

# Benign and premalignant disease of the cervix

Dr Sushma Sharma

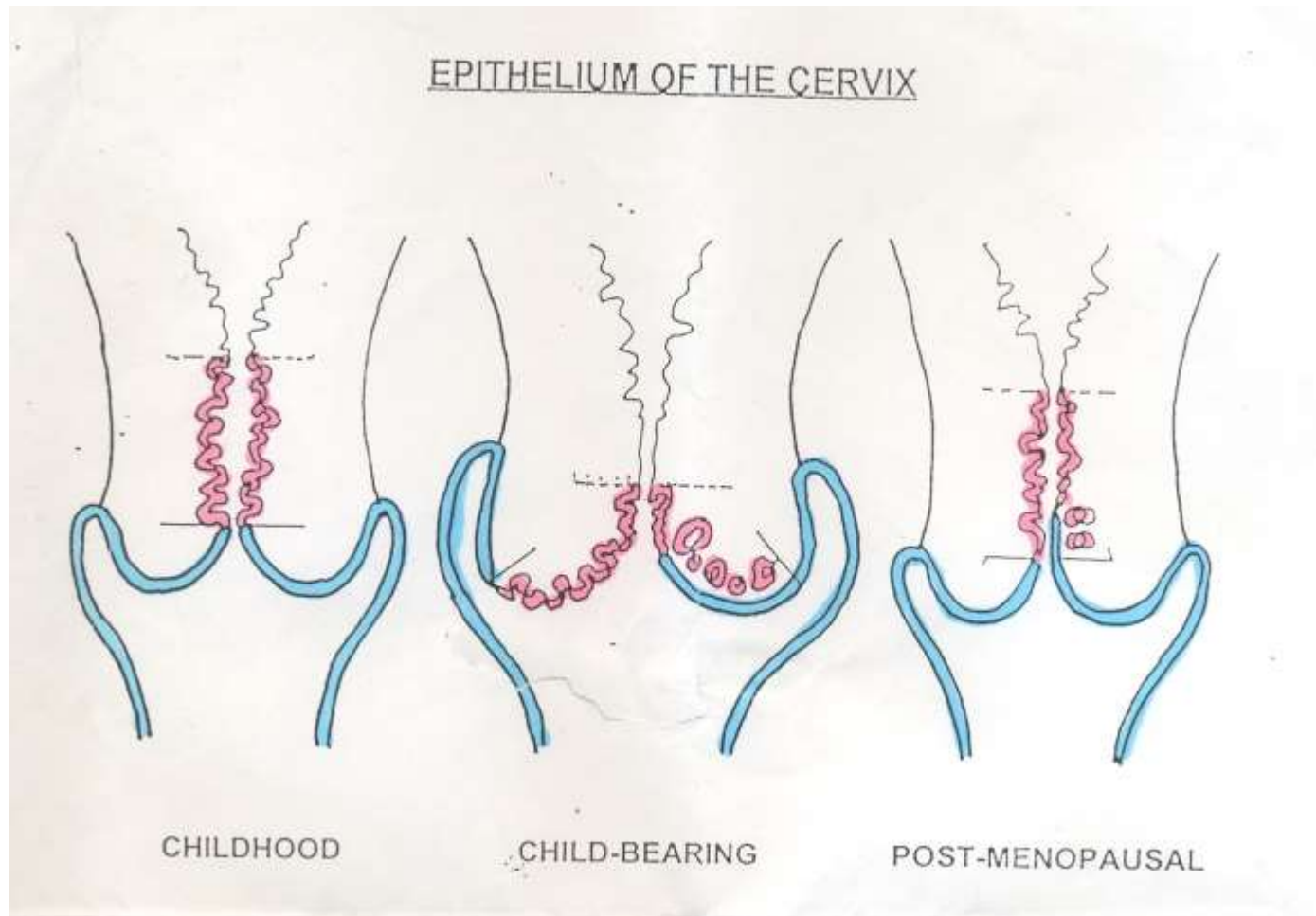
# Introduction

- Benign diseases of the cervix are common and are unusually asymptomatic or cause minor symptoms but must be differentiated from malignancy.
- Cervical cancer is the second commonest cancer in women. It is preceded by a premalignant form years before its invasion.
- Screening for premalignant disease of the cervix markedly reduces the deaths from cervical cancer.

# objective

- To understand the normal cervical epithelium
- To be able to define metaplasia and dysplasia.
- To understand the concept of cervical screening.
- To outline the principles of colposcopy.
- To outline the management of CIN

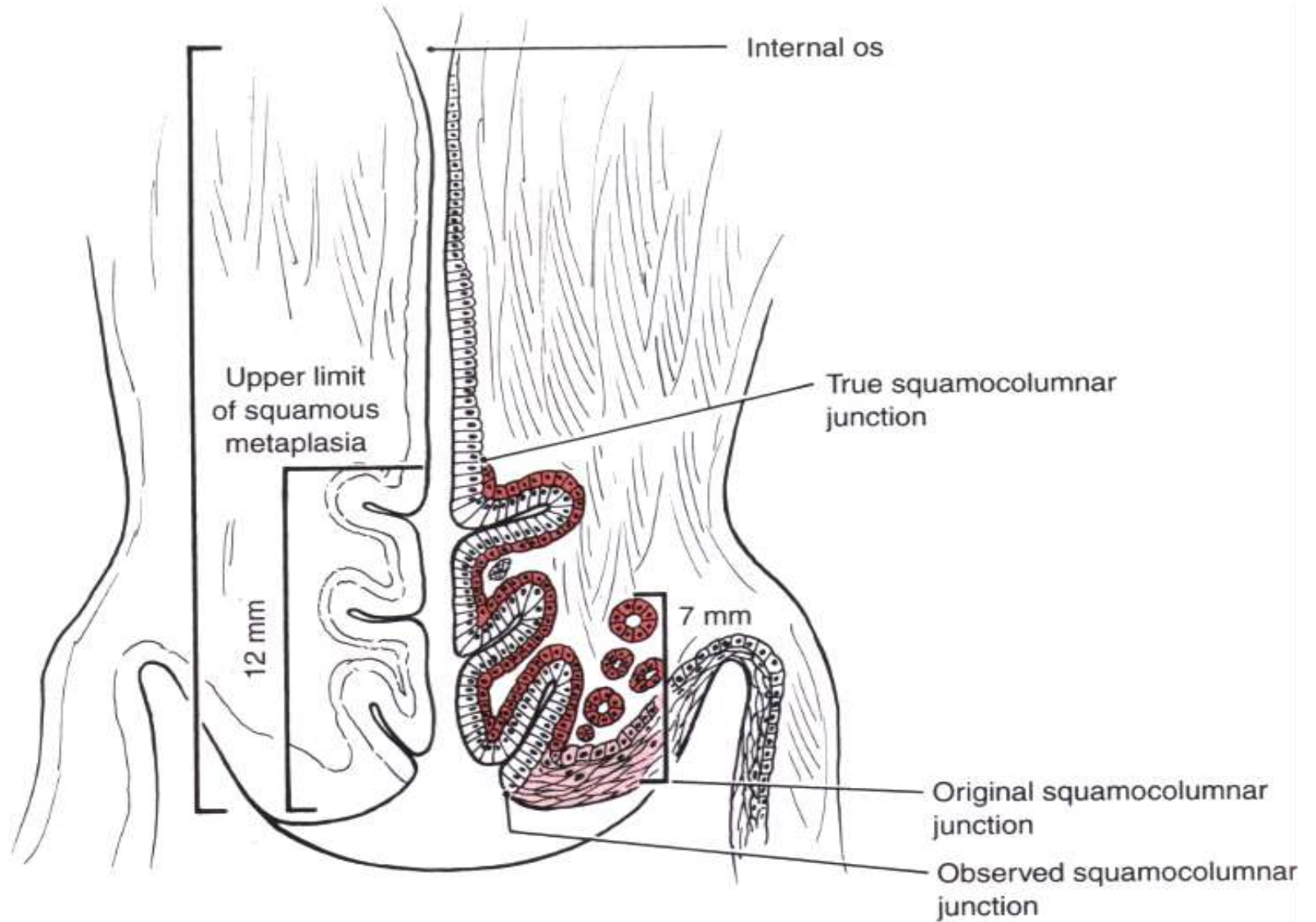
# Epithelium of the cervix



# THE CERVICAL TRANSFORMATION ZONE

The cervical transformation zone extends from the endocervical margin of the original squamous epithelium of the ectocervix to the identified squamo-columnar junction.

Over 95% of all cervical intraepithelial neoplasias (CIN) arise within the transformation zone of the cervix.



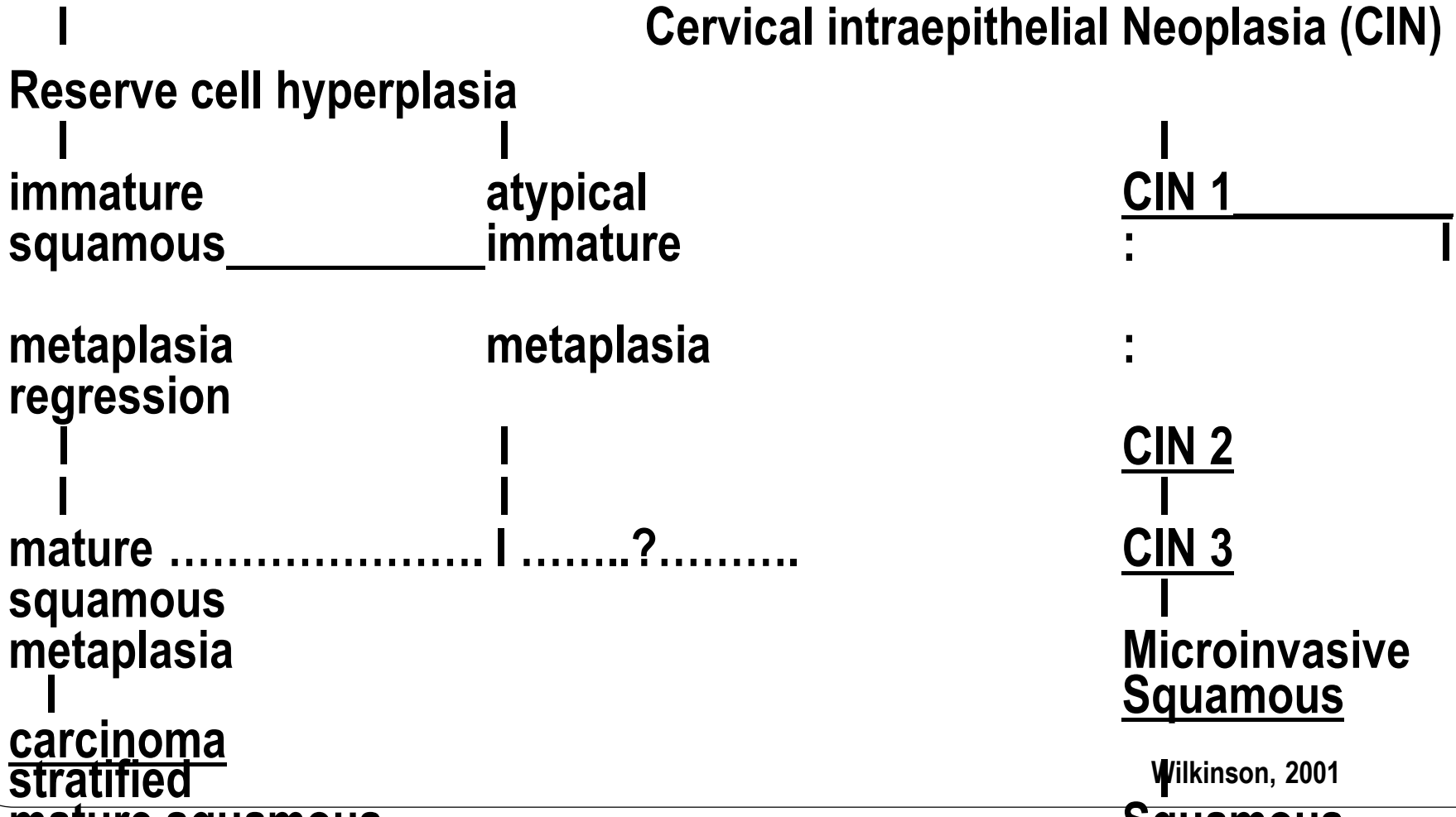
**Figure 8.3** The anatomy of the transformation zone.

# NORMAL AND NEOPLASTIC CELLULAR CHANGES WITHIN THE TRANSFORMATION ZONE

Normal Reserve Cell

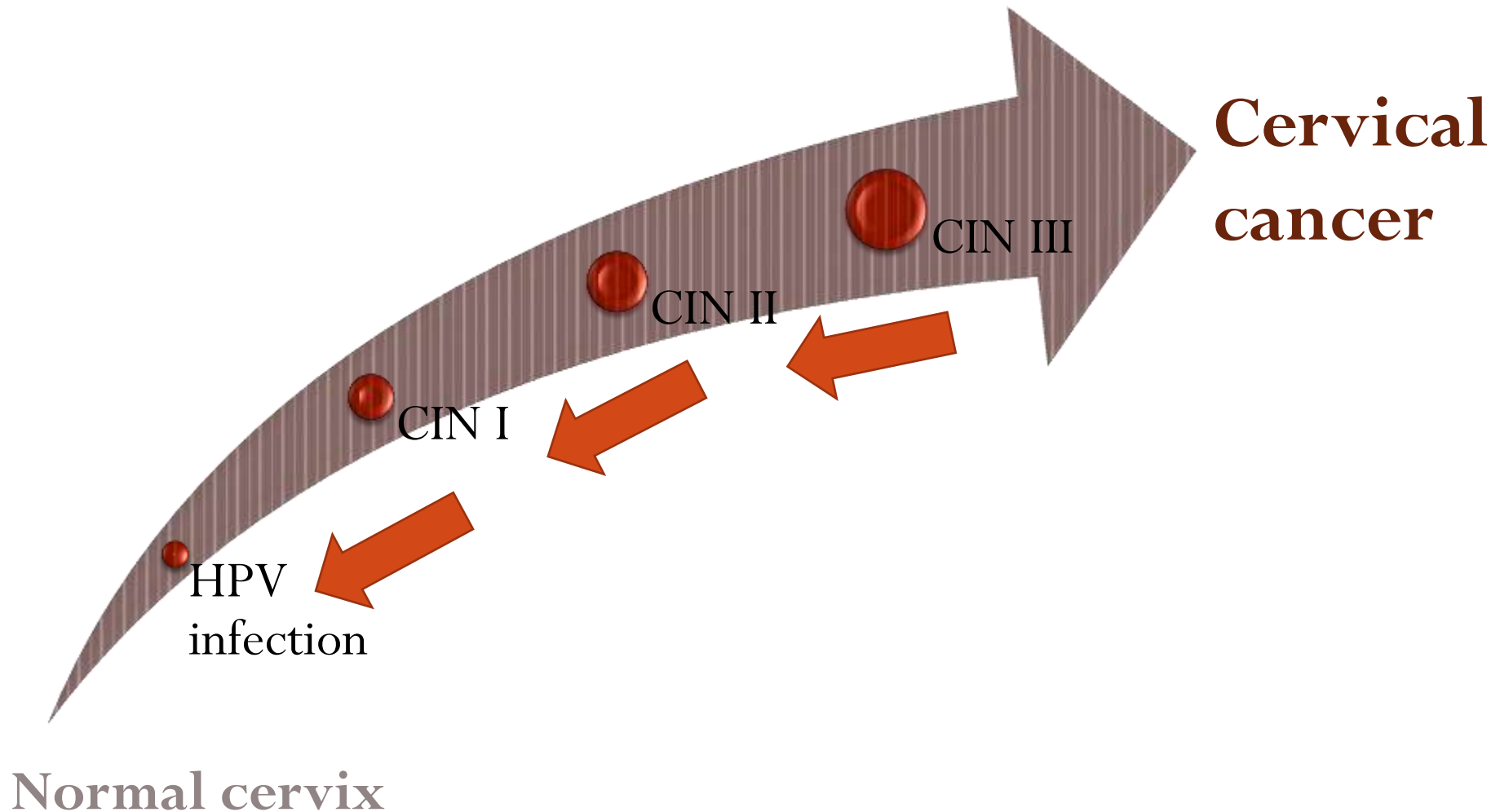
Neoplastic Transforming Factors

Cervical intraepithelial Neoplasia (CIN)



Wilkinson, 2001

# Premalignant disease of the cervix





# HPV infection

- DNA virus.
- Over 100 different types and subtypes of this virus.
- Common infection effecting epithelial surface.
- Genital HPV is divided into
  - Low risk type (HPV 6,11) cause genital warts.
  - High risk types (HPV **16, 18**, 31, 33, 45, 56).
- HPV is a common infection while cervical cancer is a rare disease.

# HPV is Epitheliotropic

- **No viremia**
- **Infection is confined to where it initiated**
- **Spreads by infected cell dividing.**

## **Factors that increase risk of transmission:**

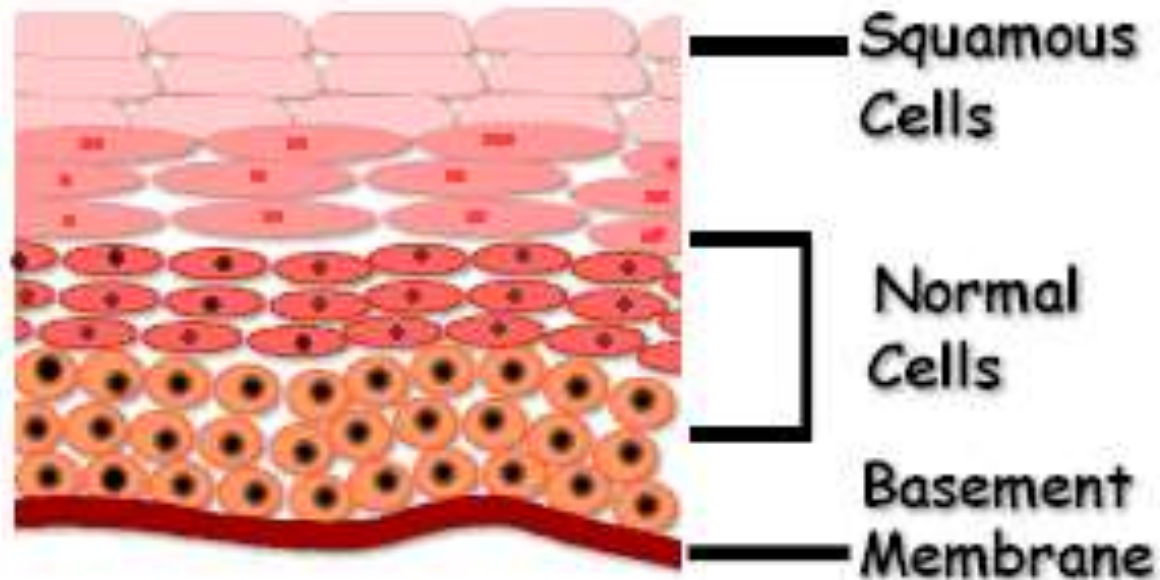
- Smoking.
- Increasing parity.
- Early age of intercourse.
- Oral contraceptive pills.
- Immunity.

# Cervical intraepithelial neoplasia

- Metaplasia: change of epithelium from one cell lining (columnar) to another (squamous).
- Dysplasia: abnormal epithelial cells that fail to mature. (hyperchromasia, larger, variable size, mitosis).  
it may be mild, moderate or severe

# Cervical Dysplasia: Classification

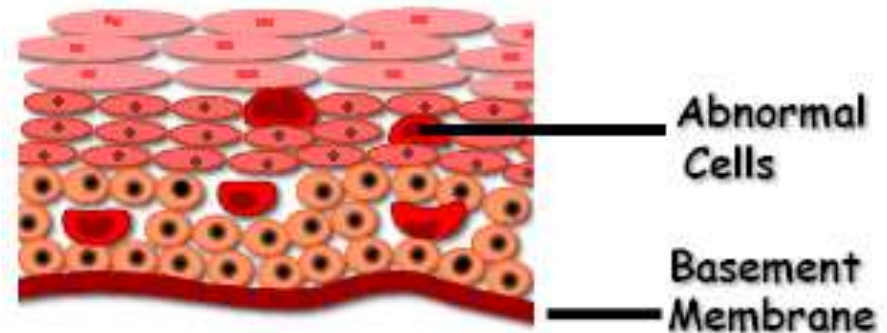
## Normal Cervix



# Cervical Dysplasia: Classification

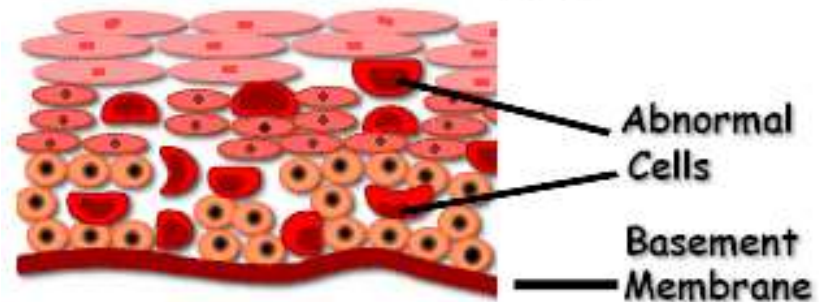
Cervical  
Intraepithelial  
Neoplasia (CIN 1)

## Mild Dysplasia



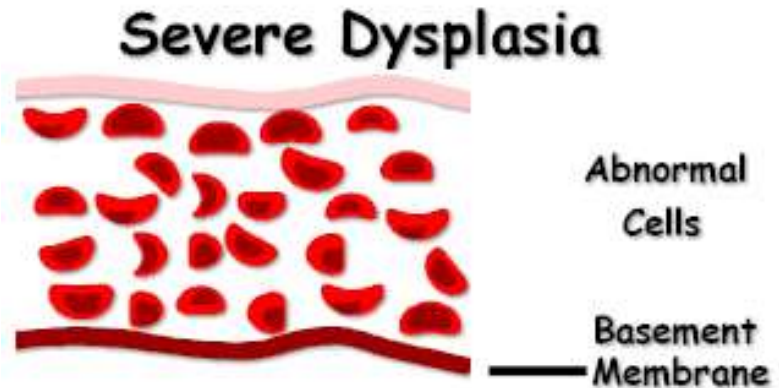
Cervical  
Intraepithelial  
Neoplasia (CIN 2)

## Moderate Dysplasia

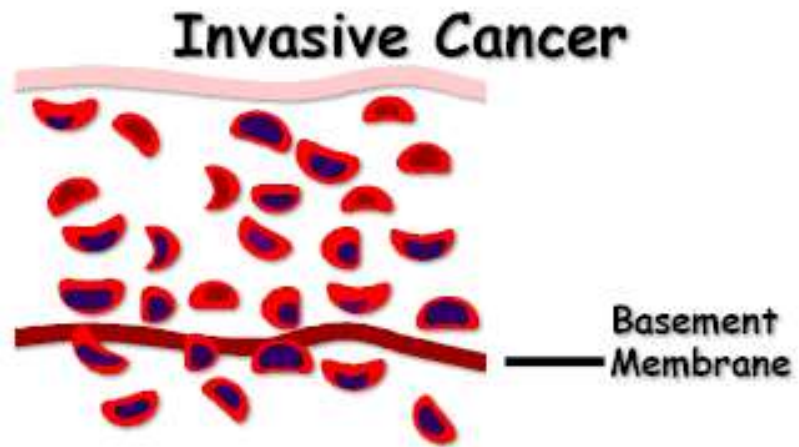


# Cervical Dysplasia: Classification

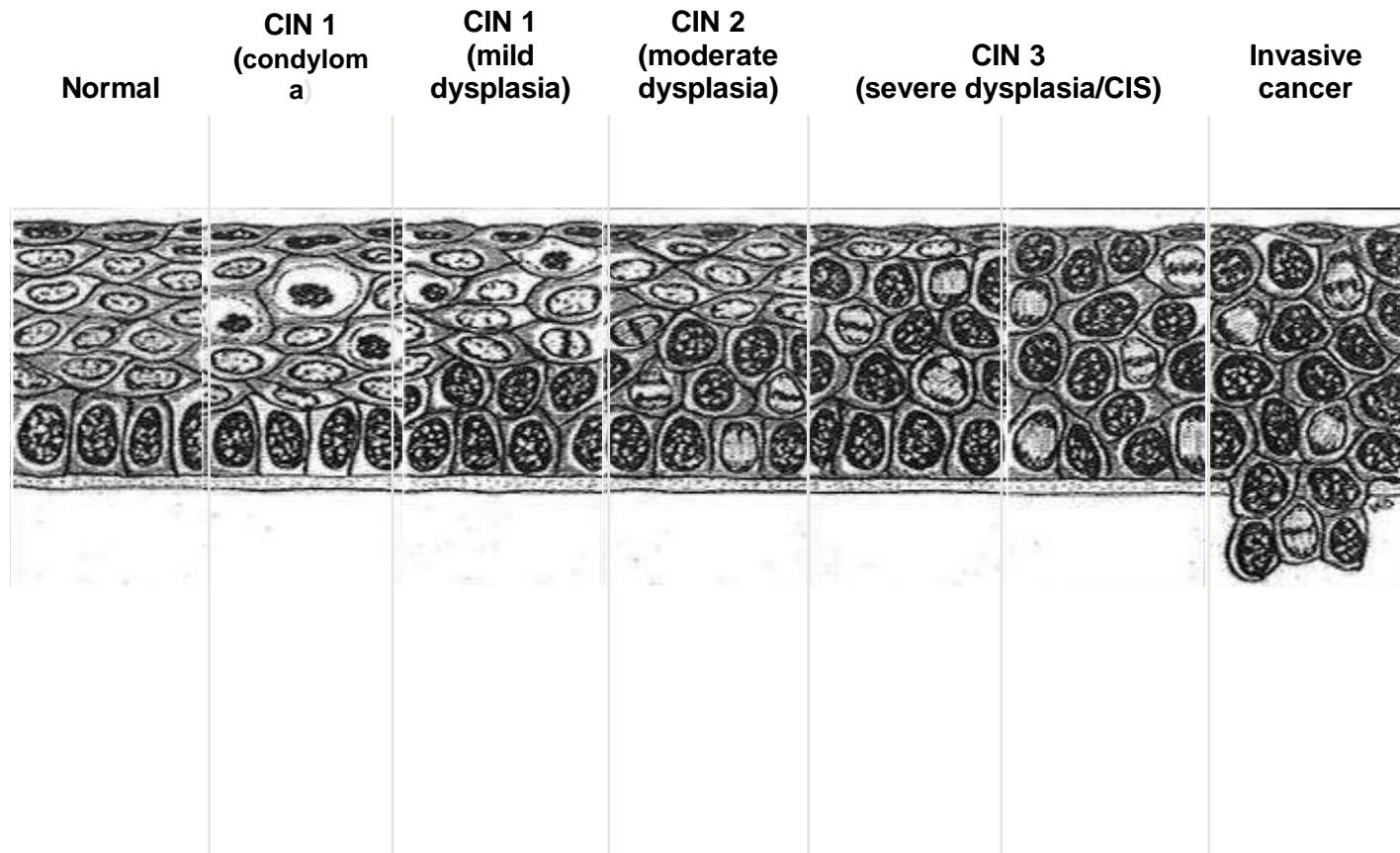
Cervical Intraepithelial  
Neoplasia (CIN 3)



Invasive Cervical  
Cancer (ICC)



# Classification of CIN





**CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN):**  
**Mild Dysplasia / CIN 1: Dysplasia confined to the lowest third of the epithelium.**

**Moderate Dysplasia / CIN 2: Dysplasia involving the lower two thirds of the epithelium.**

**Severe Dysplasia / CIN 3: Dysplasia extending into the upper third of the epithelium, but not involving the full thickness.**

**Carcinoma In Situ / CIN 3: A squamous intraepithelial lesion in which nuclear abnormalities involve the full thickness of the epithelium.**

# Bethesda 2001 Cervical Cytology

## Classification

**Negative for squamous intraepithelial lesion or malignancy**

## **Epithelial cell abnormalities: Squamous Cell**

**Atypical Squamous cells of undetermined significance (ASC-US)**

**Atypical Squamous Cells, cannot exclude HSIL (ASC-H)**

**Low-Grade Squamous Intraepithelial Lesion (LSIL)**

**encompassing: HPV / mild dysplasia / CIN 1**

**High-Grade Squamous Intraepithelial Lesion (HSIL)**

**encompassing: moderate and severe dysplasia, CIS / CIN 2 &**

**CIN 3**

**-with features suspicious for invasion (if invasion is**

**suspected)**

**Squamous cell carcinoma**

# The Bethesda 2001 System

## **Major New Changes from Bethesda 1991:**

**\* Negative for intraepithelial lesion or malignancy replaces “within normal limits”.**

**\* Benign Cellular Changes Eliminated.**

**\* ASCUS changed to ASC : either ASC-US or ASC-H**

**\* AGUS changed to AGS**

# COMPARISON OF THE WHO AND BETHESDA SYSTEM TERMINOLOGY

WHO histopathologic terms	Bethesda Cytology Terms
<b>CIN 1 / Mild Dysplasia</b>	<b>LSIL</b>
<b>CIN 2 / Moderate Dysplasia</b>	<b>HSIL</b>
<b>CIN 3 / Severe Dysplasia</b>	<b>HSIL</b>
<b>CIN 3 / Carcinoma in Situ</b>	<b>HSIL</b>

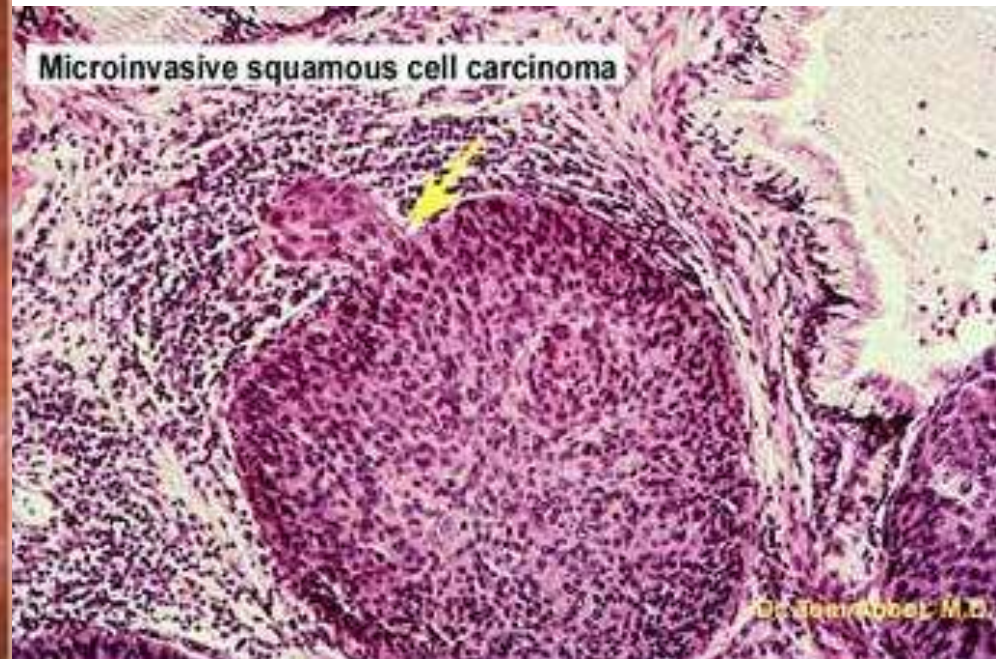
\*LSIL: low-grade squamous intraepithelial lesion

\*HSIL: high-grade squamous intraepithelial lesion

# Cervical Cancer



Gross pathology of  
Cervix



Micro pathology of  
Cervix

# Normal, Ectopic and Cancerous Cervixes



Slide courtesy of ITECH

## **Outcome of CIN**

- Spontaneous regression.
- Progression to invasive cancer.
- Progression from one stage to another takes years.
- Detection and treatment of CIN prevents cancer cervix.

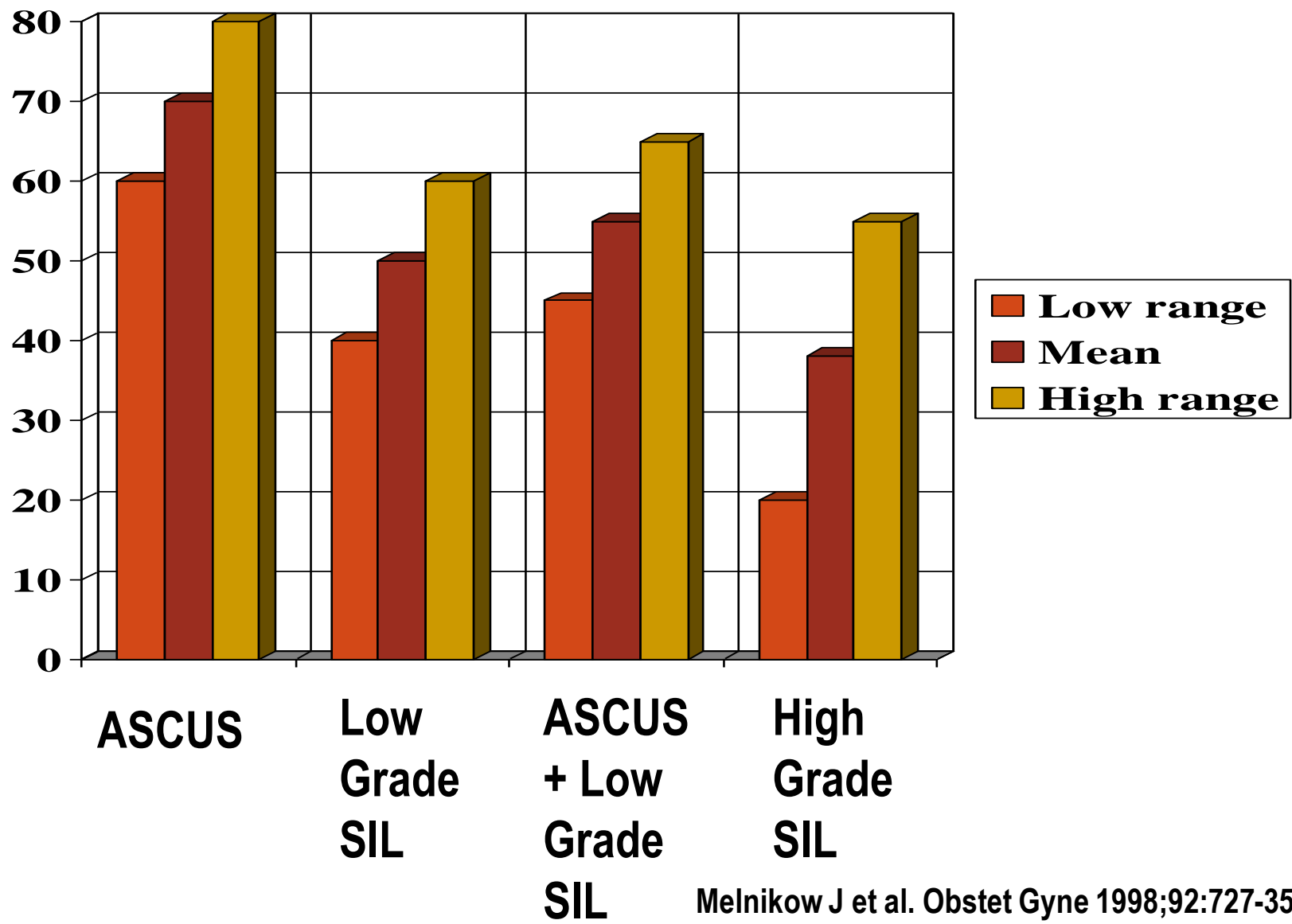
# Natural history of CIN: *summary*

	<b>Regress</b>	<b>Persist</b>	<b>Progress to CIS</b>	<b>Progress to invasion</b>
<b>CIN 1</b>	<b>57%</b>	<b>32%</b>	<b>11%</b>	<b>1%</b>
<b>CIN 2</b>	<b>43%</b>	<b>35%</b>	<b>22%</b>	<b>5%</b>
<b>CIN 3</b>	<b>32%</b>	<b>&lt; 56%</b>	<b>--</b>	<b>&gt;12%</b>

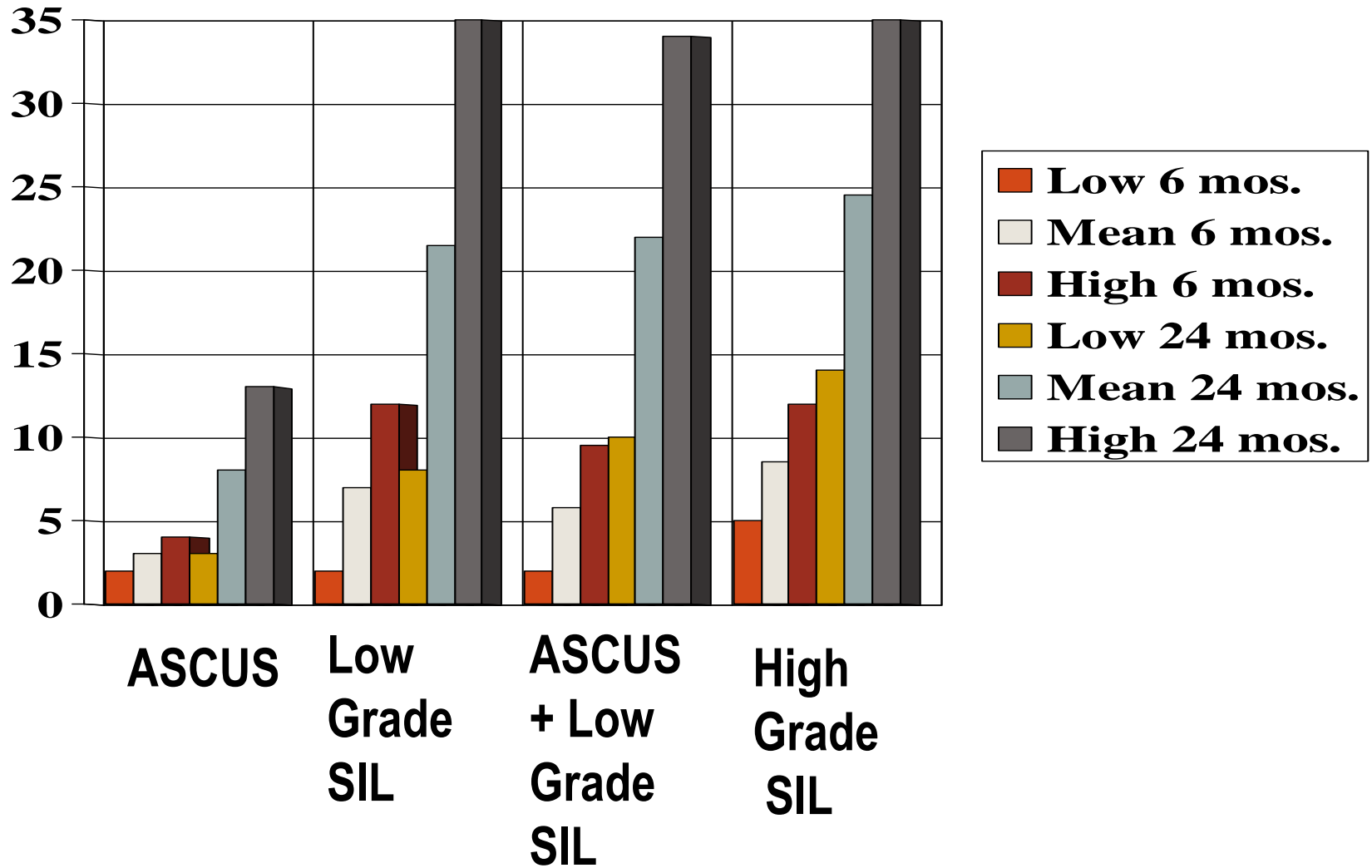
**64 studies, 274 carcinomas, 15,473 CIN cases**  
**Followup <1-12 years**



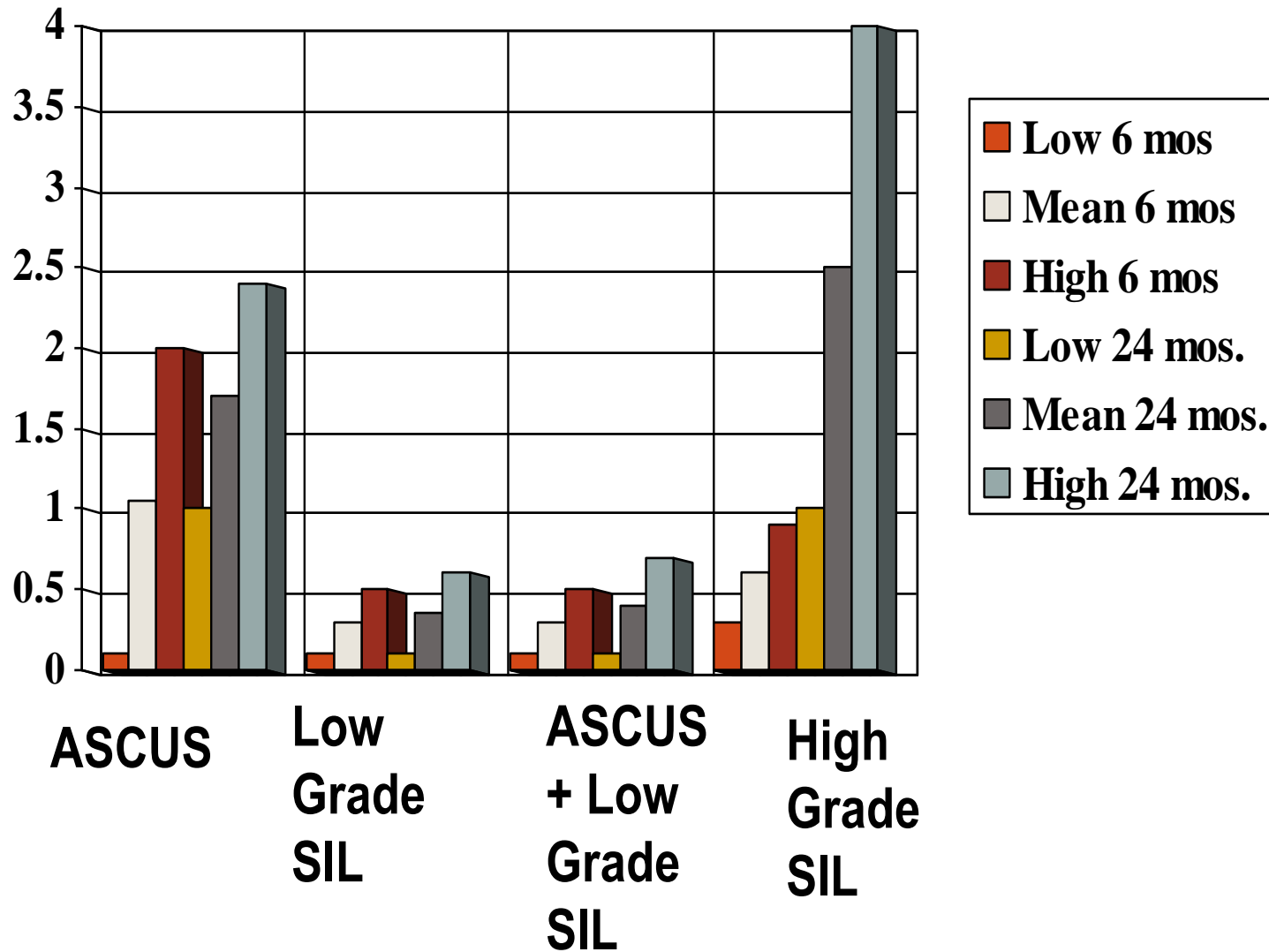
# Regression



# Progression



# Invasive Cancer



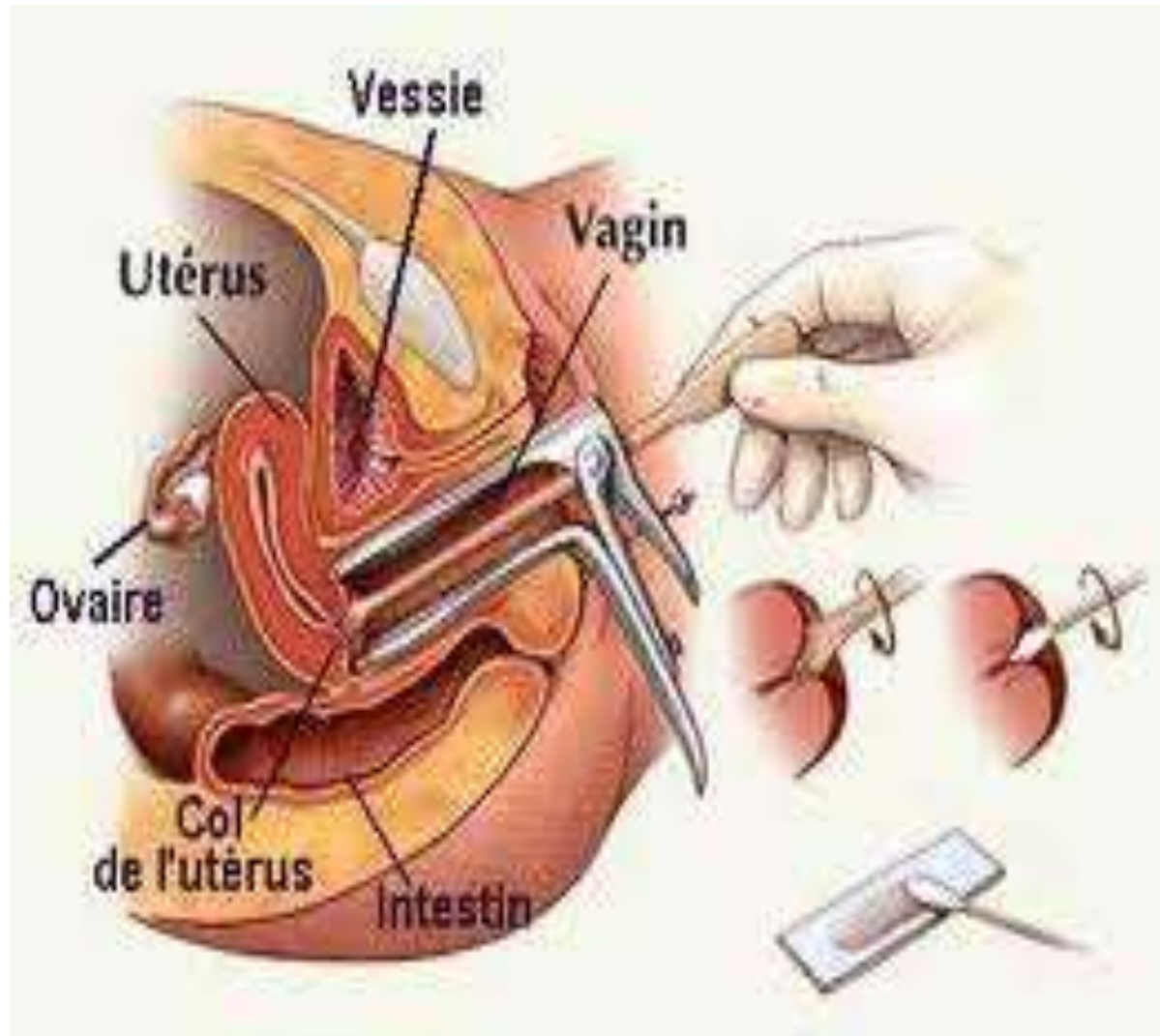
# Cervical Cancer: Risk Factors

- Early onset of sexual activity
- Multiple sexual partners
- High-risk sexual partner history of sexually transmitted diseases
- Smoking
- High parity
- **Immunosuppression**
- Low socioeconomic status
- Prolonged use of oral contraceptives
- Previous history of vulvar or vaginal squamous dysplasia

# Screening for CIN

## cervical smear

- Screening for dyskariosis by obtaining cervical cytology.
- Cervical screening should be carried out every 3-5 years in all sexually active women from 20-60 years of age.
- There is a 10-15 % chance of false positive or false negative results.



# Colposcopy

- Is the inspection of the cervix with a low powered microscope.
- Magnifies the cervix 4-20 times.
- The patient is put in lithotomy position.
- Passing a bivalve speculum gently into the vagina.

- Inspection of the cervix and its vasculature.
- Green filter may help studying vasculature.
- Abnormal vascular structure includes punctuation and mosaicism.
- Acetic acid test: application of 3% acetic acid stained the abnormal area. The degree of staining correlates with severity of the lesion.
- Schiller test: application of Lugol's iodine stains the normal cervix brown.
- Colposcopy gives a clinical diagnosis.
- Punch biopsy from the abnormal area gives a histopathological diagnosis.

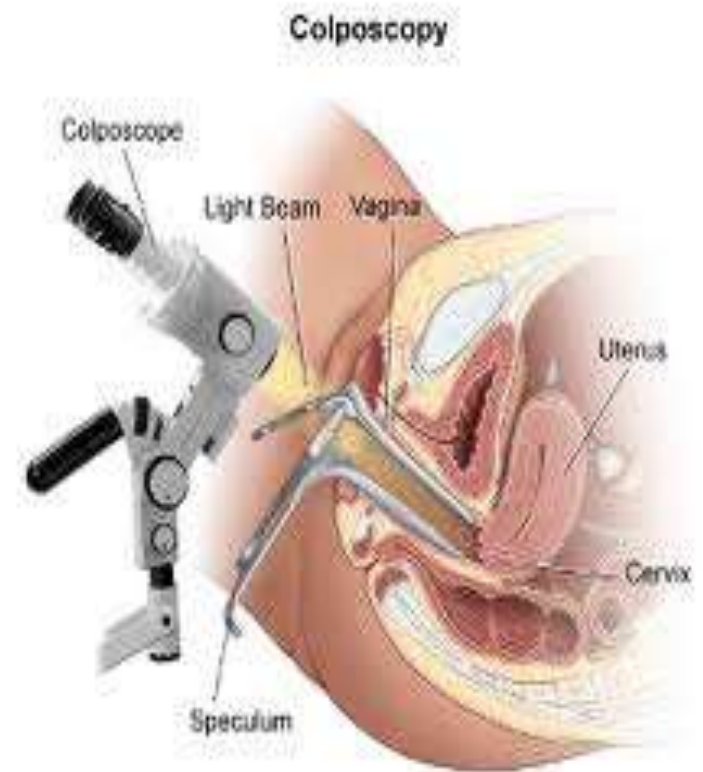


# Colposcopy

- **Accurate delineation of suspicious areas for tissue biopsy.**
- **Suspicious areas appear as acetowhite areas.**

## ❖ **Indications**

- ✓ **Abnormal papsmear cytology.**
- ✓ **To locate abnormal areas.**
- ✓ **To obtain directed biopsy.**

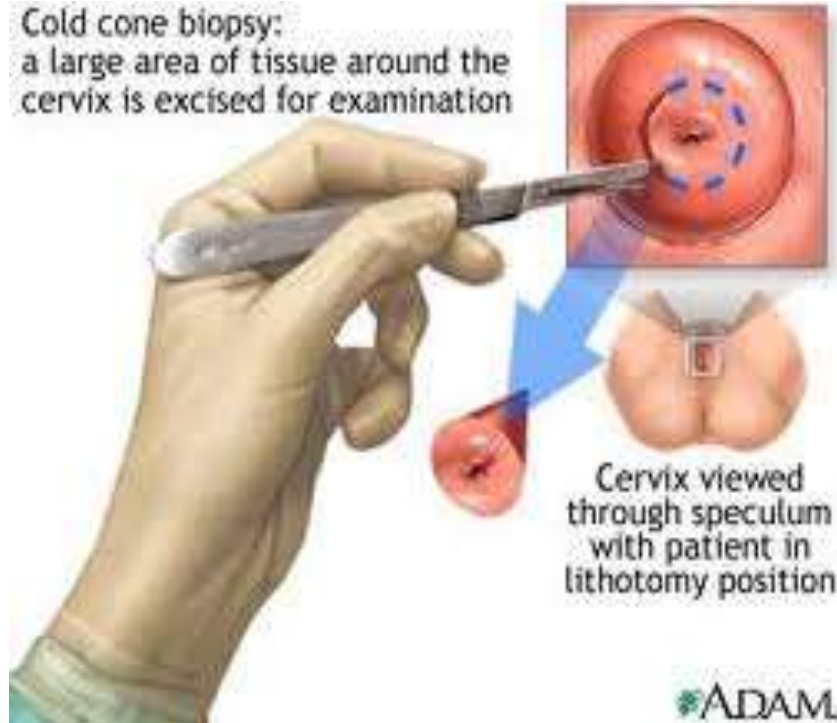


# t/t of dysplasia & cin

- ❑ **Mild dysplasia : Treat inflammation & advise follow up pap test every 3 to 6 months**
- ❑ **Moderately severe to severe dysplasia/CIN II,III**
  1. **Local destructive**
    - a. Cryosurgery
    - b. Fulguration
    - c. Laser ablation
    - d. Cauterisation
  2. **Excision of abnormal tissue :**
    - a. Cold knife conization
    - b. Laser conization
    - c. LLETZ /laser large loop excision of the transformation zone
  3. **Surgery**
    - a. Hysterectomy
    - b. Therapeutic conization

# Tissue biopsy

Cold cone biopsy:  
a large area of tissue around the  
cervix is excised for examination



Cervix viewed  
through speculum  
with patient in  
lithotomy position

ADAM

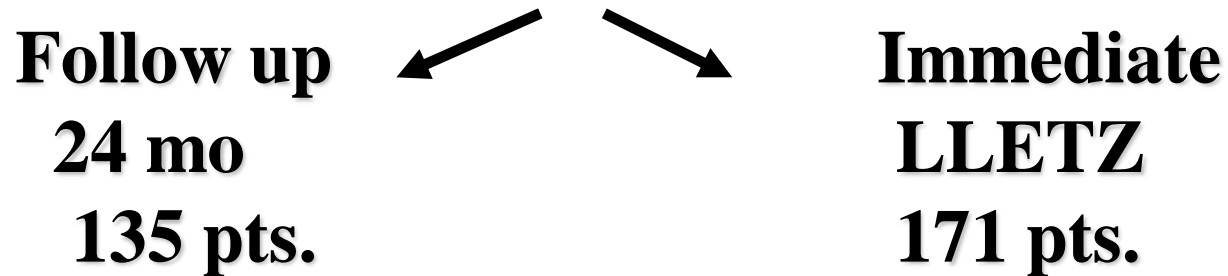
# MANAGEMENT OF CIN 1

**Risk of follow up** of CIN 1 -

1. Invasive cancer already exists and was missed by Pap, colpo and biopsy.
2. Invasive cancer develops between follow up visits.
3. Patient lost to follow up and develops invasive cancer.

# FOLLOW UP FOR CIN 1

## Atypia / LSIL Pap



## Histology

20%	Negative	< 1 %
55%	CIN 1/HPV	76%
24%	CIN 2-3	23%
1 pt.	Invasion	--

Shafi, BJOJ, 1997

# **FOLLOW-UP: OBSERVATION VS. THERAPY**

**Patients with Pap smears interpreted as LSIL may have colposcopy directly if reliable and have the ability to be followed, may be followed by repeat smears at 4 to 6 months.**

**A meta-analysis of women with LSIL Pap tests had a pooled rate of regression reported as 47.39%, with a very low risk of invasive carcinoma, varying from 0.00% to 0.74% of the patients.**

## **OBSERVATIONAL FOLLOW-UP, CIN 1**

**If the patient has a follow-up Pap smear that is**

**within normal, or benign cellular changes,**

**repeat follow-up at 4 to 6 month intervals should continue. If the smears remain**

**within**

**normal, or benign cellular changes, the patient**

**may return to annual yearly screening if**

# **METHODS TO TREAT CIN**

**There are a variety of accepted methods of therapy to treat CIN, including:**  
**cryosurgery ablation,**  
**laser ablation or excision,**  
**electro-loop excision,**  
**cone biopsy**

**ACOG: 1997; Nuovo et al, 2000; Wright et al, 1995**



# Management of abnormal colposcopy

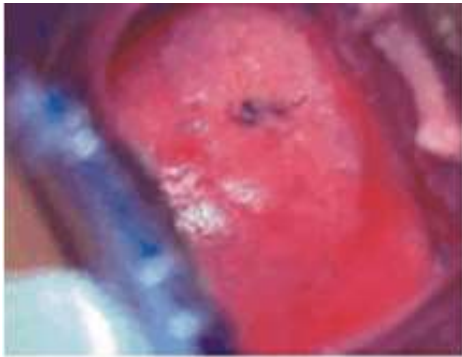
- CIN II, CIN III. ?CIN I.

Techniques for treatment:

*Excisional:* LLETZ, laser cone, knife cone, hysterectomy.

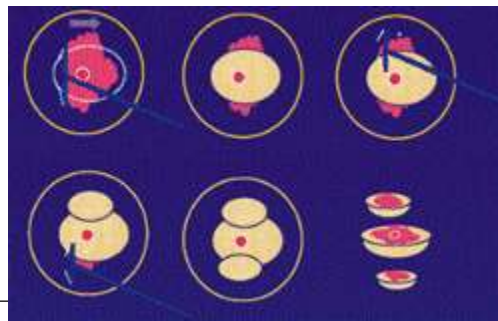
*Ablative:* radical electrodiathermy, cold coagulation, cryocautery, laser.

- 90-95% cure rate



**BEFORE SURGERY**

**IN SURGERY**



# HPV vaccine

- In 2006, an HPV vaccine against HPV16 and HPV18 (types most commonly responsible for cervical cancers) and HPV6 and HPV11 (cause most anogenital warts) was licensed for use in females 9-26 years old.
- The vaccine appears to be highly efficacious in preventing HPV infection and high-grade CIN in HIV negative women.
- No specific data in HIV+ women is available to date.
- The vaccine is available in Vietnam but use is limited due to the high cost.

# Summary

- Benign diseases of cervix are harmless but malignancy should be excluded.
- Cervical intraepithelial neoplasia precedes cancer cervix by years.
- Screening for CIN reduces mortality from cancer cervix.
- Those with positive screening test should be referred to colposcopy for diagnosis and treatment.

Thank You

Questions?