세포병리의 역사

George N. Papanicolaou (1883~1962)

- American of Greek descent
- Anatomist of Cornell university

- Vaginal epithelial cell change during menstrual cycle (small glass pipette)

- Incidental observation of cancer cell in vaginal smears of women

“Pap smear”

- Late 1980s
  - 70% reduction in the mortality
- 1980s~today
  - New collection & automated processing method of cervical material
    - Liquid media
    - Monolayer preparation

세포 검체 채취방법에 따른 분류

- Collection of exfoliated cells
- Collection of cells removed by brushing or similar abrasive technique
- Aspiration biopsy or removal of cells from palpable or deeply seated lesions by means of needle
- Intraoperative cytology

Exfoliative cytology

- Spontaneous shedding of cells derived from the lining of an organ to into body cavity whence they can be removed by non-abrasive means

- Principal target
  - Female genital tract (Vaginal smear)
  - Sputum, voided urine, body fluid (effusions), etc.

Body fluids

- to determine the **cause of fluid accumulation** in body cavities
- to detect primary or metastatic cancer
- to detect many infectious processes in body cavity

Vaginal smear

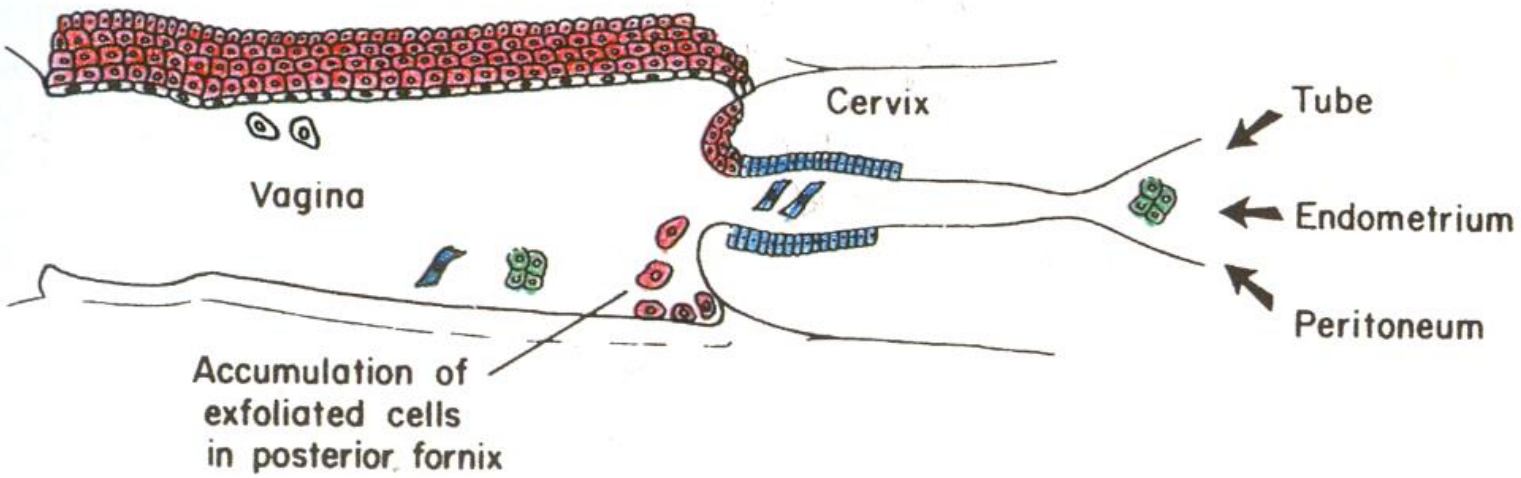


Figure 1-5 **Exfoliative cytology.** A schematic representation of the cross section of the vagina, uterine cervix, and the lower segment of the endometrial cavity. Cells desquamating from the epithelial lining of the various organs indicated in the drawing accumulate in the posterior vaginal fornix. Thus, material aspirated from the vaginal fornix will contain cells derived from the vagina, cervix, endometrium, and sometimes fallopian tube, ovary, and peritoneum. Common components of vaginal smears include inflammatory cells, bacteria, fungi, and parasites such as *Trichomonas vaginalis* (see Fig. 1-2). Red indicates squamous epithelium, blue represents endocervical epithelium, and green is endometrium.

Abrasive cytology

- Purpose : to enrich the sample with cells obtained directly from the surface of the target organs

- Cervical scraper or spatula
- Gastric balloon and esopha
- Brushing instruments
- Fiberoptic endoscopic Inst
  - Respiratory system : tra
  - Colonic brush cytology

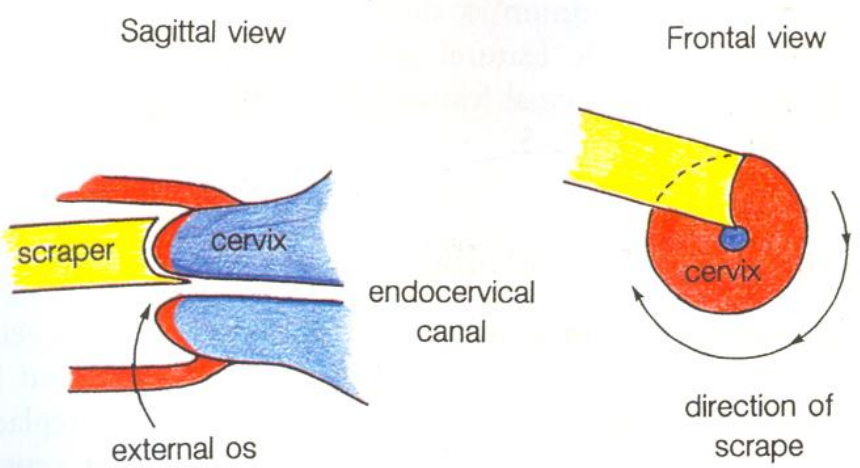


Figure 1-6 Method of obtaining an abrasive sample (scraping) from the uterine cervix by means of Ayre's scraper. Red indicates squamous epithelium and blue indicates endocervical mucosa.

Washing or Lavage techniques

- developed as a direct offshoot of rigid endoscopy
- With the development of flexible fiberoptic instruments, brushings replaced the washing technique

- Principal techniques
  - Peritoneal lavage
  - Bronchoalveolar lavage
  - Lavage of the urinary bladder

Aspiration cytology (FNA)

- Virtually any organ in the body sampled using either palpation or imaging techniques
- Well tolerated, easily adaptable as an outpatients procedures, rapid and cost-effective
- Throid gland, breast, Lung, Liver, Pancreas, Intraabdominal mass, Lymph nodes, etc.

Intraoperative cytology

- Intraoperative cytology is applicable to <u>all organs and tissues</u>
  : biopsy of breast, parathyroid, uterine cervix, etc.

- **Advantages**

1. easier, faster, and cheaper to prepare -> **<u>a rapid diagnosis</u>**!
2. If the sample is very small and brittle
3. Organs such as <u>pancreas</u> that are not suitable for freezing and cutting

- **Disadvantages**

1. Interpretation of intraoperative smears requires training and experience
2. False-positive (specificity), **false-negative (sensitivity)**

검체의 고정과
슬라이드 제작 및 염색

Classification of fixatives

1. **Aldehydes** : formaldehyde, glutaraldehyde, acrolein, glyoxal
2. **Oxidizing agents**
   : asmium tetroxide, potassium permanganate, potassium dichromate
3. **Protein-denaturing agents or coagulant**
   : acetic acid, methyl alcohol, ethyl alcohol
4. **Other cross-linking agents** : carbodiimides
5. **Physical** : heat, microwaves
6. **Miscellaneous** : mercuric chloride, picric acid, non-aldehyde-containing fixatives, dye stuffs

Fixation for Pap stain

- **Goal** : 세포의 단백성분, 형태의 변성 방지
- **Method** : 95% Ethanol에 15분이상 고정 (sample의 두께에 따라 변동 가능)
- **Fixatives**
  : 95% ethanol (m/c used)

- **Caution!!!**
  : Pap stain 검체는 건조 시켜서는 안됨.
  (건조될 경우 세포가 커져 염색성이 약해진다.)

∴고정액을 미리 준비하여 도말 직후 slide를 바로 넣도록 함.

세포 검체의 염색

- **Papanicolaou stain**

  - 진단세포학에서 일반검사 목적으로 사용하고 있는 가장 기본적인 염색법.

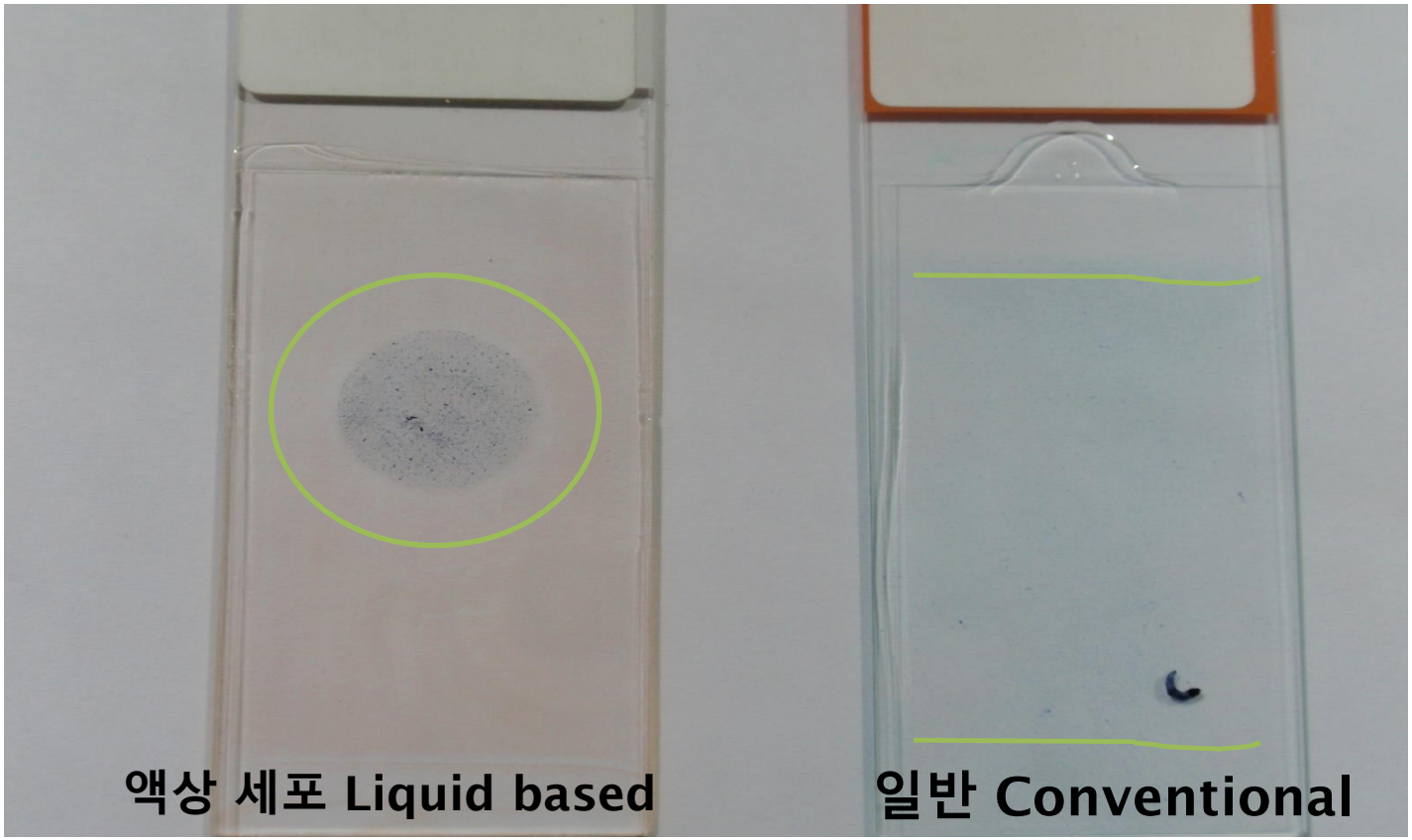
  - 단일 감별 염색법인 Shorr 엽색법을 도입하여 전통적인 H&E 염색법을 수정한 것으로 두 가지의 염색방법을 결합한 방법.

  - 핵의 미세구조가 명확하며, 염색질이 뚜렷하고 선명하게 나타남.

  - 세포질이 여러 염료(dye)에 의하여 대조적으로 감별 염색되고, 세포질이 투명하게 보임.

세포검체 제작

- Conventional method
- Liquid based method



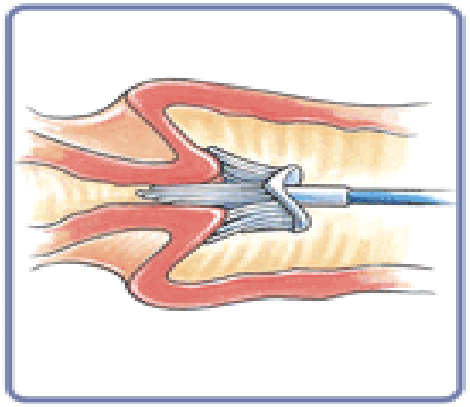
Liquid base cytology
원리와 이용

Liquid based cytology 예

- ✓ "SurePath" and "ThinPrep 2000"

  approved by the FDA for cervicovagina testing

- ThinPrep 검사는 재래식 검사의 한계를 극복하기 위해 미국에서 새로 개발된 기술로서1996년 미국 식품의약청(FDA)에 의해 재래식 자궁경부 세포도말 검사의 대체 검사법으로 공인되었습니다.
- 이방법에 의하면 세포 보존액이 들어있는 Vial에 채취도구를 잘 흔들어 세포를 씻어낸후 그 보존액을 전용장비로 처리하여 엉킨 세포를 분산시켜줌과동시에 혈액,점액,염증,세포등 진단 에방해가 되는 성분을 제거한 뒤 특수필터를 통해 진단 세포만을 선택적으로 수거하여 현미경 슬라이드상에 직경2cm크기의 균일하고도 박층으로 도말된세포군을 형성시켜줍니다.



Step 1: Collect

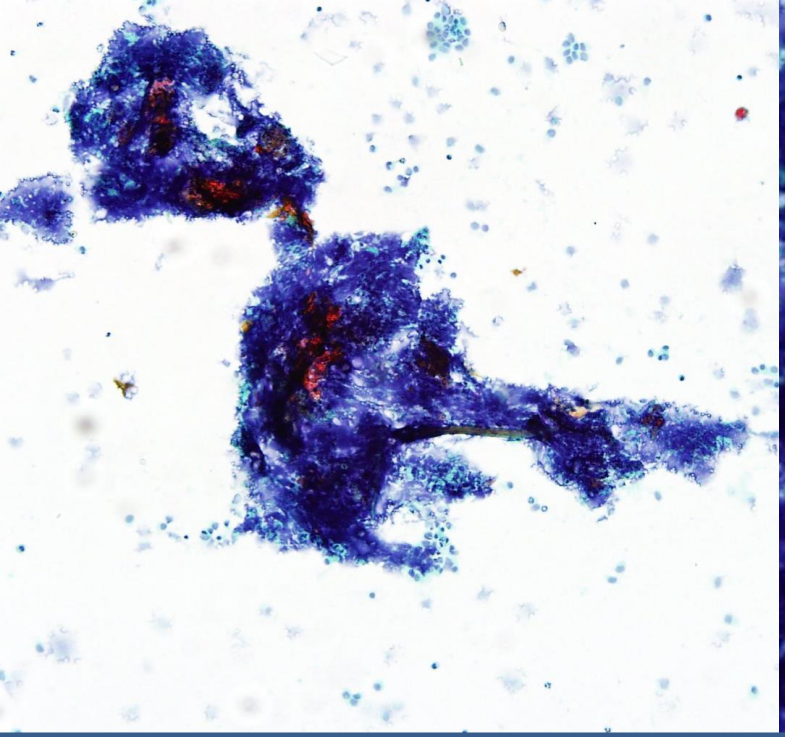
SurePath® uses a unique, easy to use sample collection process. A cytologic sample is collected by a healthcare professional using a broom-like or a brush/spatula combination of collection devices.

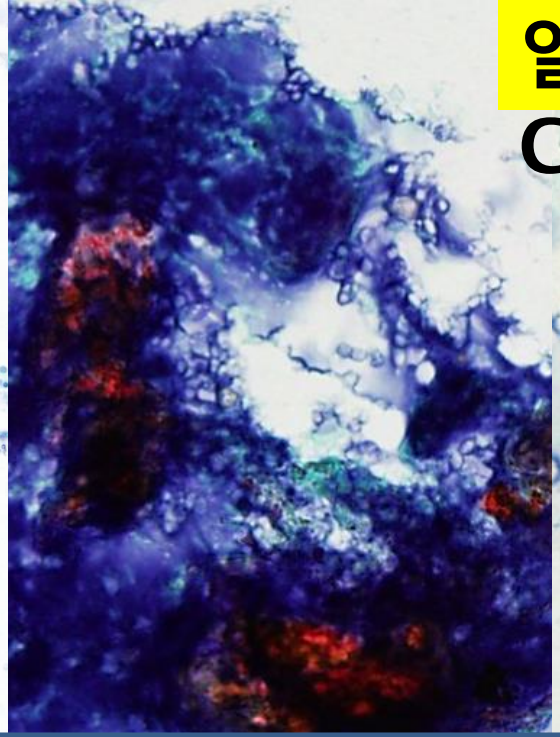
Step 2: Drop

Once the sample is collected, the detachable head(s) of the collection device(s) is dropped into the proprietary SurePath® preservative vial to retain 100% of the cells collected.

Step 3: Send

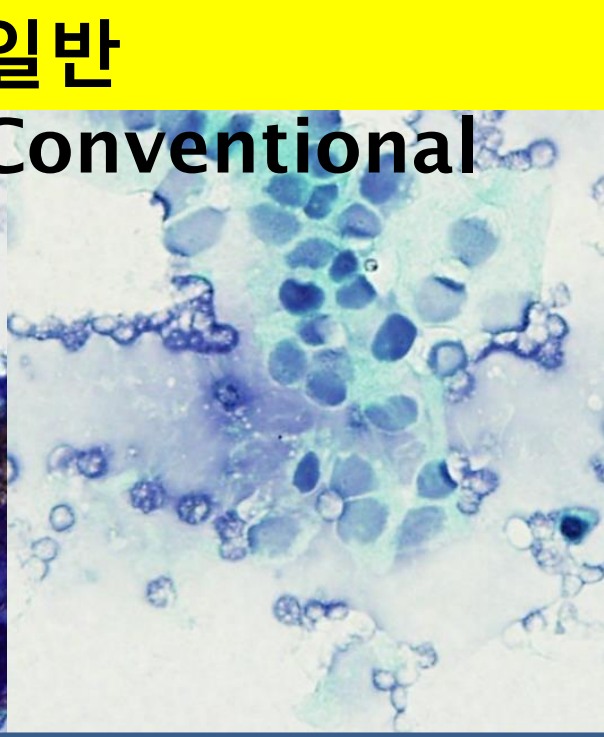
The vial is then sealed and sent to the lab for processing and analysis.

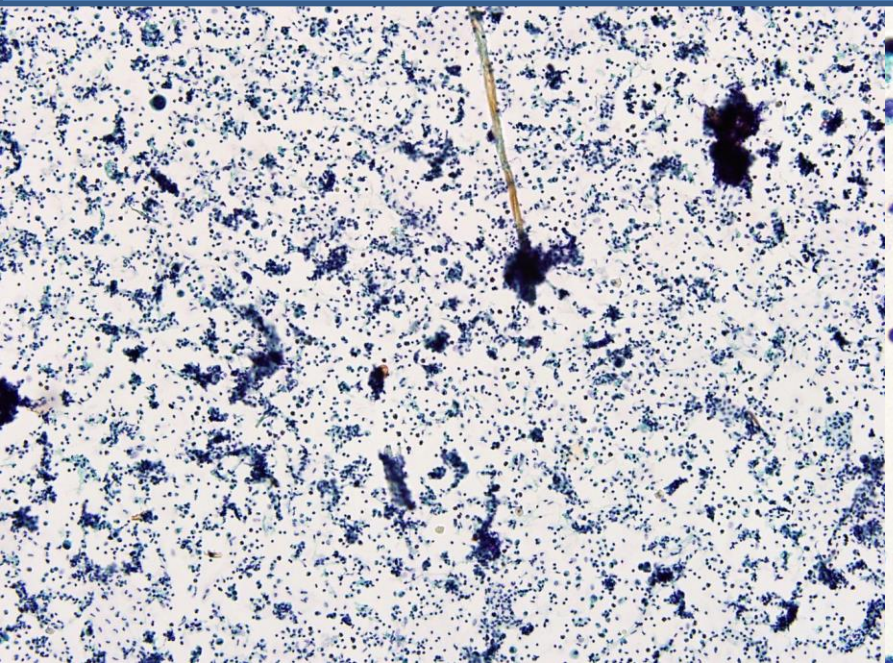




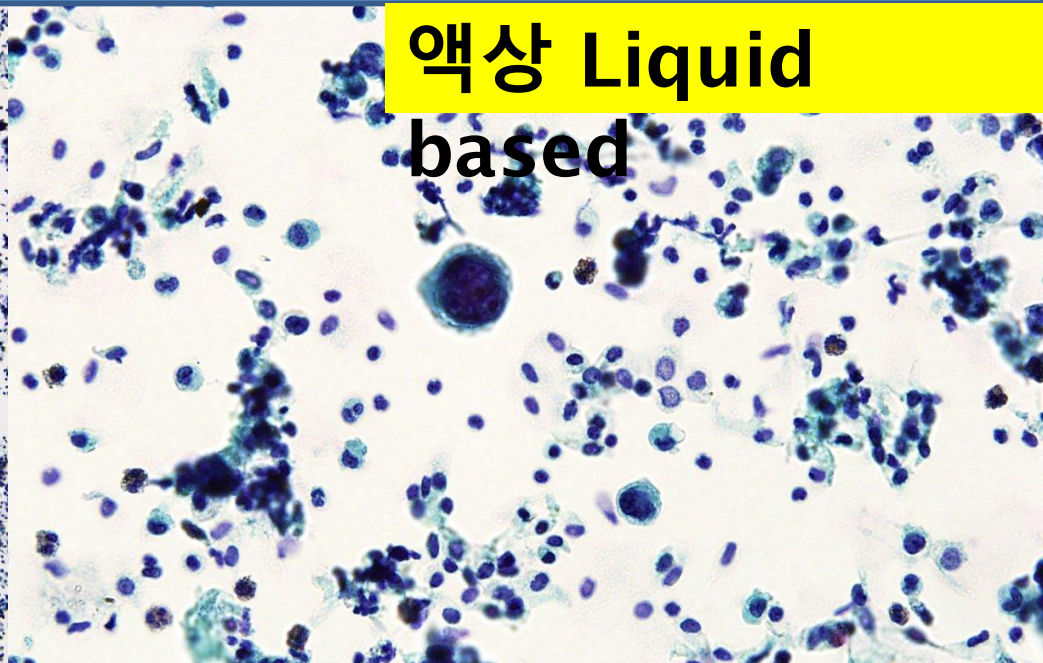
일반

Conventional





액상 Liquid based



부인과 세포병리 진단체계

The Bethesda system for reporting cervical/vaginal diagnosis

Specimen Adequacy

Satisfactory / unsatisfactory

General Categorization

1. Negative for intraepithelial lesion or malignancy (NILM)
   (infection, inflammation, radiation and etc.)
1. Epithelial cell abnormality :

A. Squamous cell

1. Atypical squamous cells
   1) of undetermined significance (ASC-US)
   2) cannot exclude HSIL (ASC-H)
1. Low grade squamous intraepithelial lesion (LSIL) Encompassing:

1) HPV /
   2) mild dysplasia / CIN 1
3. High grade squamous intraepithelial lesion (HSIL) Encompassing:
   1) moderate / CIN 2
   2) severe dysplasia, CIN 3
   3) CIS
   4) With features suspicious for invasion (*if invasion is suspected*)
4. Squamous cell carcinoma

A. Glandular cell

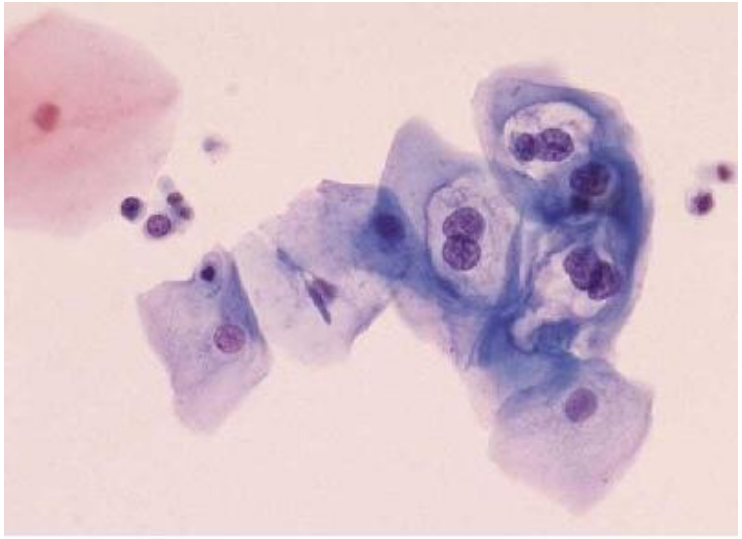
1. Atypical
   1) endocervical cells (NOS *or* favor neoplastic)
   2) endometrial cells (NOS *or* favor neoplastic)
   3) glandular cells (NOS *or specify in comments*)
2. Endocervical adenocarcinoma *in situ*
3. Adenocarcinoma
   1) Endocervical
   2) Endometrial
   3) Extrauterine
   4) not otherwise specified (NOS)

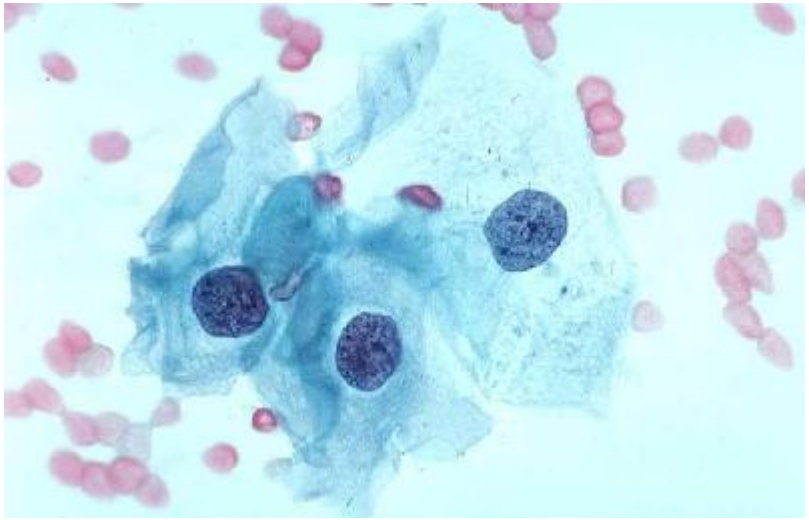
1. Others
2. Interpretation

Cytologic diagnosis of pap smear

- SQUAMOUS CELL
  - **Low grade squamous intraepithelial lesion (LSIL)**

    encompassing: HPV/mild dysplasia/CIN 1



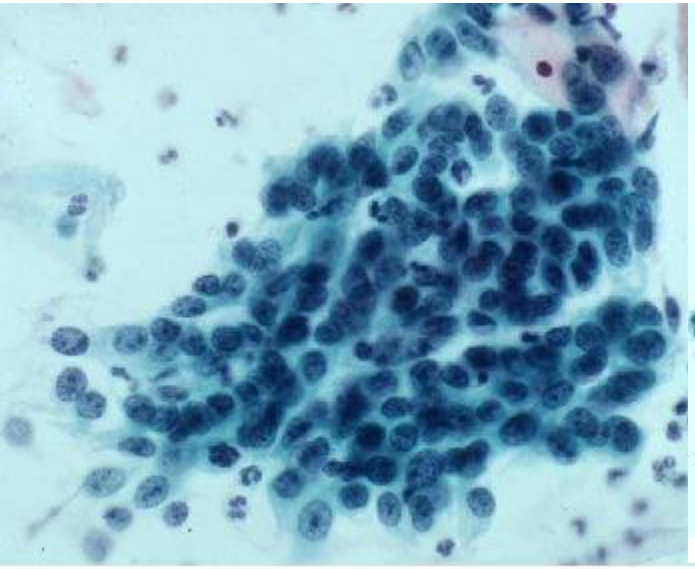
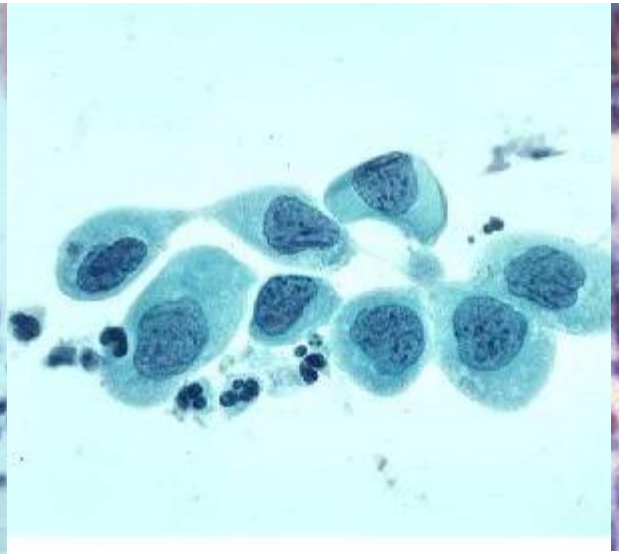
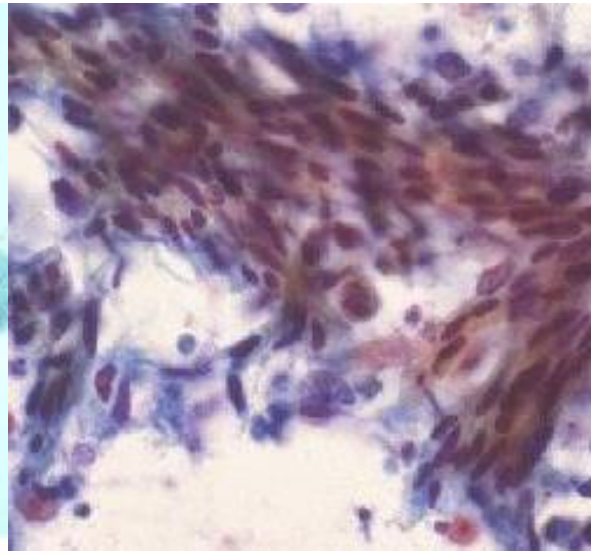


EPITHELIAL CELL ABNORMALITIES

- SQUAMOUS CELL
  - **High grade squamous intraepithelial lesion (HSIL)**

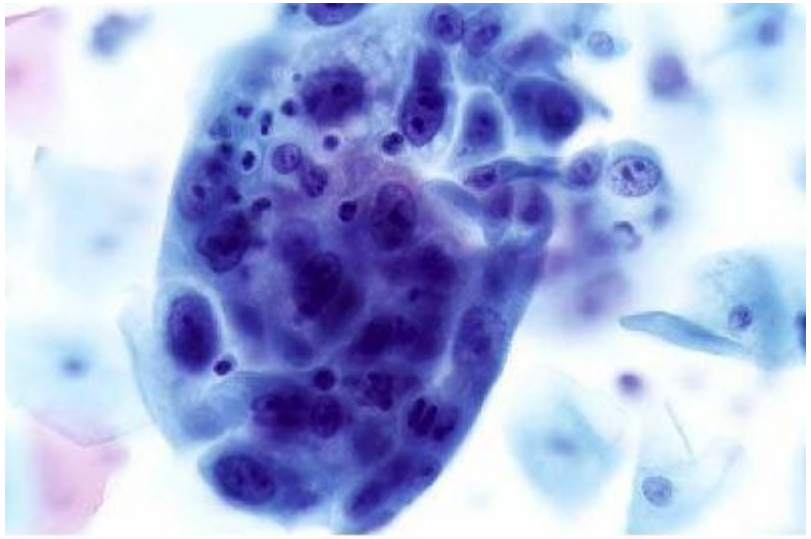
    encompassing: moderate and severe dysplasia, CIS/CIN 2 & CIN 3

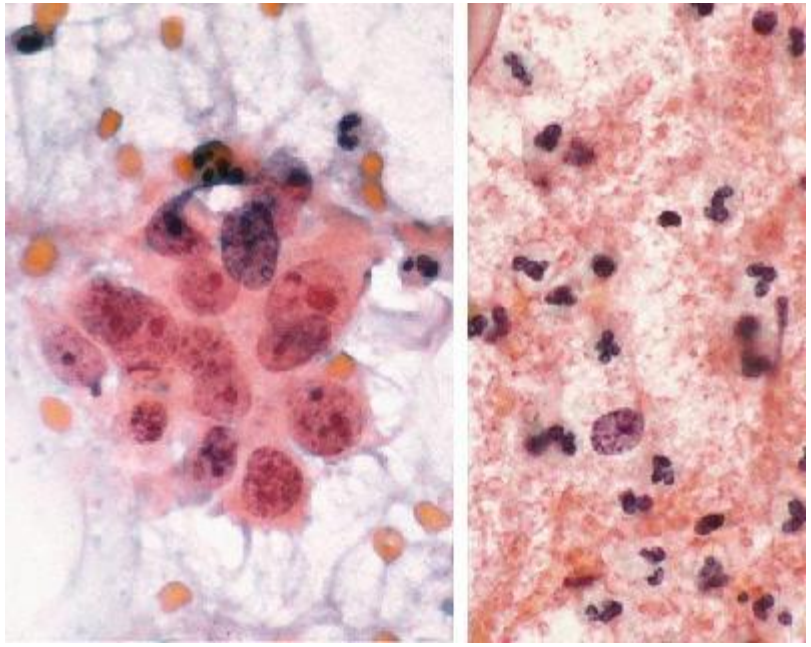
    - with features suspicious for invasion (*if invasion is suspected*)

EPITHELIAL CELL ABNORMALITIES

- SQUAMOUS CELL
  - **Squamous cell carcinoma**





Focal point system-computerized screening system