

Gynecologic Cytology Laboratory Practice and Methodology

Clinical Laboratory Advisory
Committee Meeting
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Outline

- What is a pap smear? What a pap smear **isn't!**
- Workflow in the cytopathology laboratory
- Pap smear terminology
- Ancillary testing
- Quality systems, educational programs and accreditation

What is a pap smear?

- Screening test for cervical carcinoma and precursor lesions
- Exfoliative cytology pioneered by George Papanicolaou in 1920's
- More than 60 million tests in U.S. annually
- An effective way of saving lives!

What a pap smear **isn't!**

- Not highly sensitive
- Not able to completely eliminate morbidity and mortality from cervical cancer
- Not a primary test for other gynecologic malignancies

Workflow in the cytology laboratory

- Technical processing
- Personnel and training
- Pap interpretation (screening and diagnosis)
- Pap test result reporting

Pap collection and staining

- No real changes for many decades
- 5 dyes in 3 solutions
- Spatula, broom or brush collection
- Conventional or liquid based processing
- Manual or highly automated



Personnel in the cytopathology laboratory

- Couriers
- Cytology processing technicians
- Cytotechnologists
- Pathologists
- Supervisory/administrative support





Cytology technical processors

- Typically non-degree trained
- Mostly trained "on the job"
- Small number of highly technical procedures
- No standardized proficiency testing



Cytotechnologists

- Bachelor level degree is required, with...
- Specialized training in cytotechnology from an accredited program
- Certification by National Registry Examination by the ASCP
- Enjoy independent, meticulous microscopic work
- Comfortable with a high degree of responsibility



Pathologists

- Are M.D. or D.O. degreed
- Residencies in anatomic and/or clinical pathology; certified after examination by the American Board of Pathology
- Residencies provide full and sufficient training for examination of pap tests and other cytology specimens
- Specialized fellowship programs, examination and subcertification available

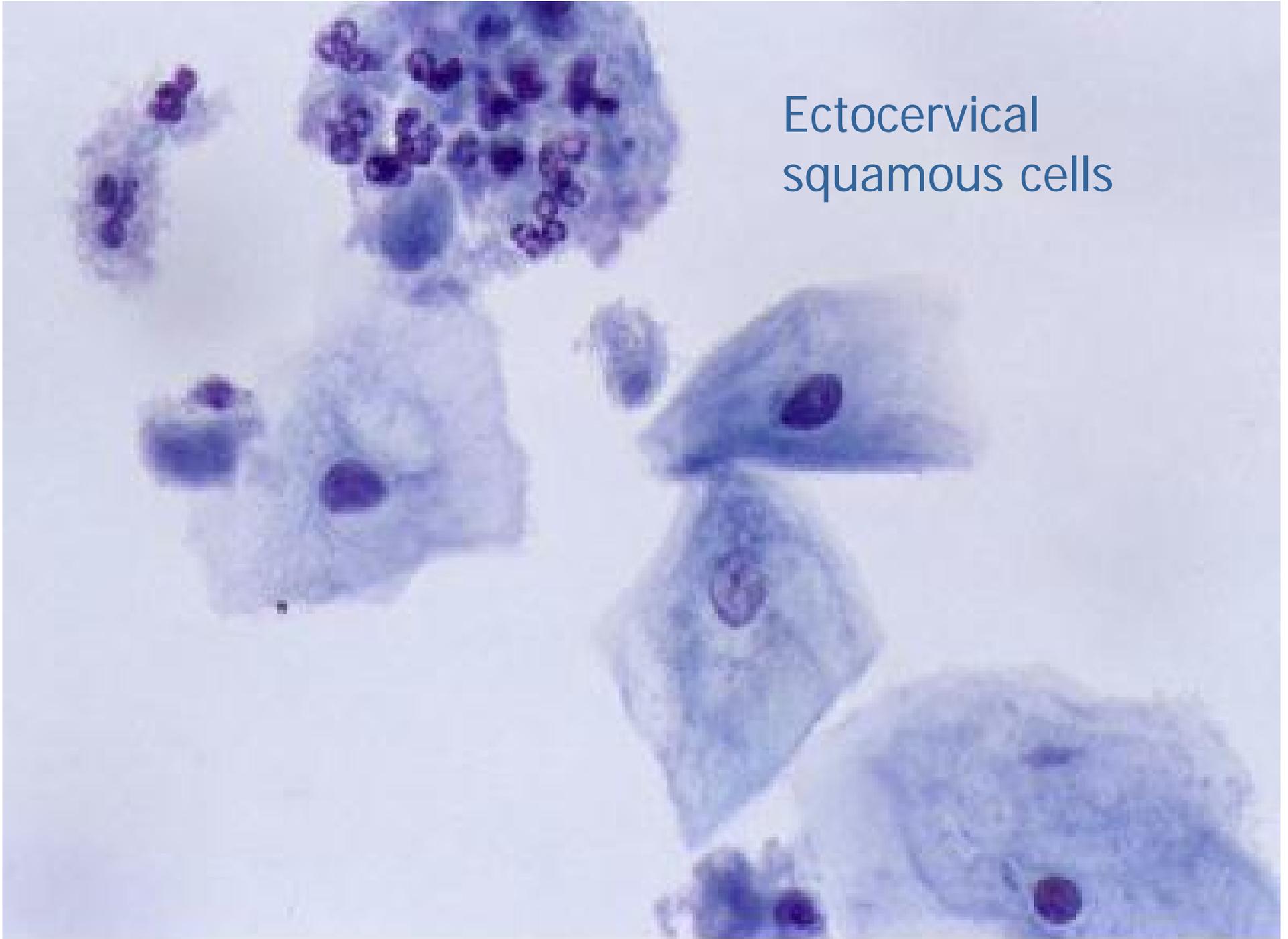
Skills needed for pap test evaluation

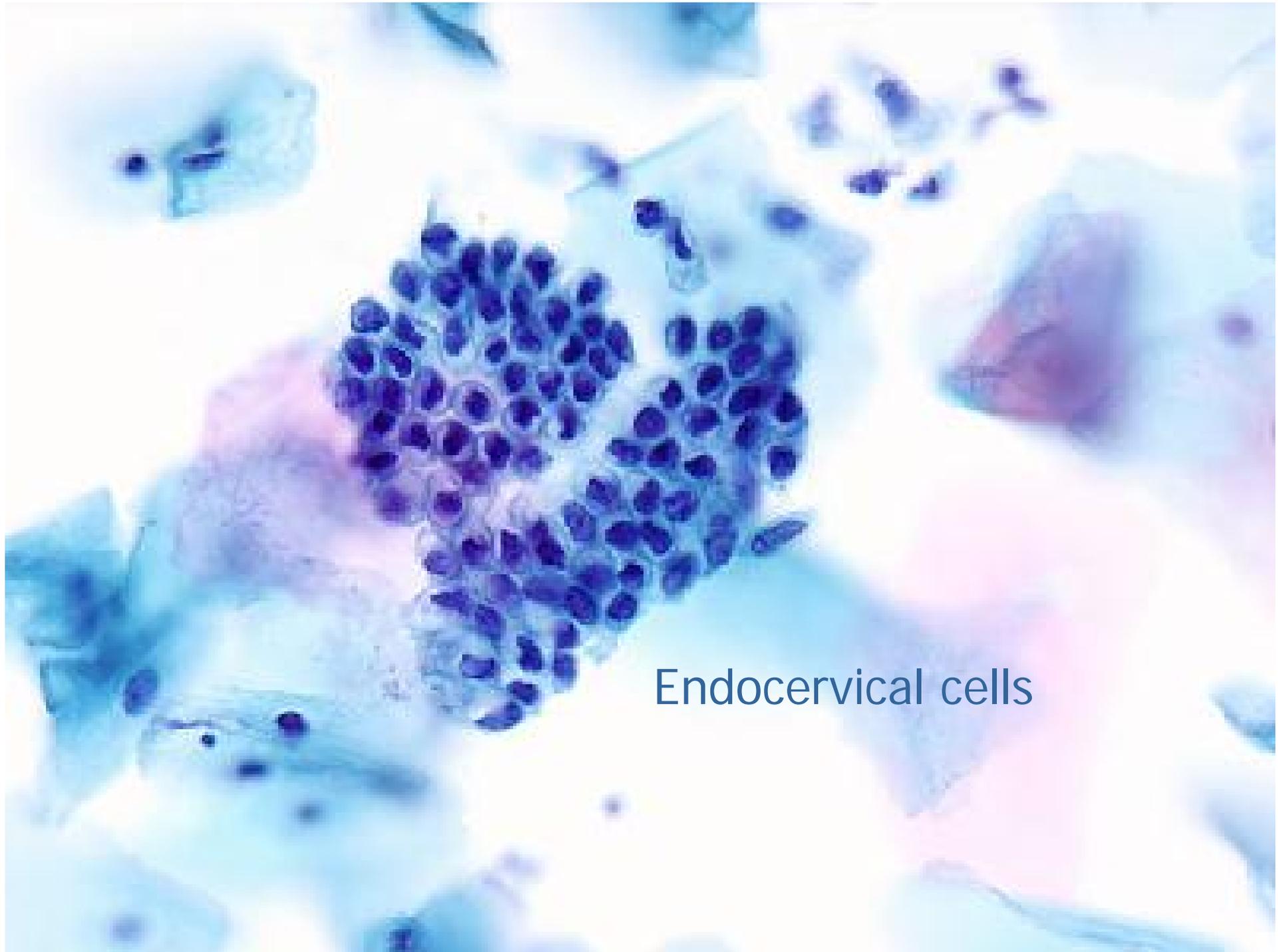
- Fund of knowledge of gynecologic diseases, including infectious, neoplastic, and degenerative processes
- Locator skills
- Interpretive skills
- Communication skills

Locator skills

- Conventional pap smears: 50,000 – 300,000 epithelial cells
- Liquid based tests: 50,000 – 75,000
- Minimal cellularity guidelines are established
- Percentage of abnormal cells may be as low as one hundredth of 1% of all cells on a smear
- Typical screening time per test: 5-10 minutes

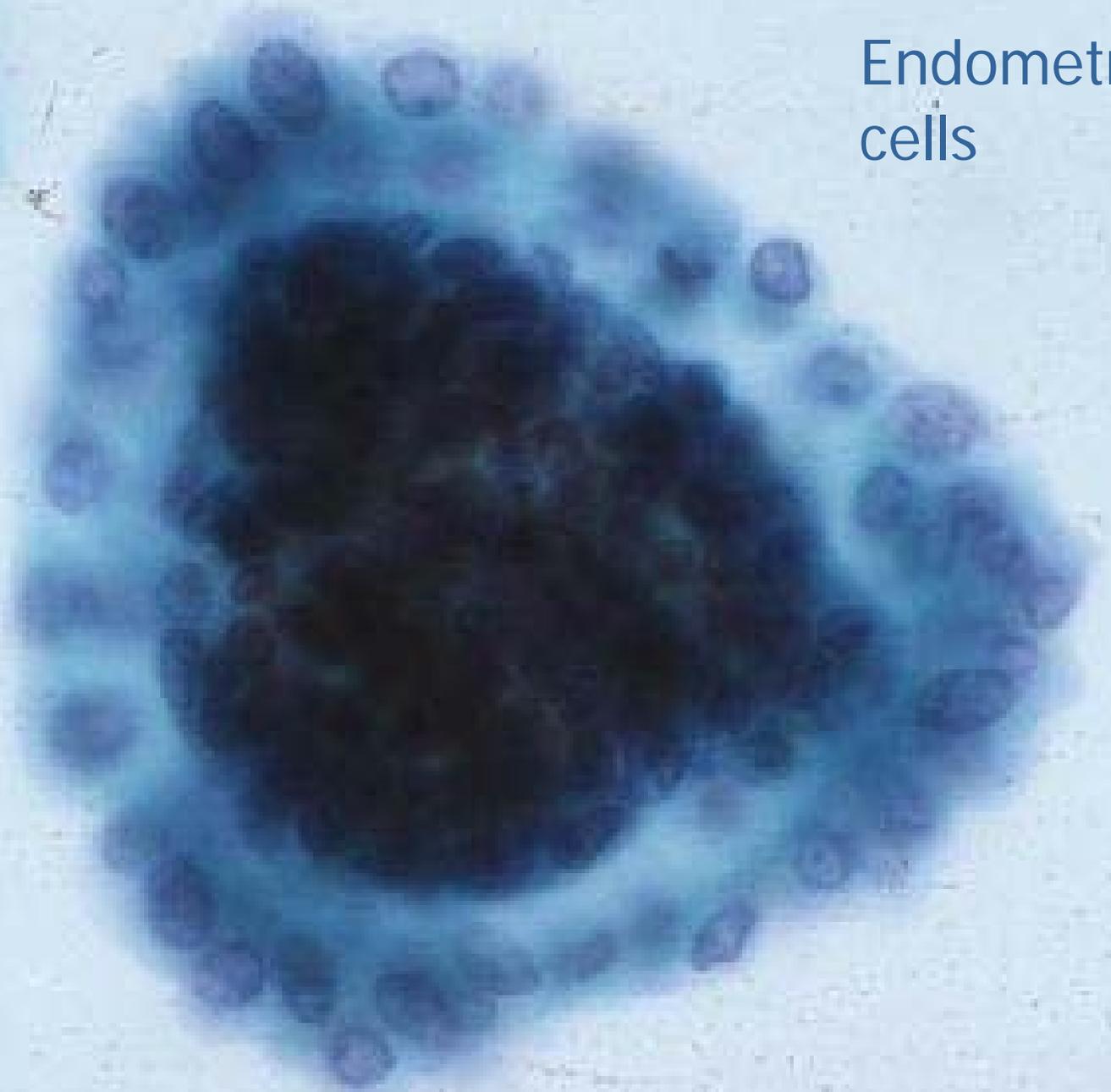
Ectocervical
squamous cells





Endocervical cells

Endometrial
cells



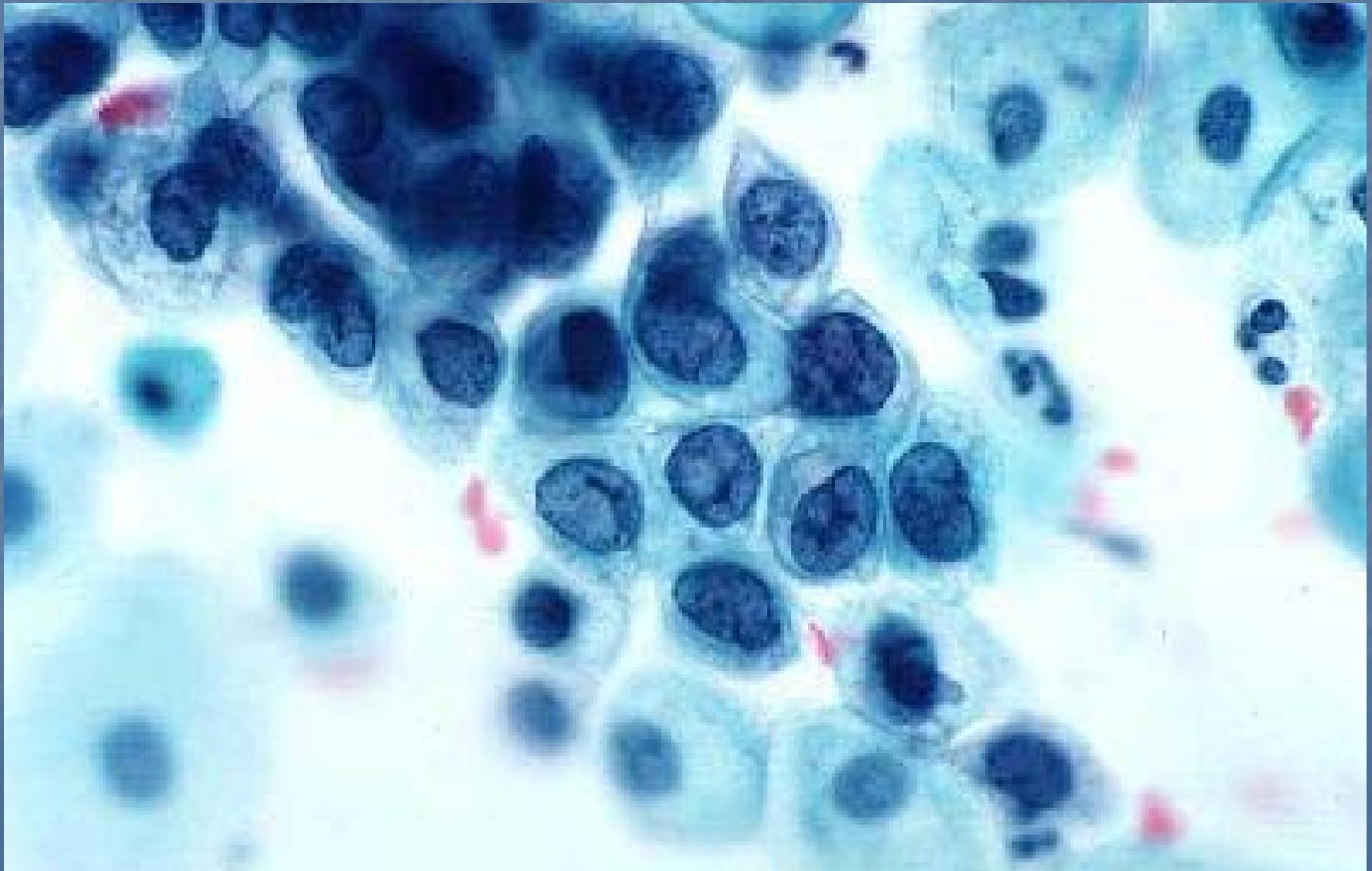
Like finding a needle in a haystack?

- **No, much harder!**
- A needle and a piece of hay are fundamentally dissimilar
- The background pieces of hay are essentially homogeneous
- You can rely on more than one sense (ouch!) to find the needle

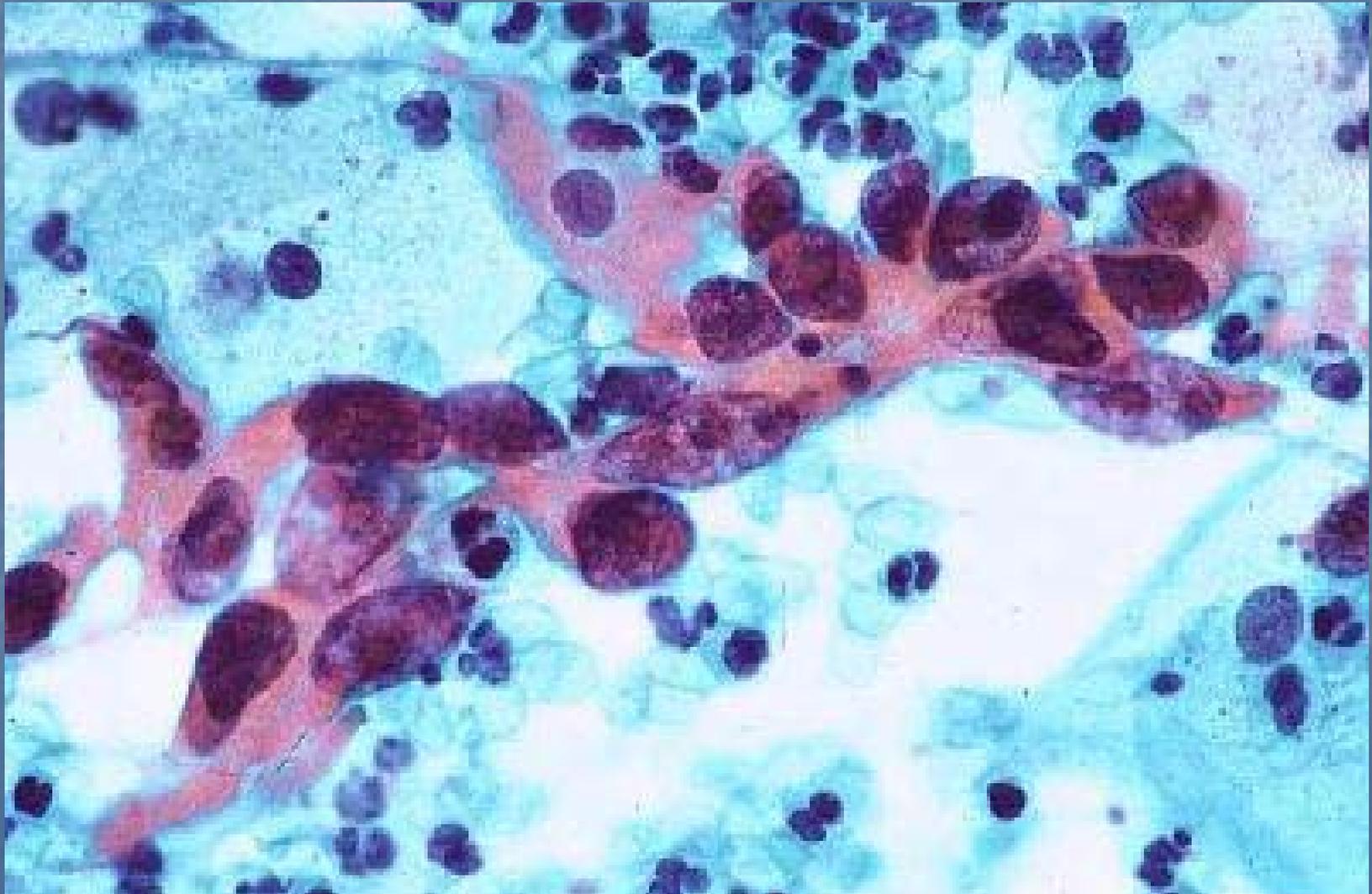
Low grade squamous dysplasia



High grade squamous dysplasia



Squamous cell carcinoma



Conventional vs liquid based smears

- The conventional pap smear has proved highly effective over several decades
- Liquid based (monolayer) techniques use cell suspensions to produce a standard sized image field, and use a slightly modified pap stain

Advantages of liquid based pap tests

- Reduces obscuring material
- Fewer "unsatisfactory" cases
- Higher sensitivity, especially in detection of high grade dysplasia
- Liquid reserve for ancillary testing

Terminology – a historical perspective

- Use of Papanicolaou "Class System, I-V"
- Dysplasia system (mild, moderate, severe, in situ carcinoma)
- Cervical intraepithelial neoplasia (CIN 1, 2 and 3)
- Squamous intraepithelial neoplasia (low grade, high grade)

The Bethesda System (TBS) 2001

- TBS revised twice since developed in 1988
- Bethesda Workshop 2001, 400 cytopathologists, cytotechnologists, clinicians and patient advocates
- Reviewed terminology and reporting of cervical cytology
- FINAL TBS 2001 Terminology reflects workshop recommendations

Bethesda 2001 Terminology

- Specimen type
- Specimen adequacy
- General categorization (optional)
- Automated review
- Ancillary testing
- Interpretation/result

“Negative for intraepithelial lesion or malignancy (NIL)”

- Replaces “within normal limits”
- May include smears with no epithelial abnormalities but with specific microorganisms requiring treatment, or other non-neoplastic findings

Epithelial cell abnormalities – Bethesda 2001

Squamous cell

- Atypical squamous cells of undetermined significance (ASC-US)
- Atypical squamous cells cannot exclude high grade intraepithelial lesion (ASC-H)
- Low grade squamous intraepithelial lesion (LSIL)
- High grade squamous intraepithelial lesion (HSIL)
- Squamous cell cancer

Glandular cell

- Atypical glandular cells (AGC)
- Adenocarcinoma in situ (AIS)
- Adenocarcinoma

CLIA terminology vs Bethesda 2001

- “Unsatisfactory” retained in both systems
- “NIL” present in both systems
- For PT, CLIA has eliminated ASCUS/AGUS challenges and responses
- CLIA responses include four classes:
 - **Class A - unsatisfactory**
 - **Class B – normal or benign changes**
 - **Class C – Low grade squamous intraepithelial lesions**
 - **Class D – High grade intraepithelial lesions and malignancies**

HPV Testing – Hybrid Capture 2

- Nucleic acid solution hybridization assay with signal amplification using probes complementary to the DNA sequences of 13 high risk HPV types
- Easy to perform – amenable to automation
- Two FDA approved uses: screening test in women over 30, and in women with slightly abnormal paps to determine if more testing or treatment might be needed.

Quality Systems in Cytopathology

- Quality control for staining and processing
- Initial 100% rescreening of newly hired technologists
- Statistical evaluation of individual performance to guide daily workload limits
- 10% random rescreen of "normals"
- Cytology-histology correlation and look backs
- Educational programs (ASCP, CAP)
- Proficiency testing

Additional roles of the pathology laboratory in GYN cytology

- HPV testing in the clinical laboratory
- Evaluation of related surgical pathology specimens
- Consultation with practitioners regarding pap test results
- Education and evaluation of new methods

Pap Test - Key points

- Effective, despite low sensitivity
- Most effective when tested at regular, repeated intervals
- Most effective when laboratory practices are optimized
- Role of pap test in cervical cancer prevention is evolving