Cervix

→ HPV pathogenesis:

Pathogenic strains – HPV 16, 18, 31, 33, 45 (high risk strains)]→ Non enveloped, double stranded DNA virus

↓

Basal cell of epidermis

↓

Integration of viral genome into host genome.

↓

2 oncoproteins

↙ ↘

E6 → p53 inactivation

E7 → pRB inactivation

Environmental factors (smoking / alcohol) (+) → Genomic instability ← (+) Coinfection with other STDs

↓

HPV associated SCC

Protective factors

- Intrauterine devices
- circumcision in men

lowers incidence of HPV in men and their female partners.

→ HPV prevention

* Primary prevention

- Prevention before disease occurance.
- HPV vaccination

Bivalent
CERVARIX
HPV 16, 18

Reduce the risk of CIN-1, 2, 3 by vaccine specific subtypes by 95%.

4 valent
GARDASIL
HPV 16, 18, 6, 11

9-valent
GARDASIL-9
HPV 16, 18, 31, 33, 45, 52, 58, 6, 11.

↓

Approved in male & female.

Vaccination schedule :- By CDC for Gardasil-9 (by Merck)

A two-dose series (0, 6-12 months) for most persons who initiate vaccination at ages 9 through 14 years.

A three-dose series (0, 1-2, 6 months) for persons who initiate vaccination at ages 15 through 45 years, and for immunocompromised persons.

India vaccine
CERVEVAC - quadrivalent against 6, 11, 16, 18.
By serum institute

* Secondary prevention

- For early detection & treatment

HPV screening by HPV DNA testing
Pap smear
Pap smear + HPV co-testing

↓

more sensitive
No observational bias in CIN lesions.

Current screening guidelines by USPSTF 2018

Pap smear cytology from 21-29 yrs every 3 years

Hb
- → Pap smear 30-65 yrs every 3 years
- (or)
- → Pap smear + HPV cotesting every 5 years.

No screening for > 65 years if past 20 years reports normal.

Woman >65 years without any prior screening → Pap smear + HPV cotesting.

Post hysterectomy & No Hx of CIN 2 or greater → No screening recommended.

→ Pathology - Pre-invasive - on Pap smear

→ Bethesda system
→ CIN system
→ Papanicolaou system

1) ★ Specimen type
→ Conventional Pap
- smeared directly on slide
→ Liquid based cytology
- cells suspended in bottle / preservative & sent to lab.
- Thin prep Pap slides.

2) Specimen adequacy:
Unsatisfactory
Satisfactory
→ min squamous cellularity
- atleast 5000 squamous cells in liquid prep
- atleast 8000 - 12000 cells in conventional prep.
→ Endocervical / transformation zone
- atleast 10 cells in single / clusters.

3) Reporting

* NILM - Negative for Intraepithelial lesion or Malignancy.
Epithelial abnormalities

Squamous
→ ASCUS - Atypical Squamous cells of unknown significance
- mc Pap smear report
- 9.1. of Pap smears.
- ↑ N:C ratio
→ ASC-H - Atypical Squamous cells cannot exclude high grade lesion
→ LSIL - low grade Squamous Intraepithelial lesion
- includes CIN-1 → abnormalities upto lower 1/3rd epithelium.
→ HSIL - High grade Squamous intraepithelial lesion
- includes CIN-2 - lower + middle 1/3rd
← CIN-3 - lower + middle + upper 1/3rd epithelium.

Adeno (endocervix)
→ AGC - Atypical Glandular cells
NOS | AIS | Adeno CA.
Adeno carcinoma in Situ
↓
Several benign mimics
- Reactive glandular atypia
- Endometriosis.

→ Endocervical adenocarcinoma classification:

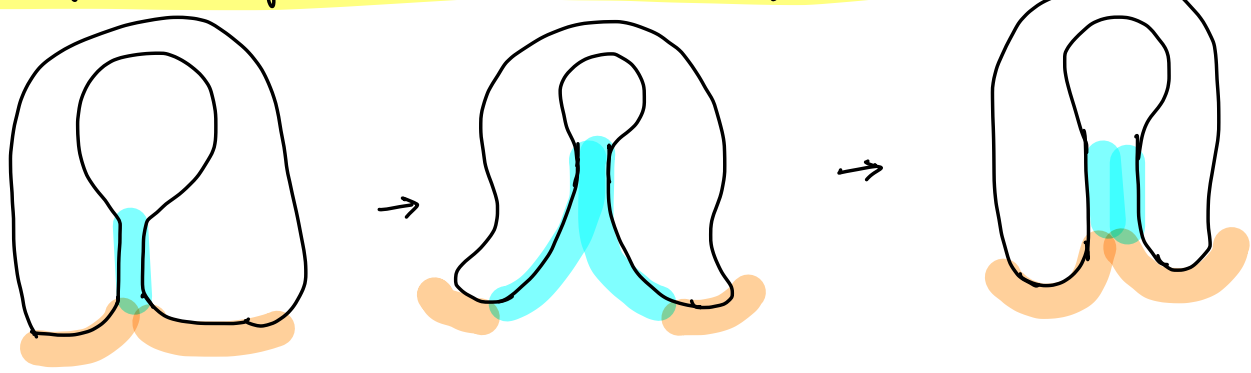
TABLE 48.3

International Endocervical Adenocarcinoma Criteria and Classification (2018)

Main Categories	Morphologic Subcategories (Optional)	World Health Organization
1. HPV-related endocervical adenocarcinoma	HPV adenocarcinoma, usual type HPV adenocarcinoma, villoglandular type HPV adenocarcinoma, mucinous NOS type HPV adenocarcinoma, mucinous intestinal type HPV adenocarcinoma, signet-ring cell type HPV adenocarcinoma, stratified mucin-producing type	1. Usual type adenocarcinoma 2. Villoglandular adenocarcinoma 3. Mucinous adenocarcinoma NOS 4. Mucinous adenocarcinoma, intestinal type 5. Mucinous adenocarcinoma, signet ring cell
2. Non-HPV adenocarcinoma, gastric type – mc in Southeast Asian women		6. Mucinous adenocarcinoma, gastric type
3. Non-HPV adenocarcinoma, endometrioid type – from Endometriosis		7. Endometrioid carcinoma
4. Non-HPV adenocarcinoma, clear cell type – diethylstilbesterol exposure		8. Clear cell carcinoma
5. Non-HPV adenocarcinoma, mesonephric type — very rare		9. Mesonephric carcinoma
6. Non-HPV adenocarcinoma, serous type		10. Serous carcinoma
7. Invasive adenocarcinoma, NOS		11. Invasive adenocarcinoma, NOS

HPV, human papillomavirus; NOS, not otherwise specified.

→ management of abnormal screening results: → ASCCP Guidelines



At birth

Young adult
- Ectropion of cervix
= columnar metaplasia

Adult.
- involution of cervix

columnar epithelium

Squamous epithelium.

Transformation zone (TZ) – Area between old & new squamocolumnar junction.
- prone to develop malignancy
- Pap test taken from TZ.

★ Co-testing vs Reflex Testing

↓ Co-testing: HPV + Pap smear testing

↓ Reflex: Pap smear only if HPV test is positive.

★ Management of abnormal HPV testing

- HPV negative → Return to normal screening protocol
- HPV positive
  - HPV Genotyping if 16 / 18
  - Pap test if ≥ Ascus
  - Pt. not willing for Pap test

→ Colposcopy & Biopsy.

✱ Abnormal Pap smear test

- **ASCUS**
  - HPV (+) → Colposcopy & Bx
  - HPV (−) → normal screening
- **LSIL**
  - HPV (+) → Colposcopy Bx
  - HPV (−) → Repeat cytology at 1 year
- **HSIL / ASC-H** → Colposcopy & Bx irrespective of HPV status.

✱ management of abnormal colposcopy Bx :

- **CIN – I** → co-test after 1 year (or) Ablative procedure if pt is anxious.
- **CIN – II, III**
  - **Ablative procedure**
    - Thermo ablation (5–7mm)
    - Cryotherapy (N_2O) (5mm destruction)
    - Laser ablation i.e CO_2 Laser.

    → Done only if
    - entire T2 is visualised
    - Non pregnant.
    - No suspicion of malignancy.
  - **Excisional procedure** → Preferred.
    - LEEP / LLETZ
    - Long loop Excision of T2. → Treatment of choice.
    - Cold knife conization
      - when lesion extends into endocervix
      - Recurrent high grade lesions.
    - Laser conization.

Risk of progression to invasive malignancy

CIN – I	1%
CIN – II	5%
CIN III	10–12%

Hysterectomy directly

Indications → Adeno in situ (AIS)
→ CIN 3 in older women
→ women who are unsure to follow up.

✱ Management of abnormal LLETZ biopsy report:

- LLETZ ✓ margin Negative
  - ↓
  - Hpv colestrip at 1 year
- LLETZ ✓ margin positive
  - ↓
  - Repeat excision / hysterectomy.

✱ Complications of excisional procedures:

- Hemorrhage
- cervical stenosis
- cervical incompetence & repeated miscarriage
  - ↓
  - Procedure to be combined with cervical cerclage.