Management of abnormal cervical smear

DONE BY: GROUP C4

Outlines

- Introduction
- Screening
- Pap smear procedure
- How to take pap smear
- Pap smear classification
- Normal and abnormal results
- Diagnostic Approach to abnormal pap smear
- Management

Introduction

- Cervical cancer is the major cause of death from cancer in women worldwide, but most new cases and deaths occur in developing countries where screening for cervical cancer is poorly developed.

- Cervical cancer is caused by persistent infection with a high-risk human papillomavirus (HPV), and vaccines have been developed against some of these viruses. Vaccination of girls (and boys) before they are sexually active should significantly decrease the incidence of cervical cancer in the future.

- Persistent infection with a high-risk HPV virus initially produces an intraepithelial lesion called high-grade squamous intraepithelial lesion. This entity can be detected by screening with a Papanicolaou smear, liquid based cytology, or a primary HPV test, and successfully treated, thereby preventing the development of invasive cervical cancer

- Invasive cancer of the cervix usually occurs between 40 and 60 years of age and most commonly presents early because of post coital bleeding if the woman is sexually active. If she is not sexually active, the disease may remain asymptomatic until it is quite advanced.

Gross Anatomy

- The cervix is the **inferior part of the uterus** protruding into the vagina.

- The cervix measures **2.5-3** cm in **diameter** and **3-5cm in Length.**

Normal histology

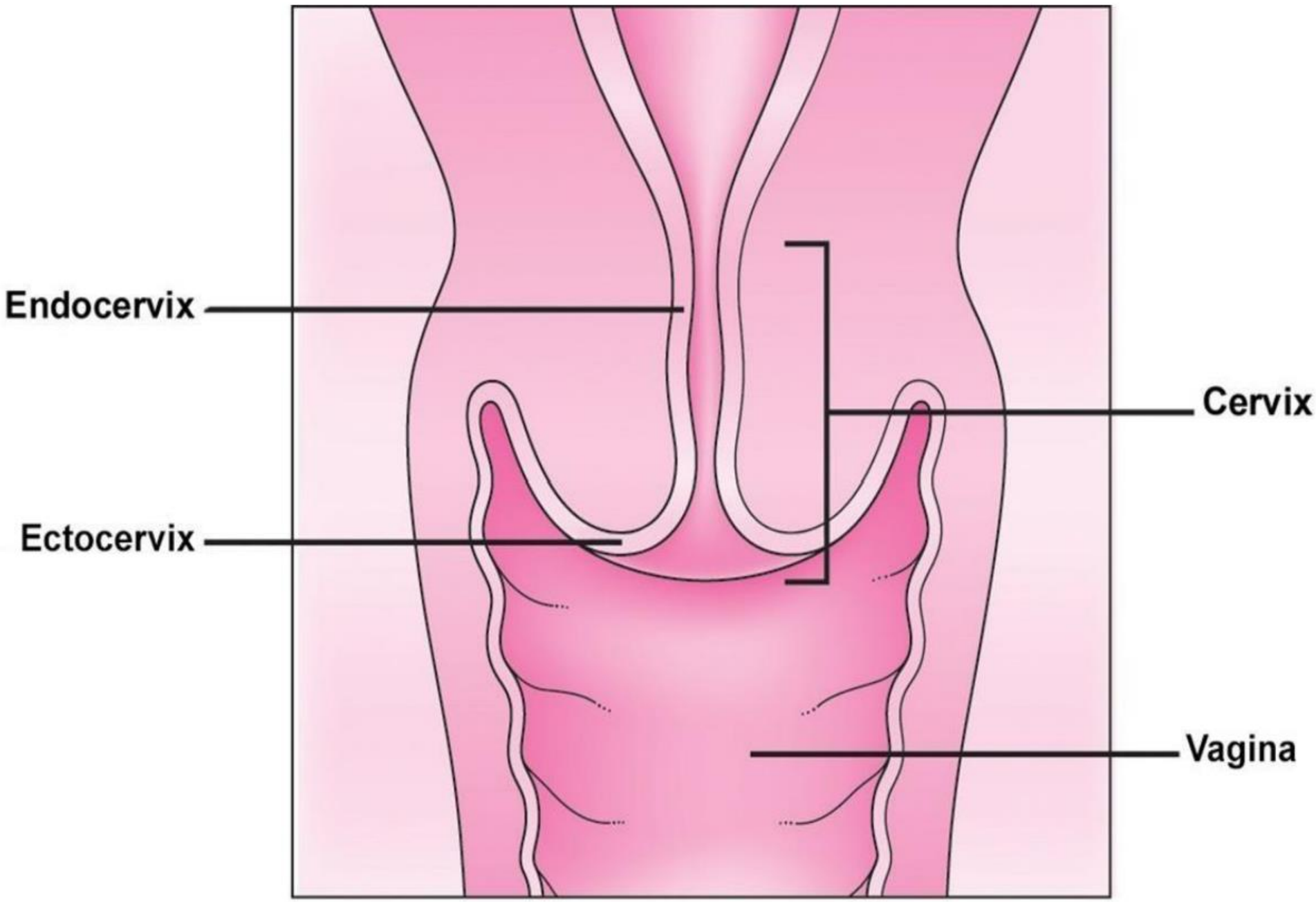
- The epithelium is

stratified squamous on the ectocervix

columnar in the endocervix..

-The exposed (i.e., vaginal) portion of the cervix is lined by nonkeratinizing stratified squamous epithelium

sensitive to estrogen and progesterone



Cervical Physiological Changes

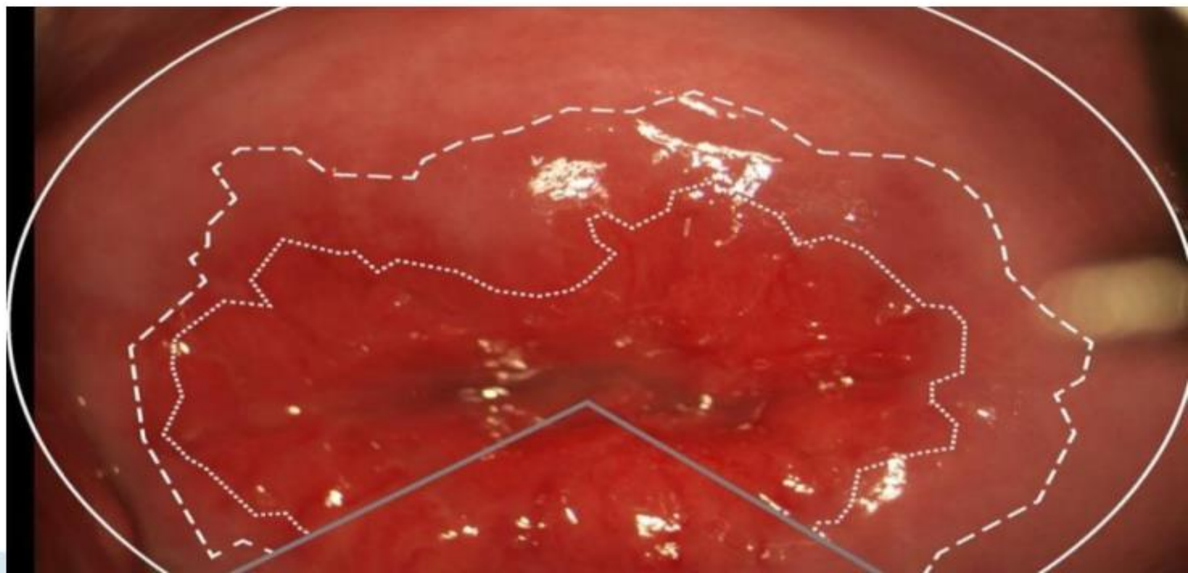
- **At birth**: squamous epithelium covers the out rim of the cervix,the inner aspect of the cervix is covered by the columnar cells and the junction between both of them is the original squamocolumnar junction.

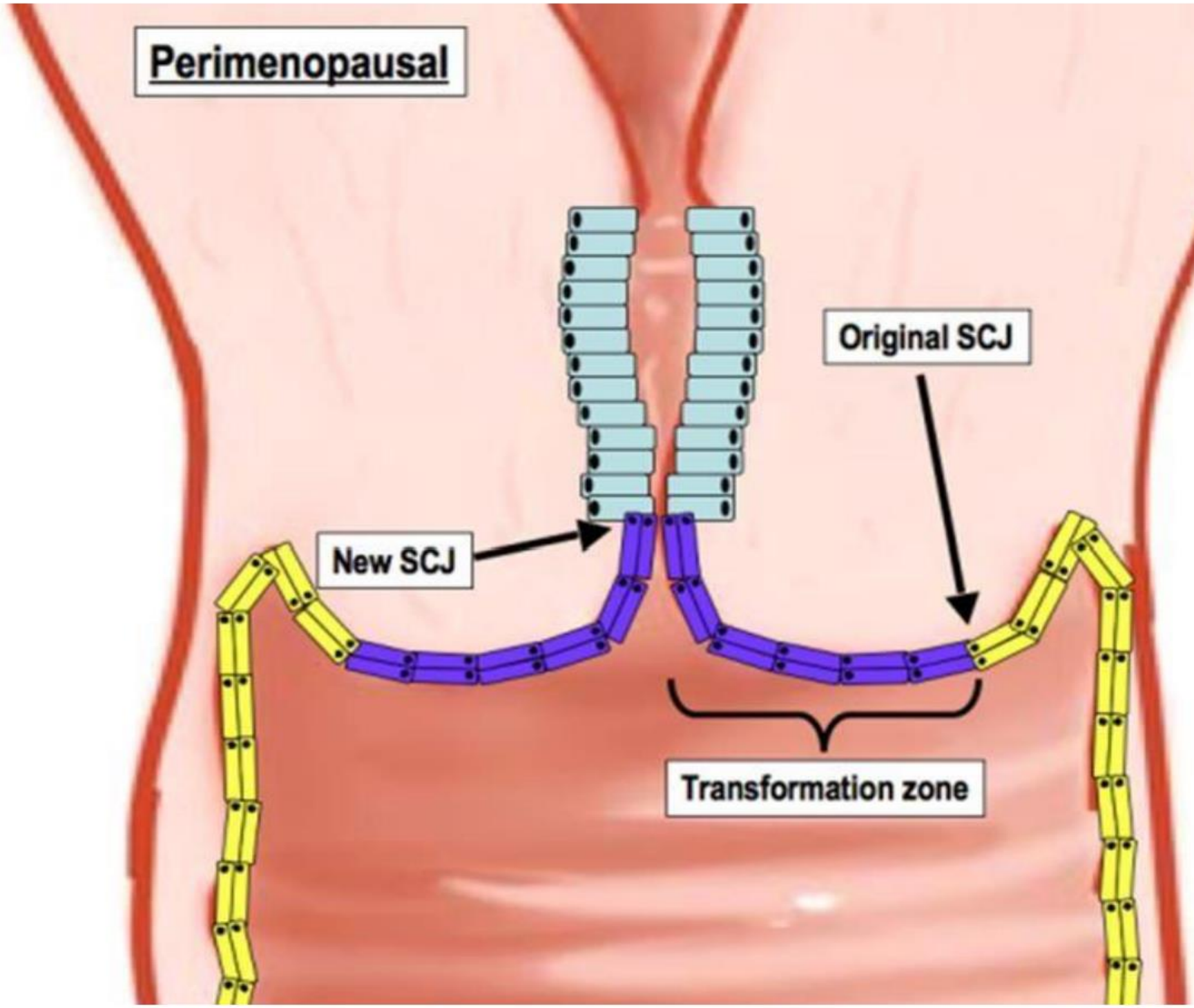
- **Adolescence and 1st pregnancy**: New squamocolumnar junction.

The transformation zone

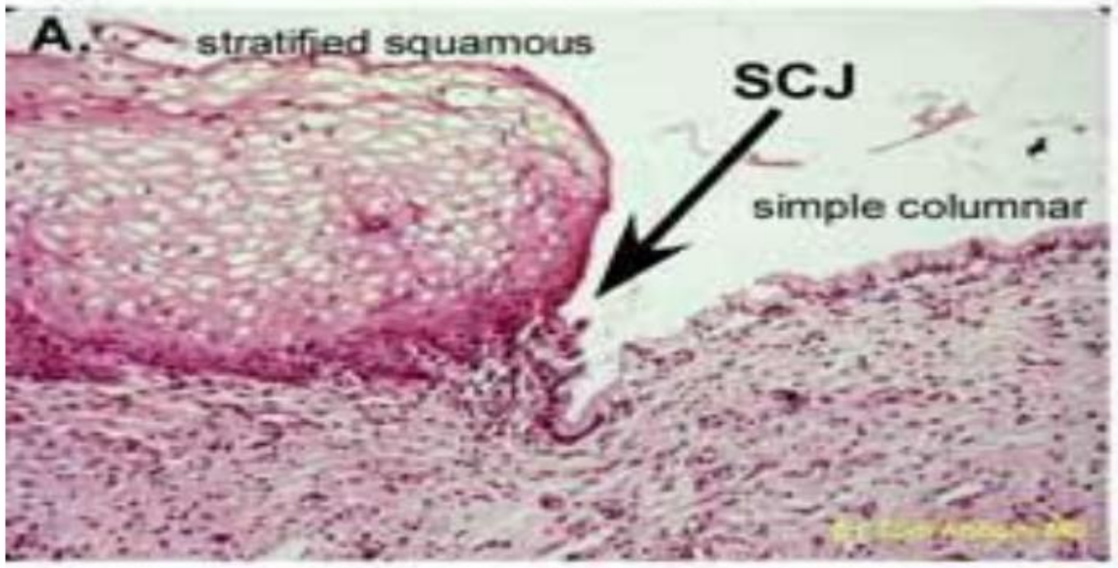
- The area **between the original squamocolumnar junction and the new squamocolumnar junction**

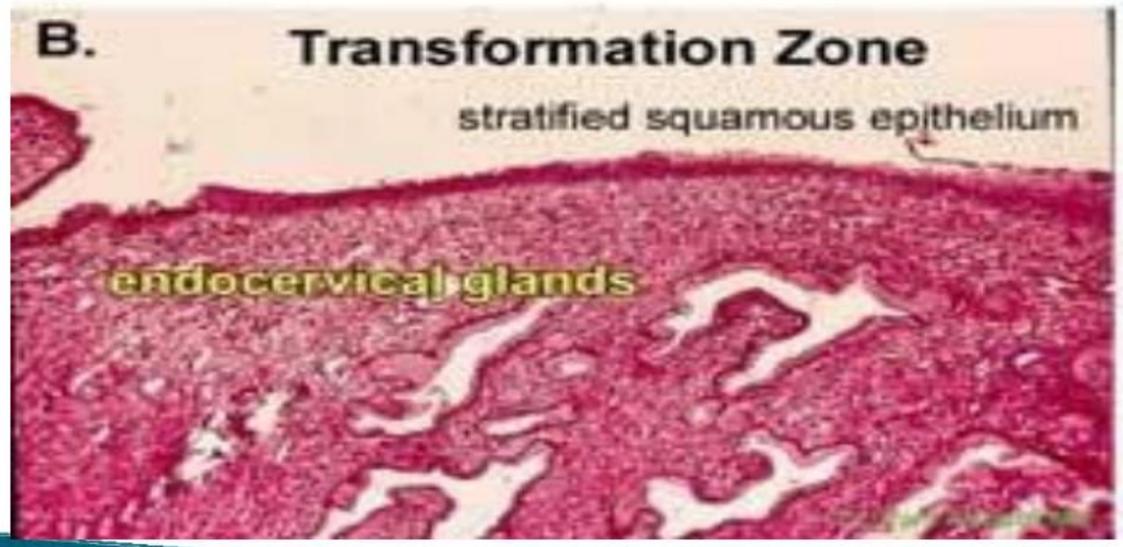
- Understanding the transformation **is important because cervical cancer and its precursors typically begin within the transformation zone.**



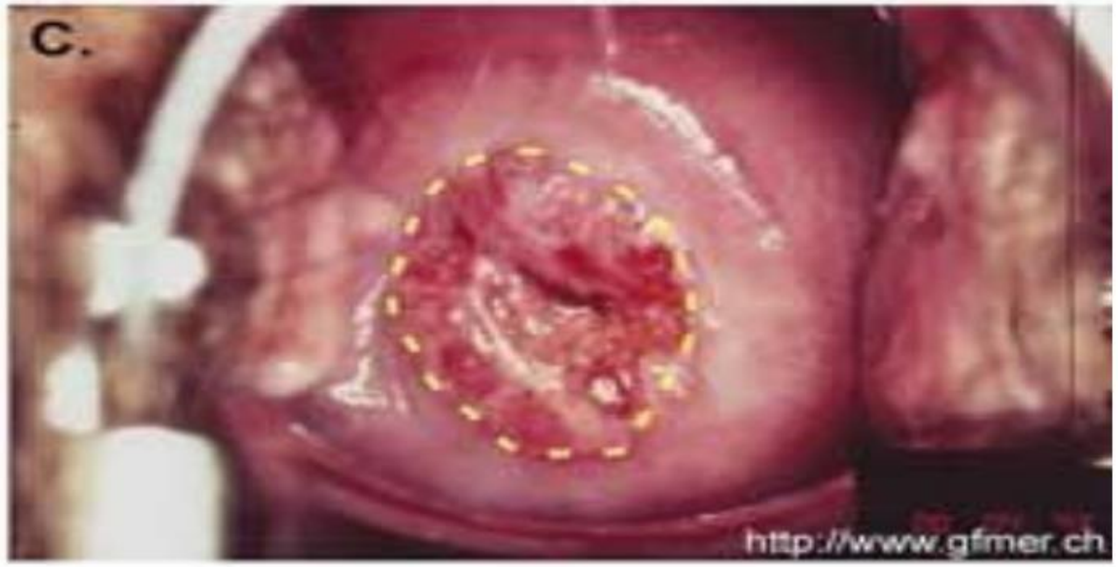

Perimenopausal
Original SCJ
New SCJ
Transformation zone

Histology





Colposcopy



Methods of screening

- Pap testing
- HPV testing
- Co-testing

Pap smear

IS a Screening tool that can detect precursors and early-stage disease for both types of cervical cancer: squamous cell carcinoma and adenocarcinoma. cervical cytology is performed to assess for cellular abnormalities.

When to begin screening

According to the American guidelines

- screening after 3 years of the first vaginal intercourse or by age 21.

Screening for ages 21-29

Cytology alone every 3 years

HPV testing "should not be used to screen"

Screening for ages 30-64

- Cytology + HPV testing (Co testing) every 5 years is preferred
- Cytology alone every 3 years is acceptable

According to RCOG guidelines

we start screening at age 25

-Women aged 25-49 are routinely recalled every 3 years.

- Women aged 50-64 are routinely recalled every 5 years.

When to Stop Screening

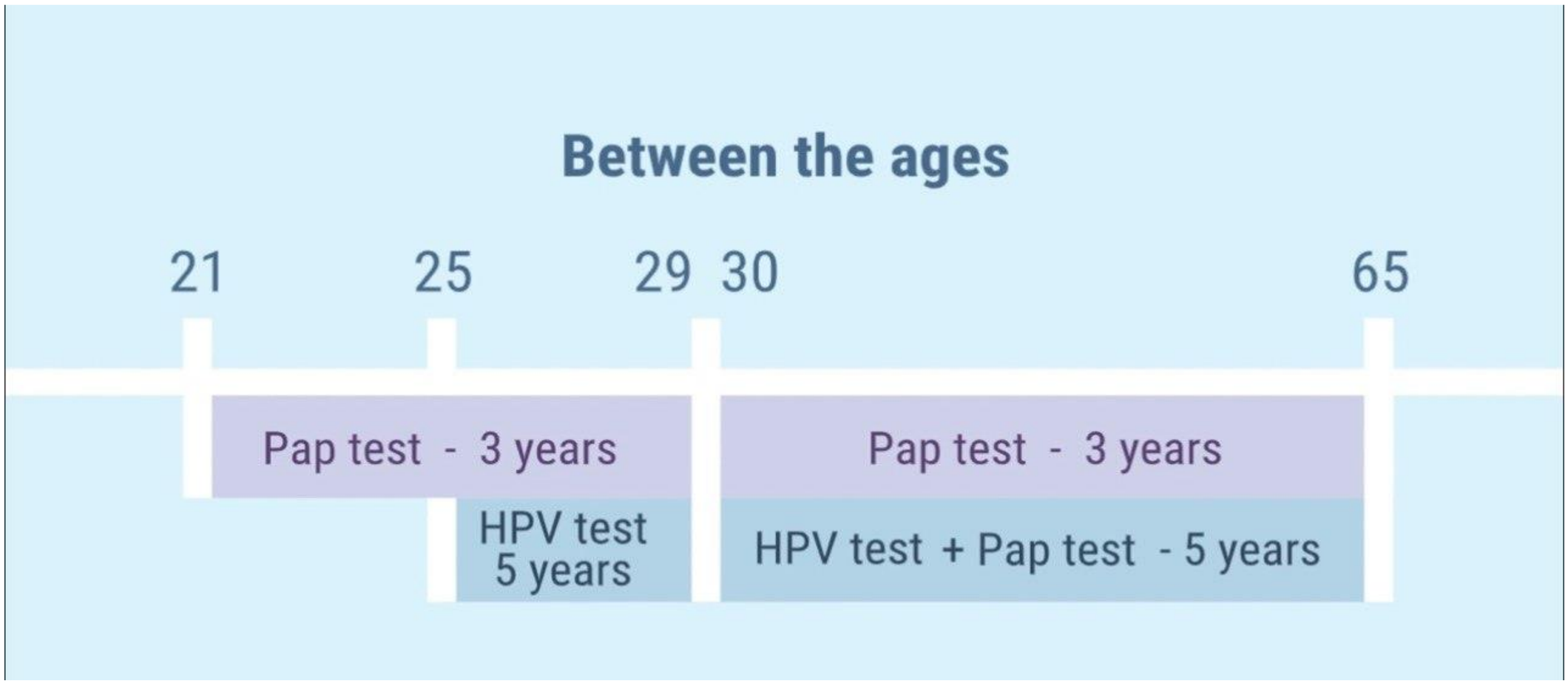
1 - **Stop at age 65 for women with adequate negative** prior screening, no CIN2+ within the last 20y.

- **Definition of adequate negative screening:**

- 3 consecutive negative Paps
  or
- 2 consecutive negative HPV tests

(Tests within 10 years of stopping; most recent within 5 years.)

2 - Stop after hysterectomy with removal of cervix and no history of CIN2+.


Between the ages
21
25
29
30
65
Pap test - 3 years
Pap test - 3 years
HPV test
5 years
HPV test + Pap test - 5 years

PAP SMEAR Prerequisite

- The optimal time for doing pap smear is **5 days after the menstrual cycle has stopped**.
- Patient should **avoid the following for 24-48h**:

1. **intercourse**
2. **douching**
3. **vaginal medications**

How to obtain a sample

1. **Collection device**

Several collection devices are available for cervical cytology sampling. A spatula and a separate endocervical brush provide a specimen with more endocervical cells than when only a spatula is used .

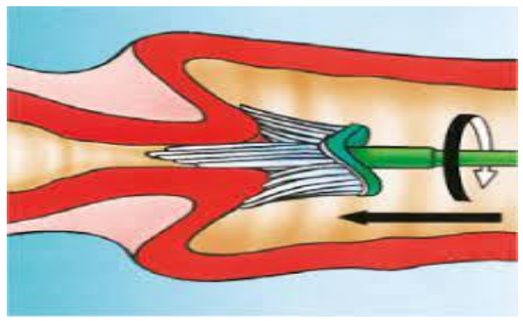
it is also slightly better for detecting any grade of cervical intraepithelial neoplasia (CIN) than the single broom device

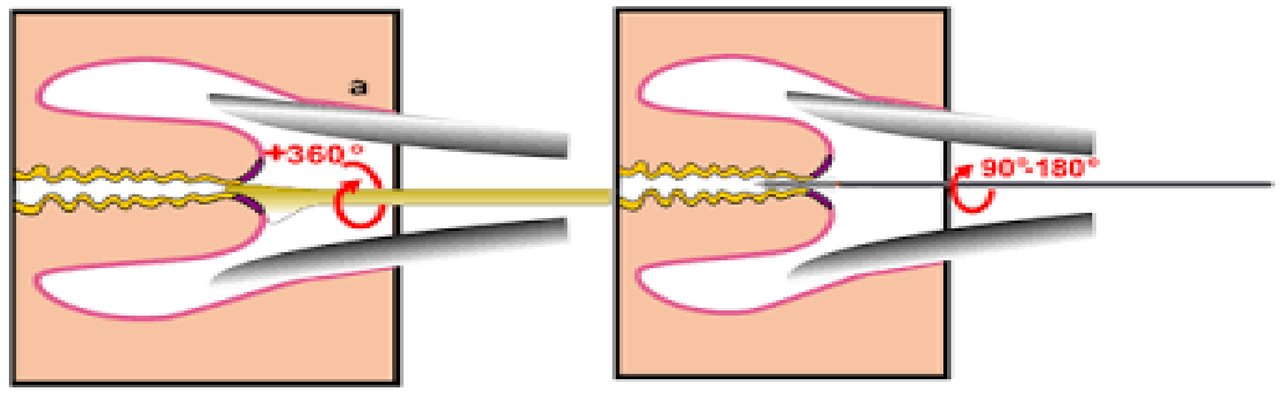
2. Sample collection

Use the spatula to circumferentially scrape the ectocervix and rotate it 360 degree, Sampling the ectocervix before the endocervix will minimize bleeding during sample collection.

Insert the endocervical brush into the endocervix so that the bristles nearest the examiner are inserted to the level of the external cervical os. Rotate the brush 180 degrees to obtain a sample.

Alternatively, if a broom is used, insert the central bristles into the endocervix with the outer bristles in contact with the ectocervix. Rotate the broom in the same direction for five turns.

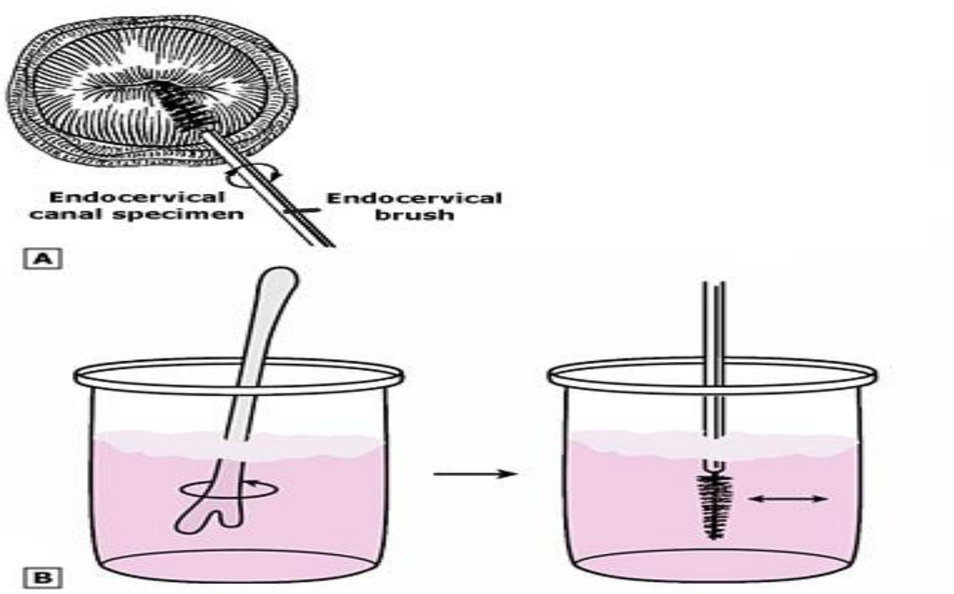




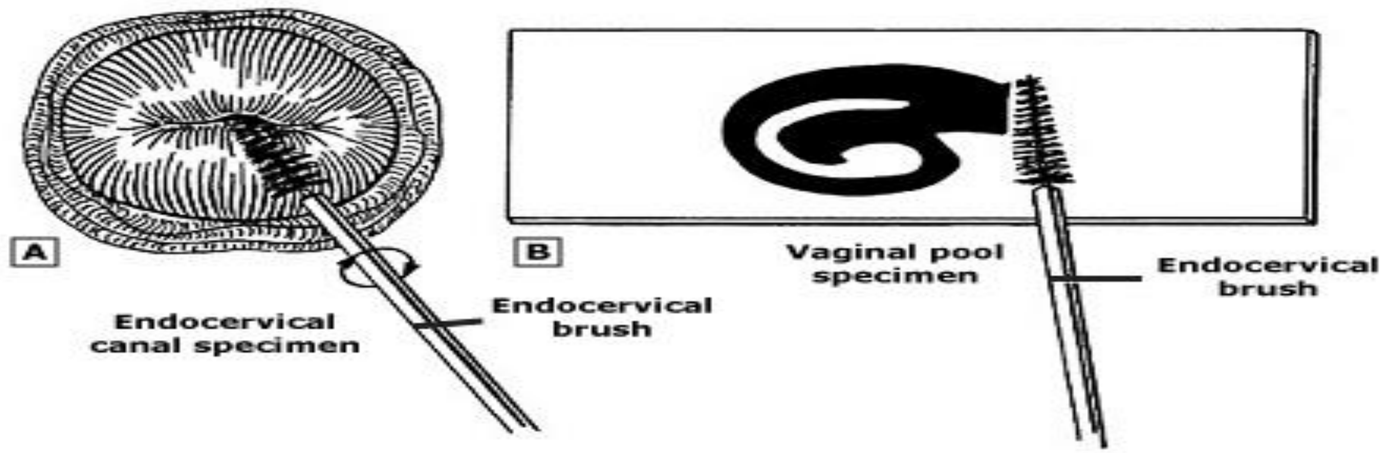
3. Preparation methods

There are two methods for preparing a specimen for cervical cytology: liquid-based thin layer preparation and conventional Pap smear .

For **liquid-based thin layer cytology**, the collecting device is placed into a liquid fixative solution and vigorously swirled or rotated ten times in the solution .

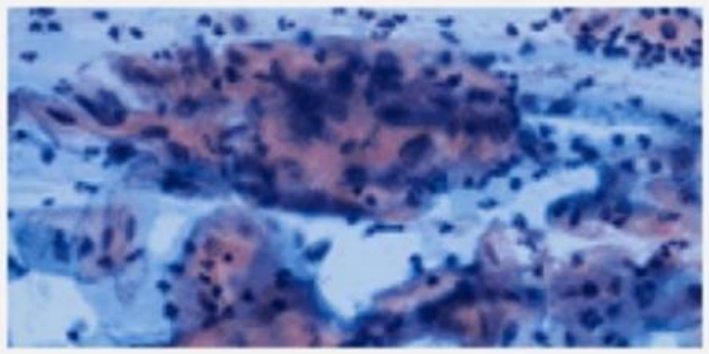
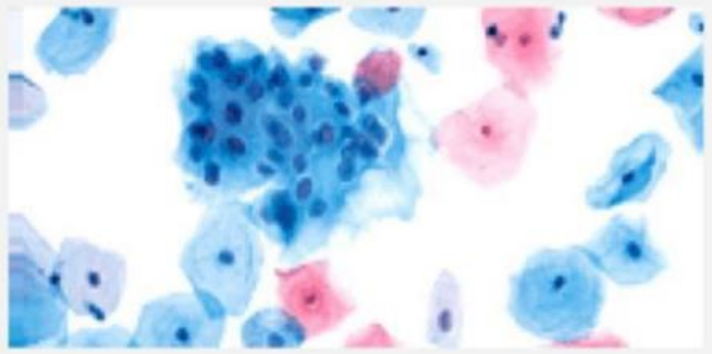


For **conventional Pap smears**, the ectocervical spatula is smeared and the endocervical brush is rolled uniformly onto a single slide promptly after obtaining the specimens, The slide is then rapidly fixed to avoid air-drying; the usual fixatives are either ethyl ether plus 95 percent ethyl alcohol or 95 percent ethyl alcohol alone. If spray fixatives are used, the spray should be held at least 10 inches away from the slide to prevent disruption of cells by the propellant.



Thin prep is more accurate because

- Cells **don't clump** on top of each other.
- **Less debris** on the resulting slide.
- **Fewer cells are required** to make adequate specimen.
- **More intraepithelial lesions are identified.**

Conventional Pap Smear	ThinPrep Pap Test
	

HPV testing

HPV testing identifies oncogenic (ie, high-risk) HPV subtypes that are associated with cervical cancer.

HPV Group	HPV Types	Clinical Association
Low Risk	6, 11, 42, 43, 44	Genital warts or benign lesions, not cervical cancer.
High Risk	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68	All types isolated in cervical cancer.

Specimens for HPV testing can be collected from the endocervix using a cervical spatula or cervical brush, which is then placed in HPV test transport medium

HPV deoxyribonucleic acid (DNA) testing is much more sensitive than cervical cytology, but less specific. It is presently being investigated as a primary screening test for women after the age of 25 to 30 in many developed countries. The negative predictive value of the HPV test is very high, so screening intervals could safely be extended to at least 5 years. If the HPV test is positive, reflex cervical cytology is performed to determine the need for referral for colposcopy.

Pap smear results Bethesda system

1 specimen type
traditional pap vs thin prep

2 adequacy
satisfactory / un satisfactory

3 categorization of cells
negative
epithelial cell abnormality
glandular cell abnormality

Adequacy

- **1-satisfactory**: describe the **presence or absence of endocervical transformation zone** component and any other quality indicators obscuring blood ,inflammation.
- **2-unsatisfactory**: should **be repeated in 6 weeks.**

Categorization

- **Negative**: mean **negative for intraepithelial lesions or malignancy.**

- **But may show other abnormalities** : organisms suggest **vaginal infection** or **cellular change in response to dryness .**

Epithelial cell abnormality

- Atypical squamous cell (ASC)

Cells are **not completely normal** but are **not pre-cancerous**

1.ASC of undetermined significance **(ASC-US)**.

2.ASC-H more **likely to be associated with pre-cancerous** cervical lesions.

Low grade squamous intraepithelial lesions (LSIL)

Mild cellular change.

90% will return to normal if left.

15% of women with LSIL there are more serious cellular change on the cervix that were not identified.

Further testing is always recommended.

High grade squamous intraepithelial lesions (HSIL)

Moderate to sever change that are considered to be pre-cancerous

About 20% will progress to invasive cancer if left untreated for several years

Glandular cell abnormalities

- Those cells develop from the endo cervix , endometrium, fallopian tube or ovaries

1- atypical:

endocervical.

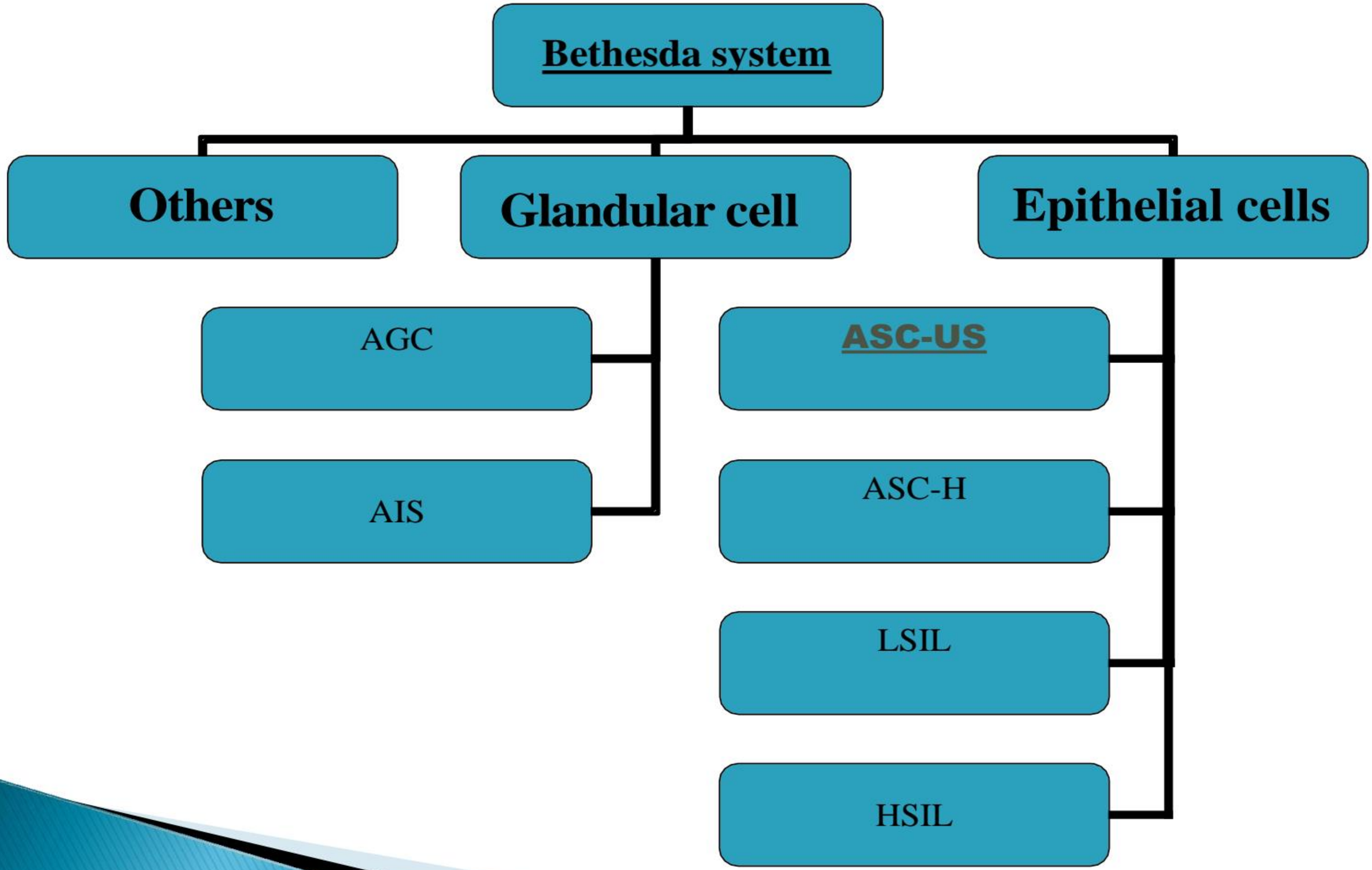
endometrial.

glandular cells not other wise specified.

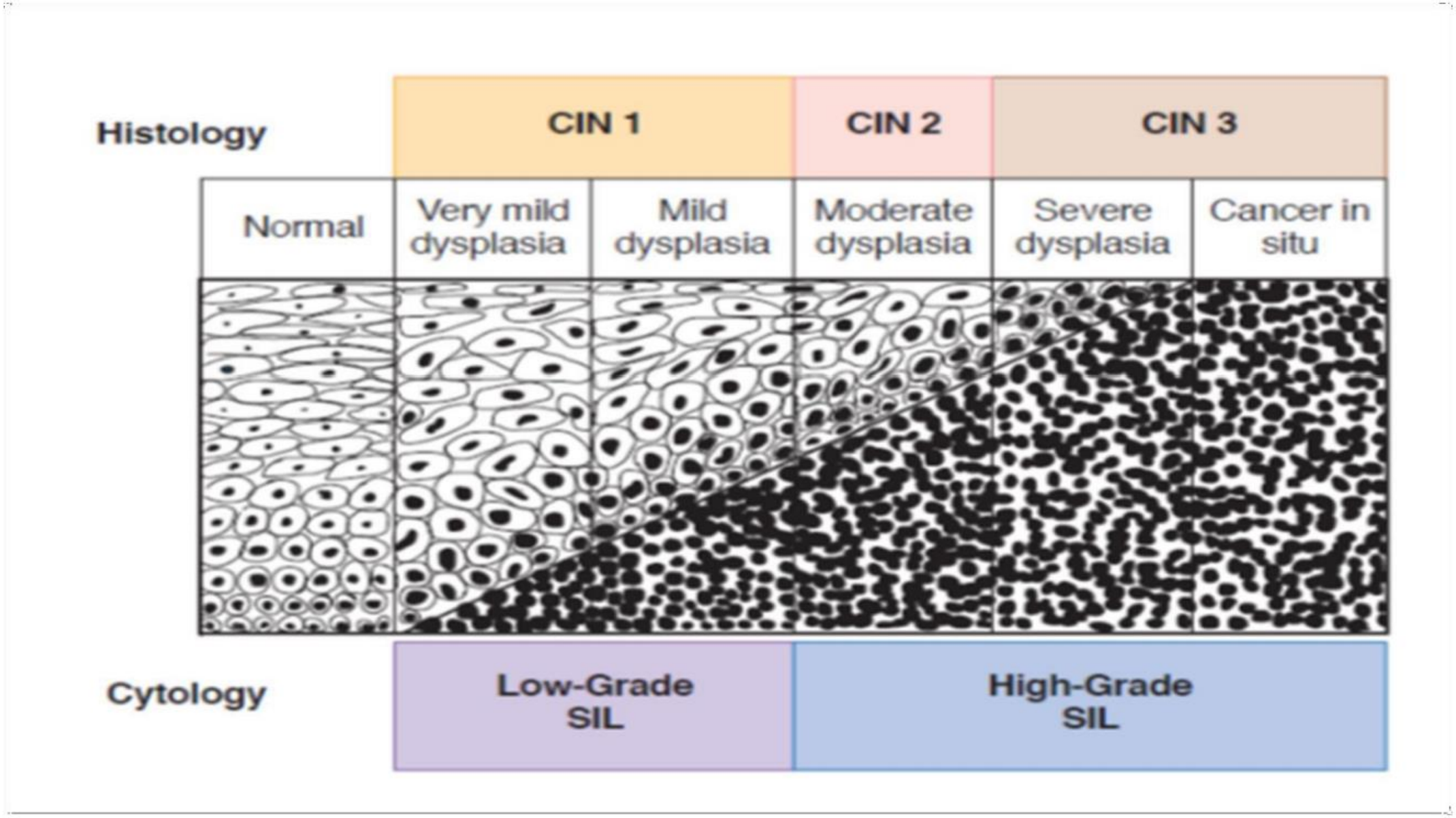
2- atypical favor neoplasia.

3- endocevical adenocarcinoma in situ(AIS).

4- adencarcinoma.


Bethesda system
Others
Glandular cell
Epithelial cells
AGC
AIS
ASC-US
ASC-H
LSIL
HSIL

Cytology vs. Histology



Relation of the pap smear (cytology) and biopsy (CIN or higher)

- **Basically :**
- **ASC-(US , H)…CIN I**
- **LSIL** encompasses cytological changes probably **consistent with CIN1 /CIN II.**
- **HSIL** denotes the cytological findings **probably corresponding to CIN II / CIN III / CIS / Invasion.**

All abnormal pap smears require further evaluation ; the objective is **to exclude the presence of invasive carcinoma and to determine the degree and extent** of any CIN.

Management options for abnormal pap smear:

- **Management of ASC-US:**

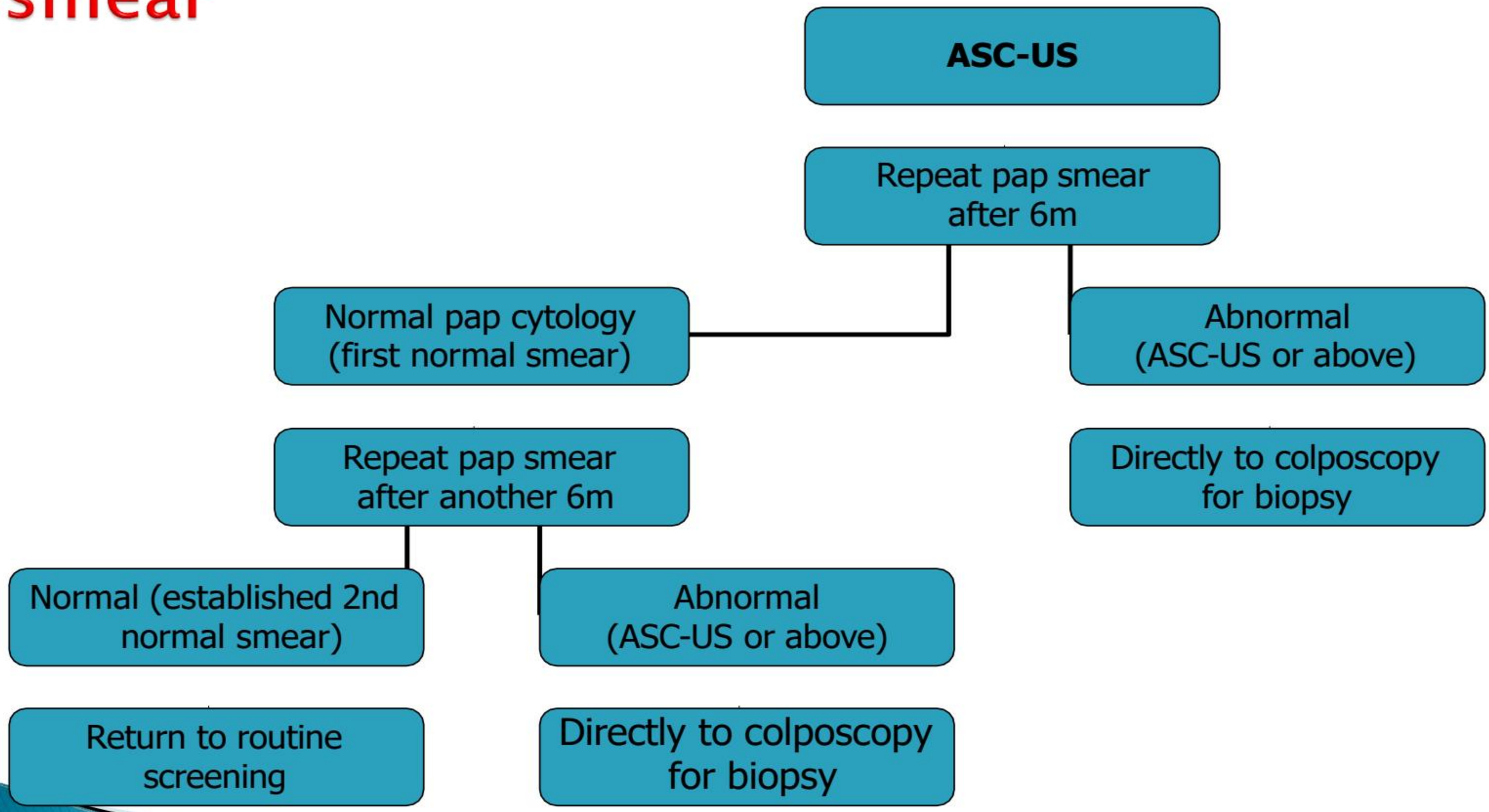
  3 options:

  1. **Repeat pap smear in 6 months.**
  2. **Test HPV with the pap smear "triage"** (new).
  3. **Immediate referral to Colposcopy and biopsy.**

- **Management of the rest (ASC-H , LSIL , HSIL, AGC, AIS)**

  Immediate referral to colopscopy and biopsy .

Option 1: Management by repeat pap smear

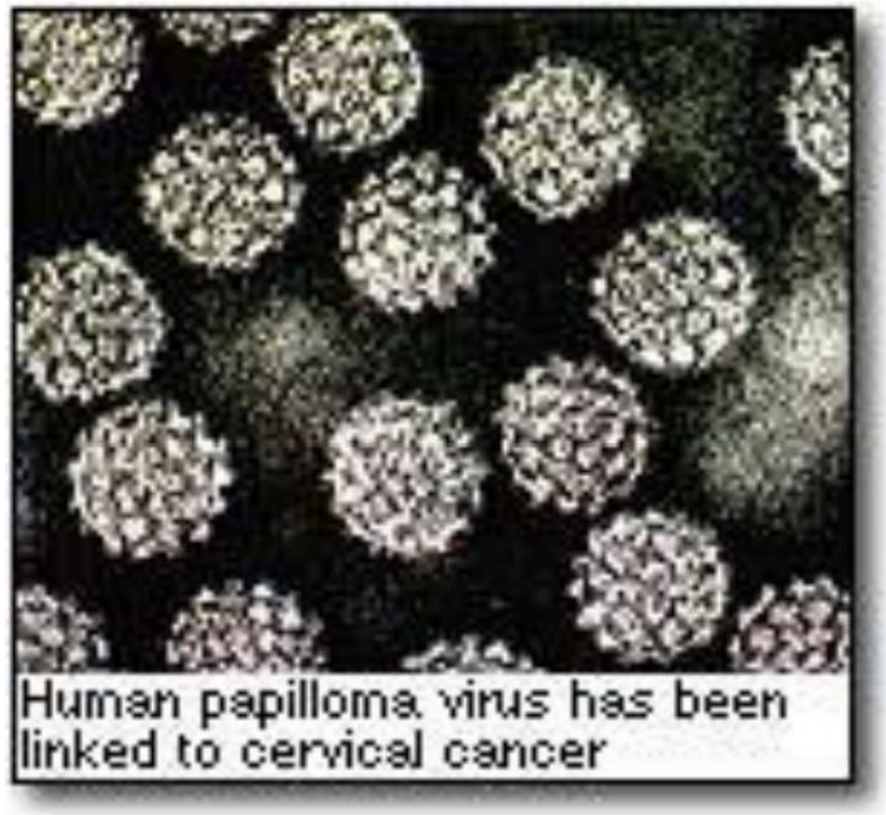


Option 2: HPV triage testing

- Test for **only high risk HPV types(16,18)**
- Method :

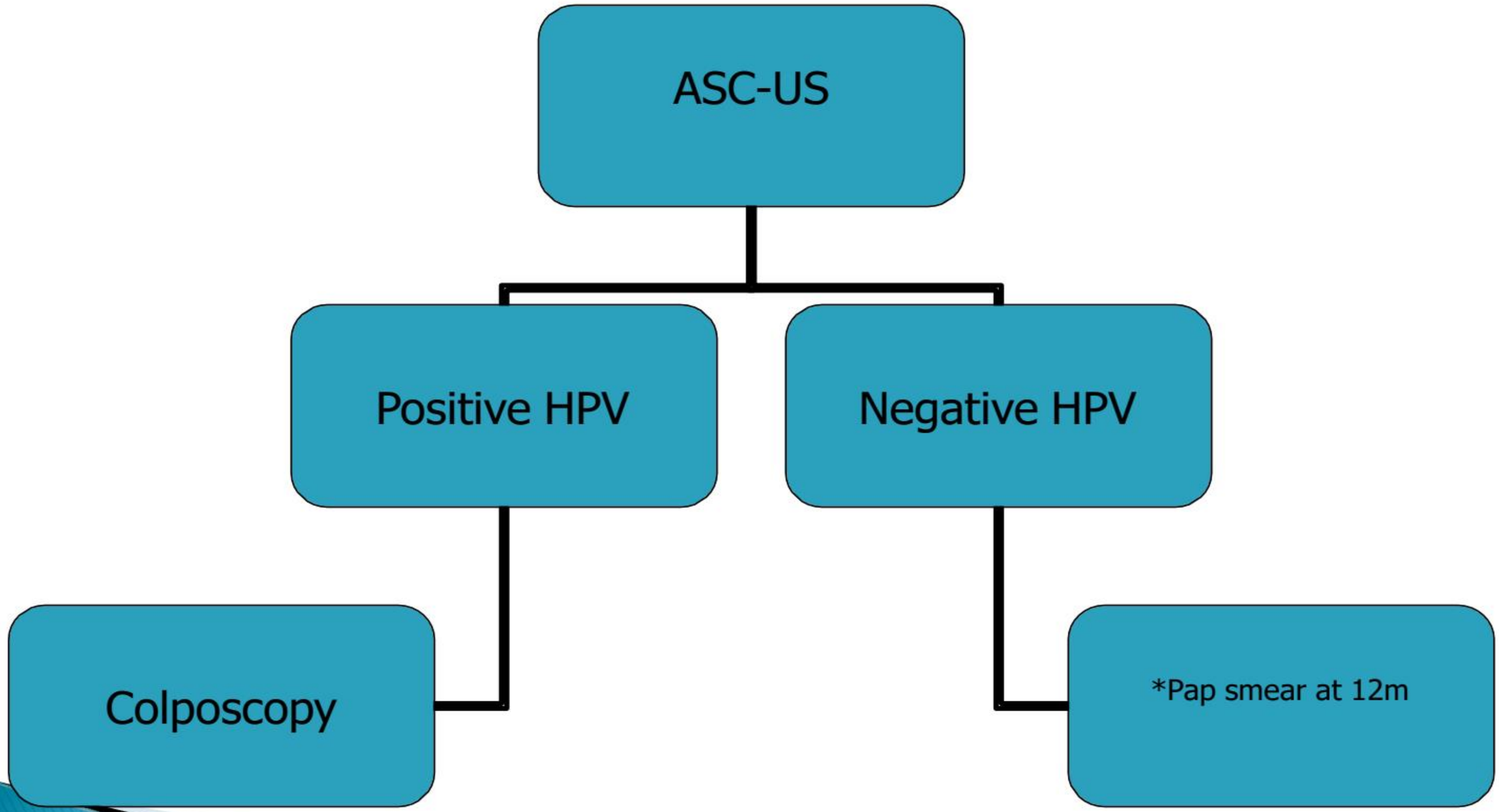
  Take **a Pap smear**

→ if it positive to ASC-US do the HPV test (in the same clinical visit).



Human papilloma virus has been linked to cervical cancer

Option 2: HPV testing

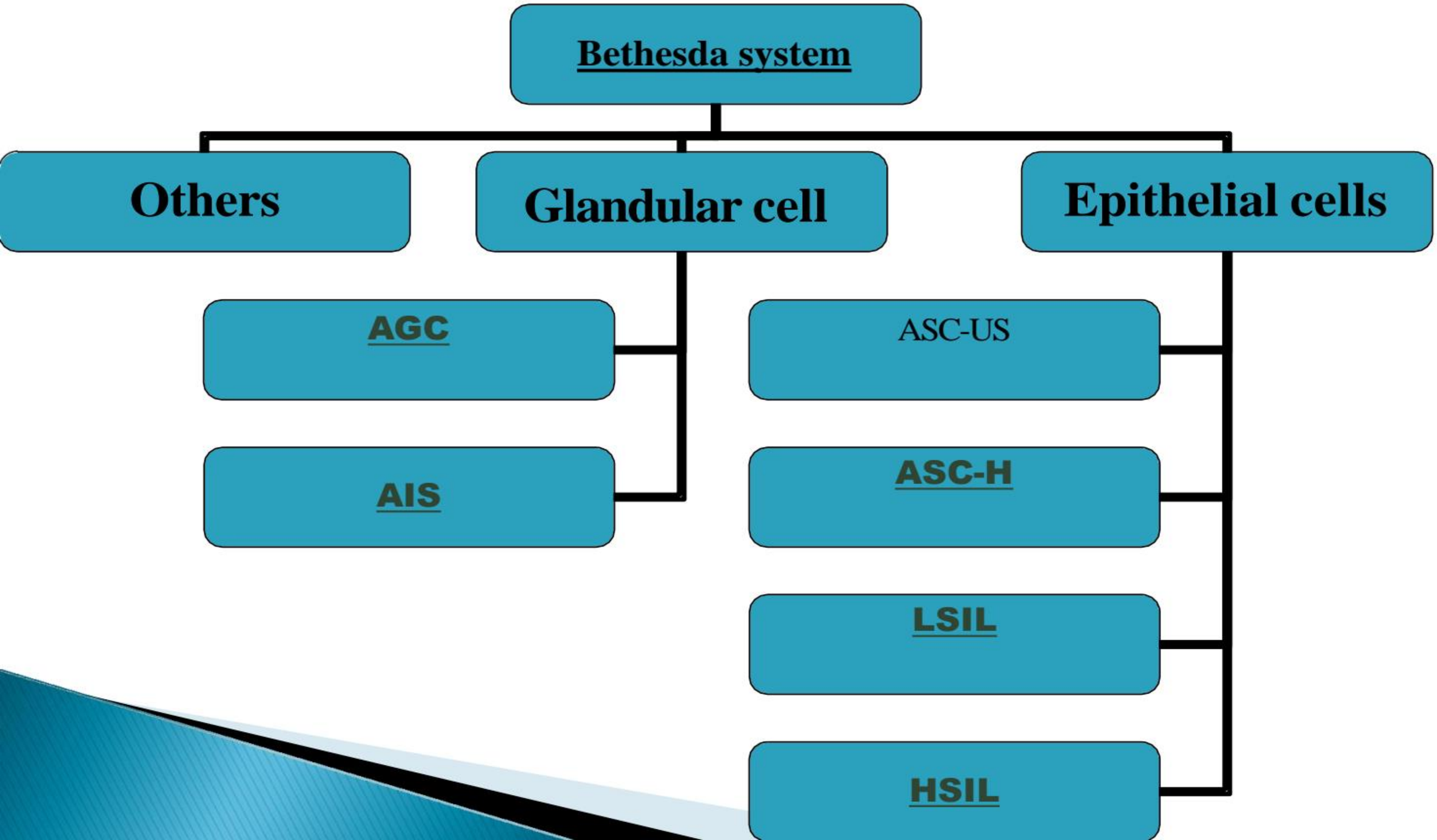


Option 3: immediate referral to colposcopy

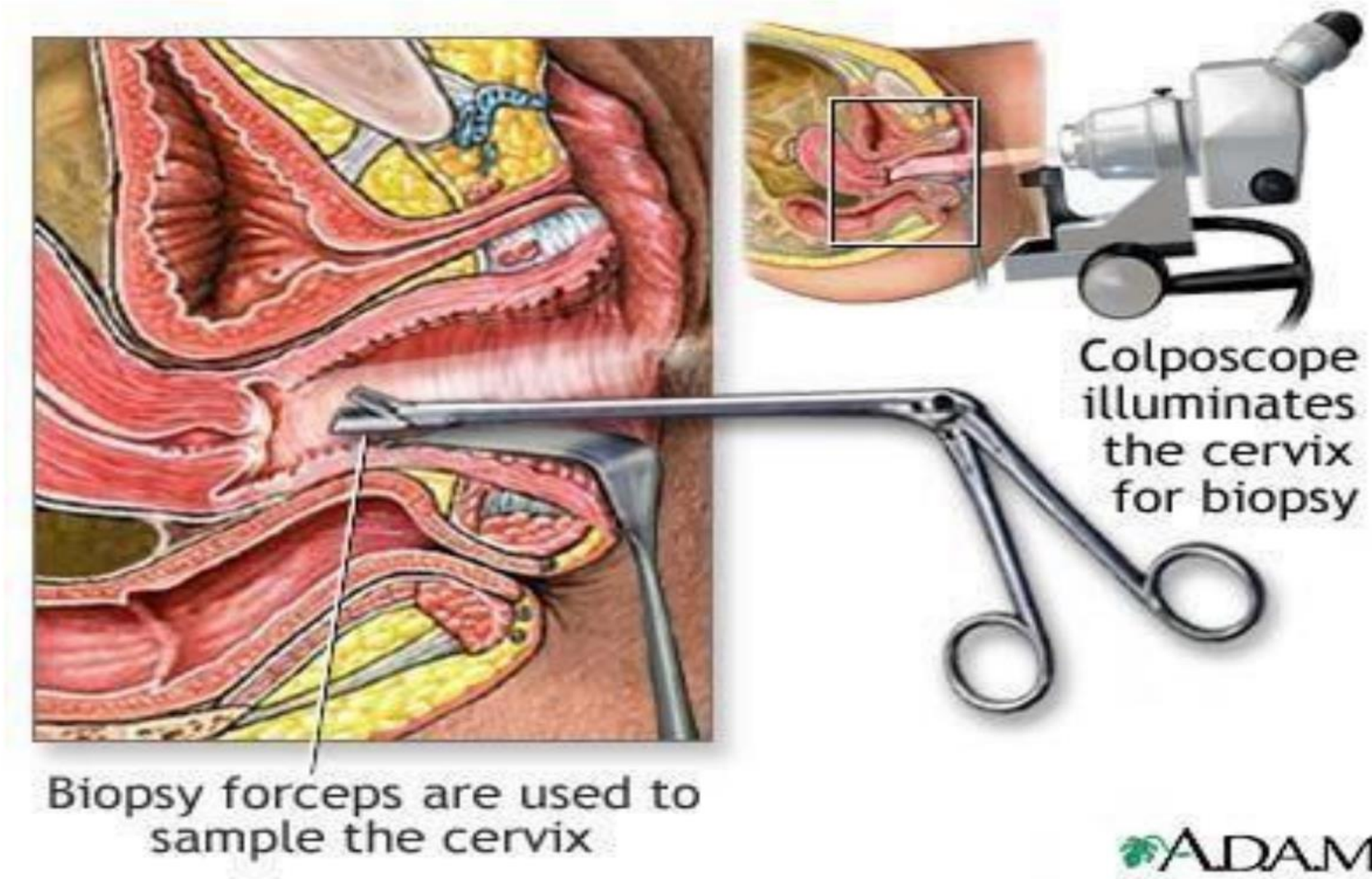
Done in these case of ASC-US if:

- Weakened immune system, i.e HIV
- If the female is unreliable

Immediately referral to colposcopy for biopsy



What is Colposcopy?



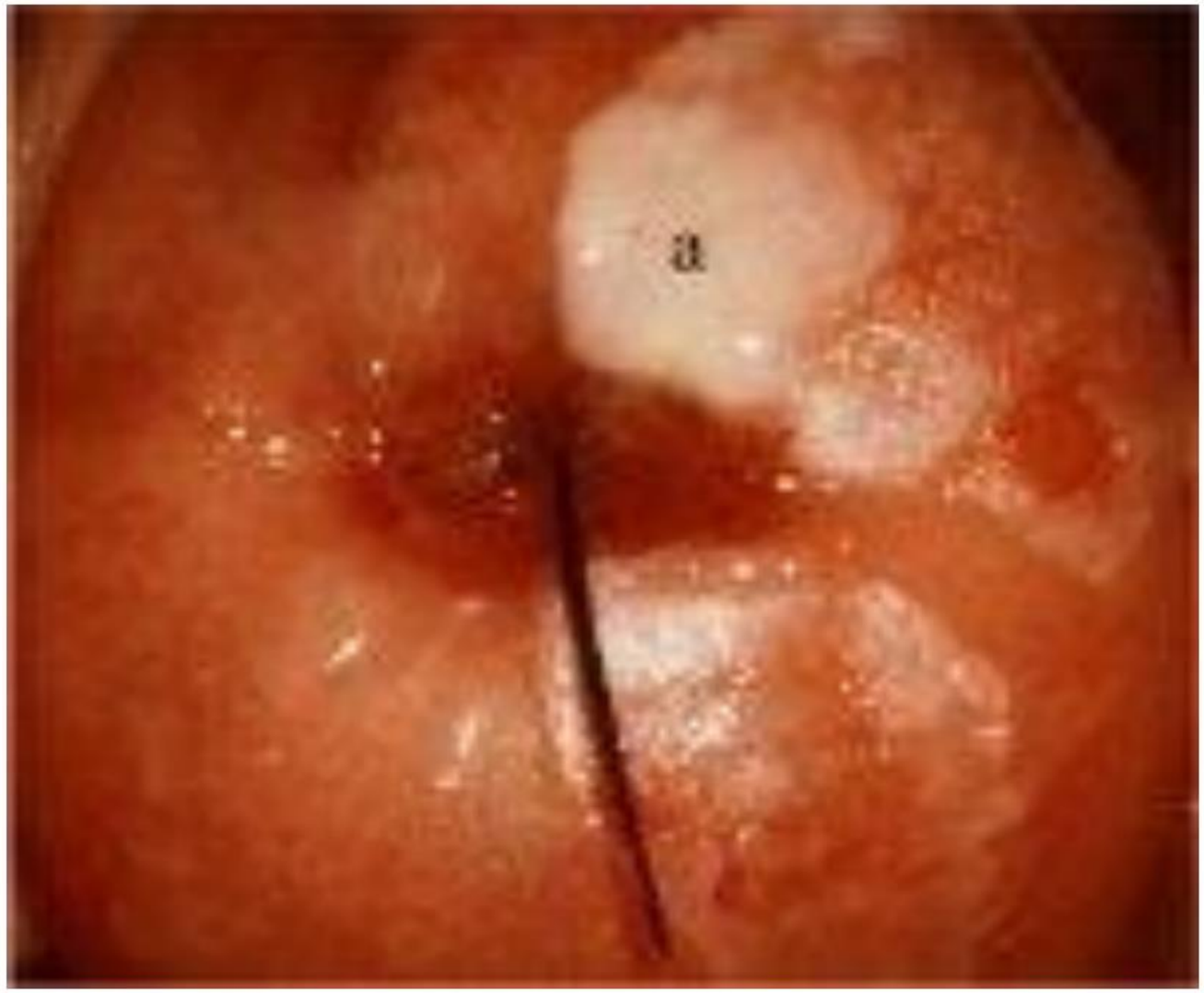
Steps of colposcopic examination

- The woman should be in the lithotomic position
- Insert the vaginal speculum and.
- Inspect the cervix with the colposcope.
- Apply acetic acid .
- Apply Lugol's iodine solution.
- Perform endocervical curettage, if necessary.
- Perform cervical biopsies .

1.The woman should be in a lithotomy position,
2.Insert the vaginal speculum
3. Inspect the cervix Looking for:

- **Gross abnormalities** (e.g., leukoplakia, condylomata).
- **blood vessels abnormalities.**
- **Identify the SCJand the transformation zone** for a satisfactory colposcopy.

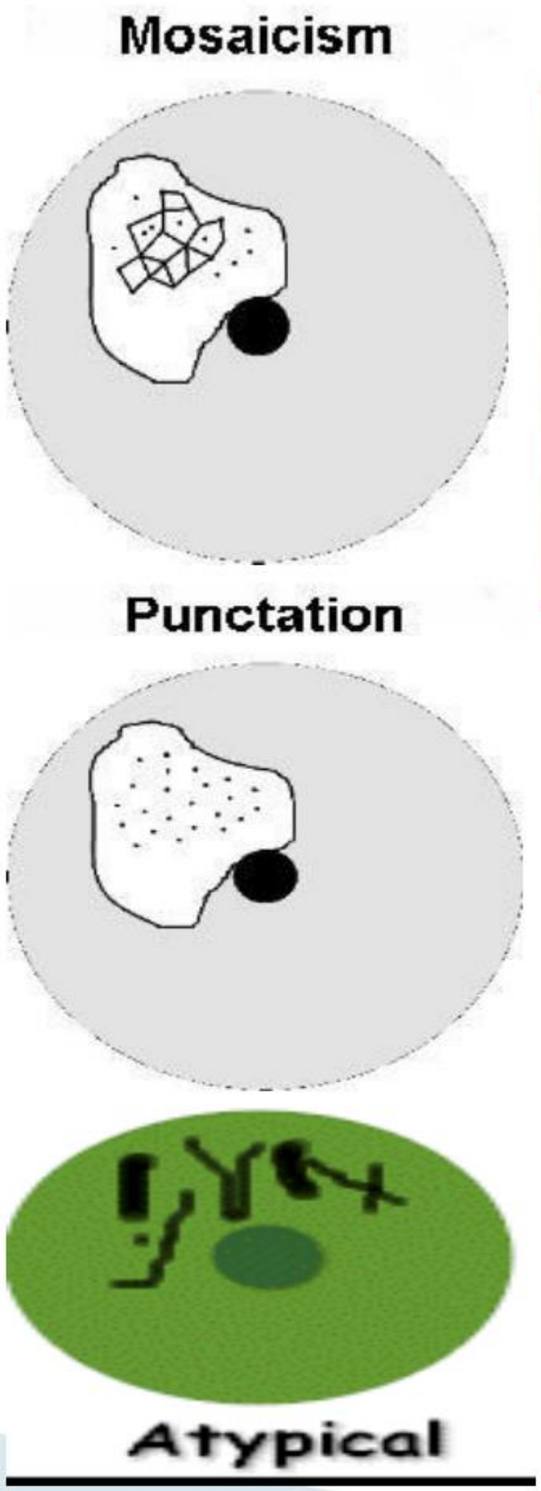
Gross abnormalities

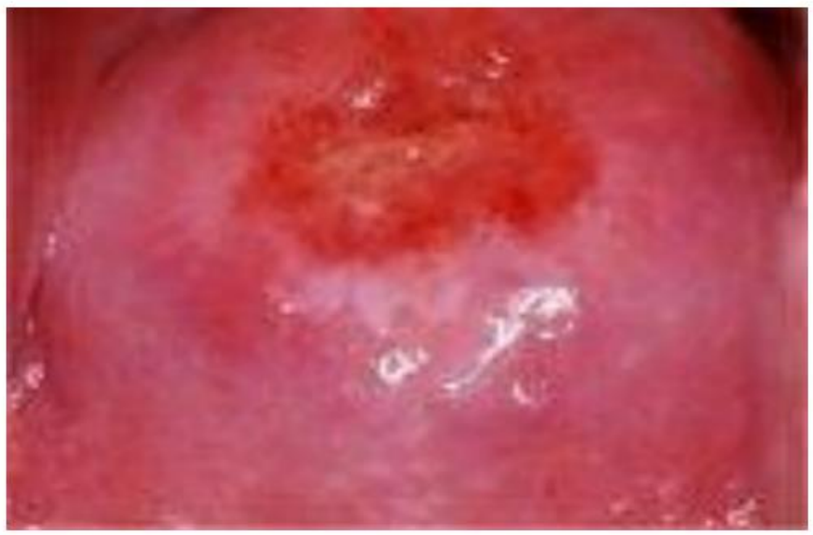


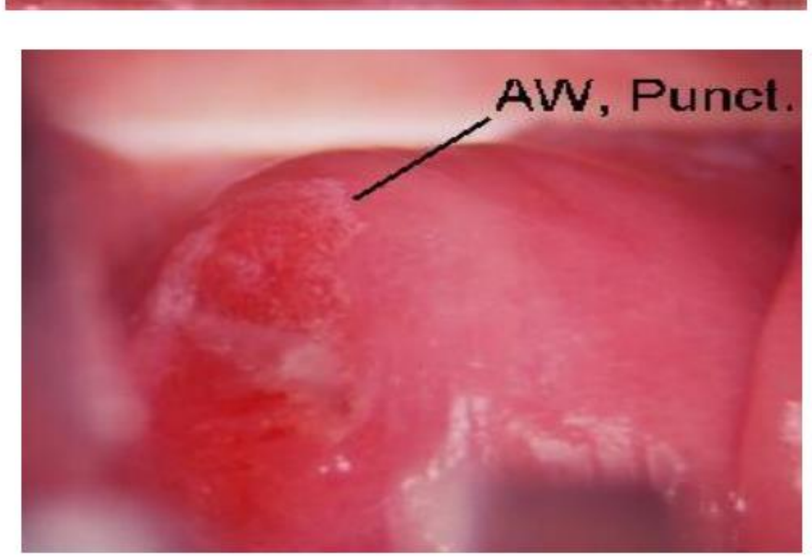
Abnormalities of the blood vessels

- **Mosaicism**
- **Punctation**
- **Atypical** : cork screw , comma-shape , spaghetti-like.

- **The higher the grade the larger and coarser the vessel abnormality.**







Identify the TZ and SCJ for a satisfactory colposcopy

- The inner border of the TZ is defined by

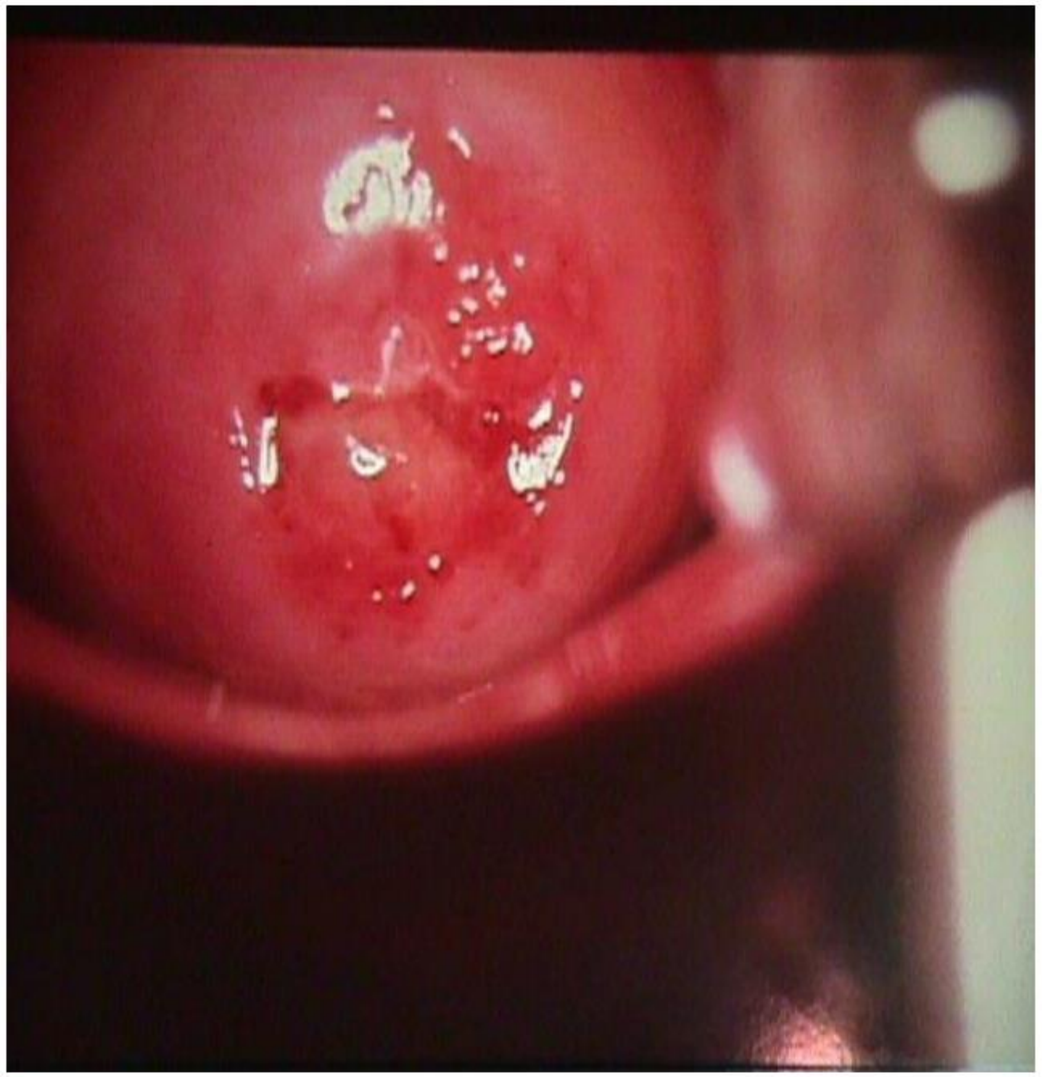
- The entire 360-degree circumference of the squamocolumnar junction.

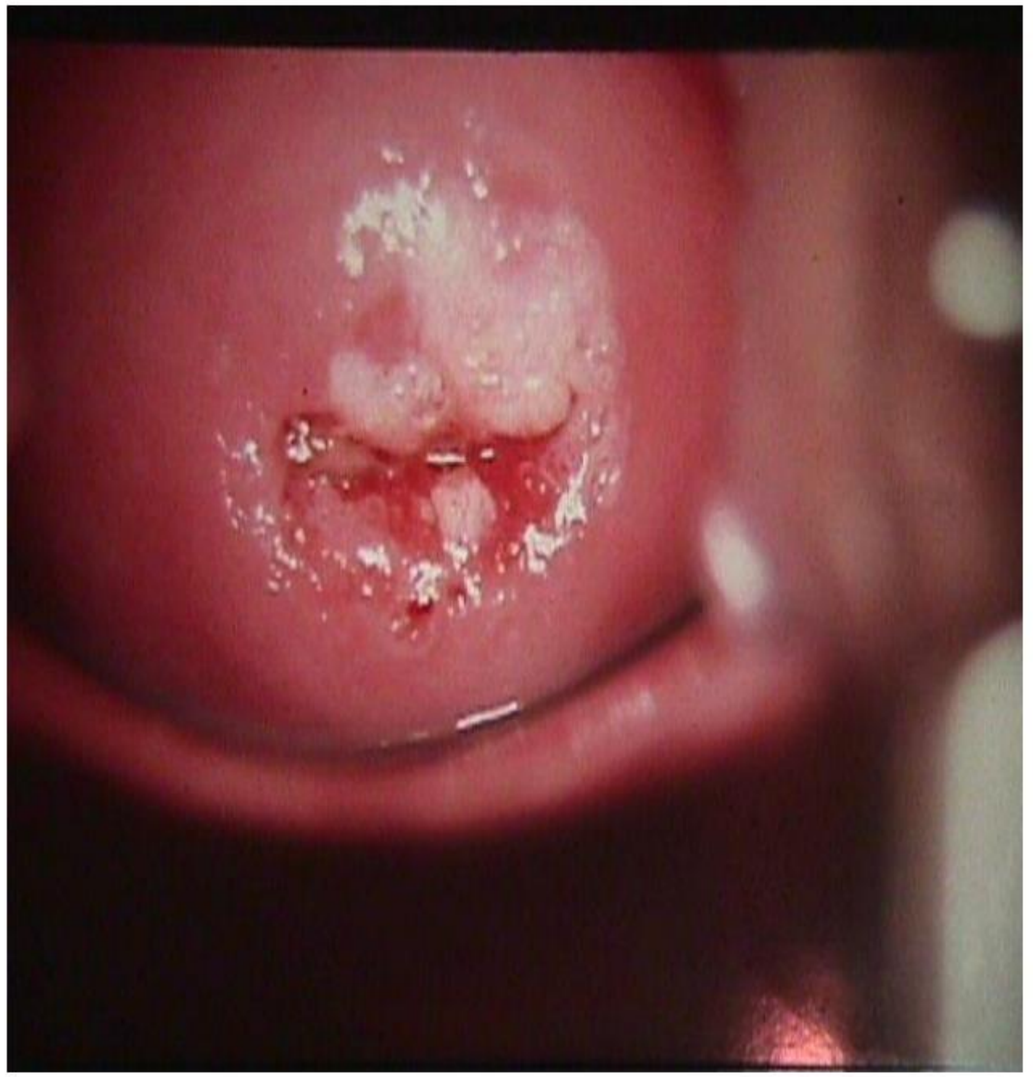
- If the junction is proximal to the external os, in the canal, it requires additional effort to visualize the entire junction.

- If the squamocolumnar junction is not visualized in its entire circumference, the colposcopic procedure is termed inadequate or unsatisfactory

Looking for hidden lesions ;

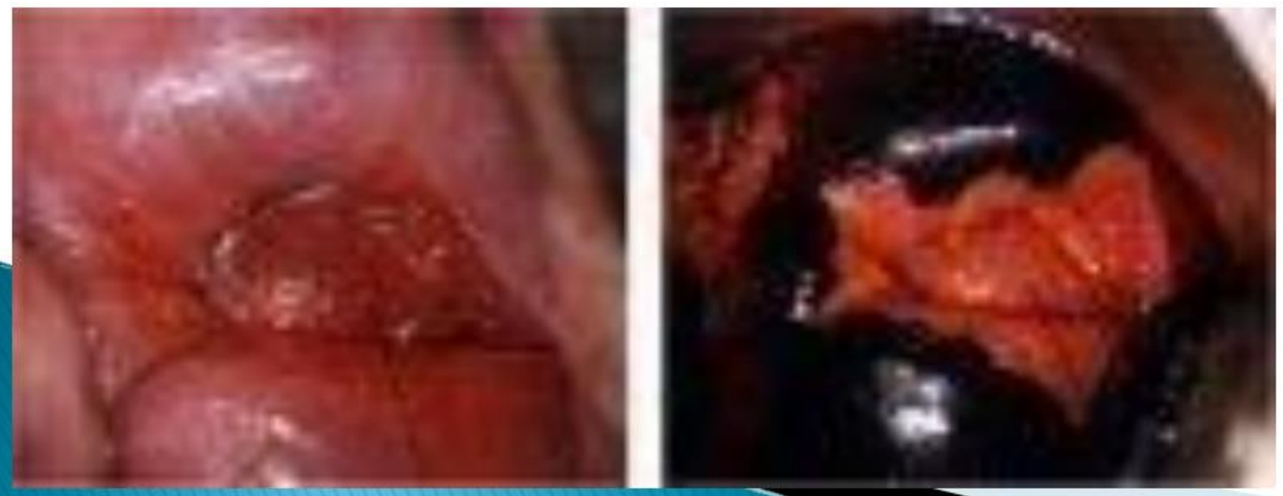
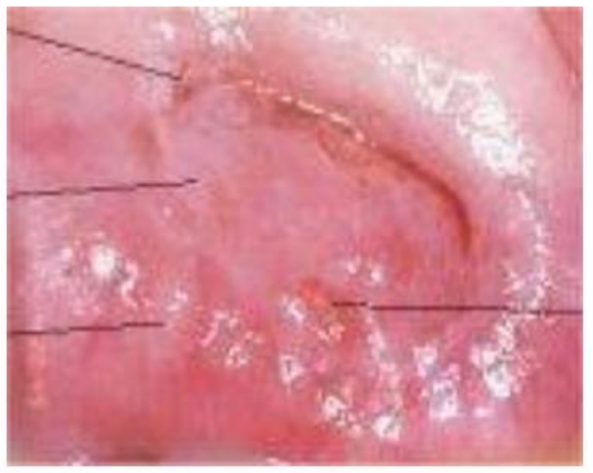
4. Applying 5% dilute acetic acid for aceto white changes

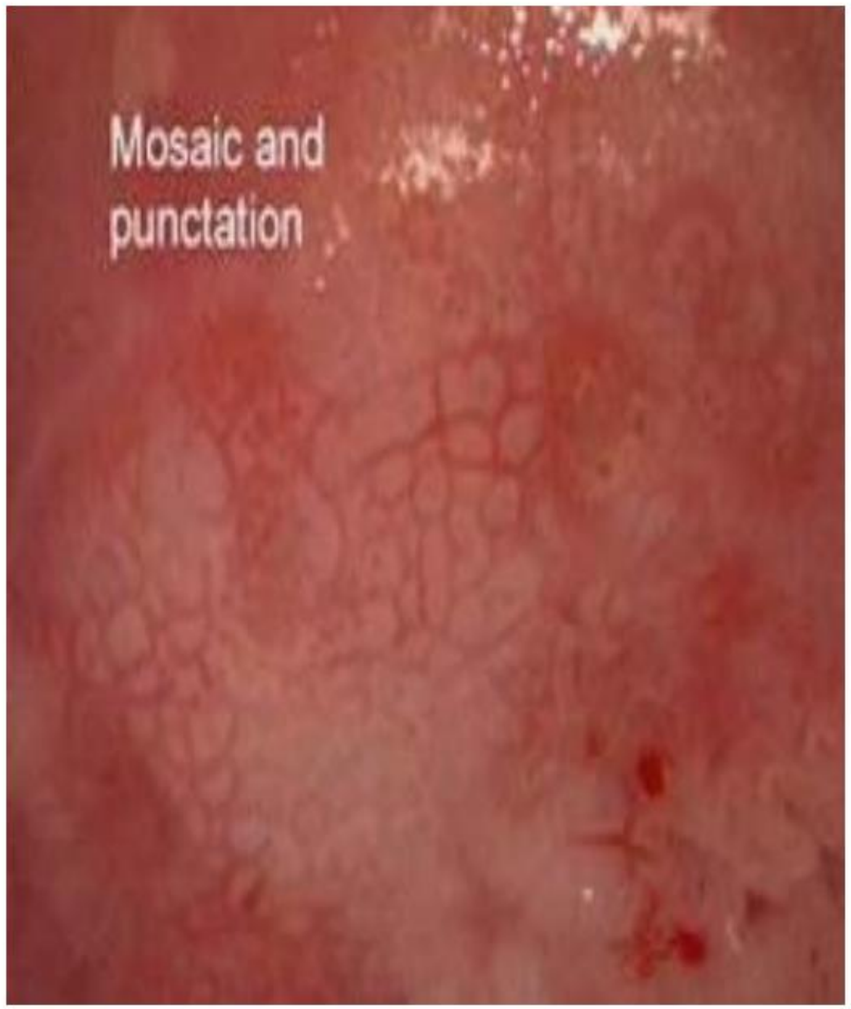


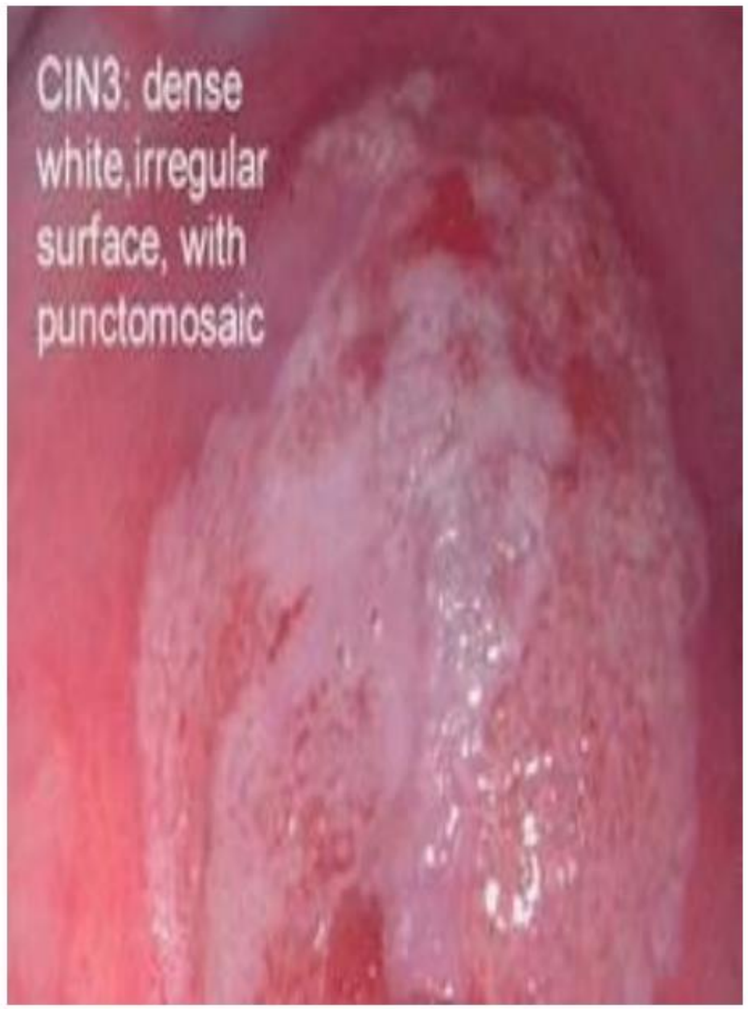


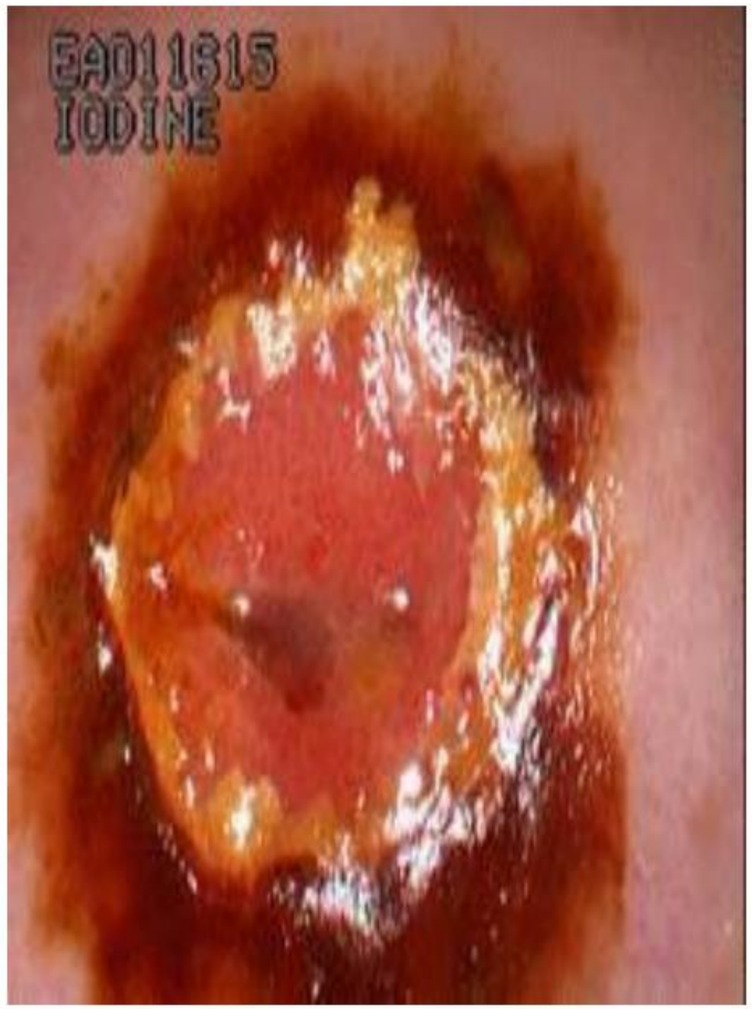
5. Applying Lugol's iodine solution

- normal squamous epithelial cells contain stores of glycogen that give a mahogany brown or nearly black stain
- Immature squamous metaplasia, inflammatory and regenerating epithelium and congenital transformation zone contain very little or no glycogen and either do not or only partially stain with iodine



Mosaic and
punctation


CIN3: dense
white,irregular
surface, with
punctomosaic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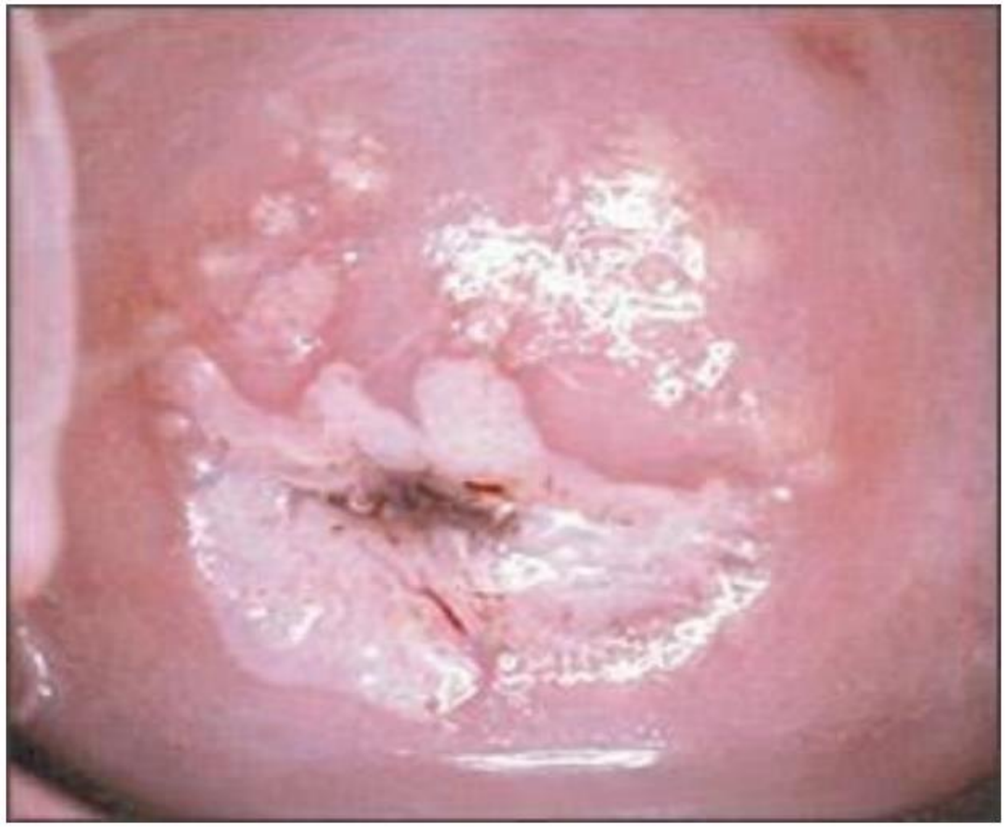
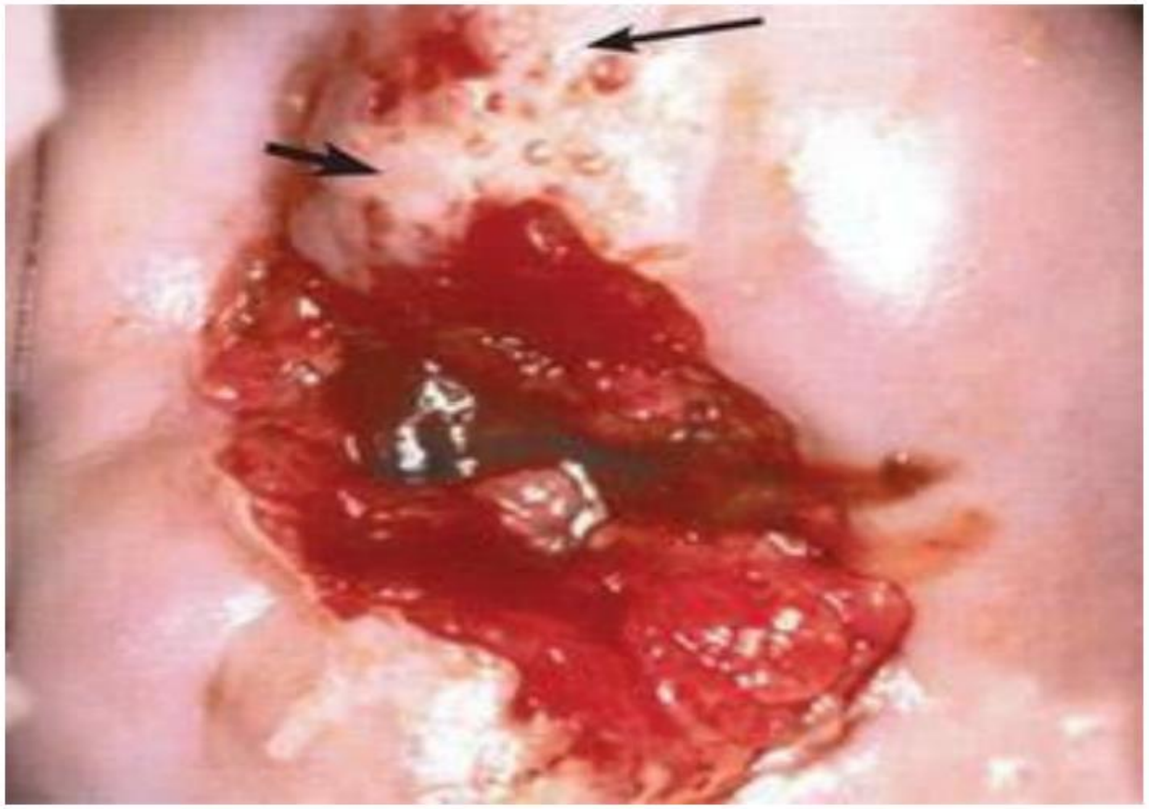


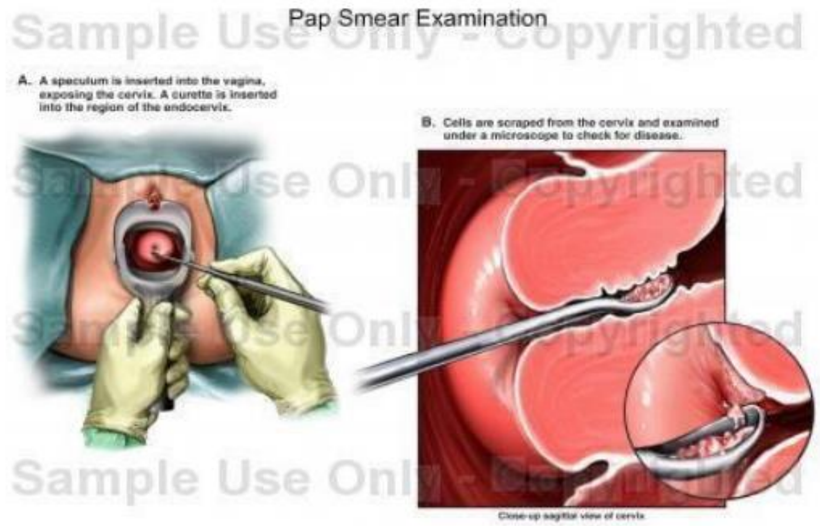


6. Perform endocervical curettage, if necessary

- the woman has been referred because of an abnormal pap smear and the colposcopic examination of the ectocervix has not revealed any abnormality,

- a glandular cell abnormality on pap smear (regardless of the findings of the colposcopic examination).

- unsatisfactory colposcopic examination (whether or not a cervical lesion has been detected)



7. take a biopsy

Depending on the colposcopic findings

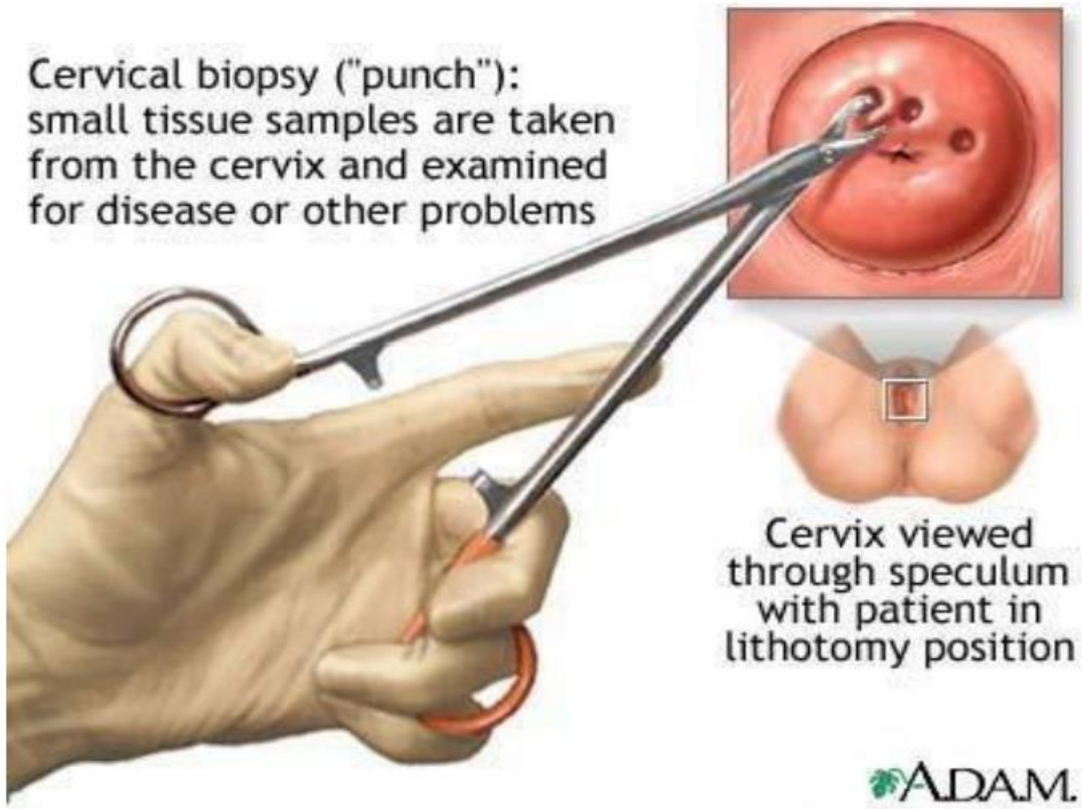
Punch biopsy (for exclusive Ectocervical lesions)

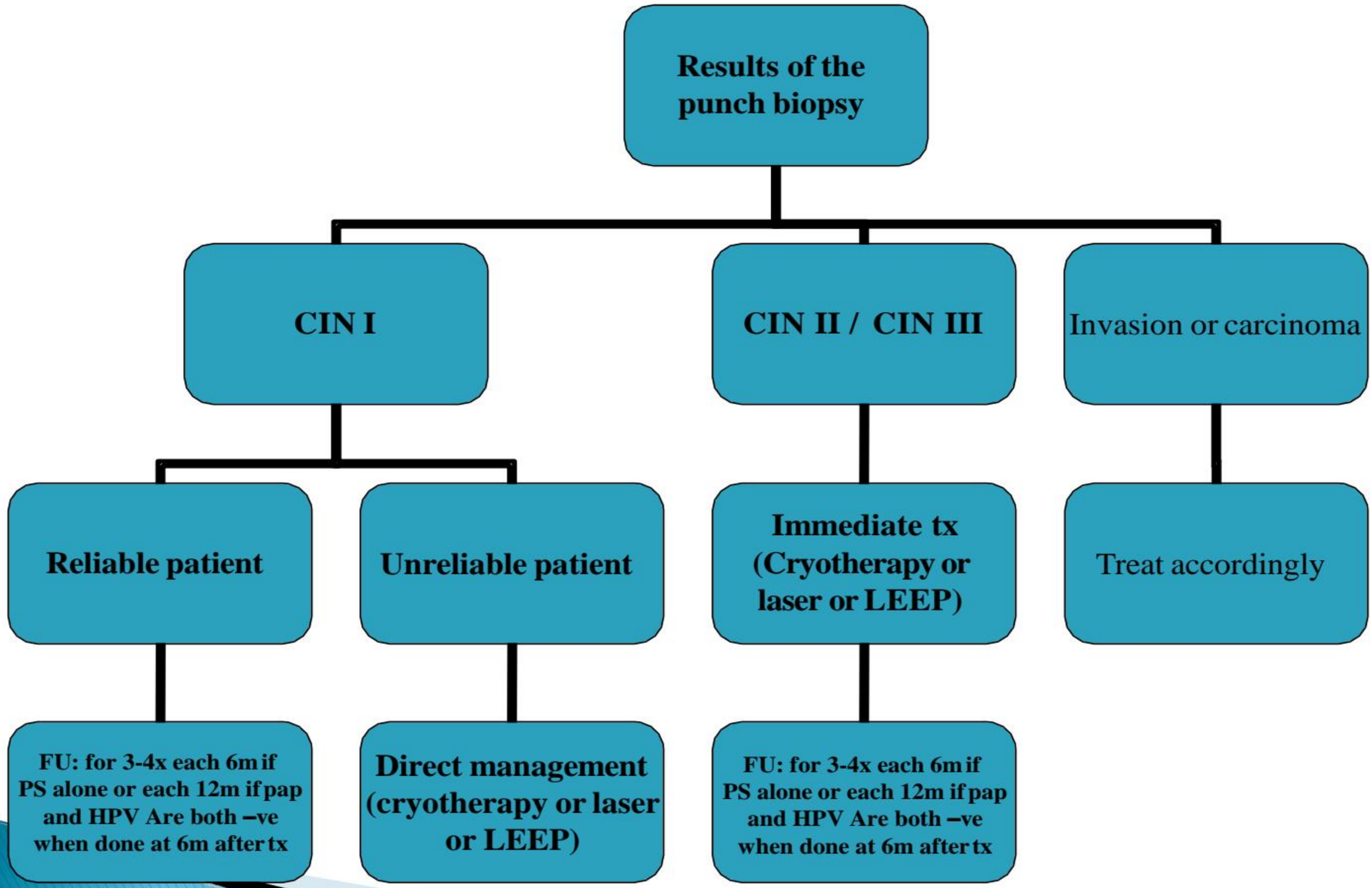
Cone biopsy (for suspected endocervical lesions)

Punch biopsy

If all,

- The colposcopy is satisfactory
- The lesion is in the ectocervix (not extending to the endocervix)
- The ECC is negative




Results of the punch biopsy
CIN I
CIN II / CIN III
Invasion or carcinoma
Reliable patient
Unreliable patient
Immediate tx (Cryotherapy or laser or LEEP)
Treat accordingly
FU: for 3-4x each 6m if PS alone or each 12m if pap and HPV Are both –ve when done at 6m after tx
Direct management (cryotherapy or laser or LEEP)
FU: for 3-4x each 6m if PS alone or each 12m if pap and HPV Are both –ve when done at 6m after tx

Treatment options

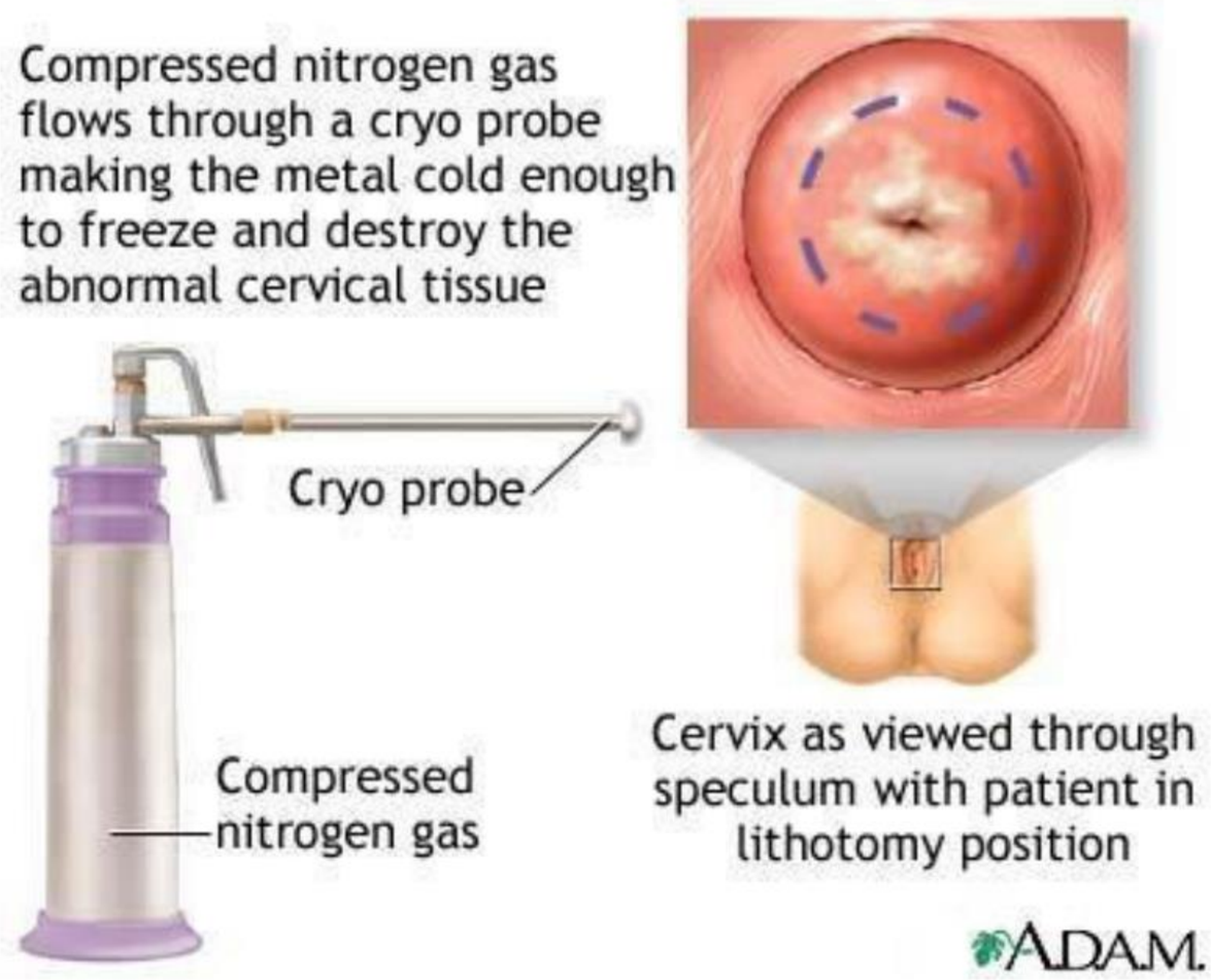
Ablative techniques
used after punch biopsy to treat Abnormal lesions)

- cryotherapy
- superficial excision by LEEP
- laser ablation

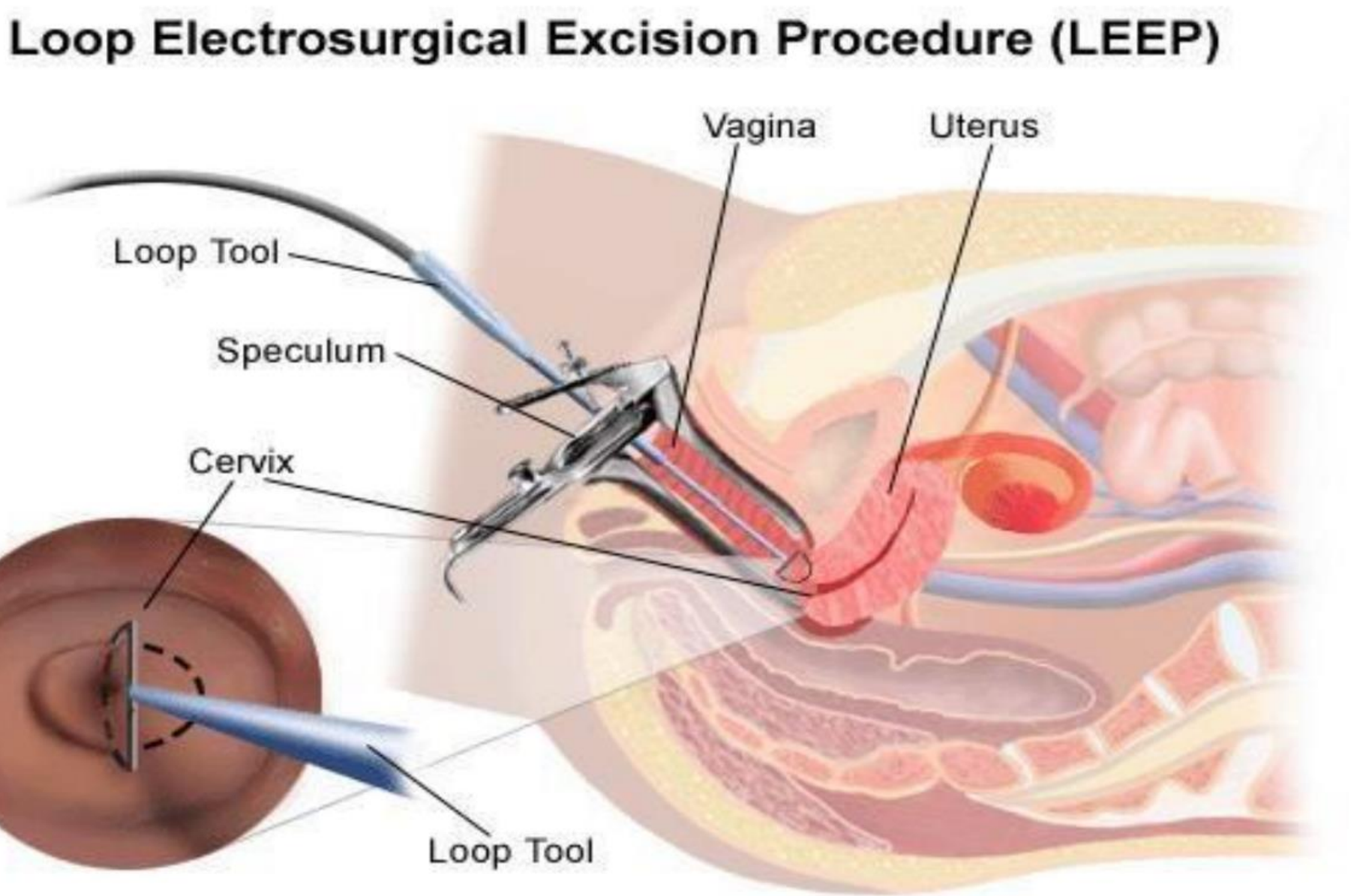
Excisional procedures
(theraputic and diagnostic)

- cold knife conization
- Deep LEEP
- laser cone excision

Killing the abnormal ectocervical cells by freezing them ; CRYOTHERAPY



Killing the abnormal ectocervical cells by burning them ; LEEP OR LASER .



Depending on the colposcopic findings

Punch biopsy (for exclusive ectocervical lesions)

Cone biopsy (for suspected Endocervical involvement)

Doing a cone biopsy

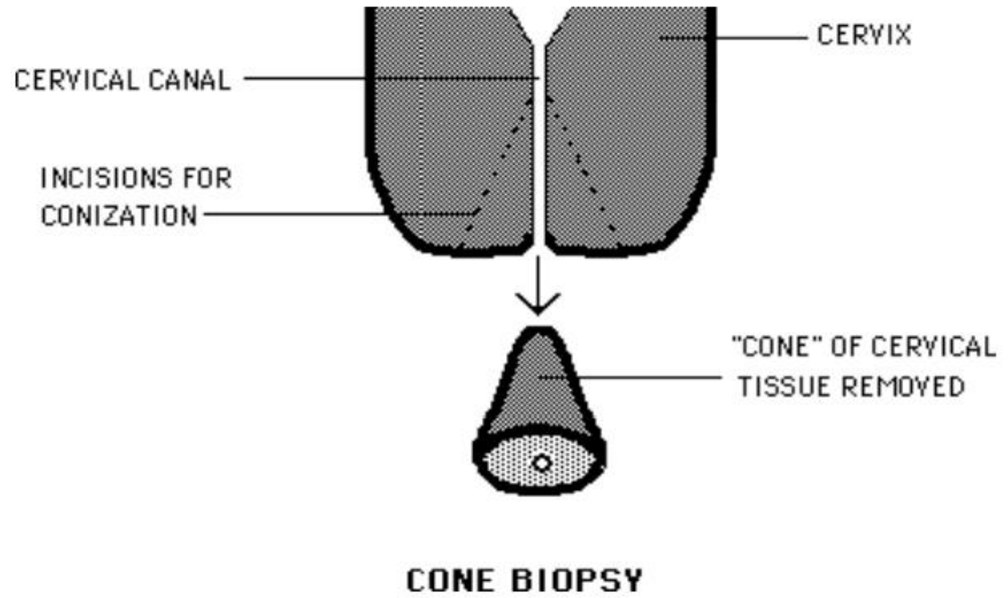
If either ,

*The colposcopy is unsatisfactory

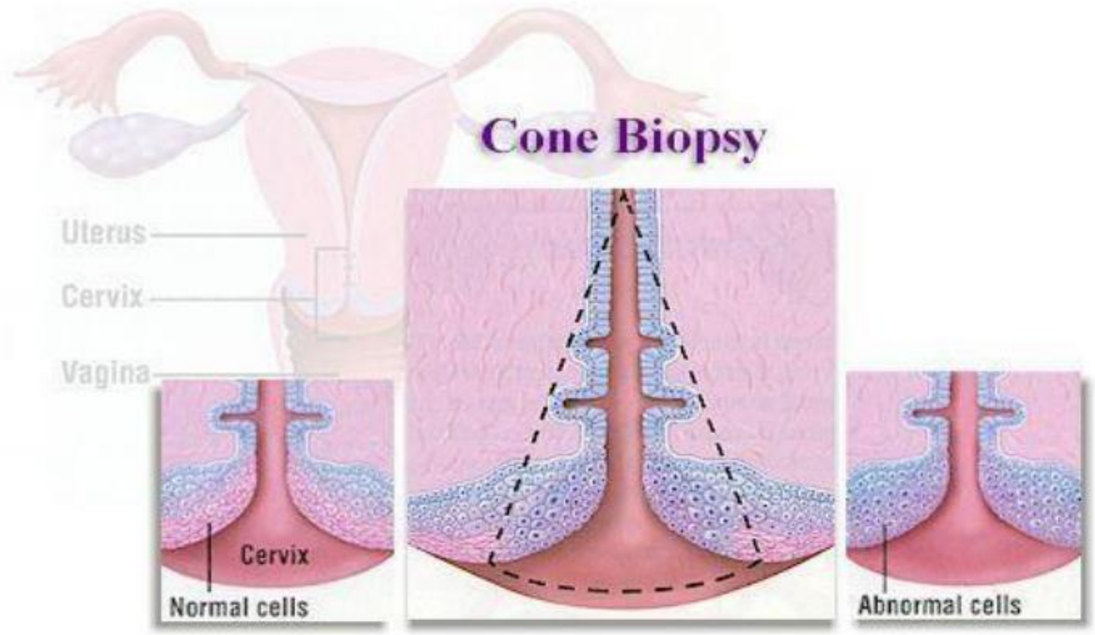
Or *The lesion extends to the endocervix

Or *The ECC is +ve for abnormal cells

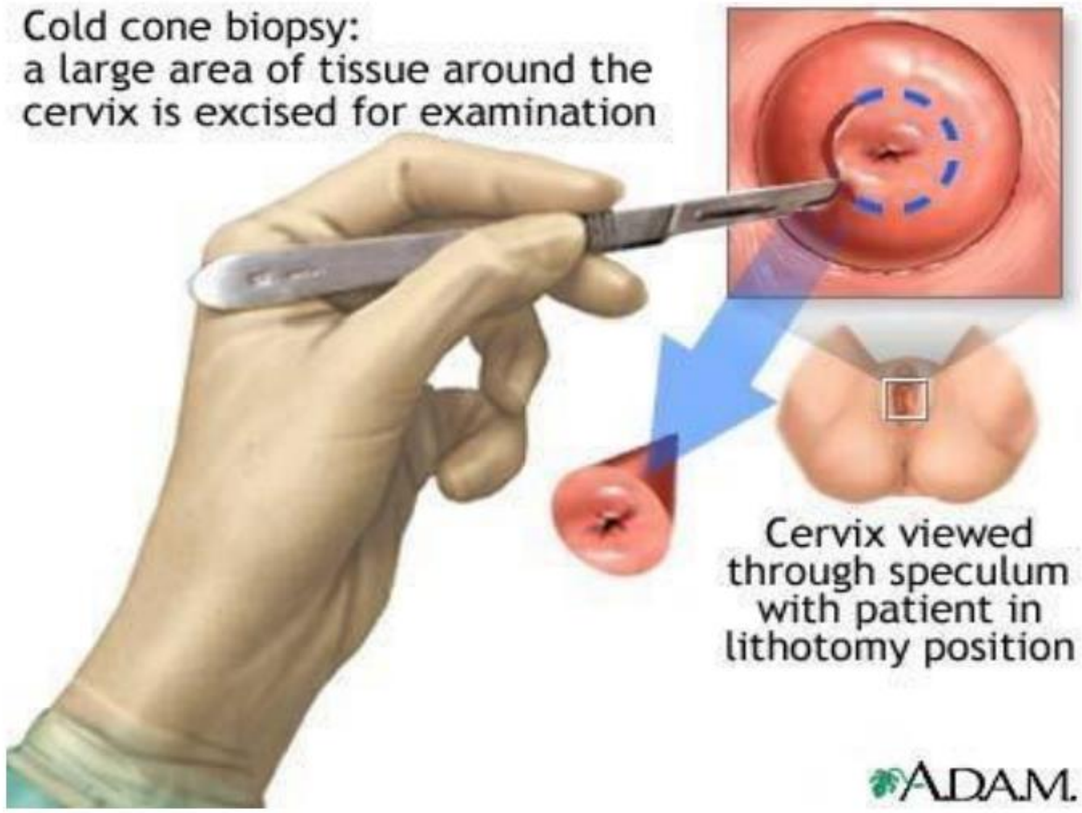
This is a Therapeutic and diagnostic method



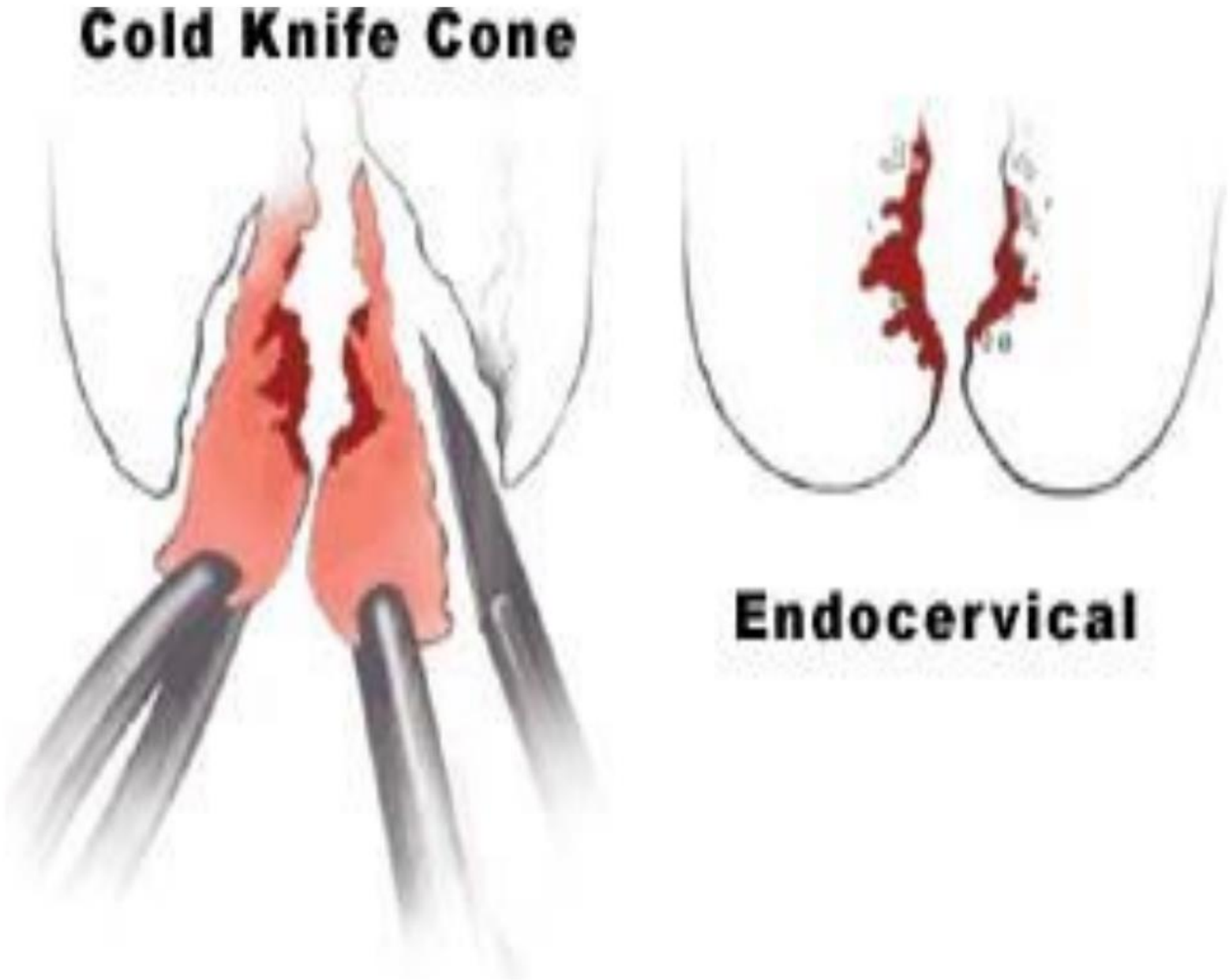
CONE BIOPSY



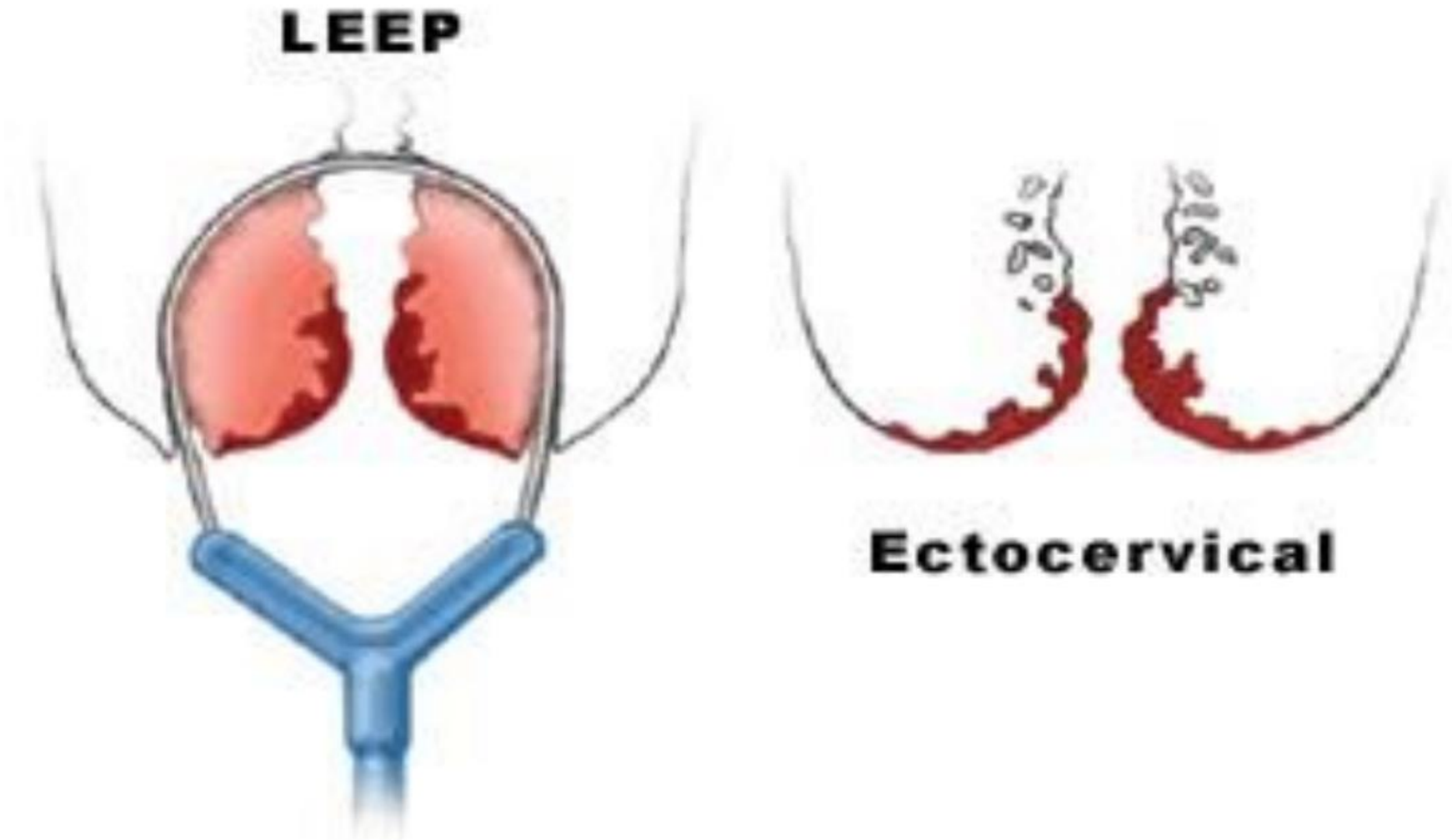
Taking a biopsy by using a cold knife ; “ COLD CONE BIOPSY ”



COLD CONE BIOPSY



Taking a biopsy by using the LEEP



Do a cone biopsy by
Cold knife or LEEP

CIN II
CIN III

FU: for 3-4x each 6m if PS alone or each 12m if pap and HPV Are both –ve when done at 6m after tx

Micro invasive

Individualize mgx depending on desire of fertility **(conservative vs. hysterectomy)_**

Invasive cancer

Definitive therapy

Follow up

- **Treatment cures over 90% of patients with CIN.**

- **Recurrent abnormalities in 12% of low risk patients and 50% of high risk patients ….so life long follow up.**

Special situations

Pregnancy..

- Done routinely at the first prenatal visit, so an abnormal cervical smear could be discovered during pregnancy .
- *Colposcopy* is performed for the same indications as in the nonpregnant women.
- *Biopsies* are limited unless there are colposcoic signs suggestive of CIS or invasive disease.
- *ECC* is NOT performed in pregnancy, cz of risk of abortion or infection
- If dysplasia is diagnose , repeat cytology and colposcopy each trimester. Repeat biopsy is only done for progressive lesions
- Treatment is postponed to the postpartum period , because
  High risk of pregnancy loss and complications
  High grade lesions discovered during pregnancy have a high rate of regression in the post partum period
  Transformation from CIN to carcinoma takes a long time (an average of 10 years or so).
- Conization during pregnancy is indicated if " early invasive disease" is suspected.

Prevention

- HPV vaccine (Gardasil®)
- Protected sexual contact
- Smoking cessation

HPV vaccine

HPV vaccine (Gardasil):

- for females in between 8-26 yo (mainly 11,12)
- 3 doses are given at 0,2,6 months
- costly
- not recommended for pregnant, lactating or immunosuppressed

- Hacker and Moore’s essentials of obstetrics and gynecology
- Up to date