Female Genital System, Lecture2

Cervix

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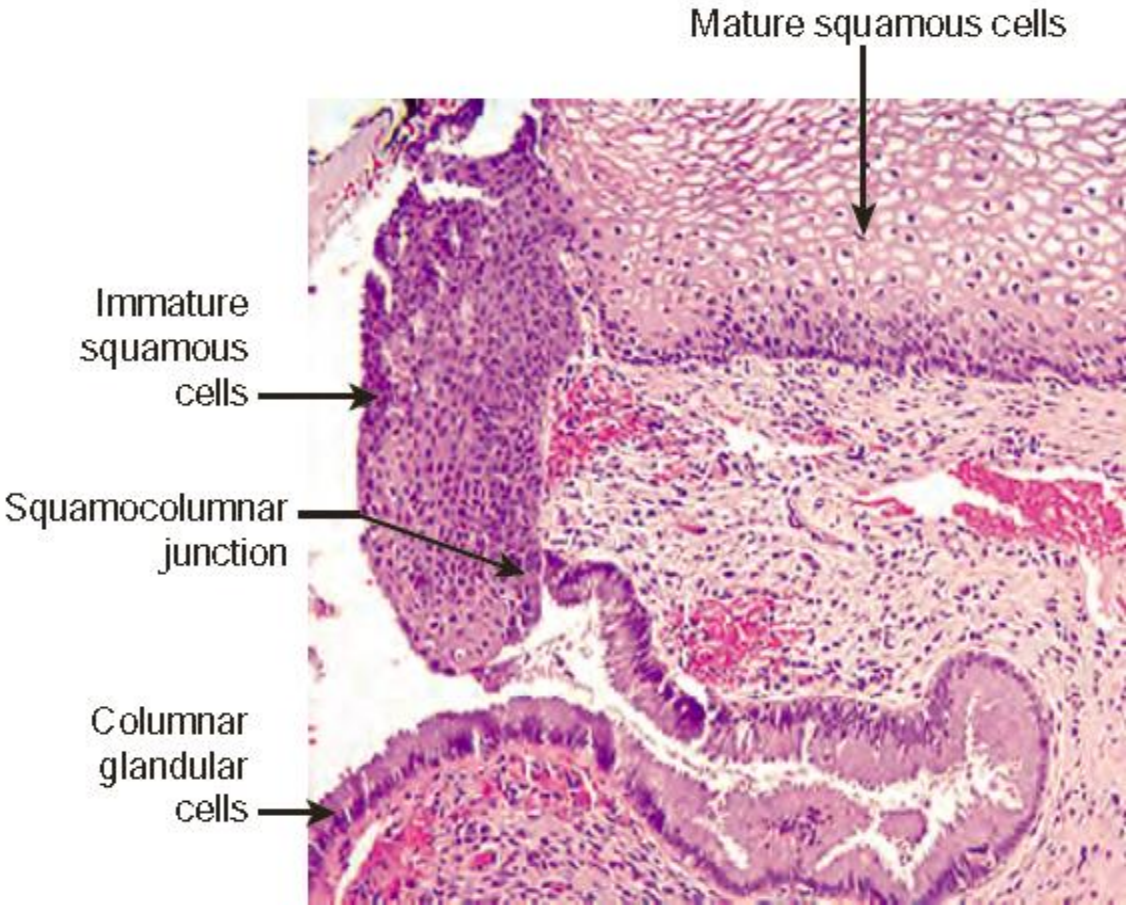

Mature squamous cells
Immature squamous cells
Squamocolumnar junction
Columnar glandular cells

Cervical carcinoma

- **Was** the most common cancers in women worldwide.
- **Was** → Papanicolaou (Pap) smear → **the most successful cancer-screening test ever developed.**
- Most common form is SCC 75%, adenoCa. & adenosquamous (mixed) Ca. 20%, & neuroendocrine Ca 5%.
- All are ass with HPV infection.
- Peak at 45 years, 10-15 years after detection of their precursors: cervical intraepithelial neoplasia (CIN).

PATHOGENESIS

- High-risk HPVs are by far the most important factor in the development of cervical cancer. HPVs are DNA viruses that are grouped into those of high and low oncogenic risk based on their genotypes.

- There are 15 high-risk HPVs that are currently identified, but HPV-16 alone accounts for almost 60% of cervical cancer cases, and HPV-18 accounts for another 10% of cases; other HPV types contribute to less than 5% of cases.

- Most HPV infections are transient; overall, 50% of HPV infections are cleared within 8 months, and 90% of infections are cleared within 2 years. The duration of the infection is related to HPV type, as infections with high-risk HPVs take longer to clear on average than infections with low-risk HPVs (13 months vs. 8 months, respectively).

- Productive, persistent HPV infection requires viral entry into immature basal epithelial cells.

- Sites in the female genital tract that are susceptible to infection include areas of squamous epithelial trauma and repair, where the virus may access basal cells, and the immature metaplastic squamous cells that are present at the squamocolumnar junction of the cervix.
- The cervix, with its relatively large areas of immature squamous metaplastic epithelium, is particularly vulnerable to HPV infection.

PATHOGENESIS & EPIDEMIOLOGY

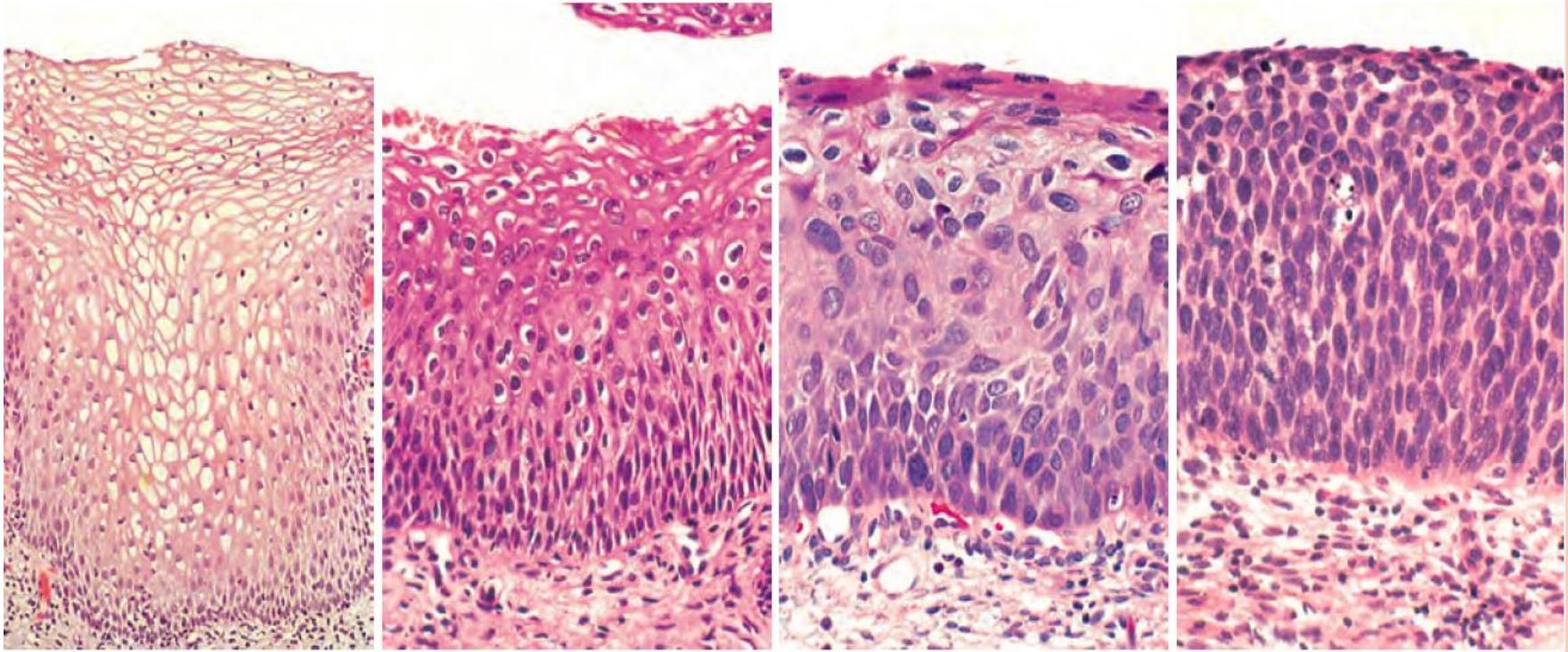
- Peak incidence at 30s (SCC at 45 years of age). The prevalence of HPV in cervical smears in women with normal Pap test results peaks between 20 and 24 years of age.
- Although HPV infects immature squamous cells, viral replication occurs in maturing squamous cells.
- These subtypes show a propensity to **integrate** into host genome, & express large amounts of E6 & E7 proteins → **inhibit** tumor suppressor genes p53 & RB, respectively.
- HPV vaccine is recently introduced → very effective in preventing HPV infections → expected to lower frequency of genital warts & cervical Ca.

Cervical intraepithelial neoplasia (CIN)

- Dysplasia in epithelial cells, graded depending on the extent of epithelial involvement:

- CIN I: Mild dysplasia (involves a third or less of thickness)
- CIN II: moderate dysplasia (involves 2/3 of thickness).
- CIN III: severe dysplasia (involves full thickness) → carcinoma in situ

CIN → Dysplasia: nuclear enlargement, hyperchromasia (darker), coarse chromatin, & variation in nuclear size & shape

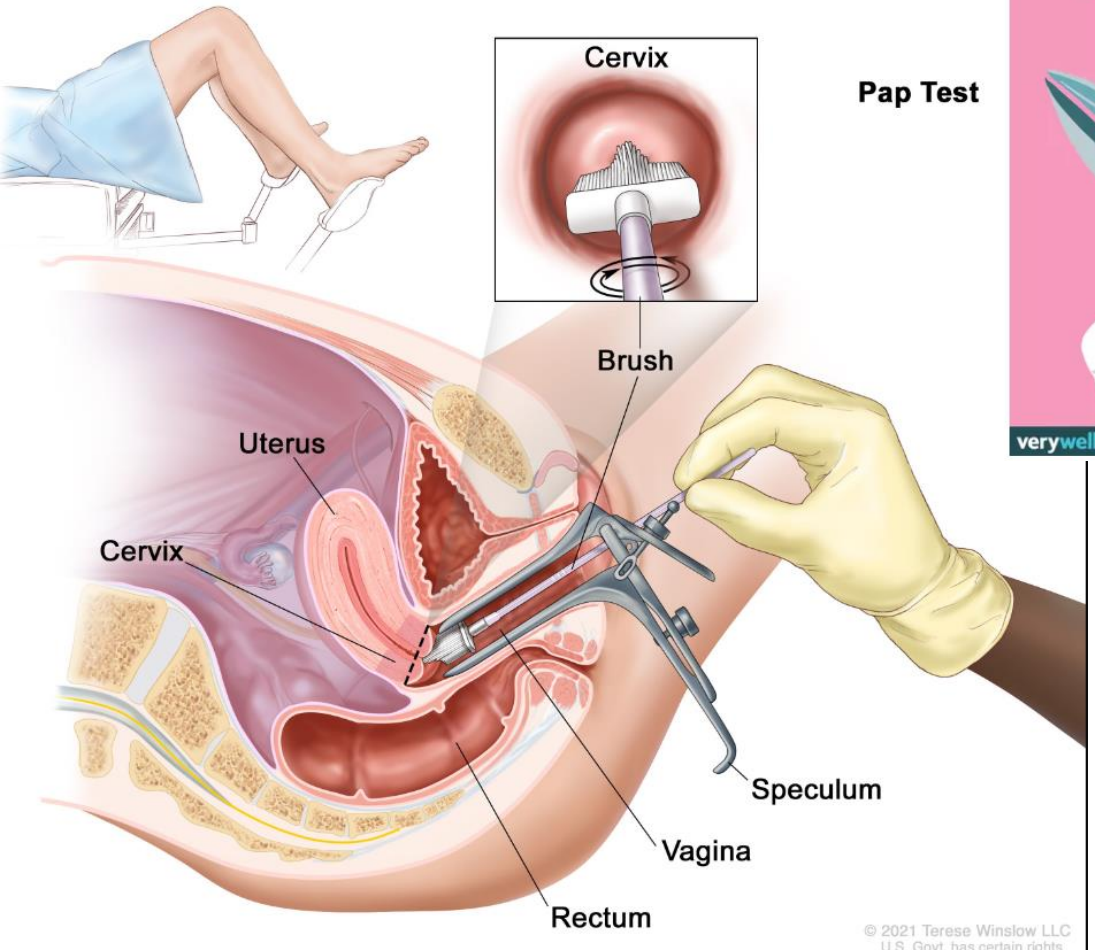


CIN AND PAP SMEAR!

- Cervical precancerous lesions are ass with abnormalities in cytologic preparations → Can be detected long before abnormality is visible on gross inspection.

- Cells are scraped from the transformation zone & examined microscopically

- Pap screening has dramatically lowered the incidence of invasive cervical tumors & it is no longer ranks among the top 10 causes of cancer deaths in U.S. women.


Cervix
Pap Test
Brush
Uterus
Cervix
Speculum
Vagina
Rectum
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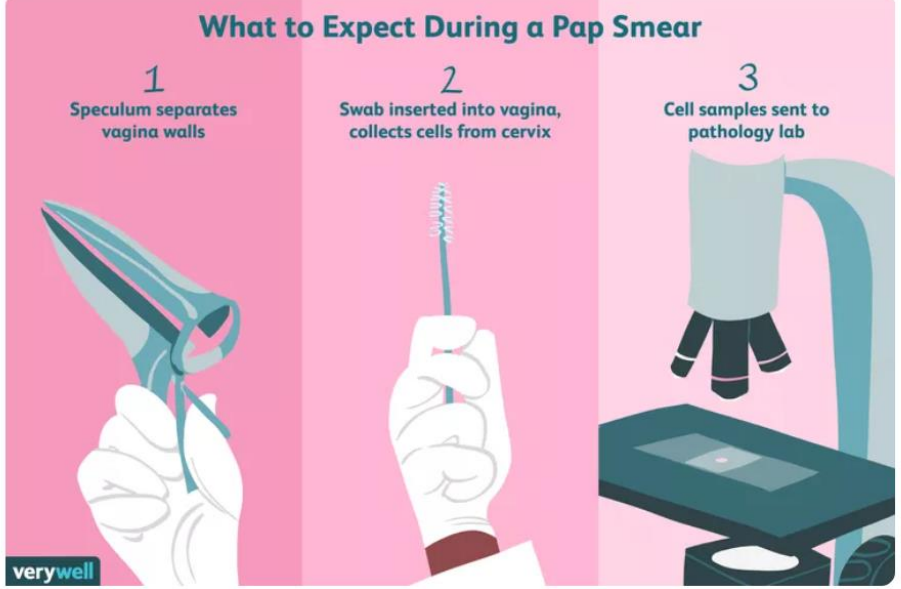
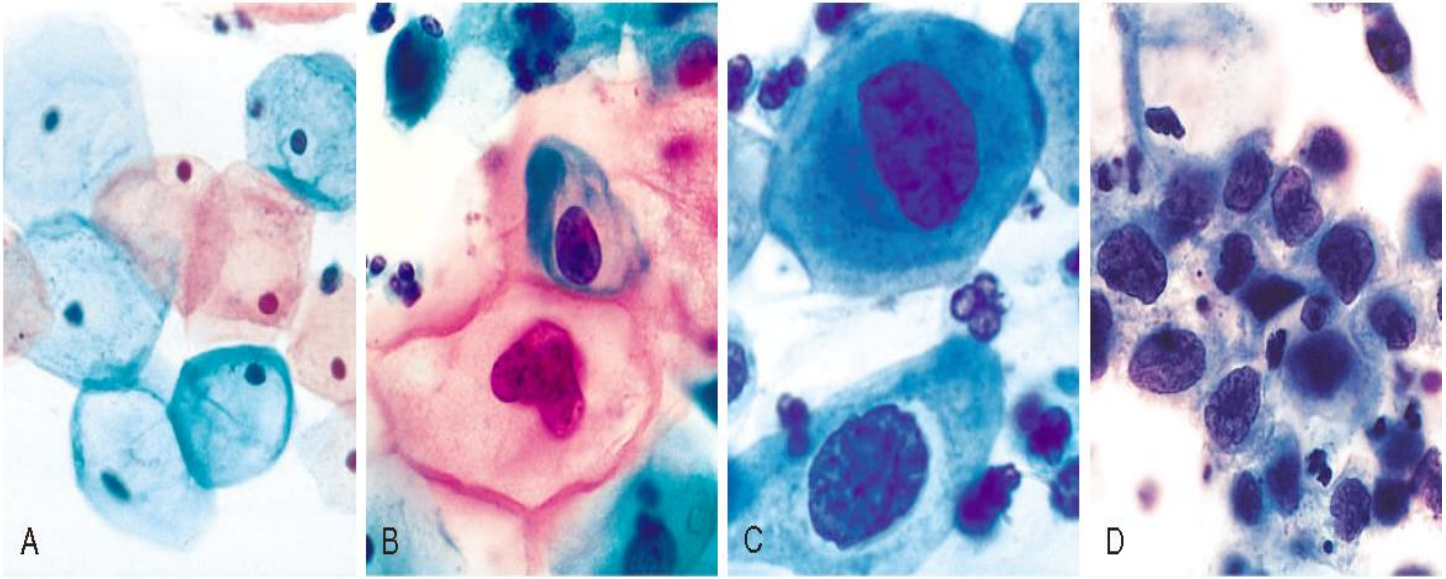

What to Expect During a Pap Smear
1
Speculum separates vagina walls
2
Swab inserted into vagina, collects cells from cervix
3
Cell samples sent to pathology lab
verywell

CIN → Dysplasia: nuclear enlargement, hyperchromasia (darker), coarse chromatin, & variation in nuclear size & shape



CIN → SIL (SQUAMOUS INTRAEPITHELIAL LESION)

The decision with regard to patient management is two-tiered (observation **versus** surgical treatment) → Three-tier classification system → recently simplified to a two-tiered system → Low grade squamous intraepithelial lesion (LSIL) & high grade squamous intraepithelial lesion (HSIL)

Dysplasia/Carcinoma in Situ	Cervical Intraepithelial Neoplasia (CIN)	Squamous Intraepithelial Lesion (SIL), Current Classification
Mild dysplasia	CIN I	Low-grade SIL (LSIL)
Moderate dysplasia	CIN II	High-grade SIL (HSIL)
Severe dysplasia	CIN III	High-grade SIL (HSIL)
Carcinoma in situ	CIN III	High-grade SIL (HSIL)

CIN, Cervical intraepithelial neoplasia; SIL, squamous intraepithelial lesion.

CIN – Clinical

- SIL is asymptomatic and comes to clinical attention through an abnormal Pap smear result.
- Women with biopsy-documented LSIL are managed with careful observation
- HSILs & persistent LSIL are treated with surgical excision (laser or cone biopsy) & follow up.

Invasive Carcinoma of the Cervix – Clinical

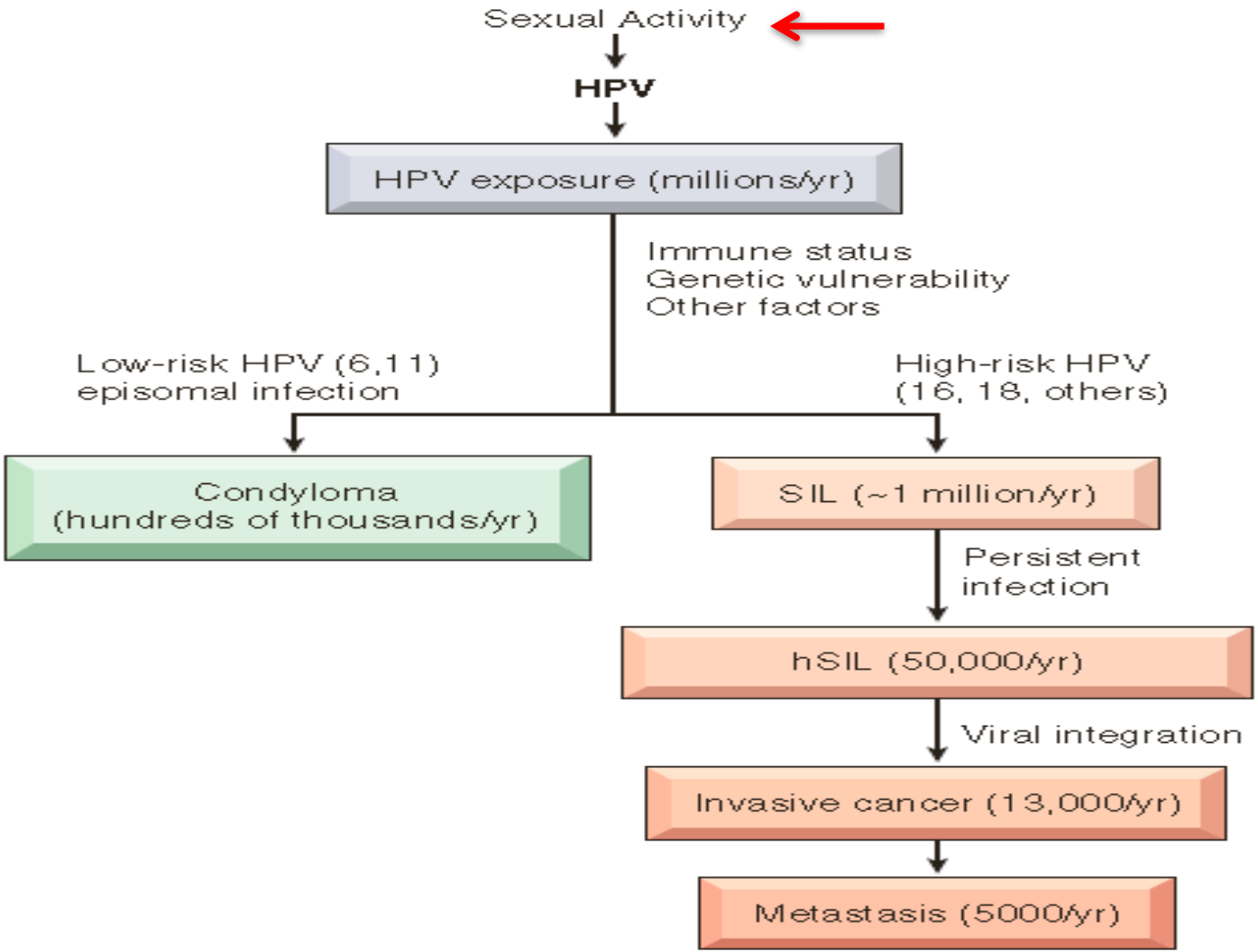
- Progression of SIL to invasive carcinoma is variable & unpredictable. (smoking is a risk factor).
- LSIL → 10% → HSIL → 10% in ~ 10 years → carcinomas.
- Most often is seen in women who have never had a Pap smear or who have not been screened for many years.
- Tx: Hysterectomy + radiotherapy and chemotherapy in advanced cases (high stage).
- 5-year survival: SIL: 100%; stage 1: 90%; stage 2 82%; stage3: 35%; & stage 4: 10%.

Table 22.2 Natural History of Squamous Intraepithelial Lesions With Approximate 2-Year Follow-Up

Lesion	Regress	Persist	Progress
LSIL	60%	30%	10% to HSIL
HSIL	30%	60%	10% to carcinoma[a]

HSIL, High-grade squamous intraepithelial lesion; *LSIL*, low-grade squamous intraepithelial lesion.

[a]Progression within 2 to 10 years.


Sexual Activity
HPV
HPV exposure (millions/yr)
Immune status
Genetic vulnerability
Other factors
Low-risk HPV (6,11)
episomal infection
High-risk HPV
(16, 18, others)
Condyloma
(hundreds of thousands/yr)
SIL (~1 million/yr)
Persistent
infection
hSIL (50,000/yr)
Viral integration
Invasive cancer (13,000/yr)
Metastasis (5000/yr)

Endocervical Polyp

- Endocervical polyps are benign polypoid masses seen protruding from the endocervical mucosa (sometimes through the exocervix).
- They can be as large as a few centimeters, are soft and yielding to palpation, and have a smooth, glistening surface with underlying cystically dilated spaces filled with mucinous secretions.
- The surface epithelium and lining of the underlying cysts are composed of the same mucus-secreting columnar cells that line the endocervical canal. The stroma is edematous and may contain

  scattered mononuclear cells.
- Superimposed chronic inflammation may lead to squamous metaplasia of the overlying epithelium and ulcerations.
- These lesions may bleed, thereby arousing concern, but they have no malignant potential.

- THANK YOU