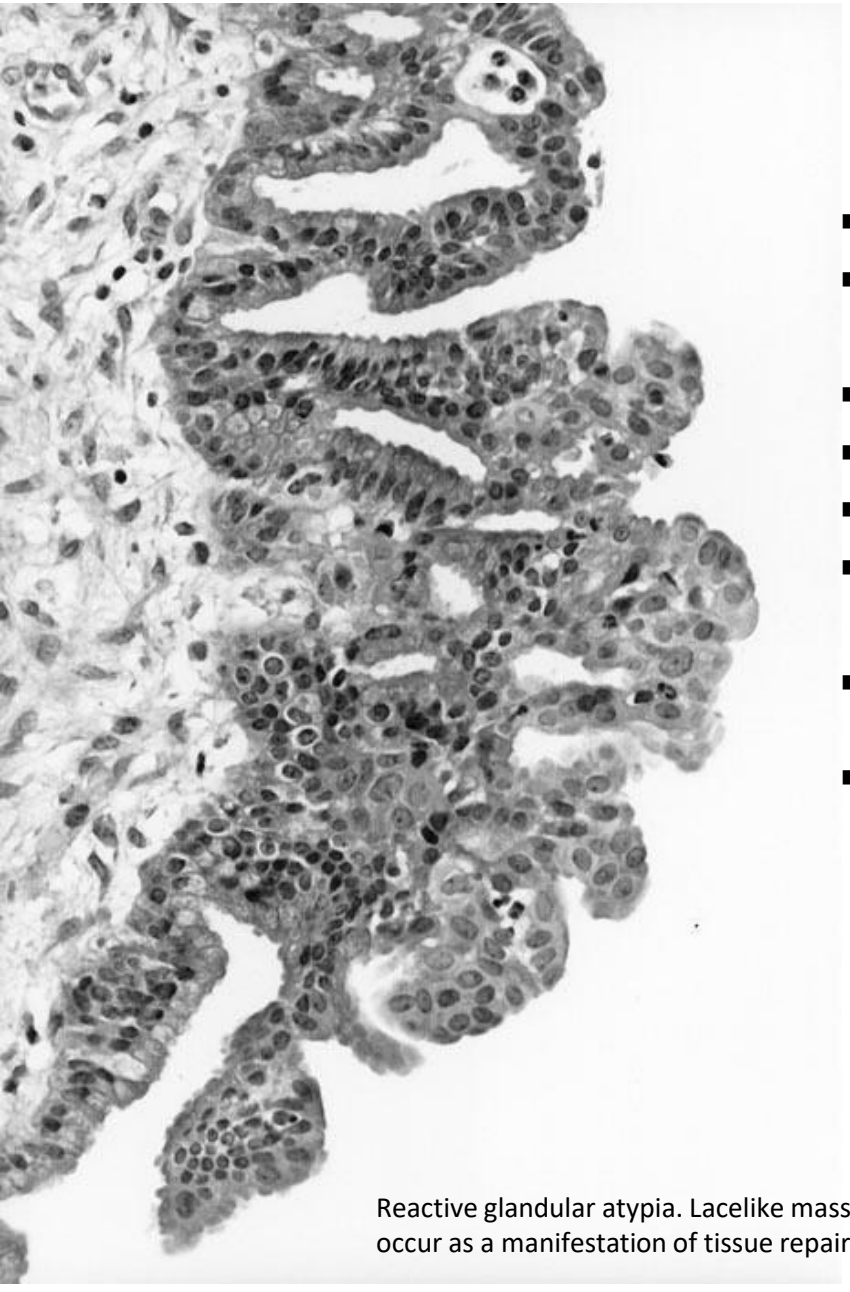


Fig. 4.16 Ectopic prostatic tissue. Gland with squamous metaplasia (left). The gland is immunoreactive for prostate-specific antigen (right).

Reactive, reparative and inflammatory lesions



Reactive glandular atypia. Lacelike masses of glandular cells, with moderately enlarged nuclei, may occur as a manifestation of tissue repair, sometimes after cone biopsy of the cervix.

Reactive changes to inflammation

- These are often seen in the form of disorganised cells with nuclear atypia
- The reactive changes affect both squamous and glandular epithelium and are often seen in ectropions
- The nuclei are uniform, they contain prominent nucleoli
- Cytoplasmic membrane is well-defined
- The epithelium is often infiltrated with inflammatory cells
- Glandular epithelium – nuclear enlargement, hyperchromasia with irregularity of nuclear size and shape, smudgy chromatin
- No mitotic activity

- The presence of a dense inflammatory infiltrate, frequently extending into the epithelium, often coupled with loss of polarity and acquisition of abundant, polygonal cytoplasm, assists in the recognition of the presence as reactive

Reactive, reparative and inflammatory lesions

Reactive changes to inflammation

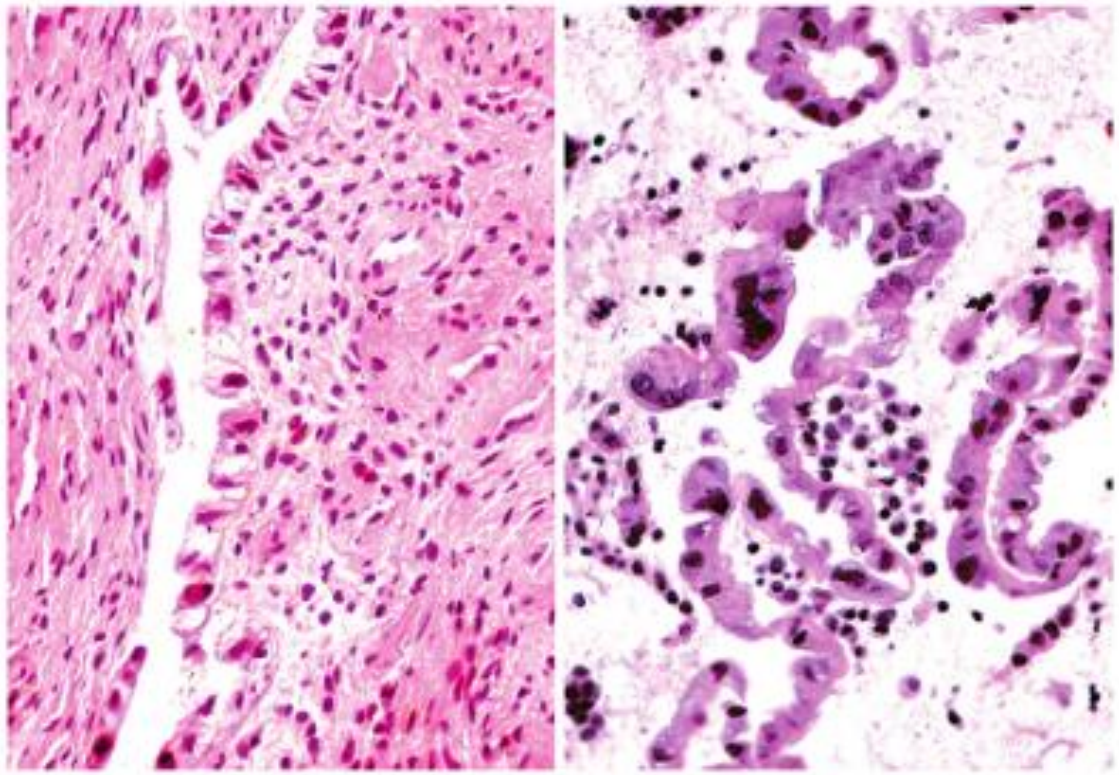


Fig. 4.33 Reactive glandular atypia. Two examples are shown, one in a biopsy specimen (left) and the other in a curettage specimen (right).

Reactive, reparative and inflammatory lesions

Reactive changes to inflammation

- With reactive change, the halo is round, uniform and less distinct, and the nuclei are minimally enlarged and normochromic
- The nuclei are more centrally located within the halo

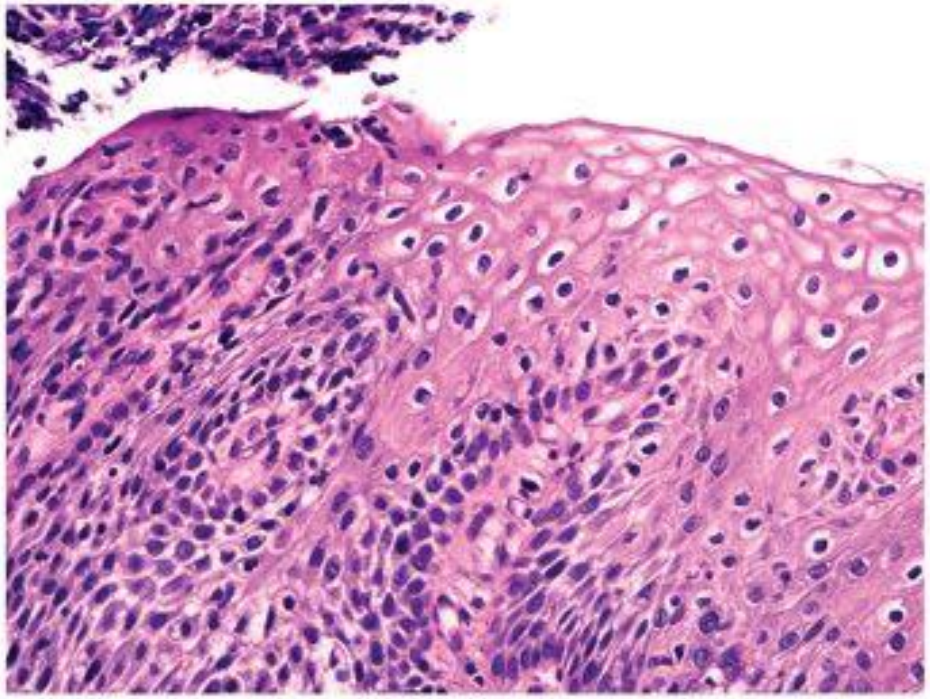


FIGURE 52.7 Inflammatory halos. Uniform, round halos with centrally located bland nuclei.

TABLE 52.2 Comparison of Morphologic Features between Nondysplastic (Benign) Squamous Mucosa and Low-Grade Squamous Intraepithelial Lesion

	Benign	LSIL
Nuclear size at surface	Smaller than basal cell nuclei	Enlarged
Binucleation	−/+	+/−
Chromatin	Normal	Hyperchromatic
Nuclear membranes	Smooth	Irregular
Nucleoli	+/−	(−)
Cytoplasmic halo	Even shape, nucleus located in center of halo	Irregular contours, nucleus located off-center

LSIL, low-grade squamous intraepithelial lesion.

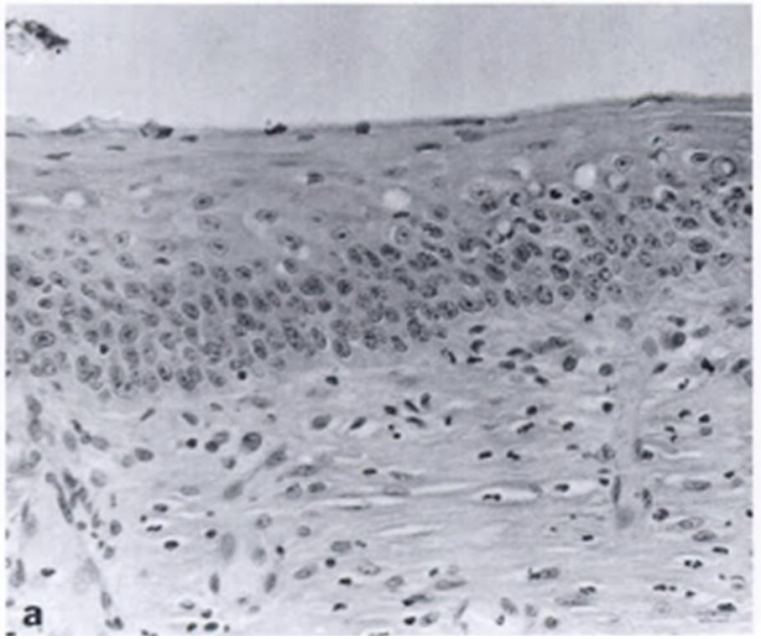
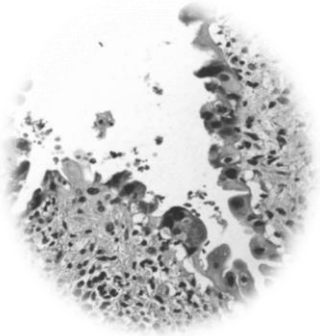


Fig. 6.1. Reparative atypia. a: Basal cell hyperplasia involving the lower one-third of the squamous epithelium of the cervix. The nuclei contain prominent chromocenters but lack nuclear abnormalities associated with neoplasia. The epithelial cells above the enlarged basal zone display normal maturation. These alterations are often associated with mucosal denudation caused by either trauma or severe inflammation.

Reactive, reparative and inflammatory lesions

Radiation atypia



- Similar to changes in other organs
- This affects both squamous and glandular epithelium

- Gross description: Fibrosis, induration, stenosis of endocervix, surface irregularity or no abnormality

- Hyalinized stroma or reactive changes with ectatic vessels
- Enlarged nucleus - but normal NC ratio
- Nuclear and cytoplasmic vacuolation
- There may be multinucleation and most nuclei contain multiple, variably sized nucleoli
- Sparse, well-spaced tubular or dilated glands in endocervix
- +/-edema, necrosis & lymphoplasmocytic infiltrate
- No/rare mitotic figures

- Knowledge of the history facilitates distinction from a premalignant lesion

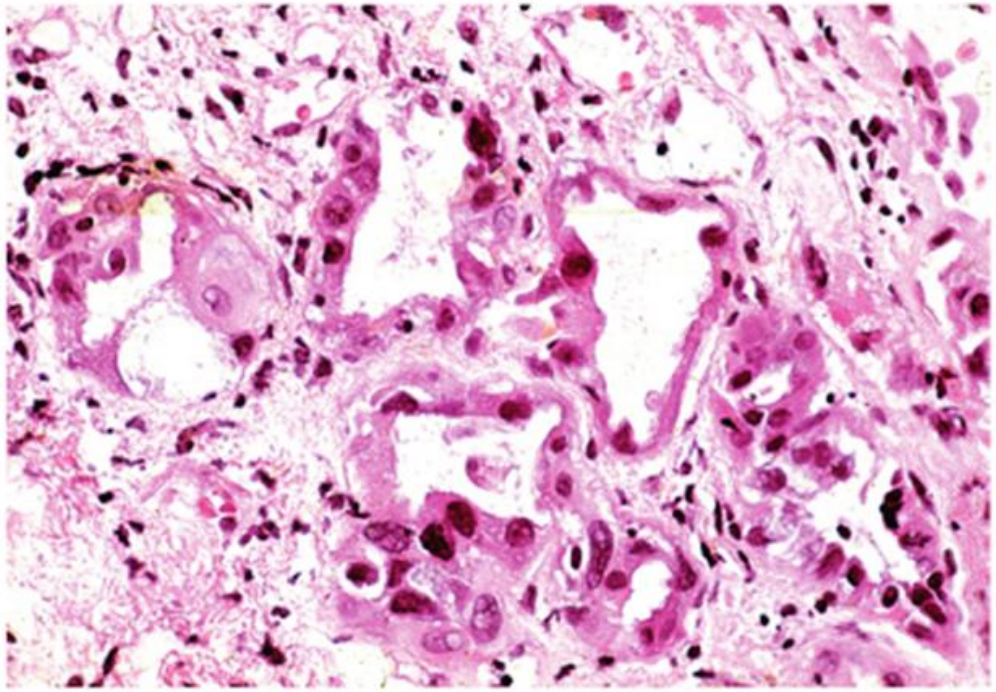


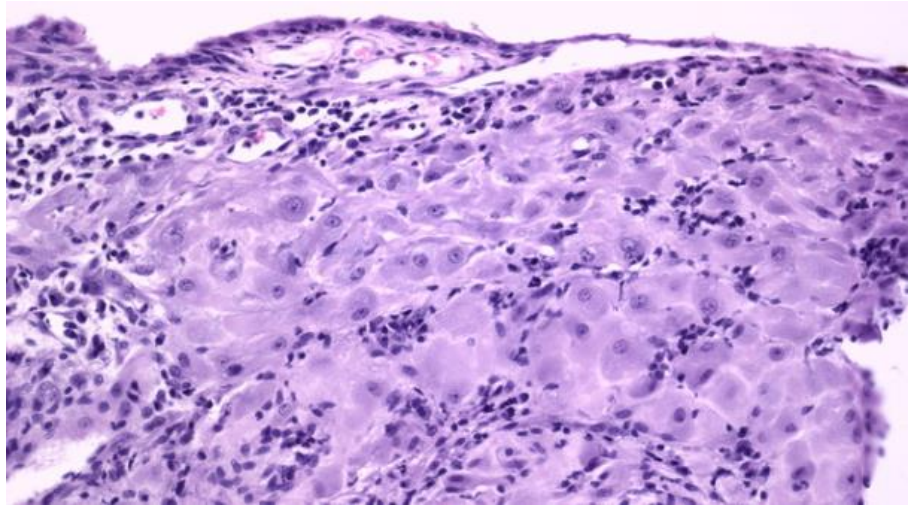
Fig. 4.34 Postirradiation glandular atypia.

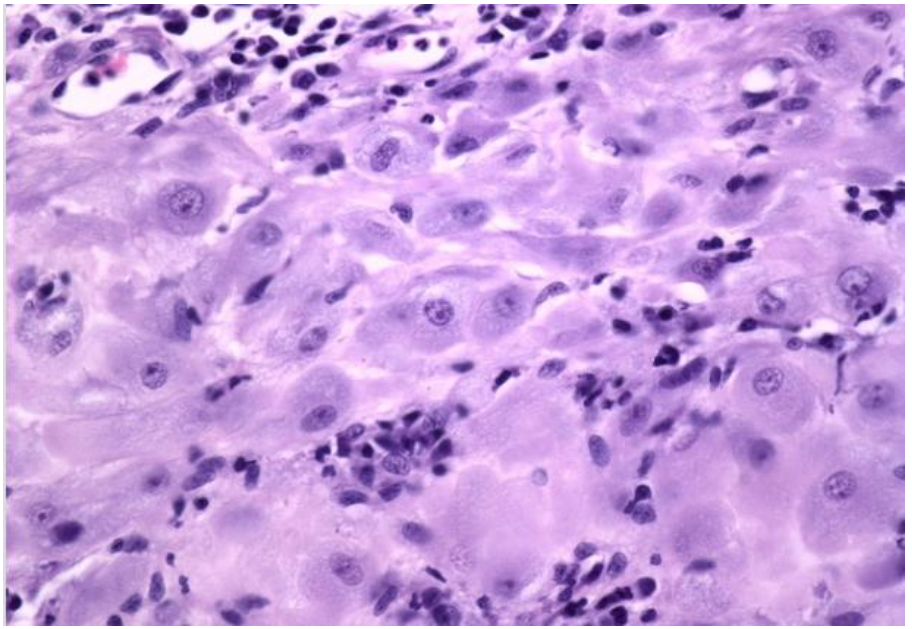
Reactive, reparative and inflammatory lesions

Decidual change

- Cervicitis decidualis, deciduosis
- Multiple small, yellow/red elevations of cervical mucosa
- Soft, friable, bleed easily
- Can be fungating, polypoidal and mimic malignancy
- It is seen in the stroma during pregnancy or affecting part of an endocervical polyp
- Decidual cells with abundant pale granular cytoplasm, bland nuclei

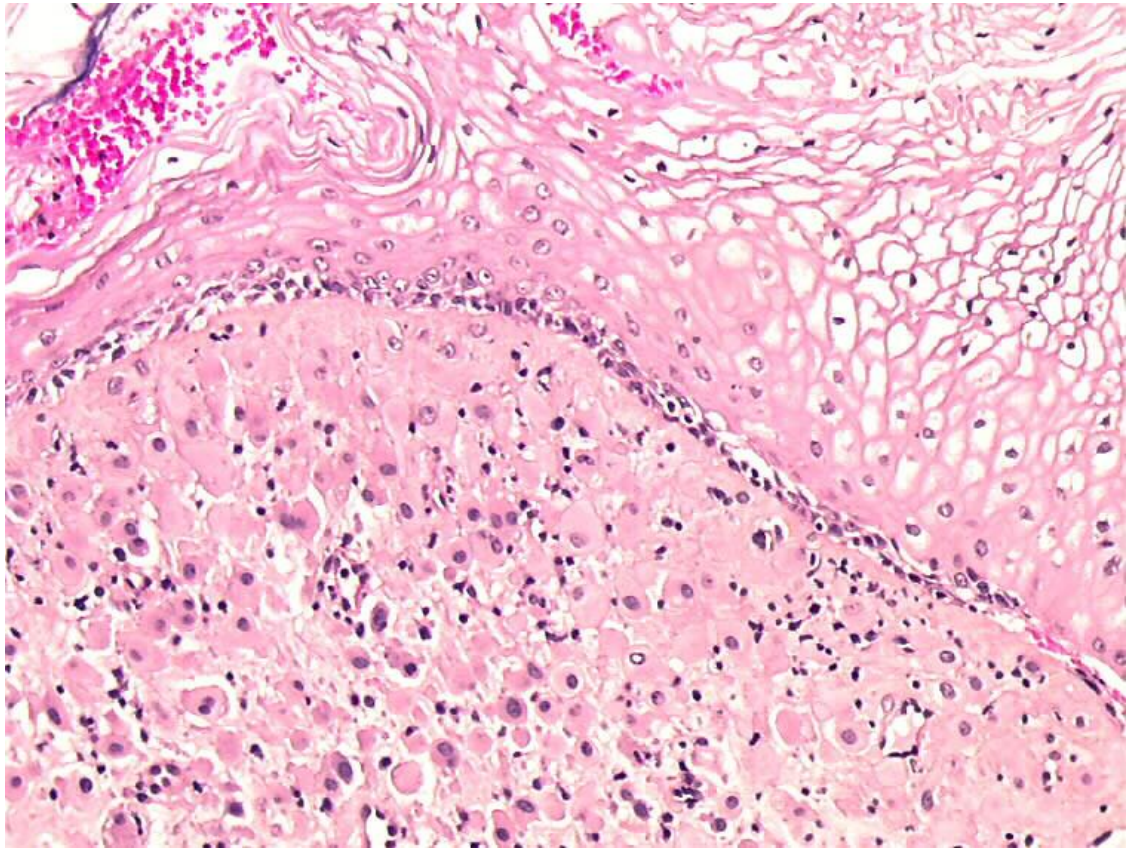
- It can microscopically mimic squamous cell carcinoma
- Correct diagnosis can be made by attention to bland nuclear features, lack of mitoses, and negativity for cytokeratin



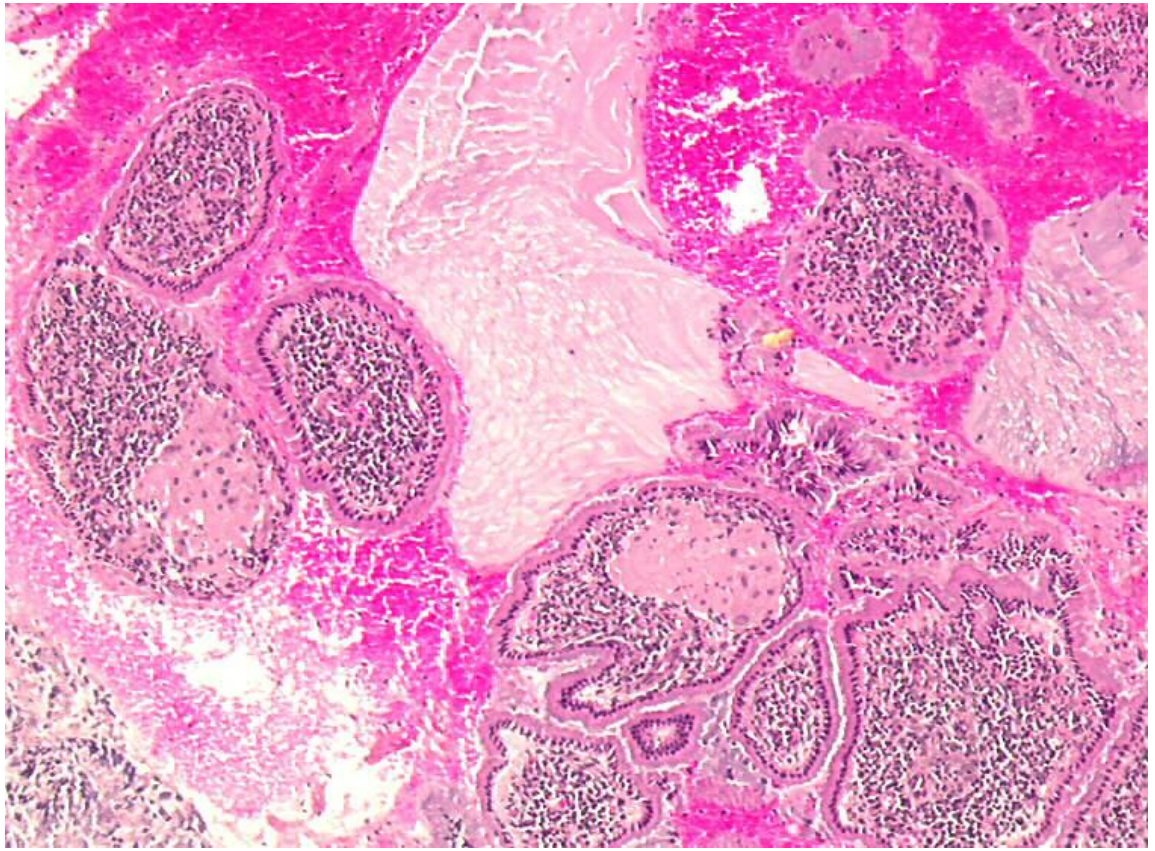


Reactive, reparative and inflammatory lesions

Decidual change



Below a non-keratinized squamous epithelium, the lamina propria is infiltrated by decidual cells with regular nuclei and large eosinophilic glycogen-rich cytoplasm



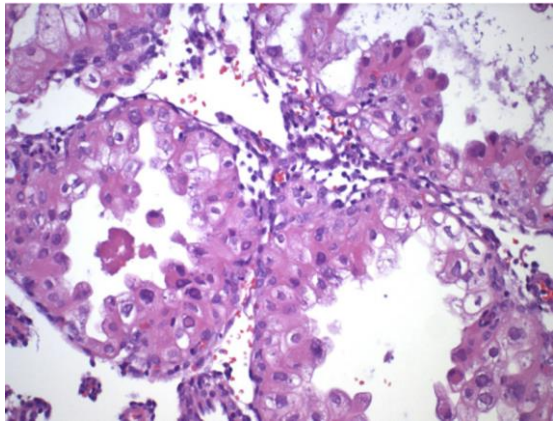
Inflammatory and papillary endocervical mucosa characterized by foci of decidual cells with regular nuclei and large, eosinophilic, glycogen-rich cytoplasms

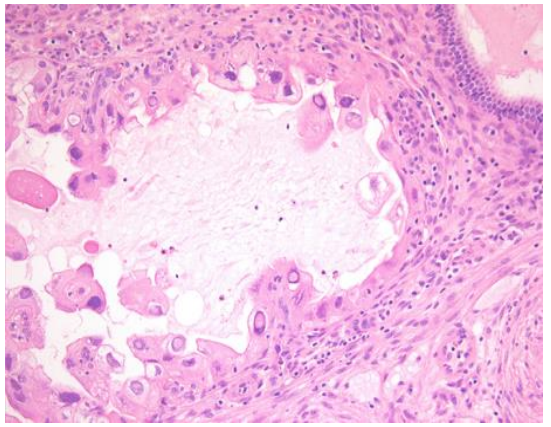
Reactive, reparative and inflammatory lesions

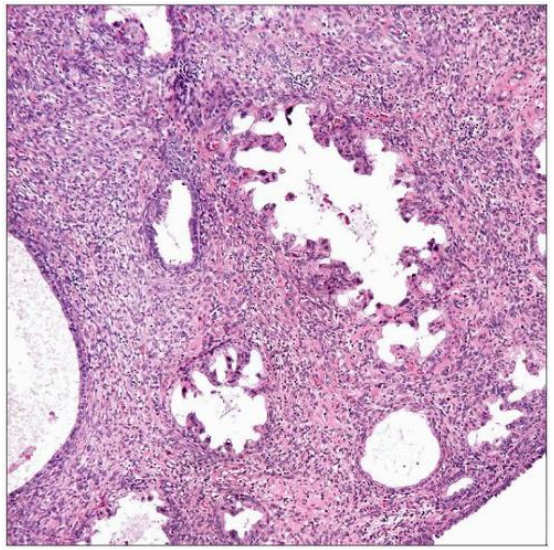
Arias Stella reaction

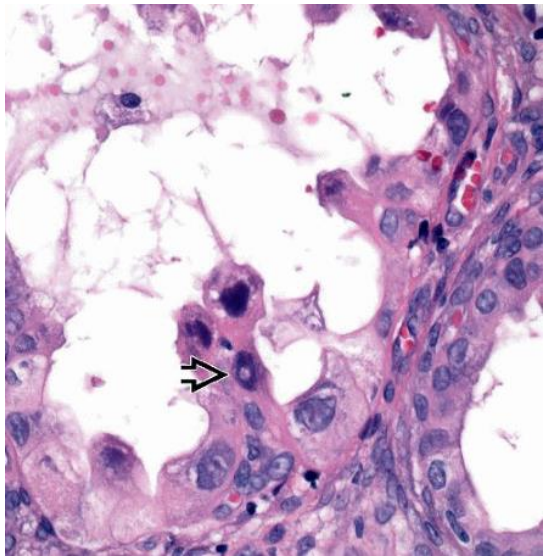
- Observed in the cervix of approximately 10% of gravid hysterectomy specimens
- Tends to be focal
- Enlarged cells with cytoplasmic vacuolation and irregular hyperchromatic nuclei
- Hobnail protrusion is a common feature
- The epithelium is usually hypersecretory
- It does not form any mass lesion
- Intranuclear cytoplasmic inclusions common
- Lack of mitotic activity

- The main neoplastic differentials - clear cell carcinoma, which presents as a mass
- The distinction from clear cell carcinoma is based on the constellation of history of pregnancy, paucity of mitoses, and absence of invasion or the tubulocystic or solid patterns of clear cell carcinoma









Reactive, reparative and inflammatory lesions

Pseudo-invasion of benign squamous epithelium following cervical biopsy

- This comprises entrapped benign squamous epithelium following loop excision or punch biopsy
- It includes hypereosinophilic cells with a giant cell reaction and granulation tissue-like and inflammatory stromal response and it mimics squamous cell carcinoma

- In cases where the displaced or disrupted epithelium is clearly benign, it becomes relatively straightforward to recognize the changes as secondary to a prior biopsy.
- However, in cases where the epithelium is dysplastic, identifying fibrin around the displaced nests or granulation tissue at the epithelial–stromal interface would support prior biopsy site changes

- Obtaining level sections can be helpful in difficult cases

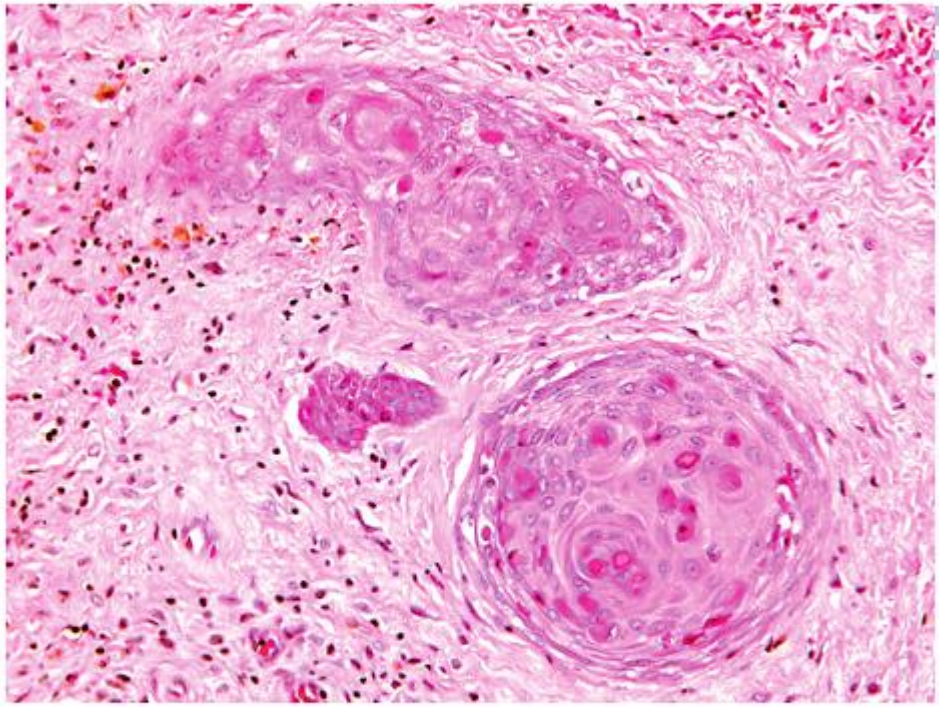


Fig. 4.32 Postbiopsy pseudoinvasion of squamous epithelium. Irregular nests of benign squamous epithelium lie within a fibrotic stroma, a finding that could be misinterpreted as superficially invasive squamous cell carcinoma, especially in a patient with a previous diagnosis of HSIL.

Reactive, reparative and inflammatory lesions

Pseudo-invasion of benign squamous epithelium following cervical biopsy

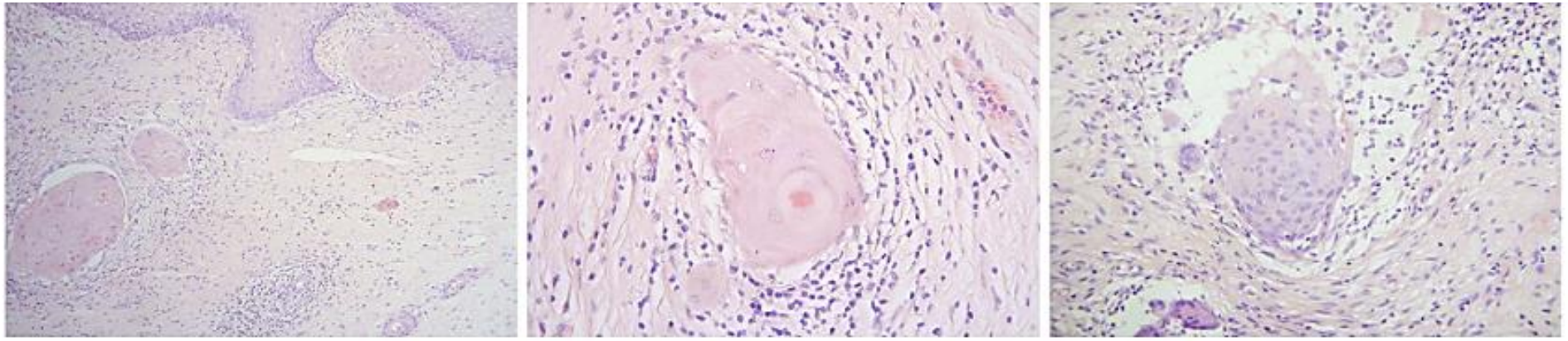
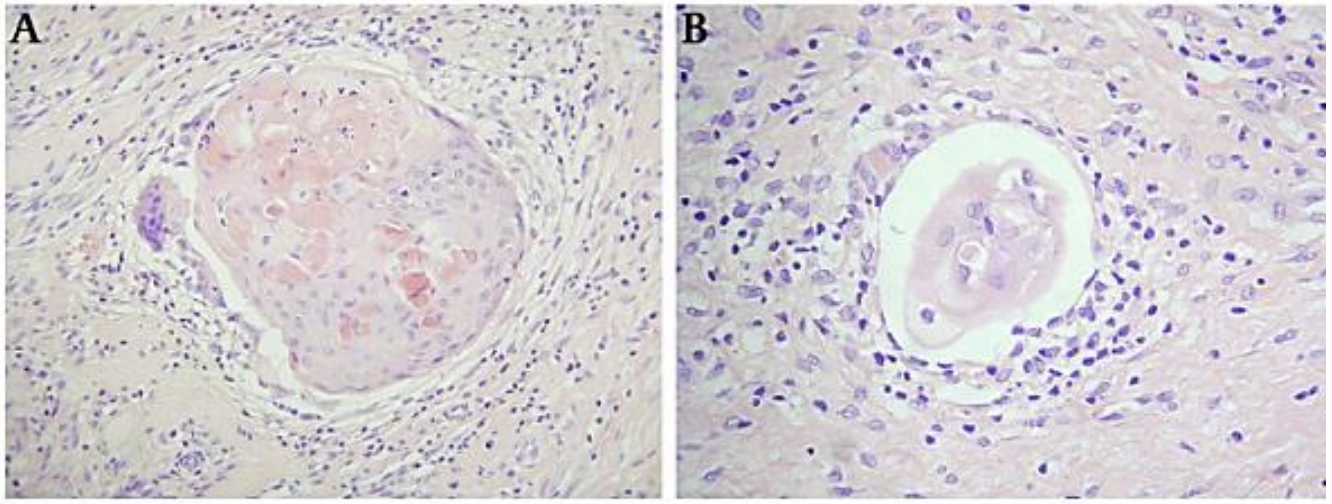


Figure 1 (A) Nest of squamous cells present deep to normal surface squamous epithelium. (B) The nests of squamous cells have a hypereosinophilic appearance. (C) The surrounding stroma is oedematous and inflamed and has a granulation tissue-like appearance.

Figure 2 (A) The nests of squamous cells are surrounded by inflammatory cells, including multinucleate giant cells. (B) Some of the nests of squamous epithelium are surrounded by clefts representing retraction artefact but simulating lymphovascular invasion.



Reactive, reparative and inflammatory lesions

Diathermy changes

- Severe nuclear damage can be seen as a result of diathermy
- Most pronounced at the edge of biopsy fragments but when severe may involve the entire tissue
- This renders enlargement and hyperchromasia-like effect and can mimic high grade CGIN, particularly when it affects glandular epithelium
- When severe, a number of problems may result, including fragmentation of the specimen and denudation and destruction of much of the surface epithelium with consequent problems in histological interpretation

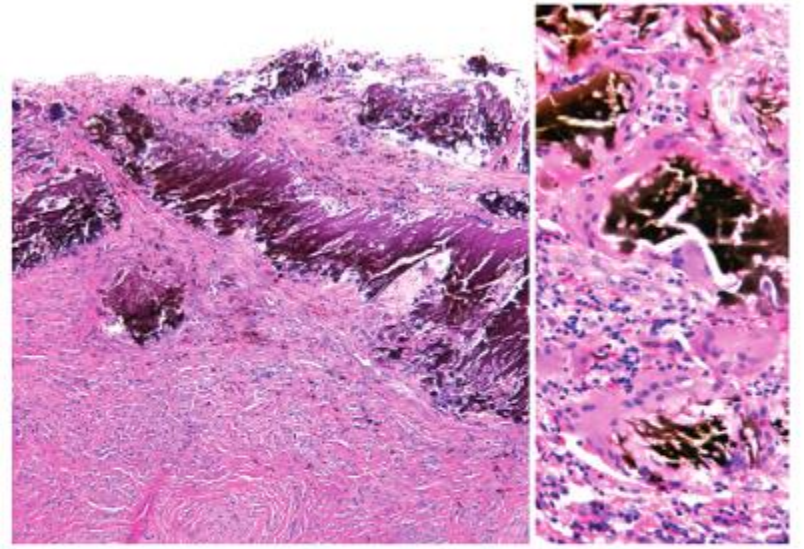


Fig. 4.43 LEEP-related changes in the mucosa of the uterine cervix within the hysterectomy specimen removed 6 months later. There is complete loss of normal epithelium with cautery-destroyed tissue (brown foci) within the superficial stroma (left) surrounded by a granulomatous inflammatory reaction (right).

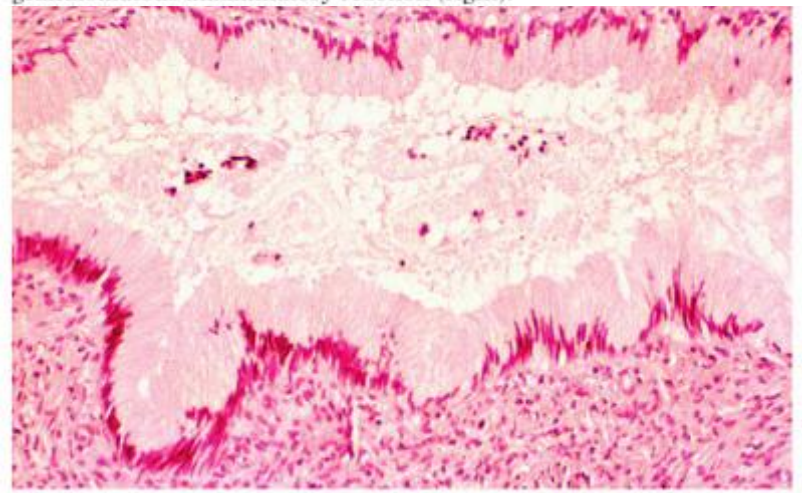
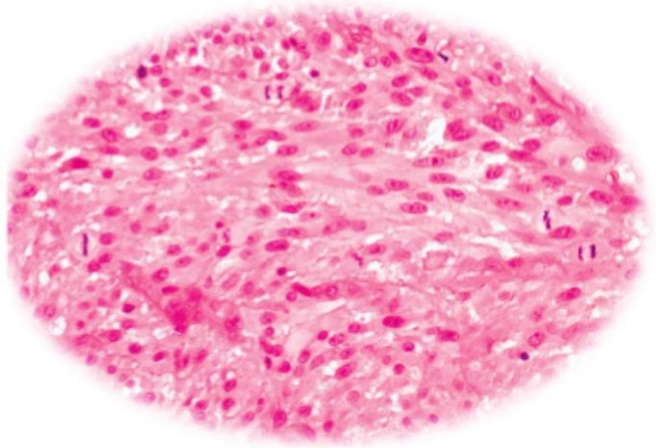


Fig. 4.41 Cautery artifact within an endocervical gland.

Reactive, reparative and inflammatory lesions

Post-operative spindle cell nodule

- This is similar to that seen in the vulva or vagina
- It can occur after therapeutic intervention or trauma and comprises spindle cells similar to cells seen in nodular fasciitis
- Often edematous stroma, delicate capillary network, neutrophils and red blood cells
- Another lesion, the inflammatory pseudo-tumour, comprises proliferation of fibroblasts, myofibroblasts and histiocytes with an inflammatory component of lymphocytes and plasma cells
- There is generally no atypia
- Mitotic rate is often high, but abnormal mitoses or atypia are absent




Thank
You