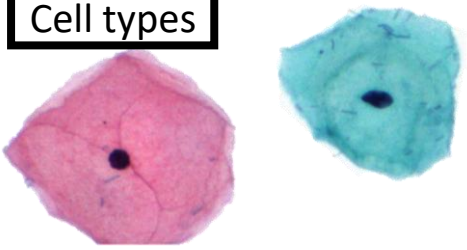
Prepared by Kurt Schaberg

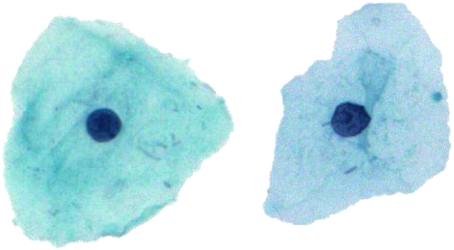
Cervical Cytology

Cell types



Superficial Cells:

Small, pyknotic nucleus
Abundant cytoplasm (Often pink, can be blue)
Polygonal shape
Indicate abundant Estrogen

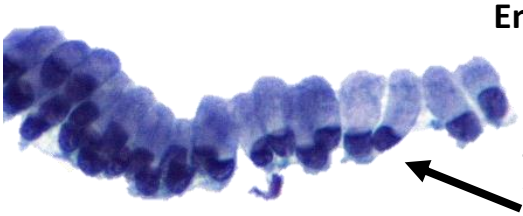


Intermediate Cells:

Abundant blue cytoplasm, polygonal shape
Larger, round to oval nuclei
Finer, normochromatic nuclei
→ Nuclei are important reference size

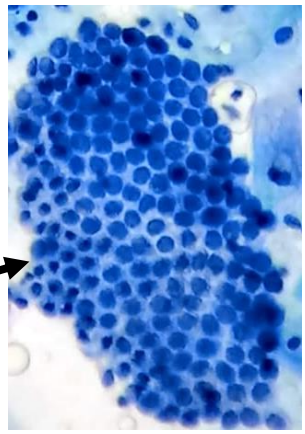
Basal/Parabasal Cell:

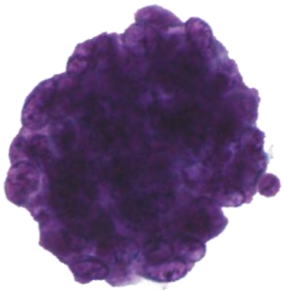
Minimal cytoplasm
Round to oval nuclei
Fine, but slightly dark chromatin
Usually few in number, unless atrophic



Endocervical Cells:

Uniform, Columnar cells
Polar, with round nucleus at one end
Majority of cytoplasm occupied by mucin
Arranged in flat sheets→ think "Honeycomb
Arranged in linear strips→ "Palisaded"





Endometrial Cells:

Small, High N:C ratio cells (almost all nucleus!)
Nucleus about the same size as an intermediate cell nucleus
Round nuclei with smooth chromatin, possible micronucleoli
Can be in large groups with outside epithelium and in inside stroma
Normal finding in first half of menstrual cycle if premenopausal
(Report if >50 yrs old)

Pap Smear Adequacy Criteria

Minimum number of well-visualized squamous cells for adequacy
Liquid-based preparation: 5,000 cells (ThinPrep and SurePath)
Conventional Preparation: 8,000 to 12,000 cells
If obscuring elements cover >75% of epithelial cells → Unsatisfactory

(In practice, the number of cells is estimated based on sample photos, and the cells aren't counted).

Quality indicator: Presence of ≥10 endocervical cells or squamous metaplastic cells (reported, but not required to be satisfactory for evaluation)

Any specimen with abnormal cells is considered adequate and should be reported!

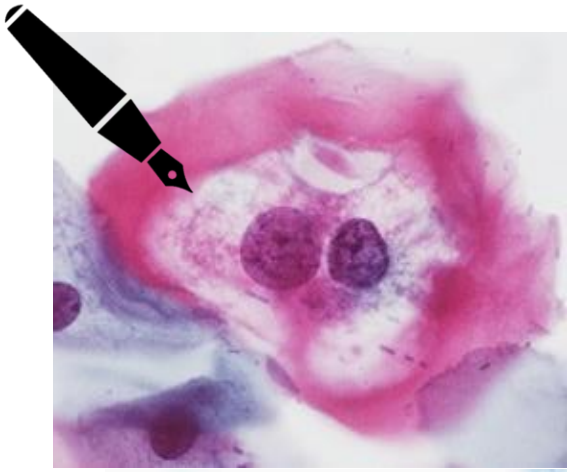
Low-Grade Squamous Intraepithelial Lesion (LSIL)

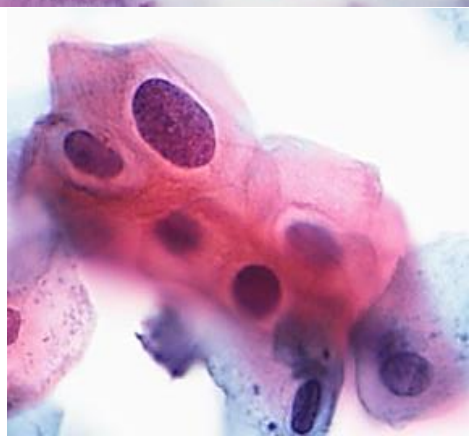
Mature Keratinocytes (with lots of cytoplasm) AND:

- **Enlarged nuclei** (>3x normal intermediate cells)
- Nuclear **membrane irregularities**
- Hyperchromasia ("Rasinoid")
- NO nucleoli

Optional:

- Perinuclear **Halos = Koilocytes**
  - Large, irregular clearing
  - Thick borders, like it was drawn with a calligraphy pen
- **Multinucleation**





Caused by High and Low-risk HPV
May regress spontaneously!

Some findings, but "not enough"?

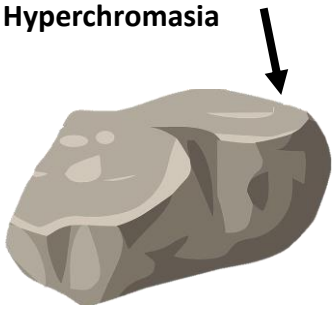
Consider "Atypical Squamous Cells of Undetermined Significance" (**ASCUS**)

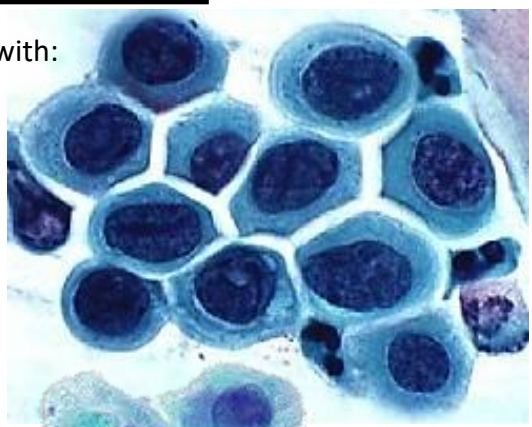
Can be either Quantitative (i.e., only rare atypical cells) or Qualitative (e.g., only 2x nuclear enlargement)

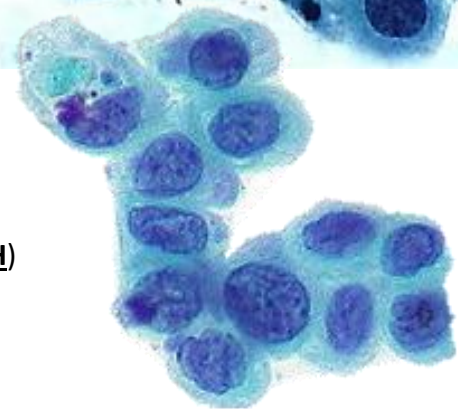
High-Grade Squamous Intraepithelial Lesion (HSIL)

Immature keratinocytes (minimal cytoplasm, **High N/C ratios**) with:

- **Markedly irregular nuclear contours**
  - *(Hint: think in 3-dimensions)*
  - *Look like boulders with all the irregularities*
- **Irregular chromatin and/or Hyperchromasia**







Some findings, but "not enough"?

Consider "Atypical Squamous Cells—Cannot exclude HSIL" (**ASC-H**)

Can be either Quantitative (i.e., only rare atypical cells) or Qualitative (e.g., only moderate atypia)

Squamous Cell Carcinoma

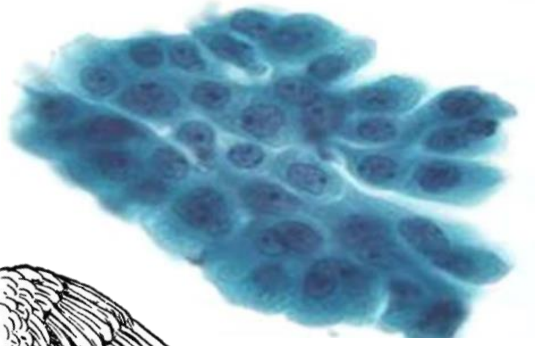
Non-keratinizing SCC may look like HSIL (similar findings)

Clues to invasion: "Tumor diathesis" (Necrotic debris)
Prominent nucleoli

Keratinizing SCC: Pleomorphic cells with hyperchromatic, irregular nuclei, prominent orangeophilic (keratinizing) cytoplasm, and bizarre shapes (like "Tadpoles" or snakes)

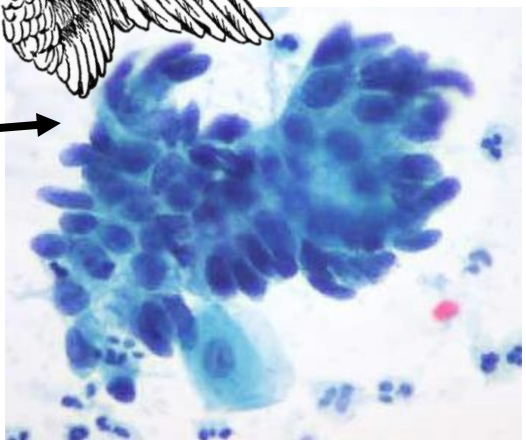
Glandular Abnormalities

Reactive Endocervical Cells
Nuclear enlargement (4-5x),
Hyperchromasia, BUT round nuclei with smooth contours and N:C ratios maintained. Prominent nucleoli.
Not too crowded. Mitoses, but no apoptosis.
Can see tubal metaplasia→ look for cilia!



*For AIS, think "**Feathery**," like a bird's wing.*

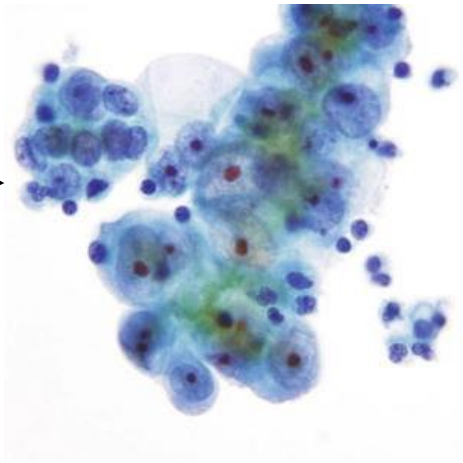
Endocervical Adenocarcinoma In Situ (AIS):
Nuclei enlargement and crowding (cigar-like, think GI adenoma)
High N:C ratios with coarse, dark chromatin.
Cellular crowding with rosettes and "feathery edges"
Mitoses and apoptosis. No nucleoli.
Most strongly associated with HPV18 subtype



Adenocarcinoma
Variable, depending on site of origin/type.
Generally, more pleomorphic/irregular.
Endometrial cell nuclei larger than intermediate cell.

Features suggesting invasion: 1)Macronucleoli, 2)Tumor diathesis, 3)increased single cells, and 4)irregular chromatin

Factors favoring endometrial adenocarcinoma (vs endocervix): Neutrophils, less cytoplasm, smaller nuclei

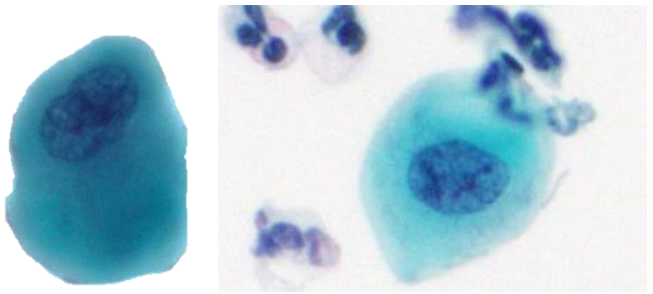


Practically speaking, often diagnose as simply: "Atypical Glandular Cells" using Bethesda System unless very pleomorphic

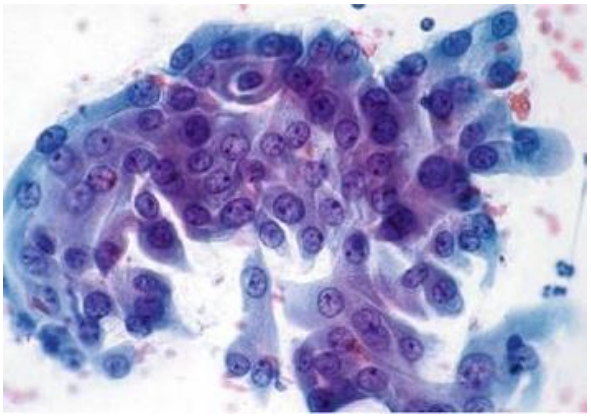
Squamous metaplasia

Thick, "Dense" cytoplasm (consistent, dark teal)
Sharply defined cell borders.
Round, usually central nuclei
Normal nuclear size

Count as sampling of transition zone

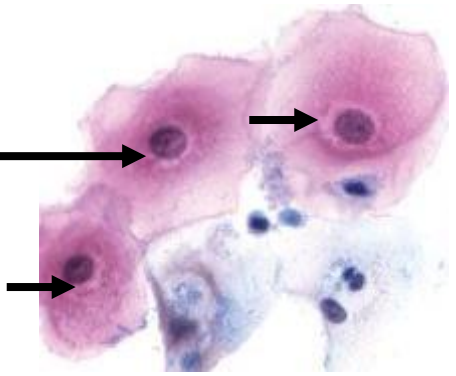


Reparative/Inflammatory Changes

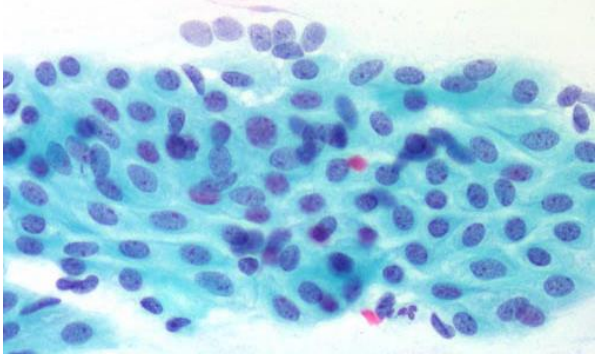


Classic "Repair"
Enlarged nuclei with Prominent Nucleoli.
Round nuclear contours with fine, pale chromatin.
Normal N:C ratios, but variably sized
Cohesive flat sheets of cells with "streaming" like pulled taffy
Background inflammation

General inflammatory change
Mild nuclear enlargement (<2x size)
Fine, pale chromatin
Often nucleoli
Can see small perinuclear clearing, but smaller, and more even than koilocytic halos

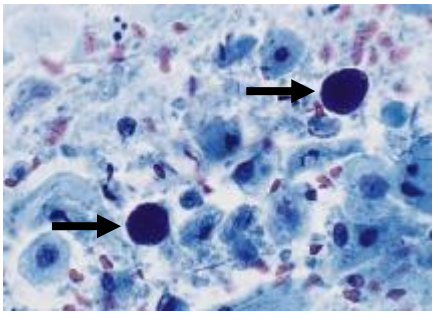


Atrophy



Seen in LOW estrogen states:
- Postmenopausal
- Postpartum
- Premenarche
- Turner syndrome

Predominance of **basal and parabasal cells** (High N:C ratios)
Prone to injury→ often inflammation



Immature cells that can mimic HSIL, BUT:
Finely granular chromatin
Smooth nuclear contours

Can see "Blue blobs" (see →) and granular debris (mimicking tumor diathesis, but no karyorrhectic nuclear debris)

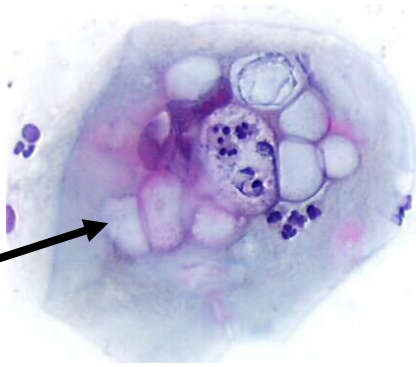
Radiation Changes

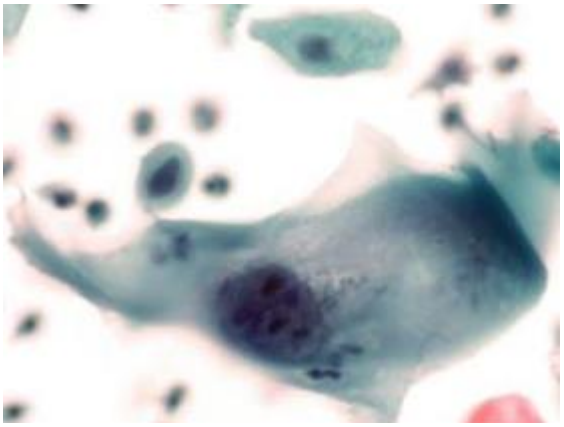
Cytomegaly: Big cells with Big nuclei (proportion N:C maintained)

Large, bizarre cells

Cytoplasmic vacuolation and polychromasia

Multinucleation



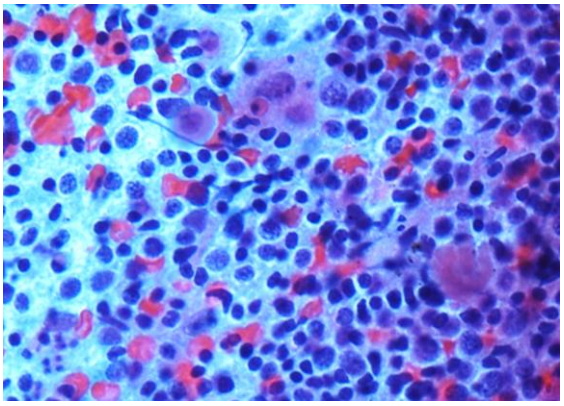


Follicular Cervicitis

Abundant **lymphocytes** (small rim of cytoplasm around round nucleus, unlike HSIL, which is irregular)

Numerous tingible body macrophages

Variably sized lymphocytes with plasma cells.



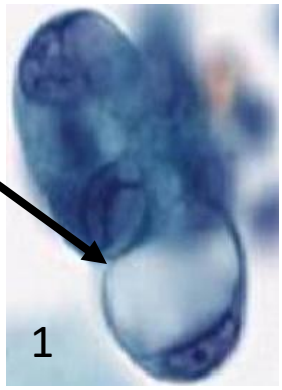
IUD-Effect

Two characteristic findings:

1) Cells with **abundant vacuolated cytoplasm** (mimicking Adenocarcinoma)

2) Cells with **small, dark nuclei** and scant cytoplasm (mimicking HSIL)

Always know history!

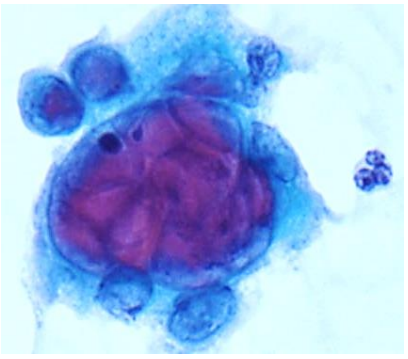


Herpes

3 M's
Molding of nuclei
Multinucleation
Margination of chromatin

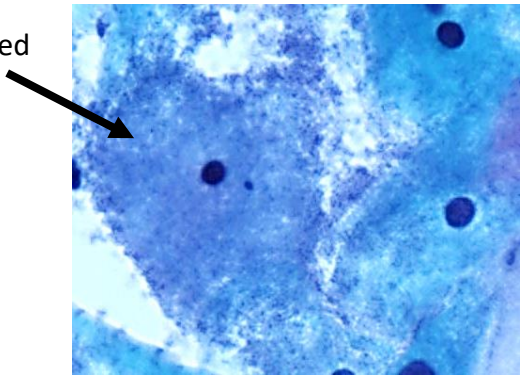
"Ground glass" chromatin with eosinophilic nuclear inclusions

Can treat with acyclovir



"Shift" in flora

"Clue Cells" = squamous cells <u>covered with shaggy bacilli</u> and mixed bacteria rather than the normal lactobacilli

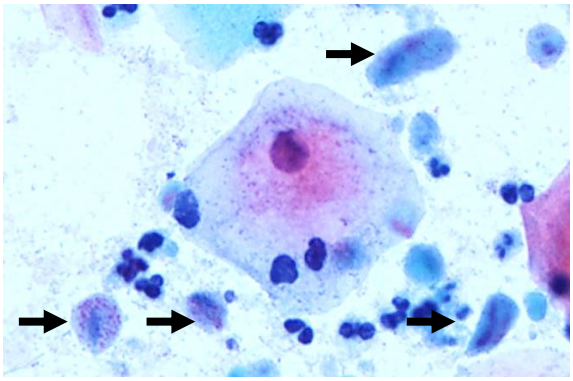


Thick, milky vaginal discharge with a foul "fishy" odor
(positive "whiff" test after adding KOH)

Most commonly attributed to *Gardenerella vaginalis*.

Treat if symptomatic.

Trichomonas Vaginalis

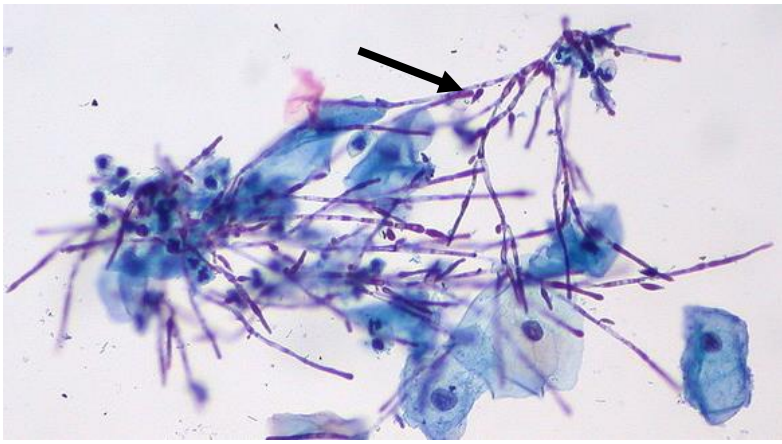


<u>Pear-shaped</u> protozoan STD
Pale, eccentric elongate nucleus
<u>Red cytoplasmic granules</u>

Often associated with Leptothrix (non-pathogenic filamentous bacterium).

Often acute inflammation and inflammatory halos
Treat with antibiotics

Candida

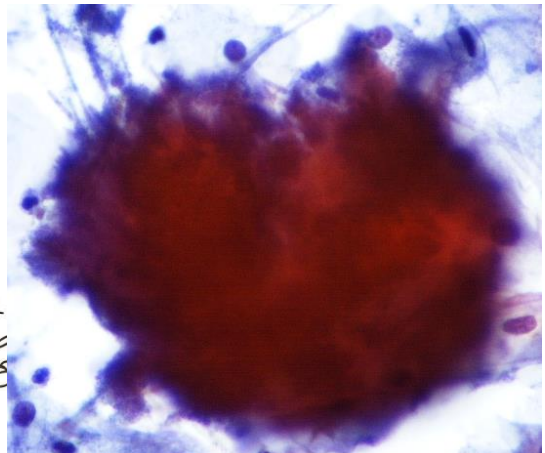


Fungal species that can cause infectious throughout the GYN tract (and other areas).
Thick, "cottage cheese" discharge
Eosinophilic yeast forms and <u>pseudohyphae</u> and hyphae ("Spaghetti and meatballs")
Often <u>tangled or skewering squamous cells</u>

Can have variable associated inflammation or inflammatory halos

Usually only treat if symptomatic

Actinomyces



Gram-positive **anaerobic bacteria**
Commonly associated with **<u>IUD</u>** (or other foreign body)

<u>Long, filamentous organisms</u>
Tangled clumps of bacteria that look like "cotton balls" or "<u>dust bunnies</u>"

No need to remove IUD or treat if asymptomatic

General Management

This is a very generalized and abbreviated (but hopefully still helpful) summarization!
For a full review of current management guidelines, please refer to the ASCCP website:
http://www.asccp.org/guidelines

Pap result → Next step

Unsatisfactory → Repeat Pap in 2-4 months

NILM, but HPV positive (> 30 yrs) → Repeat co-testing at 1 yr, OR, HPV subtyping, if high-risk→ colpo

ASCUS → HPV testing ("if you *Ask Us*, you should get an HPV test"), if positive → colpo; Neg→ routine

LSIL → Colposcopy, unless HPV negative, then can do repeat co-testing at 1 yr
21-24 yo with ASCUS or LSIL → follow-up in 12 months (likely to clear spontaneously)

ASC-H → Colposcopy

HSIL→ Colposcopy or LEEP

Atypical glandular cells → Colposcopy with endocervical sampling and endometrial sampling

Screening Recommendations (according to the USPSTF):

Women 21-65 Cytology alone every **3** years
OR Women 30-65 Co-testing (cytology + HPV testing) every **5** yrs
(Don't do HPV testing if less than 30 as high rate of positivity, but also clearance)
(Don't do any testing before age 21, after 65 if they have had good prior screening, or after a hysterectomy for benign reasons)

Human Papilloma Virus (HPV)

Sexually **T**ransmitted **D**isease.

Circular double stranded DNA virus

Infects transformation zone→ establishes itself and replicates in basal cells

Detected in the vast majority of cervical cancers.

Viral genes responsible for transforming host cells by integrating into the host DNA and disrupting tumor suppressor genes.
E6→ inactivates p53 (blocks apoptosis)
E7→ inactivates Rb (gets rid of cell cycle arrest→ uncontrolled growth)

However, many infections are naturally cleared, so only a minority persist and lead to cancer.

HPV subtypes
High-risk (associated with cervical cancer and HSIL, but can also cause LSIL)
16, 18, 31, 33
Type 16 is most commonly detected in cervical cancers
Type 18 is associated with Endocervical Adenocarcinoma

Low-risk (Not associated with HSIL. Instead associated with LSIL/condylomas)
6, 11, 42, 43