

Anatomy, Physiology and Histology

Module Overview

By the end of this module, the trainees will be able to:

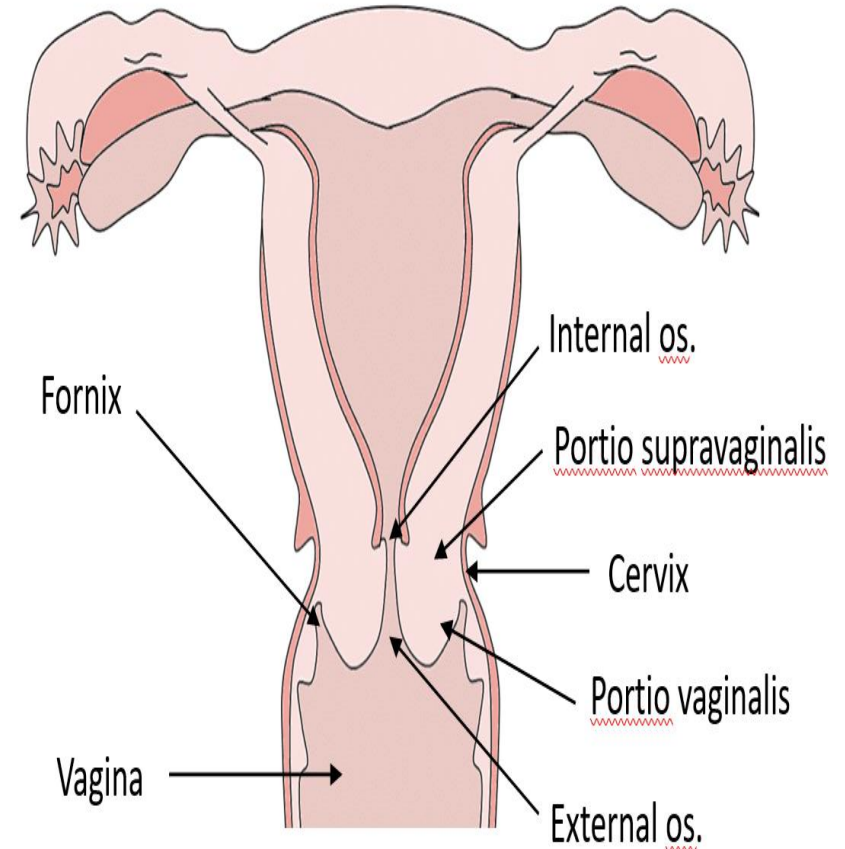
- Describe the microscopic and gross anatomy of uterine cervix
- Describe Histology of uterine cervix
- Describe normal physiological changes of the TZ
- Explain the abnormal changes occurring on the cervical epithelium relevant to neoplasia of the cervix.

Module Content

- Gross anatomy of Cervix
- Microscopic features of cervical epithelium
- The concept of squamocolumnar junction (SCJ)
- Metaplasia and concept of transformation zone (TZ)
- Features of normal TZ
- Physiological Changes in TZ across course of a women

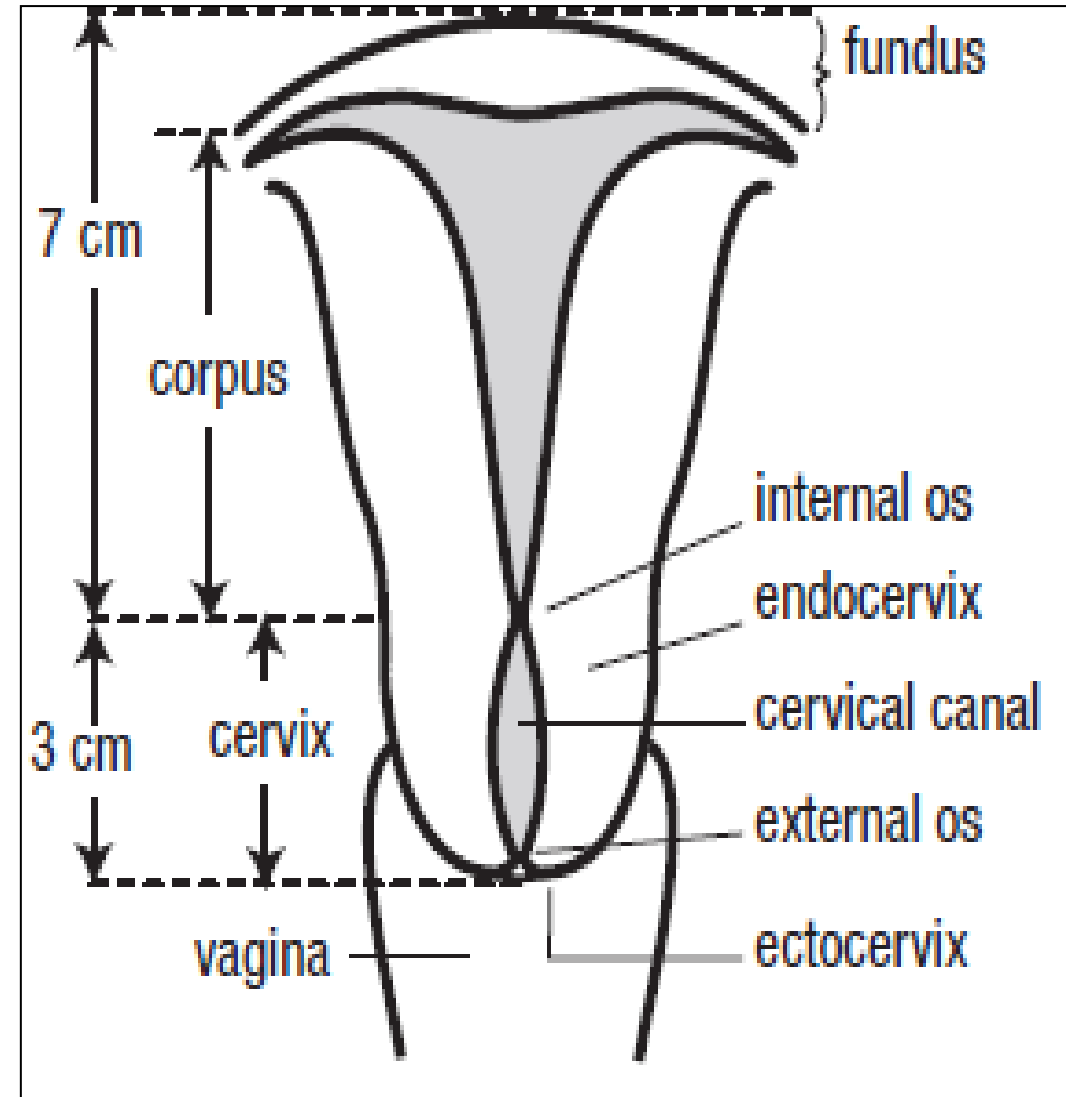
Gross anatomy : Components of uterine cervix

- Fibromuscular structure
- Internal Supra-vaginal portion within pelvis (Upper part)
- External intravaginal portion (Portio-vaginalis); Visible
 - The external os of the cervix opens into the vagina.
 - The internal os is the point at which the cervix and uterus meet, above the vagina.
 - Endocervical canal



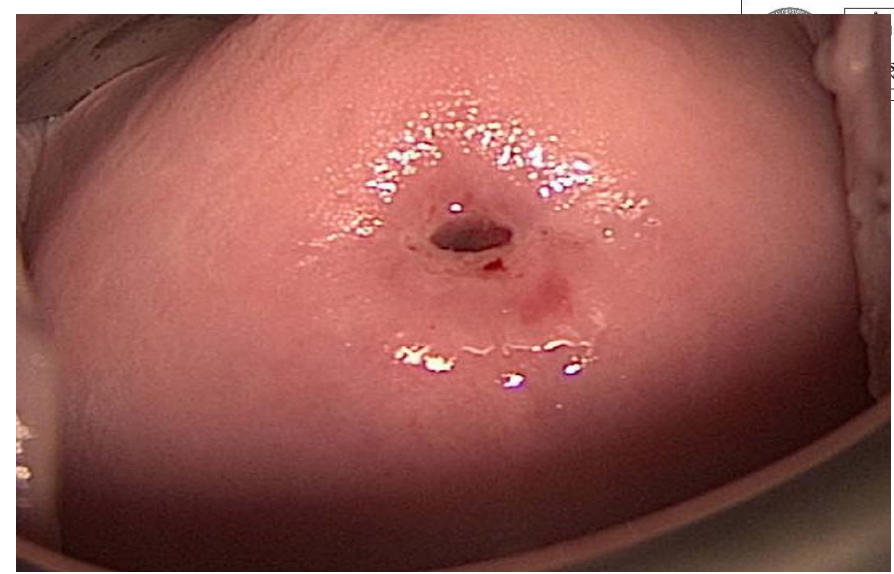
Gross Anatomy: Dimensions of the uterine cervix

- Shape and size varies with age, parity, hormonal status
- Narrow and conical in shape
- 3 - 4 cm long; 2.5-3 cm Diameter
- Endocervical canal 6-8 MM deep

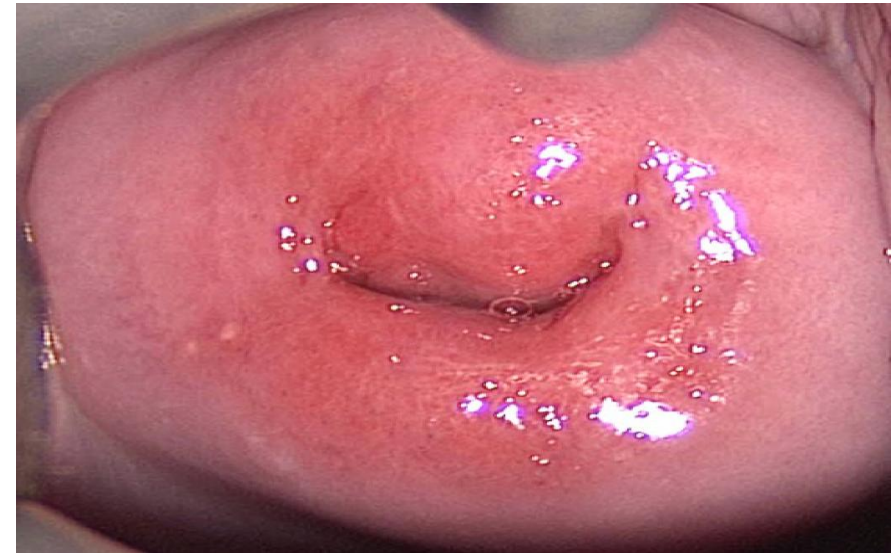


Gross Anatomy: Variation in shape

- The size and shape of the cervix vary widely with age, hormonal state, and parity.
- In the nulliparous female it is barrel shaped with a small circular external os at the centre of the cervix.
- In parous women, cervix is bulky and the external os becomes slit-like



Round in nulliparous women



**Slit-like ('fish mouth appearance')
in parous women**

STROMA

- Composed of dense, fibromuscular tissue
- The stroma contains :
 - Vascular system (Arterial supply and Venous drainage)
 - Lymphatic drainage
 - Nerve supply

Lymphatic drainage

- The lymphatic vessels from the cervix drain into the
 - Common iliac nodes
 - external iliac nodes
 - internal iliac nodes,
 - obturator and the
 - parametrial nodes.

Nerve Supply

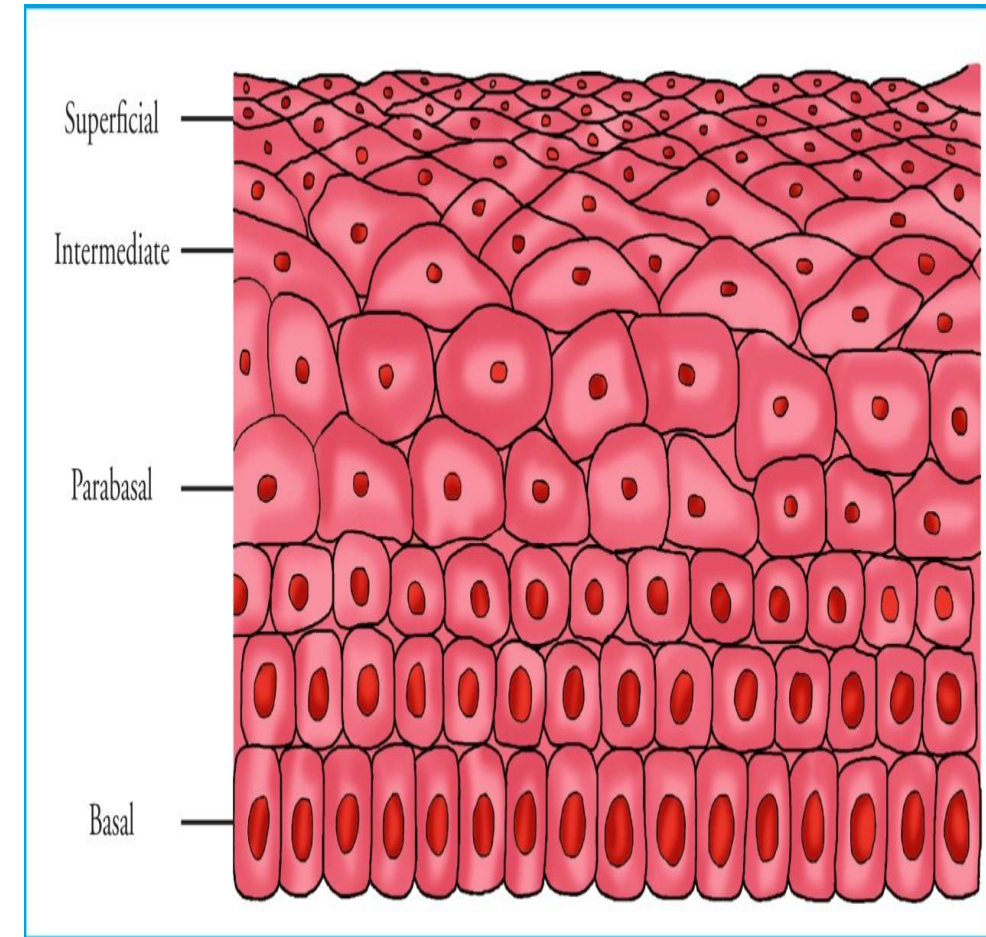
- The nerve supply to the cervix is derived from the **hypogastric plexus**.
- The endocervix has extensive sensory nerve endings, while there are very few in the ectocervix.
- Procedures such as biopsy, electrocoagulation, cryotherapy , biopsy are well tolerated in most women without local anaesthesia.
- Since sympathetic and parasympathetic fibres are also abundant in the endocervix, dilatation and curettage of the endocervix may occasionally lead to a vasovagal reaction.
- Endocervical curettage can be done without anaesthesia as it does not involve dilatation of the cervix

Cervical Epithelium

- The uterine Cervix It is covered by two types of epithelium:
 - Stratified **squamous epithelium** : Covers the external part, *multiple layers*
 - **Columnar epithelium**: covers the endocervix but may be visible on the ectocervix, *Single Layer*.

Squamous Epithelium

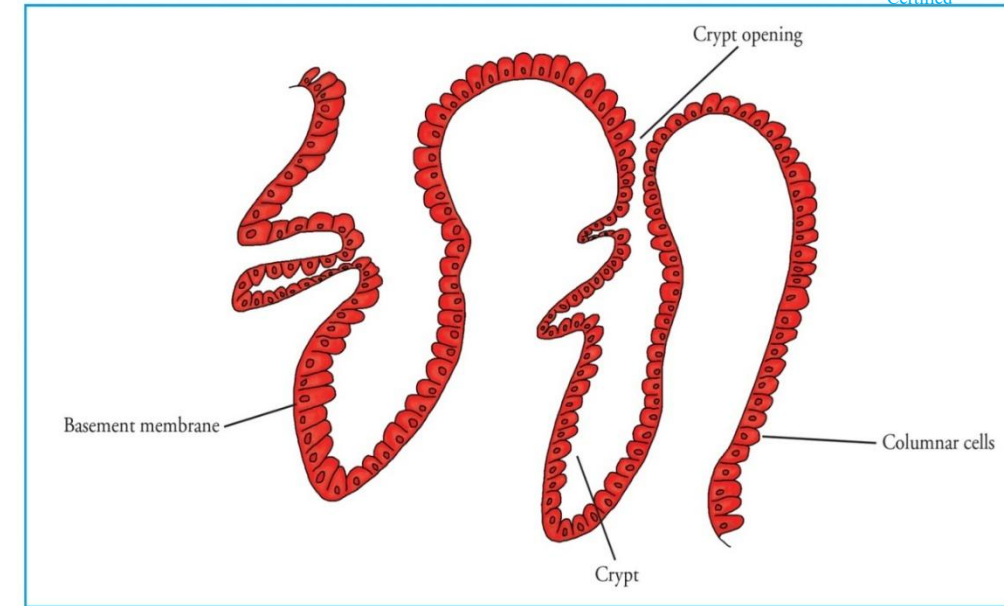
- Ectocervix is covered by **Non-keratinized, stratified squamous epithelium**
- **Multiple (15-20) layers**
- separated from cervical stroma by basement membrane
- Divided into 4 layers:
 - basal,
 - para-basal,
 - intermediate &
 - superficial
- Intermediate & superficial layers contain abundant glycogen
- Maturation dependent on estrogen hormone



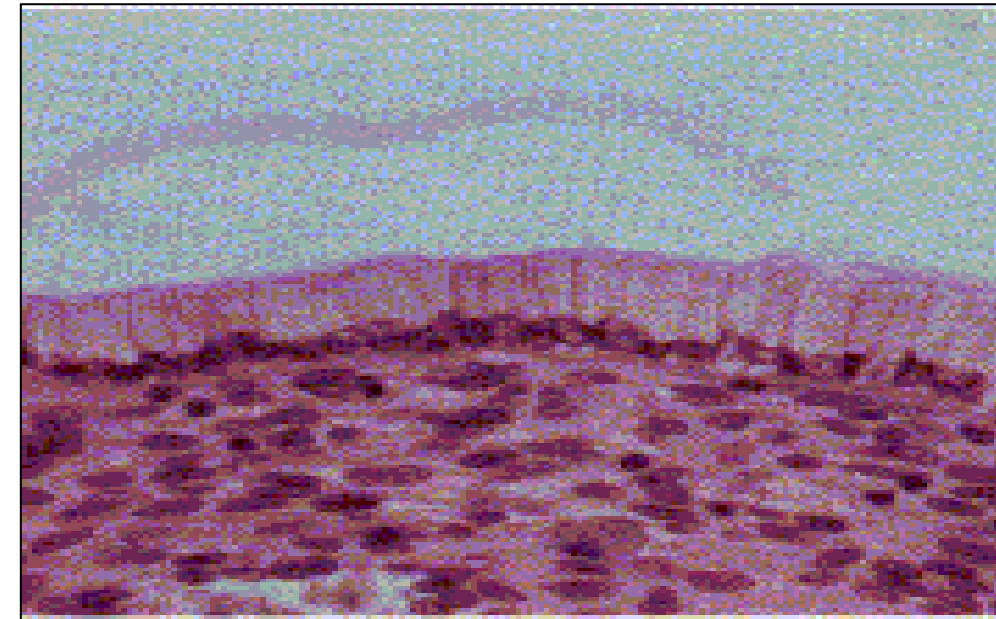
Normal stratified squamous epithelium

Columnar Epithelium

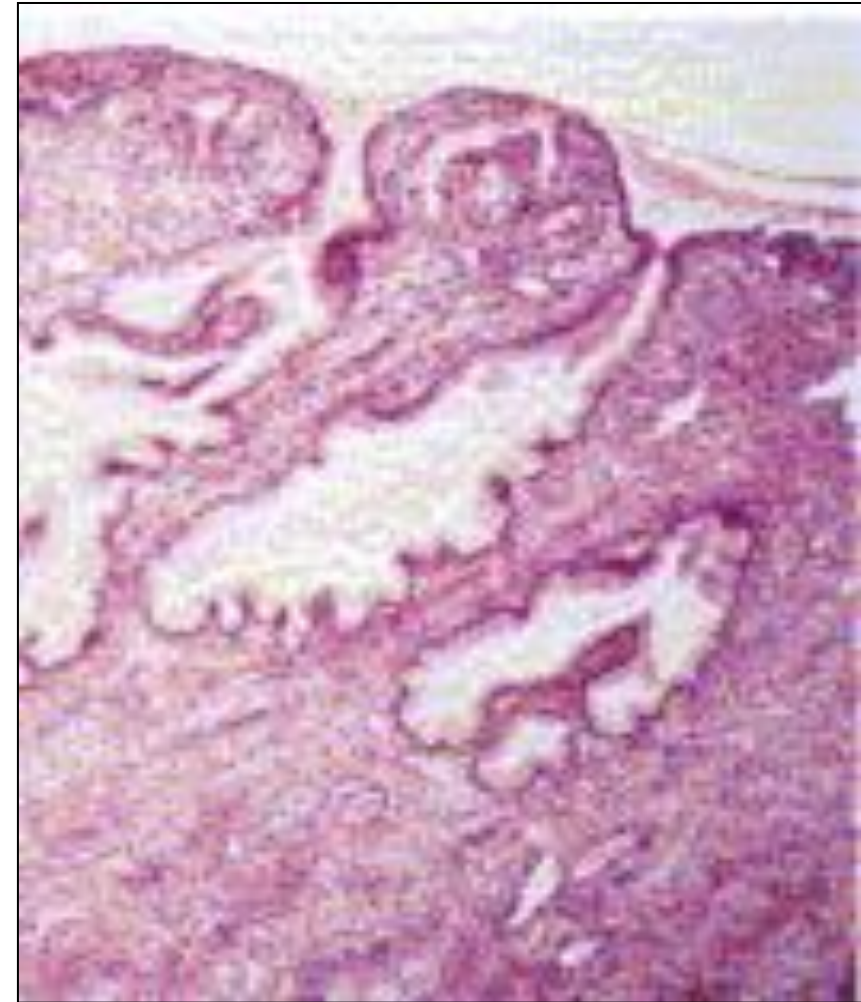
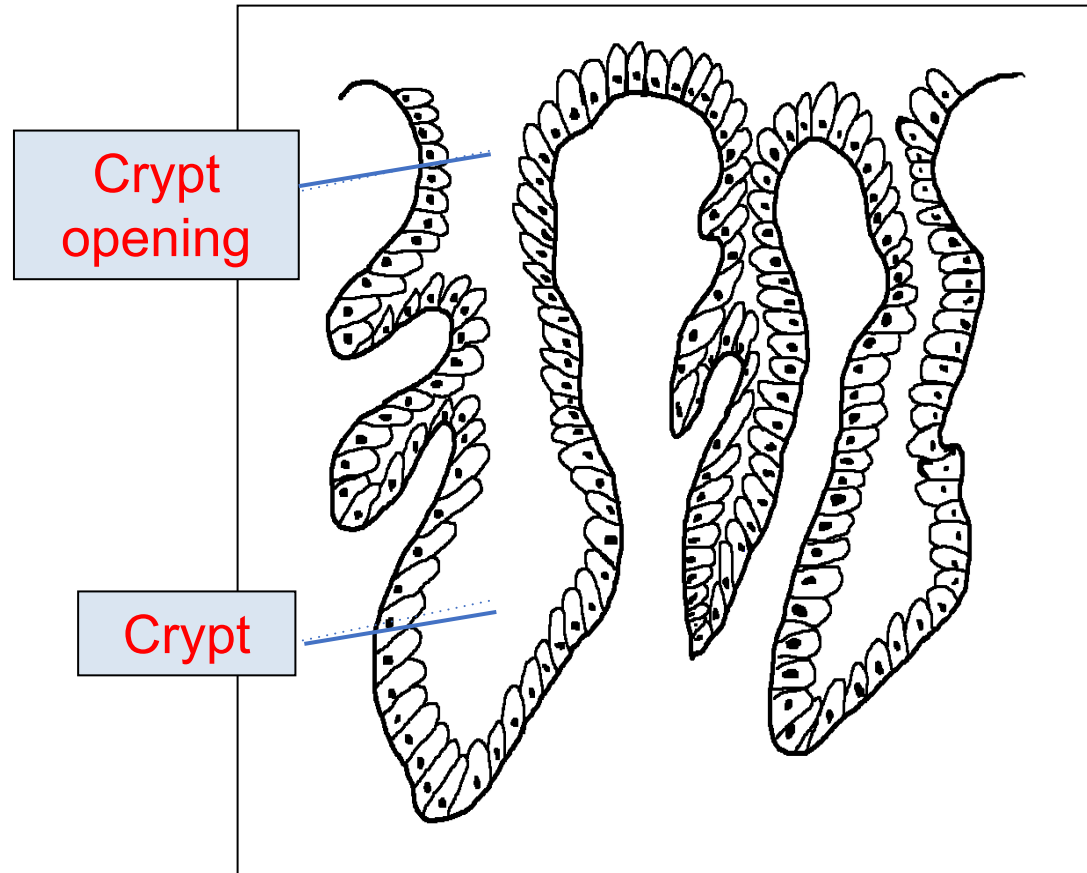
- Single layer mucin-secreting epithelium lining endocervix
- Invaginates into substance of cervical stroma forming endocervical 'crypts'
- Average depth of crypts is 5-8 mm approximately
- Does not contain glycogen



Normal columnar epithelium



Glandular Crypts of Columnar Epithelium



Source: Courtesy of L. Sankaranarayan.

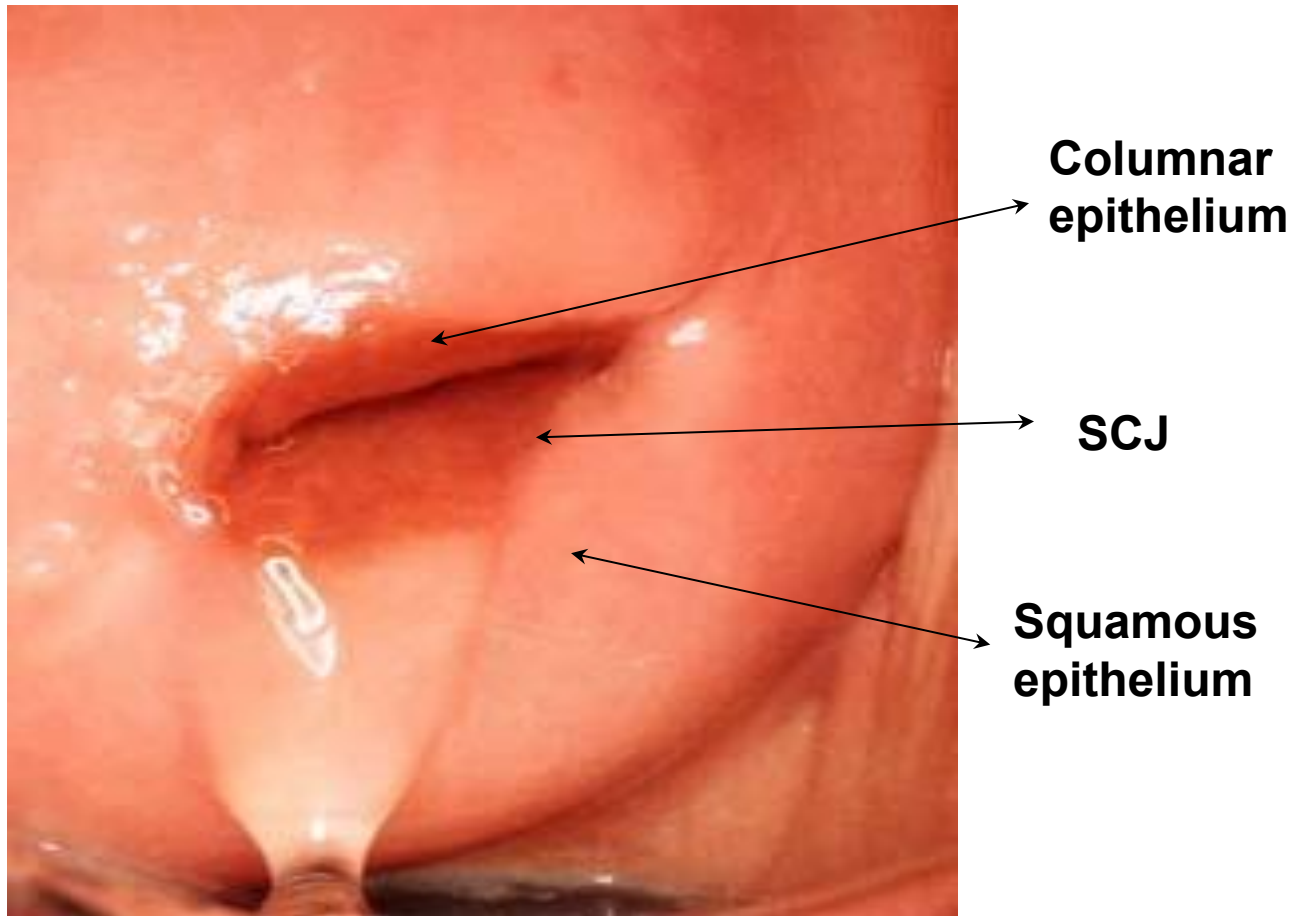
Squamocolumnar Junction (SCJ)

- The squamocolumnar junction is the place where the **squamous** and **columnar** epithelia **meet**.
- It often appears as a **sharp line of demarcation** with a slight difference in height between the two kinds of epithelium.
- Reddish columnar epithelium meets with the pink squamous epithelium at the **Squamo Columnar Junction (SCJ)**.
- After puberty and during the reproductive period, the female genital organs grow under the influence of estrogen.

SCJ -Ctd

- Thus, the cervix enlarges and the endocervical canal elongates.
- This leads to the eversion of the columnar epithelium onto the ectocervix, particularly on the anterior and posterior lips, resulting in **ectropion or ectopy**.
- Thus, the squamocolumnar junction is located on the ectocervix, far away from the external os during the reproductive years and pregnancy .
- On visual inspection, ectropion is seen as a strikingly **reddish** ectocervix .

Squamocolumnar Junction (SCJ)



- The SCJ appears as a sharp line demarcating the ectocervix and the endocervix.
- Position of SCJ influenced by
 - Age
 - Birth trauma
 - OCP use
 - Pregnancy
 - Menopause

SCJ POSITION IN RELATION TO AGE

- The **original** SCJ, laid down during embryonic life, is visible during childhood and perimenarche, after puberty, and in the early reproductive years.
- It is on the outer cervix away from the os.
- A **new** SCJ is formed where the metaplastic or growing squamous epithelium meets the columnar epithelium.
- The new SCJ moves gradually towards the external os, after menarche and throughout the reproductive life of a woman.
- The **transformation zone (TZ)** is the area bounded by the original SCJ and the new SCJ,

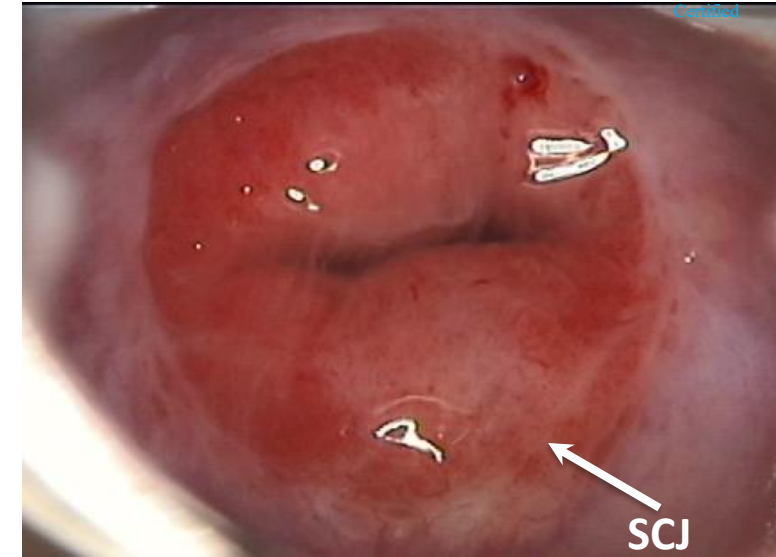


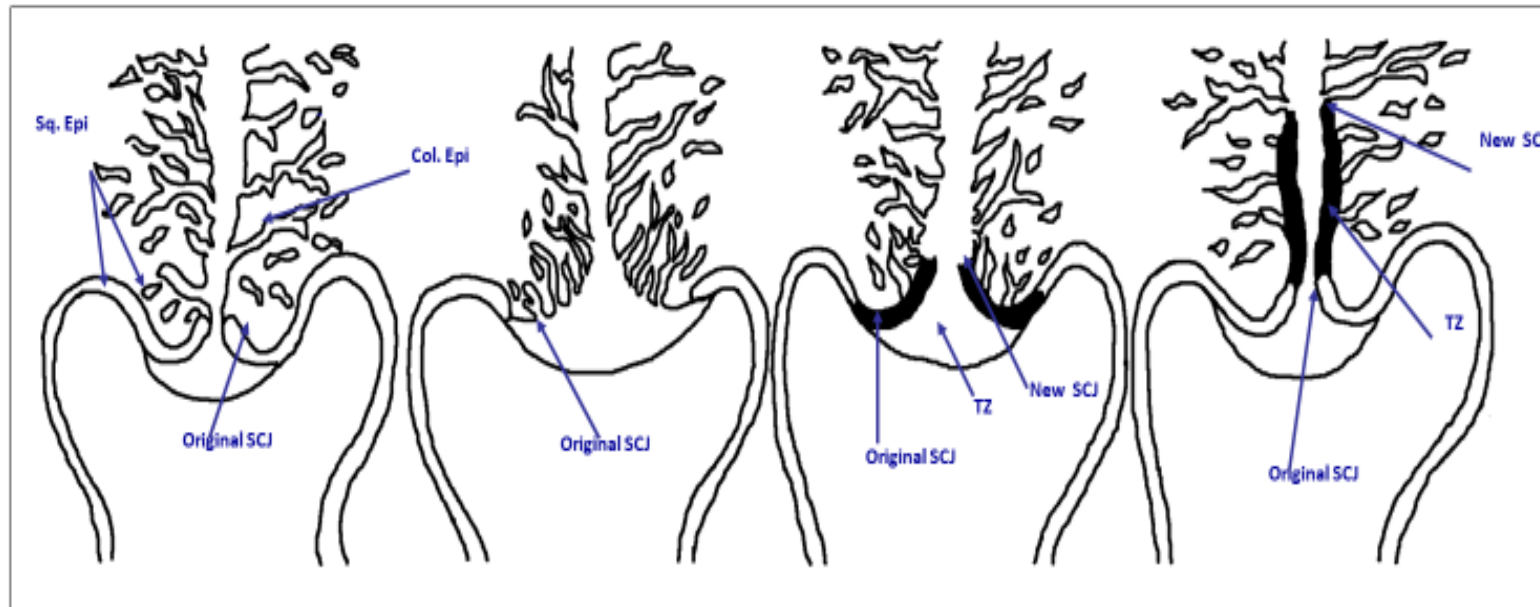
Figure 1



Figure 2

Location of SCJ and TZ: from infancy to PMP

Location of SCJ and TZ: from infancy to PMP



In Childhood

In Adolescence

In Postadolescent
Women

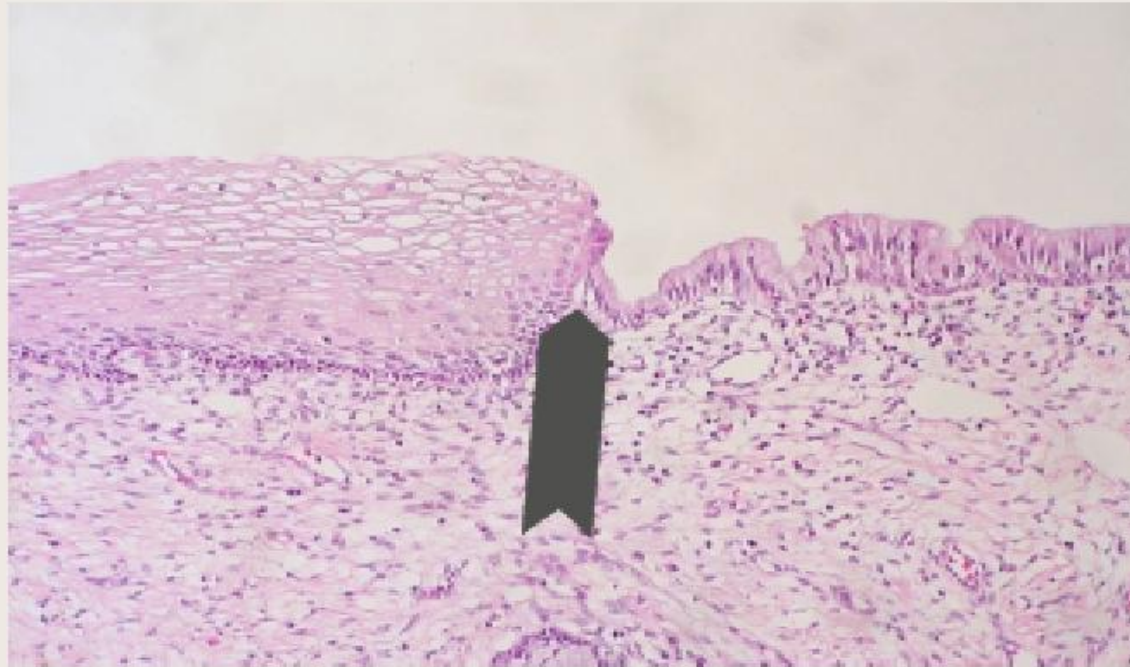
In Postmenopausal
Women

Sq. Epi—Squamous epithelium

Col. Epi—Columnar epithelium

Histology of the normal cervix: Squamocolumnar junction

Fig. 5

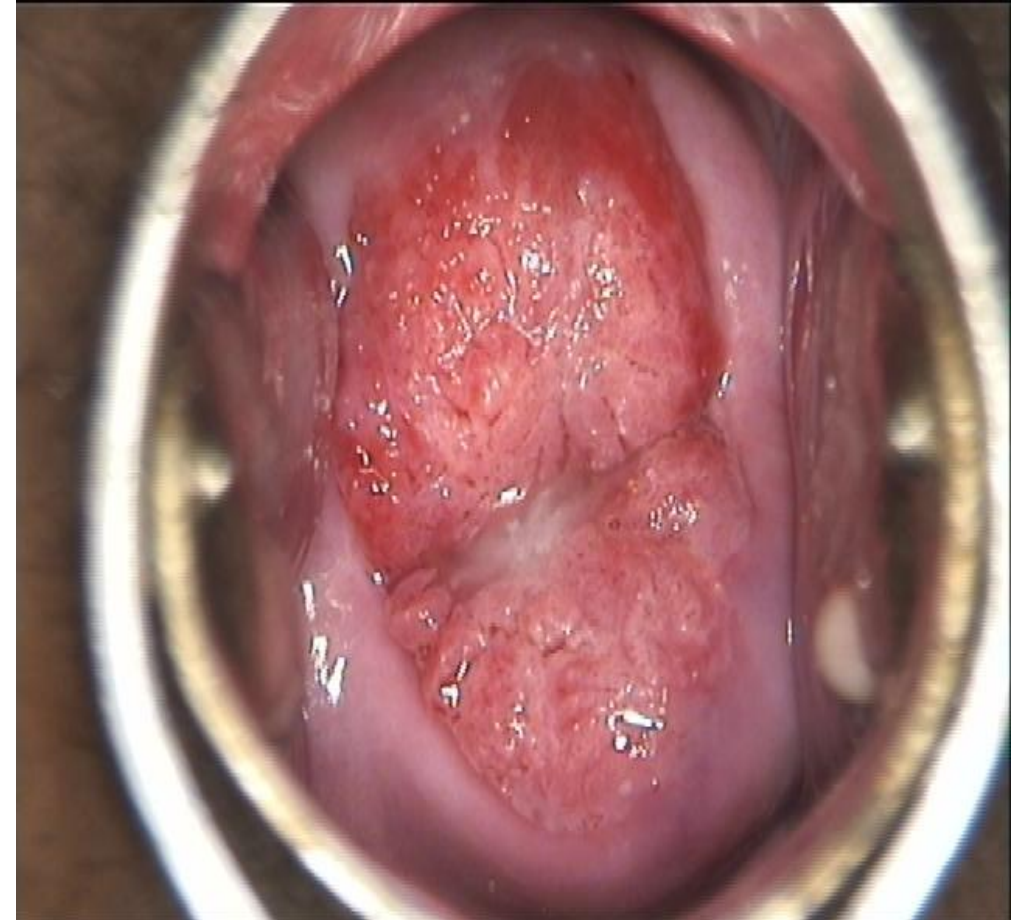


The squamocolumnar junction: marks the boundary between the squamous-lined ectocervix and the columnar-lined endocervix (arrows)

Pathological and histological images: Courtesy of Ed Uthman at Flickr

Squamous Metaplasia

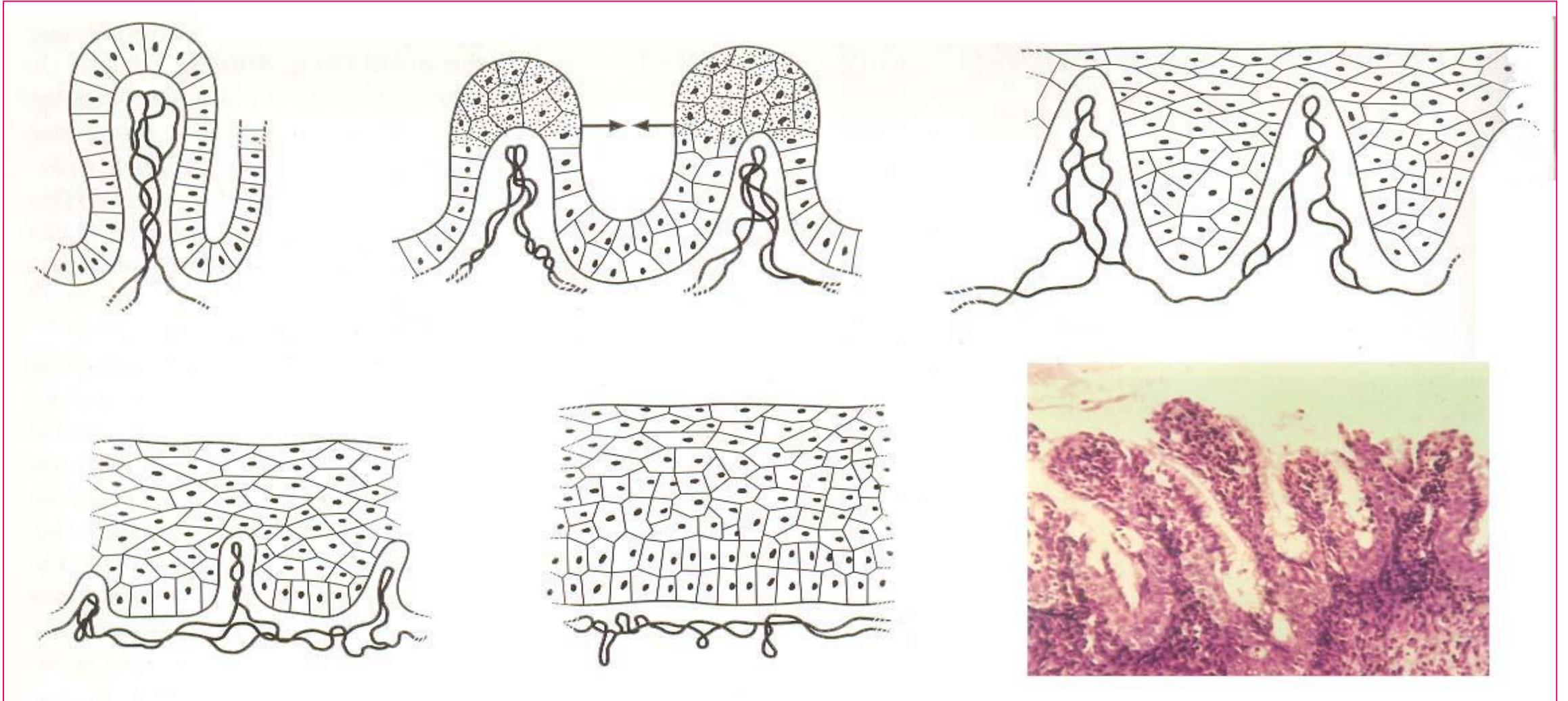
- **Metaplasia** refers to the change or replacement of one type of cell by another.
- **Squamous metaplasia** is a physiologic process that occurs on the cervix—the columnar cells on the side of the SCJ closest to the os are gradually **replaced** with squamous cells.
- This process results from the exposure of the columnar cells to the acid environment of the vagina, trauma and inflammation.



Physiological process of Squamous metaplasia

- The **irritation of exposed columnar epithelium** by the **acidic vaginal environment** results in the **activation of sub-columnar reserve cells**.
- Reserve cells are **undifferentiated, cuboidal, sub-columnar cells**.
- These cells multiply (reserve cell hyperplasia) and differentiate into **metaplastic squamous epithelium**
- Squamous metaplasia is an **irreversible** process; the transformed epithelium (now squamous) cannot revert to columnar epithelium.

Histology: Formation of METAPLASIA



Squamous metaplasia

- **Squamous metaplasia** usually **begins at the original squamocolumnar junction** at the distal limit of the ectopy, but **it may also occur in the columnar epithelium close to this junction** or as islands scattered in the exposed columnar epithelium.
- The process of conversion from columnar epithelium to squamous epithelium is **progressive** with proliferation and maturation of the reserve cells.
- The immature squamous metaplastic epithelium **do not produce glycogen** and, hence, do not stain brown or black with Lugol's iodine solution.
- Groups of mucin-containing columnar cells may be seen embedded in the immature squamous metaplastic epithelium at this stage.

Squamous metaplasia

- Further development of the newly formed immature metaplastic epithelium may take two directions:
 - Develops into a mature squamous metaplastic epithelium
 - In a minority of women, an atypical, dysplastic epithelium may develop after infection by oncogenic human papillomavirus (HPV) types
- The mature metaplastic epithelium resembles the original stratified squamous epithelium.
- Some residual columnar cells or vacuoles of mucus are seen in the mature squamous metaplastic epithelium, which contains glycogen from the intermediate cell layer onwards. Thus, it stains brown or black after application of Lugol's iodine

Histology of squamous Metaplasia

Squamous metaplasia

Fig. 7A

Immature squamous metaplasia after proliferation of reserve cells. Remaining endocervical cells on the surface.

7A

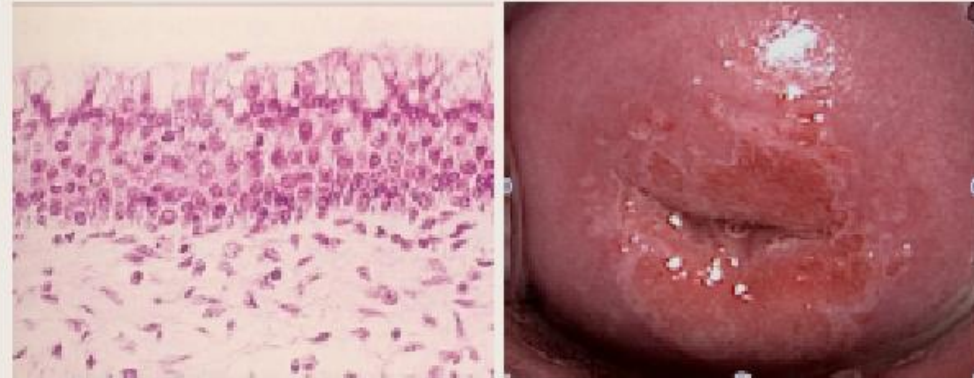
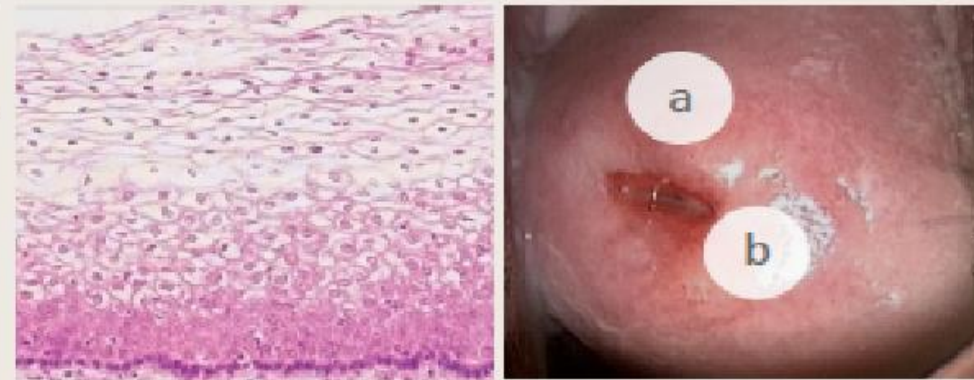


Fig. 7B

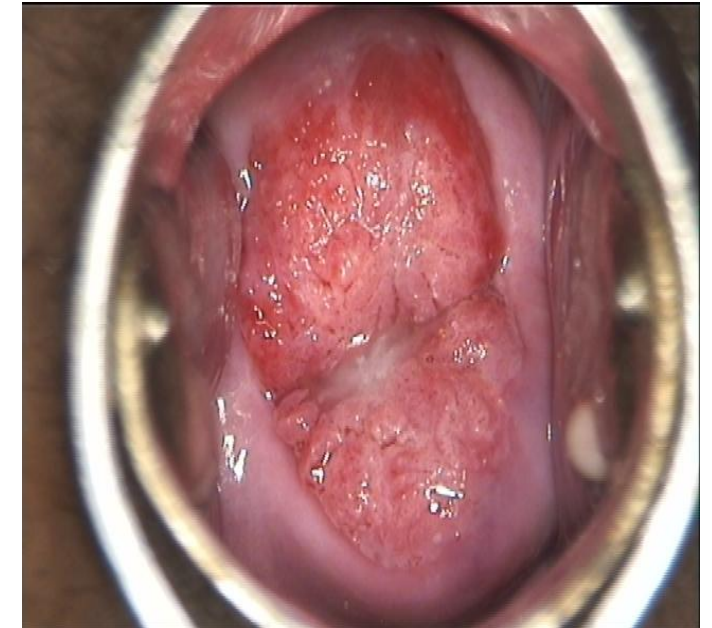
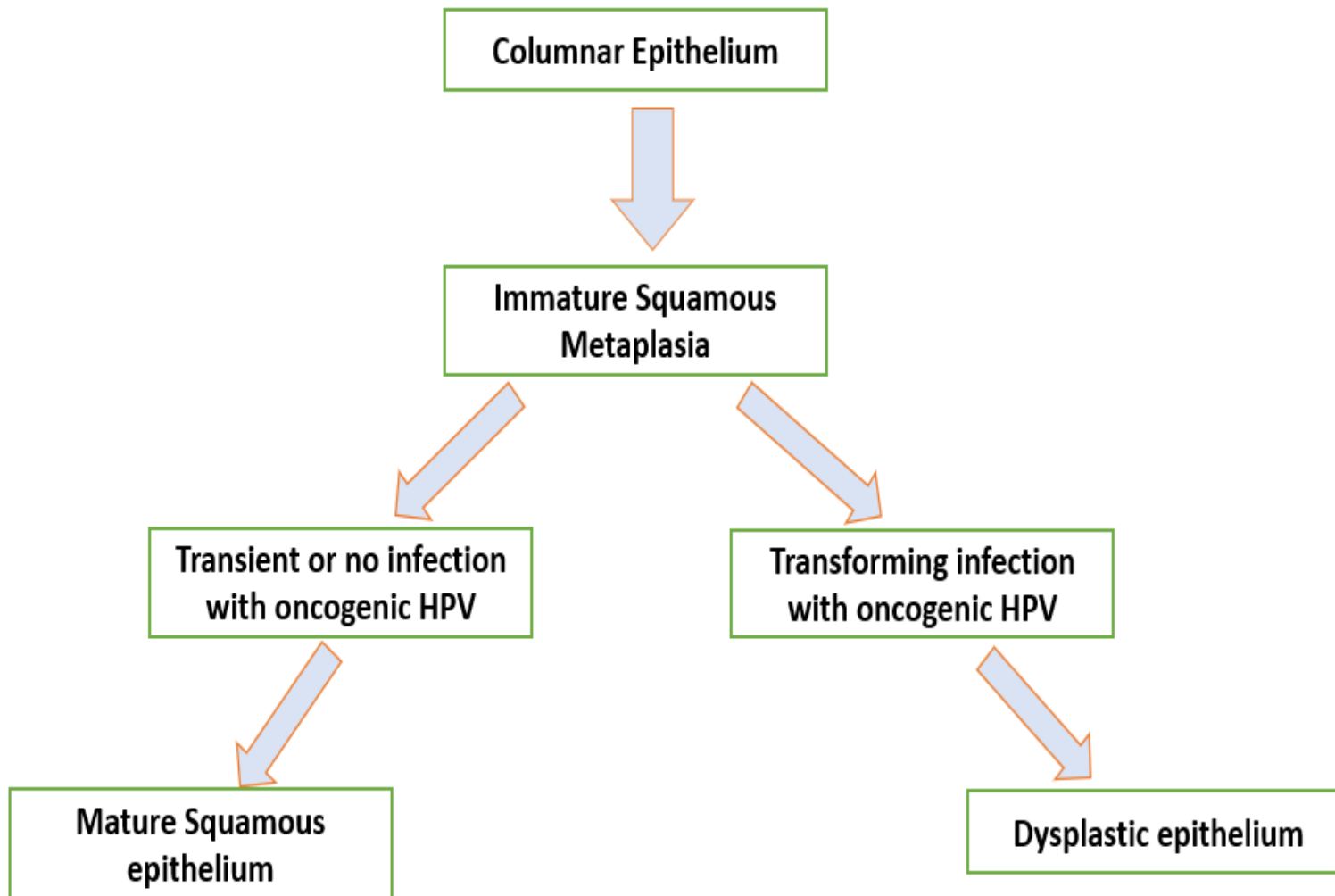
Mature squamous metaplasia (a) identical to the native squamous epithelium (b)

7B



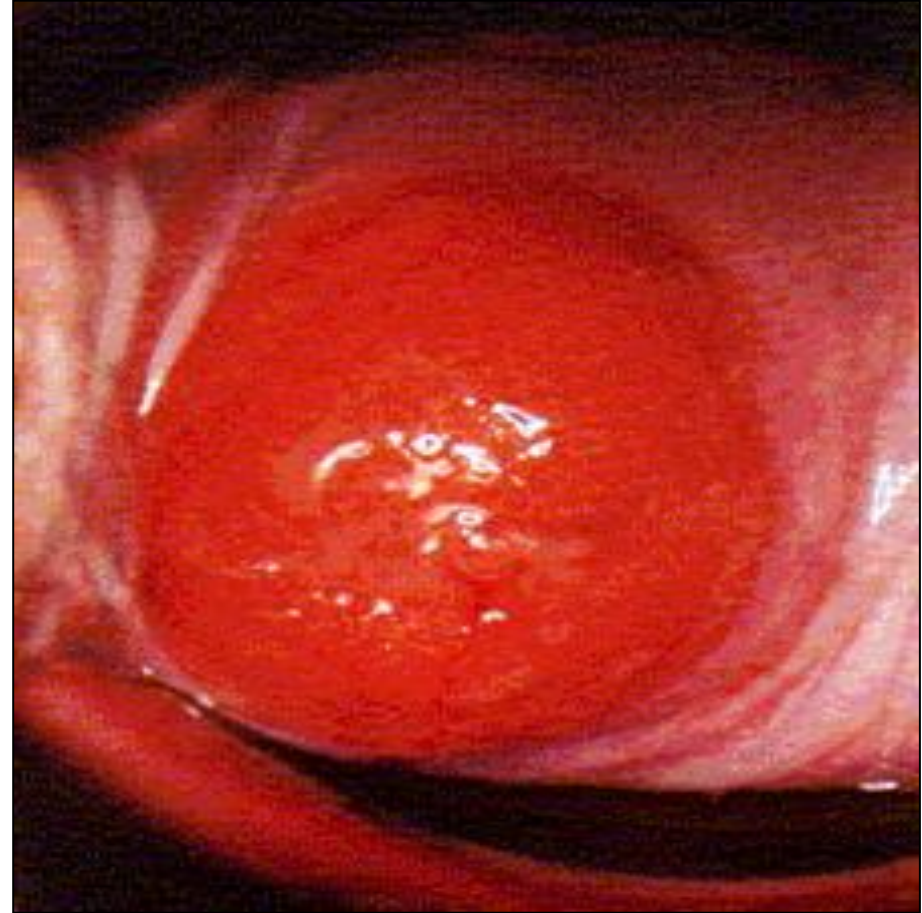
Courtesy of IARC: <http://screening.iarc.fr>

Metaplasia



Ectopy

- An **eversion onto the ectocervix** of the **SCJ** along with **large portions of columnar epithelium** is referred to as an ectropion
- Progressively through the process of metaplasia the ectropion is replaced by metaplastic squamous epithelium
- Metaplasia is a reaction of the exposed everted columnar epithelium (ectropion) to irritation by acidic vaginal environment.



Metaplasia (with iodine stain)



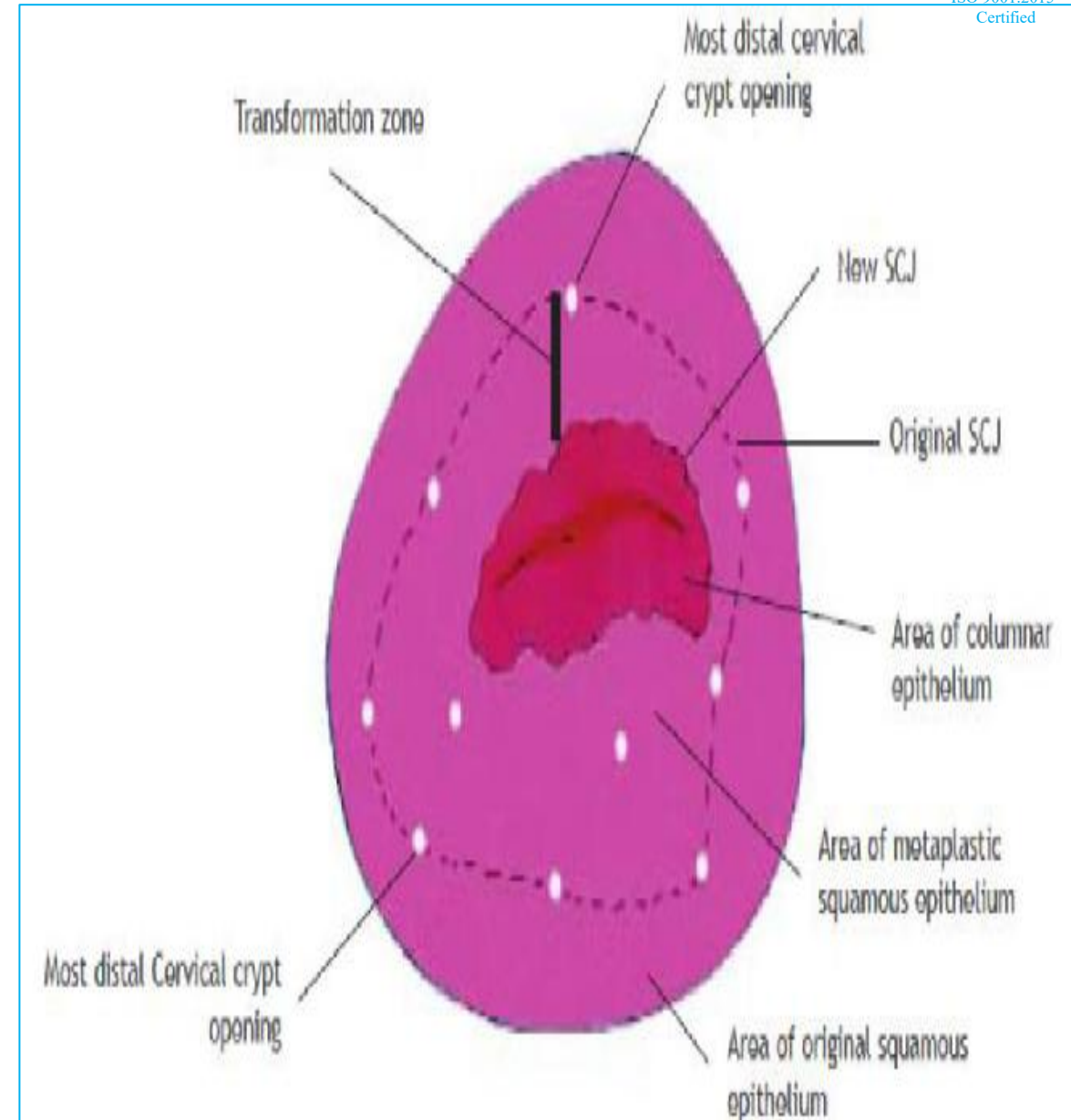
FIGURE 3.5:

VILI negative: Squamous epithelium remains brown. There are patchy areas of no or partial uptake of iodine in the transformation zone corresponding to areas of immature squamous metaplasia and inflammation.

Immature metaplastic cells do not have glycogen

Transformation Zone (TZ)

- It's the area between the **original** SCJ and the **new** SCJ where the columnar epithelium has been or being replaced by the new metaplastic squamous epithelium.
- It's an area of changing cells, and it is the most common place on the cervix for abnormal cells to develop.
- The TZ may be either wide or narrow depending on age, parity, prior infections and exposure to female hormones.

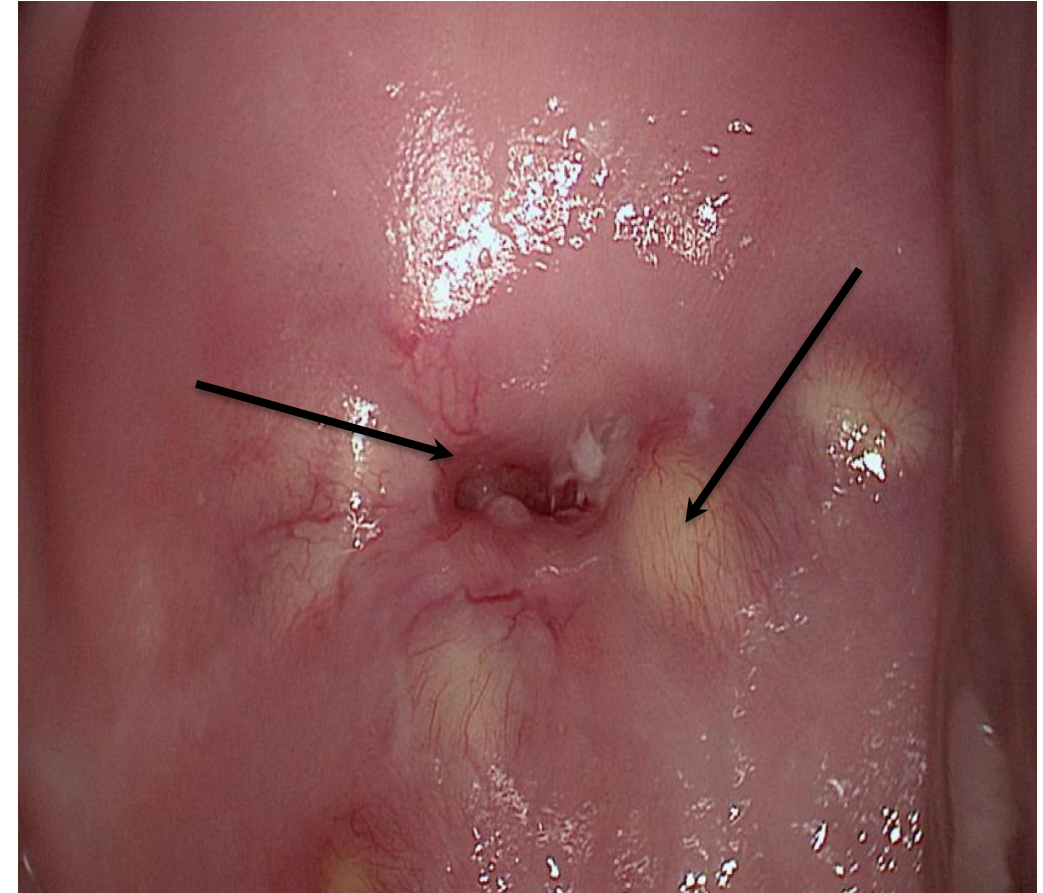


Significance of Transformation zone

- Precancerous changes almost always develop in the T-zone and specifically on or near SCJ
- Screening for precancerous lesions should focus on the T-zone and SCJ because that is where a lesion will develop

Features of a normal TZ

- The well distinguishable characteristics of a normal TZ are as follows:
- Columnar epithelium
- non keratinizing squamous epithelium, Nabothian cysts and crypt (gland) openings.
- Nabothian (Retention) cysts are due to blockage of crypts by metaplastic epithelium



Nabothian Cysts, Squamous epithelium (marked in black)

THE END

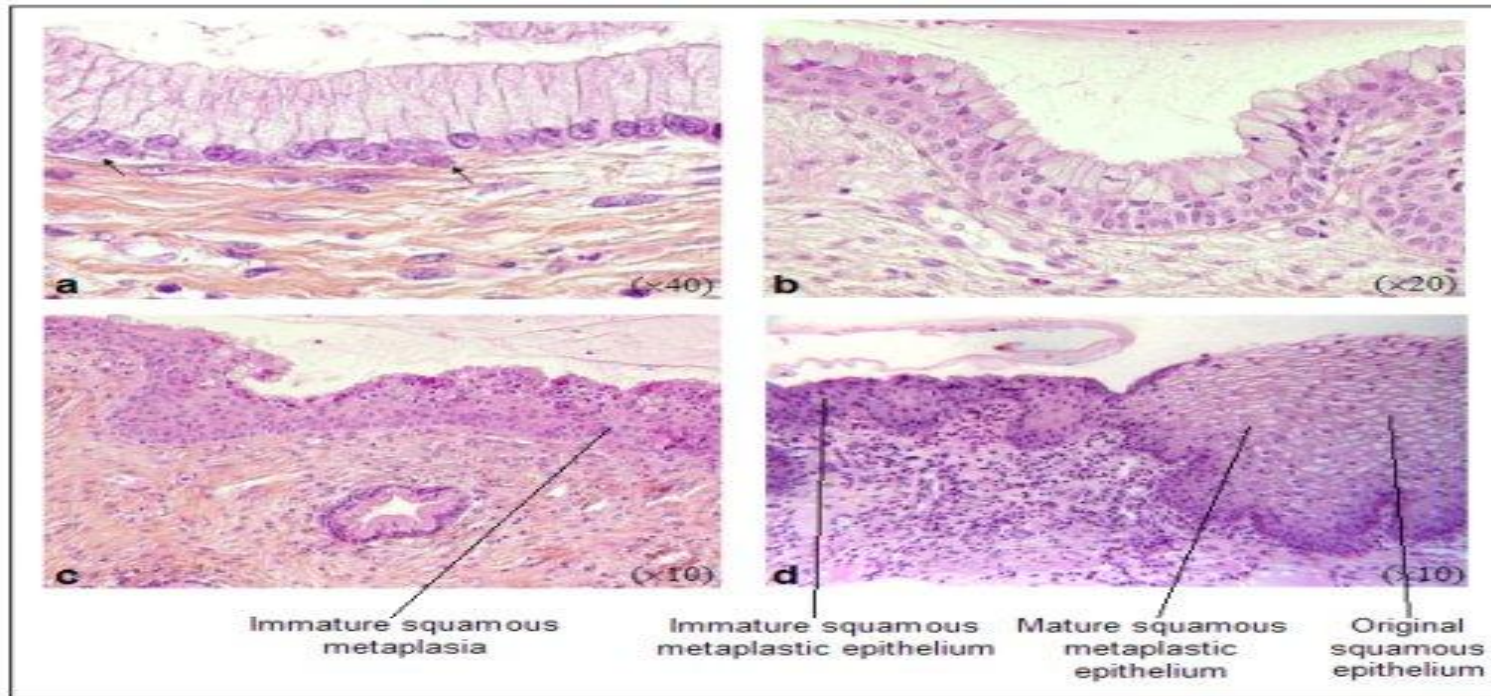


FIGURE 1.5: Development of squamous metaplastic epithelium

- (a) The arrows indicate the appearance of the subcolumnar reserve cells.
- (b) The reserve cells proliferate to form two layers of reserve cell hyperplasia beneath the overlying layer of columnar epithelium.
- (c) The reserve cells further proliferate and differentiate to form immature squamous metaplastic epithelium. There is no evidence of glycogen production.
- (d) Mature squamous metaplastic epithelium is indistinguishable from the original squamous epithelium for all practical purposes.