Cytopathology

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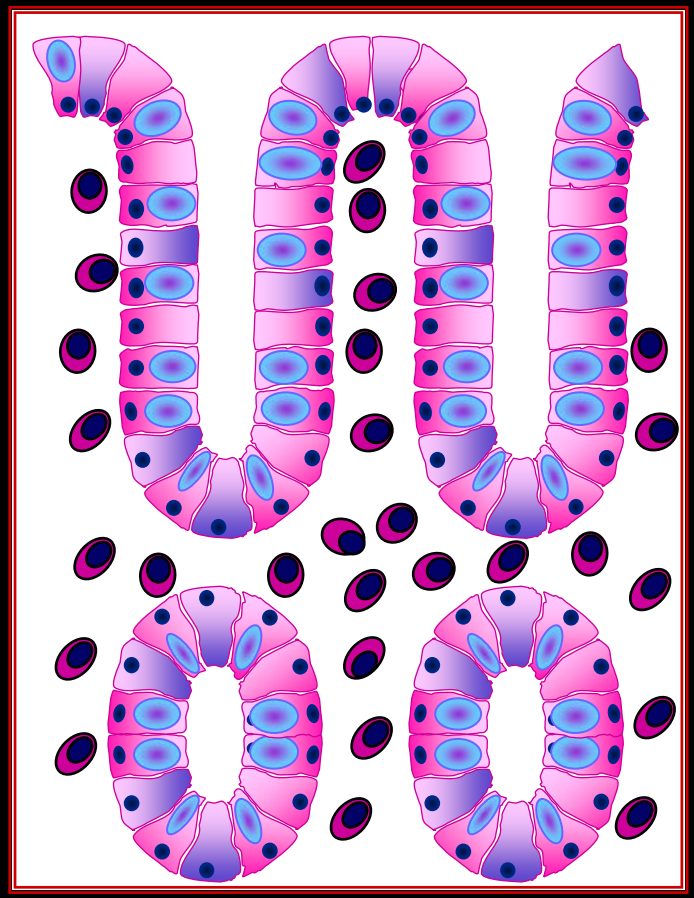
Learning objectives

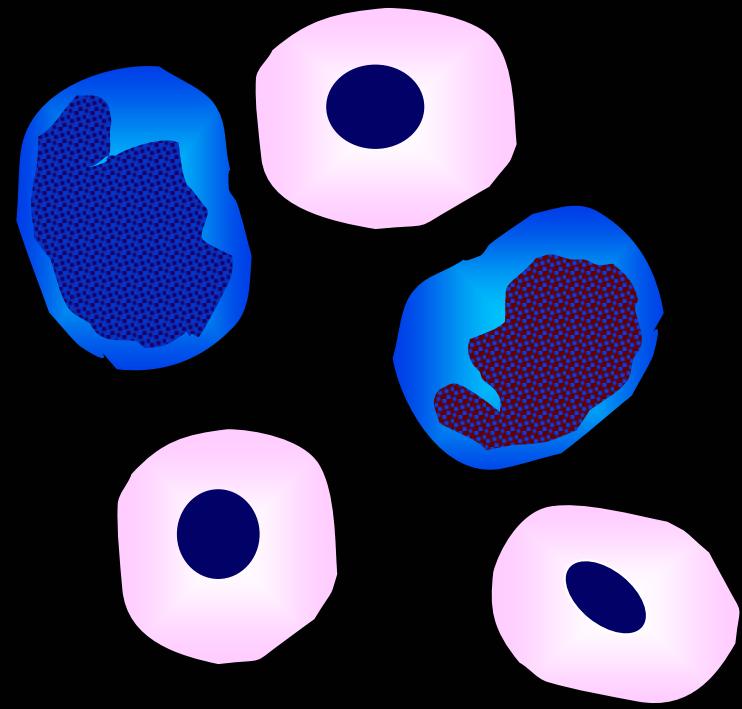
At the end of this hour you will know:

1. What cytopathology is
2. How specimens are collected, processed, and diagnosed
3. What the major problems are
4. How to design a cytopathology study
5. Where to find additional information

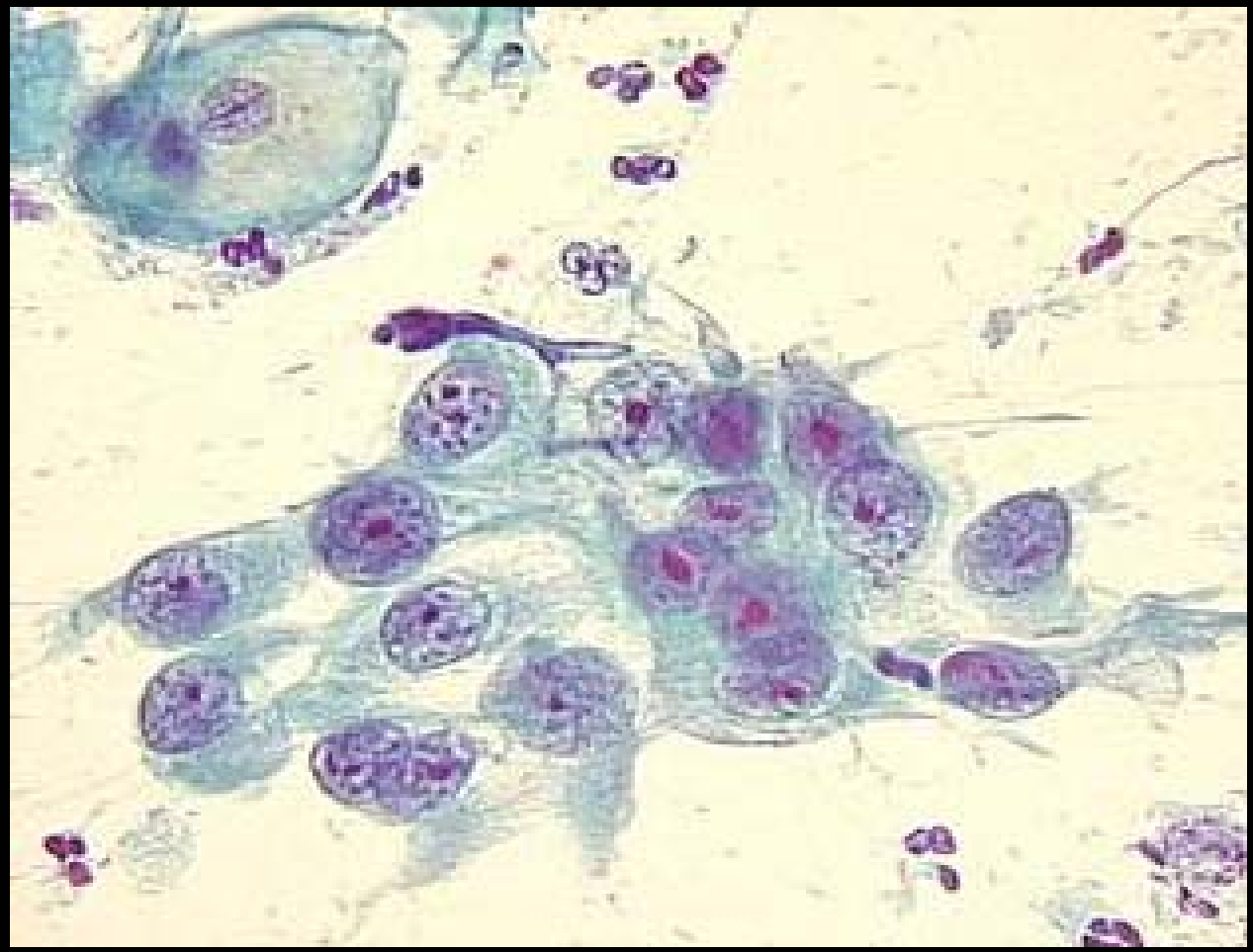
What is cytopathology?



Histopathology



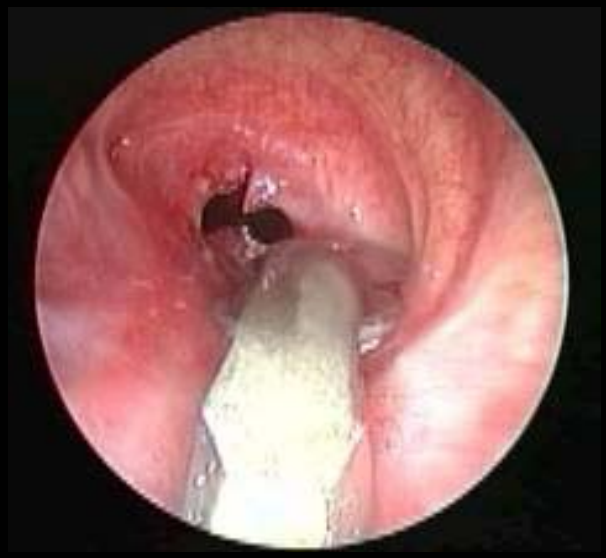
Cytopathology

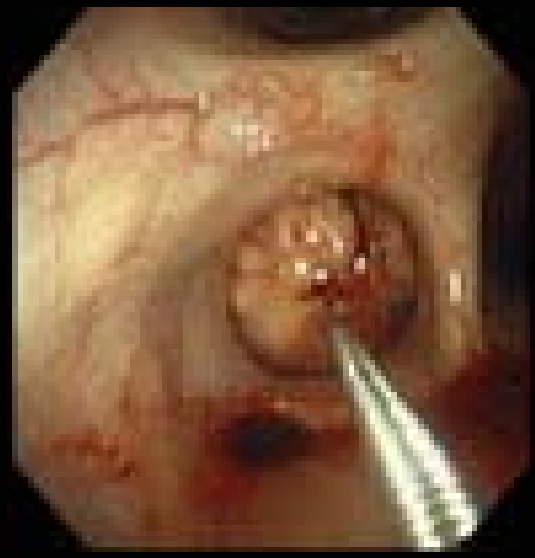


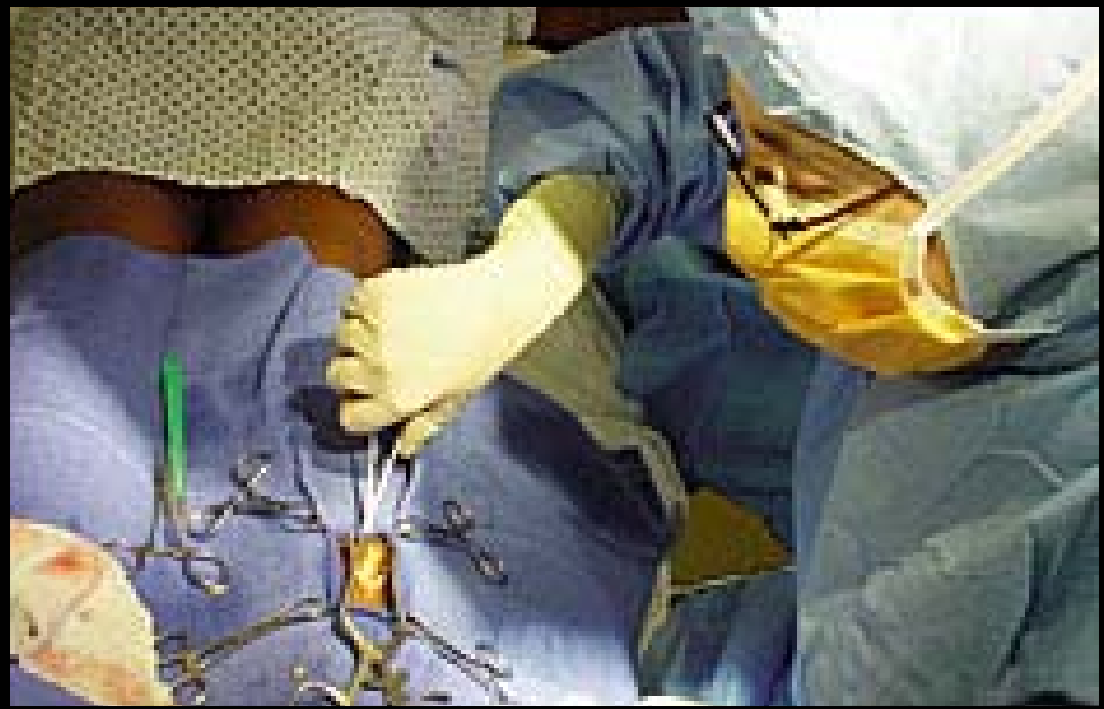
Cytopathology is the morphological study of dissociated cells

Why not always histopathology?

- Histopathology requires fragments of tissue (biopsies)
- A biopsy is usually obtained through an invasive procedure
- A forceps (or similar instrument is needed)
- There may be bleeding or trauma





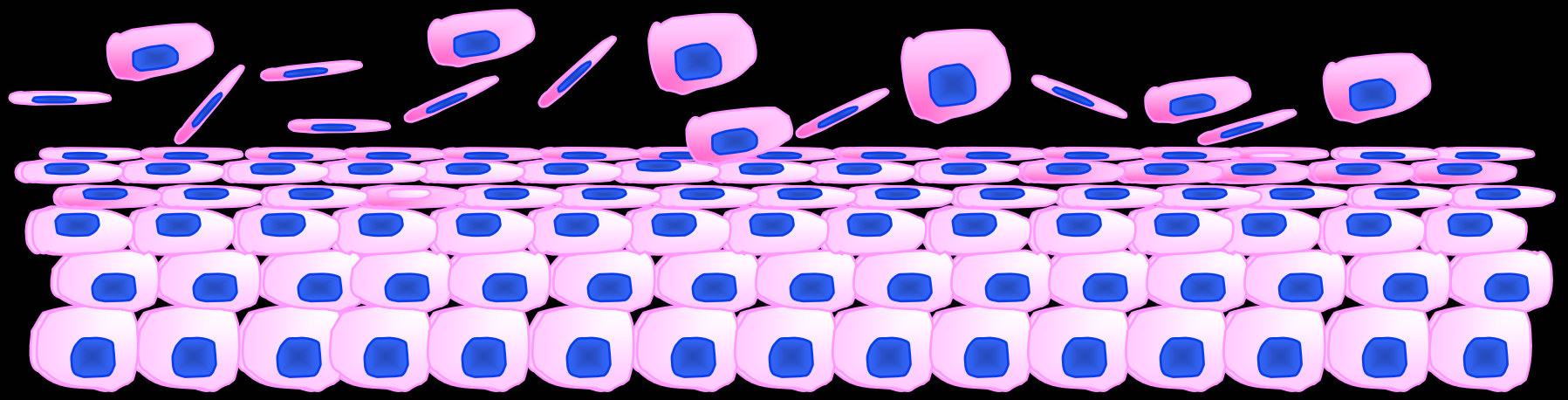


Histopathology

- Structure and architecture
- Biopsy
- Large needle, forceps
- Invasive procedure
- 30 min. – 2 hrs.
- Diagnosis: 24 – 48 hrs.
- Basic stain: H & E
- Paraffin block
- Special techniques possible

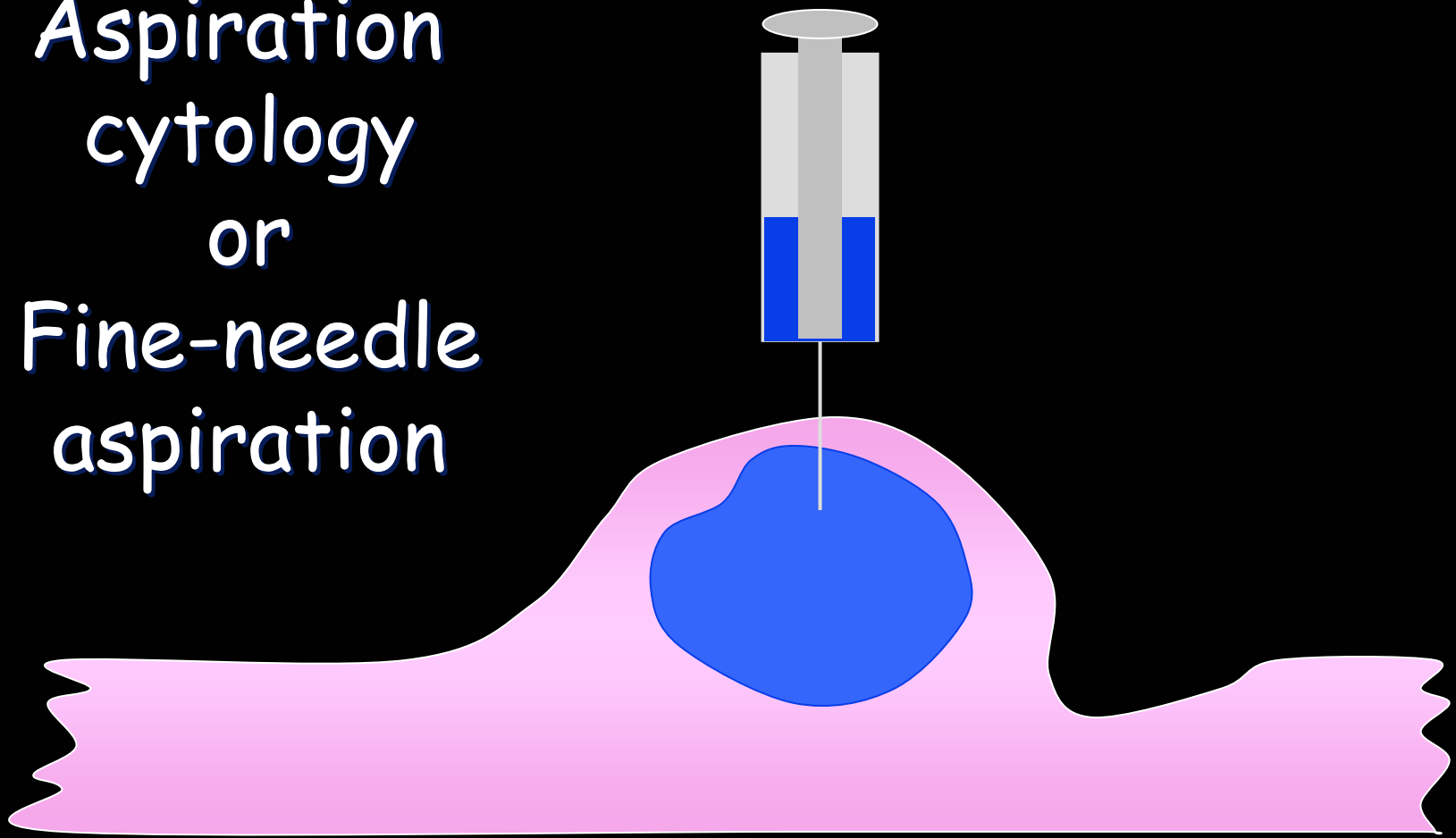
Cytopathology

- Detached cells
- Fluid, brushings
- Fine needle
- Invasive procedure
- 5 min. – 2 hrs.
- Diagnosis: mins. - 24 hrs.
- Basic stains: PAP - H & E
- Slide and/or paraffin block
- Special techniques possible

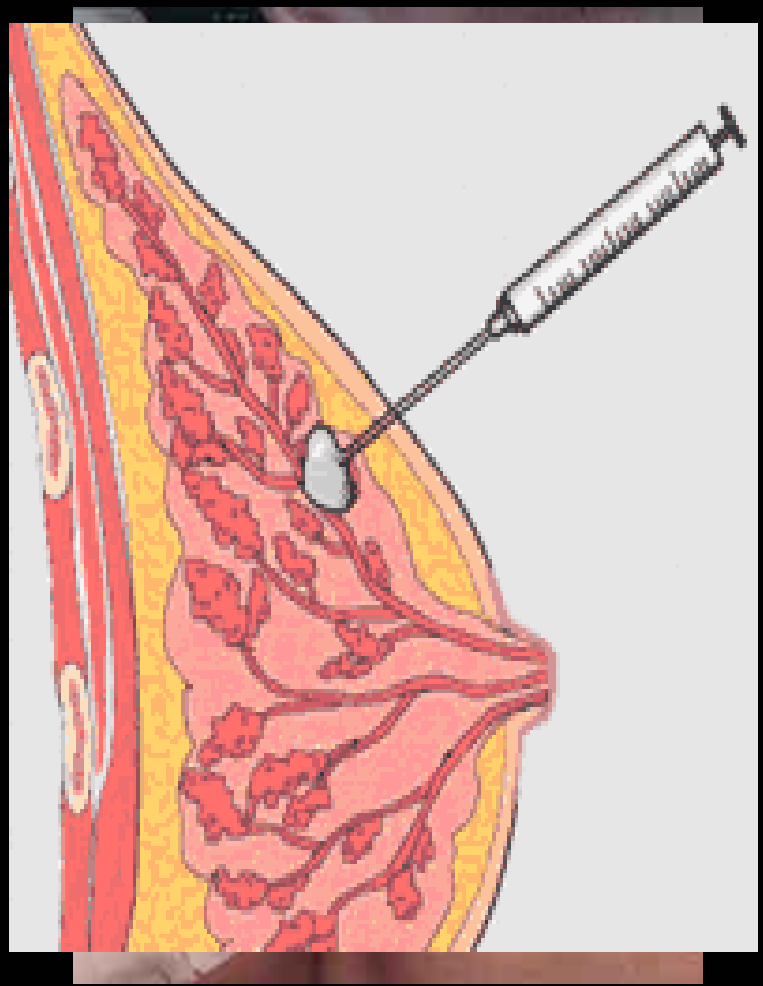


Exfoliative cytology

Aspiration cytology or Fine-needle aspiration



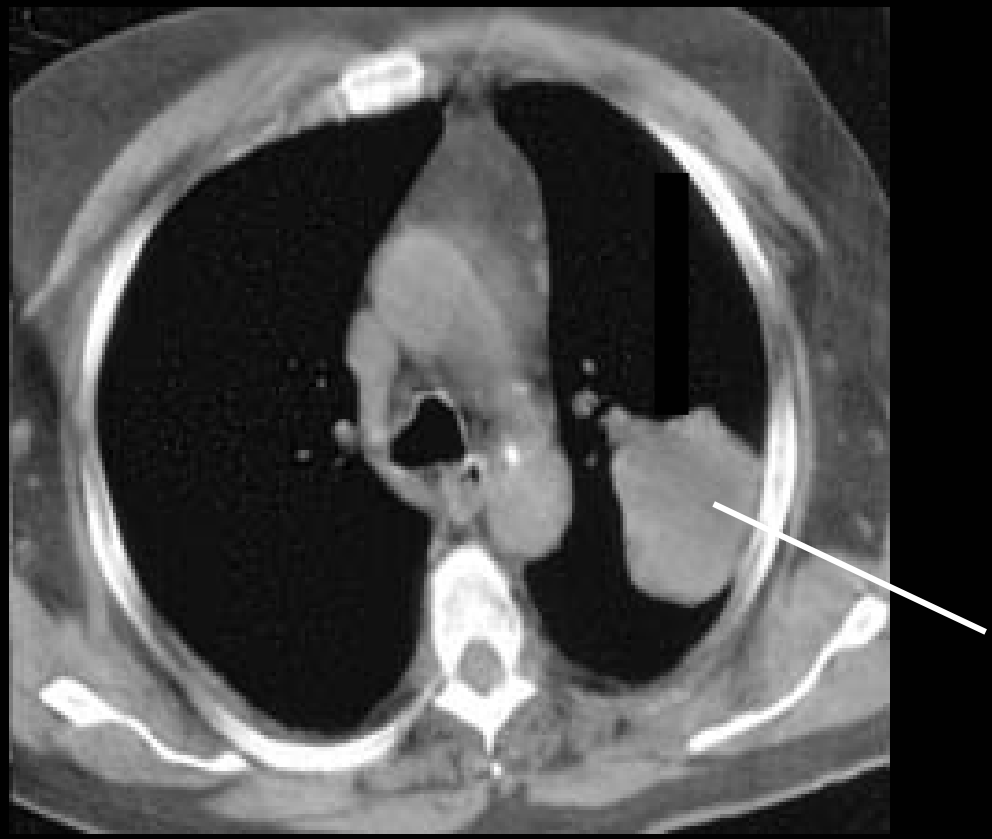
Aspiration



All superficial "lumps"
Breast growths
Thyroid nodules
Enlarged lymph nodes

Aspiration

Deep lesions may be aspirated under imaging guidance (US - CAT)

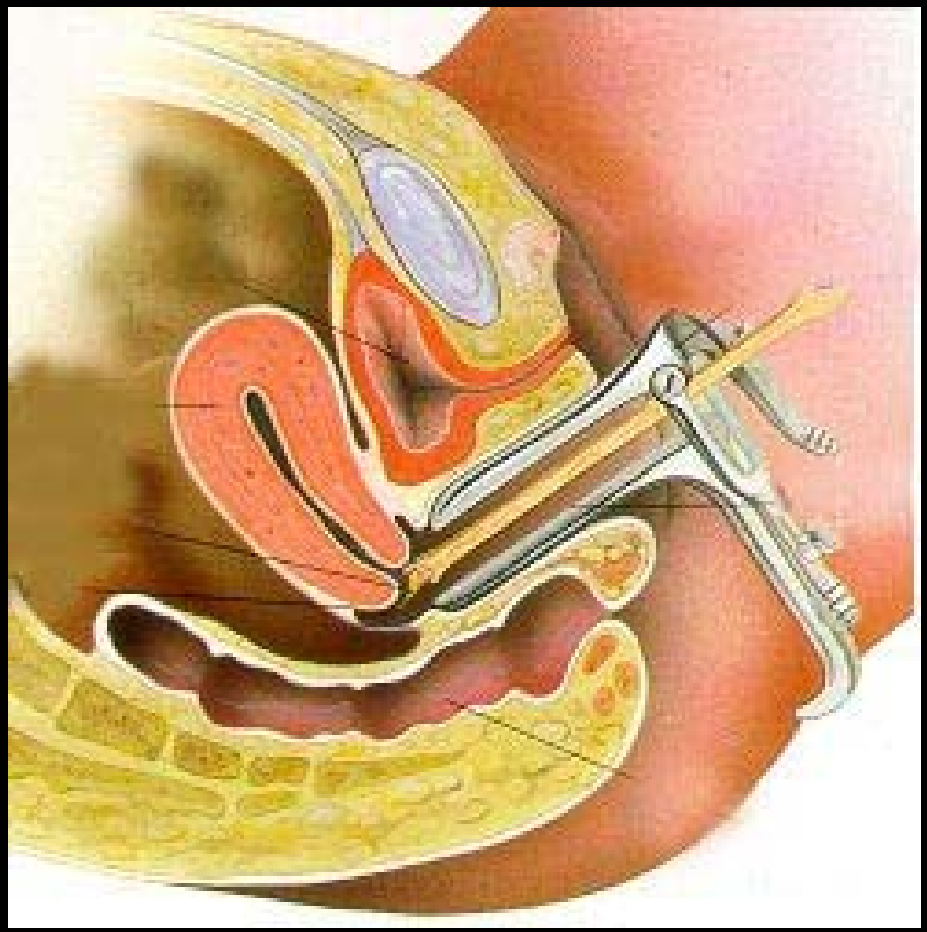


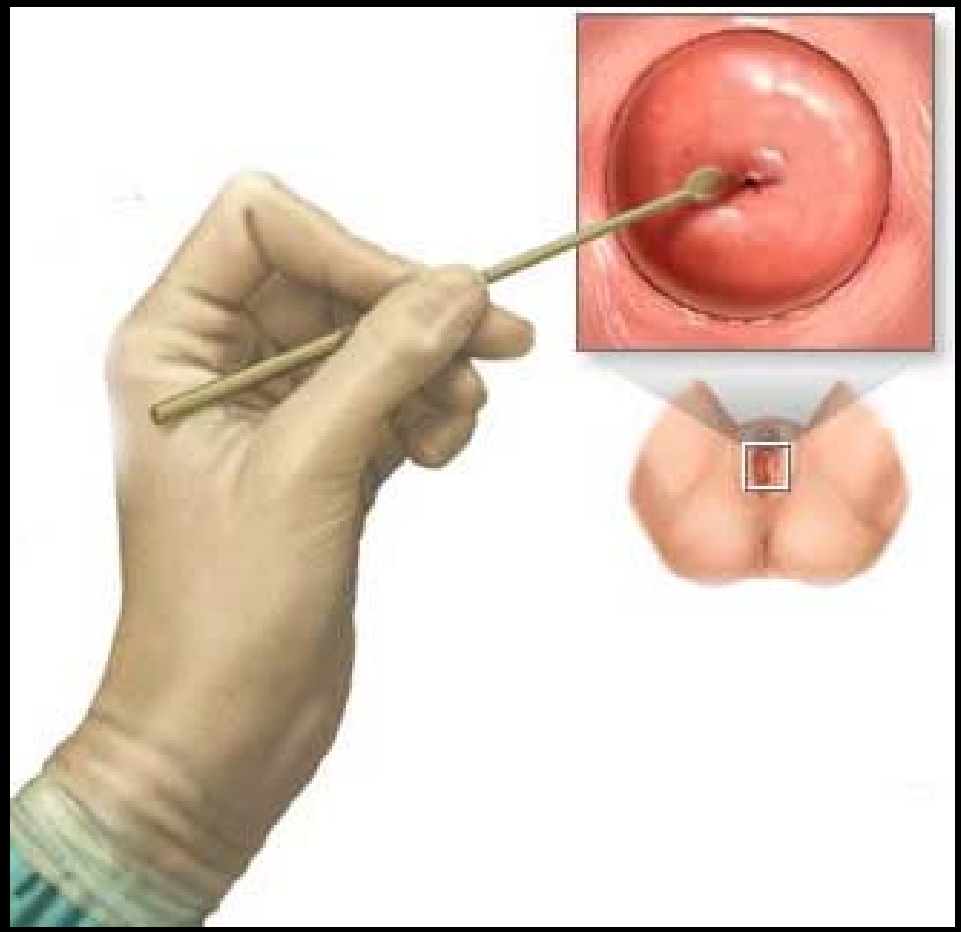
Exfoliation

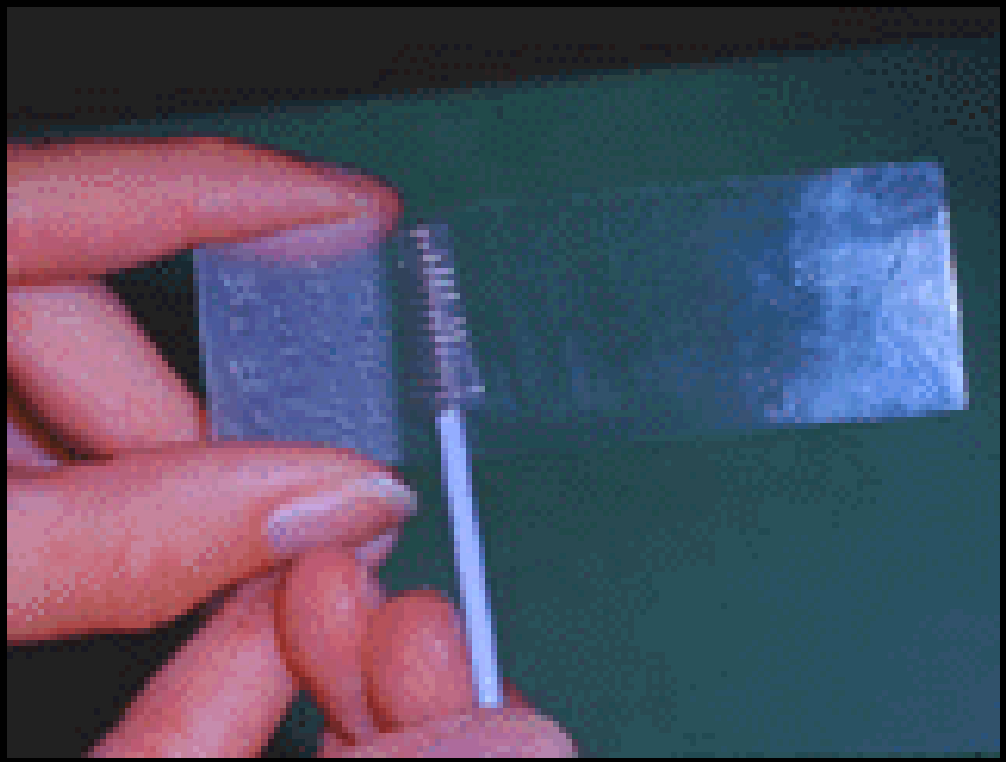
All mucosal surfaces, particularly:

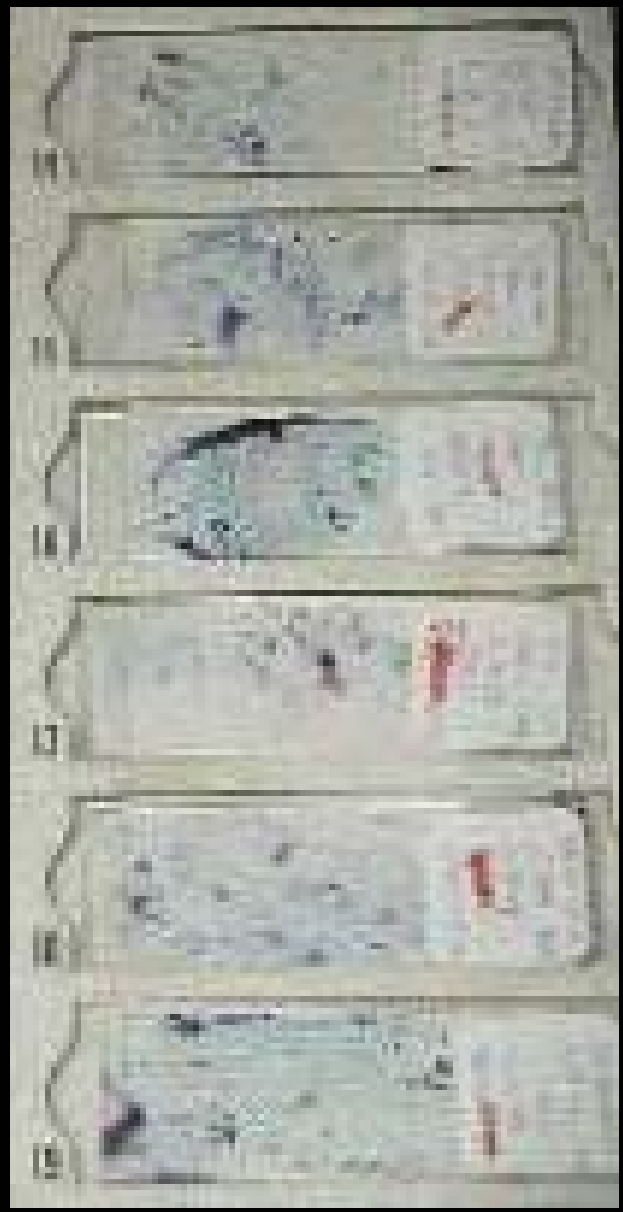
- Uterine cervix
- Oro-pharingeal mucosa
- Gastrointestinal mucosa
- Urinary tract (brush or urine)


1928
George Papanicolau









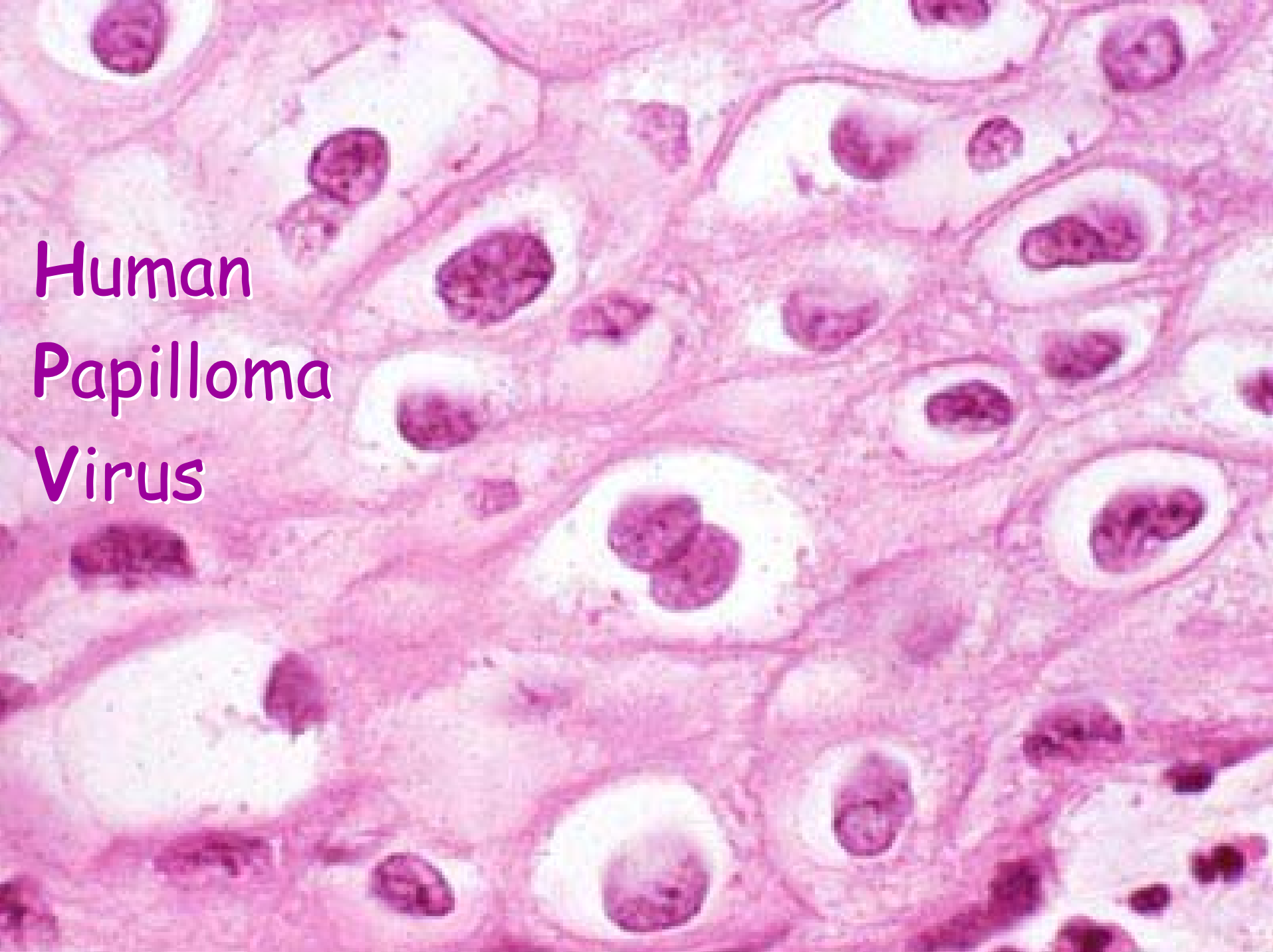
The Pap smear today

- Cervical dysplasia and cancer
- Herpes Virus Infection
- Other infections:
  - Candida
  - Fungi
  - *Trychomonas vaginalis* (*hominis*)
- Uterine carcinoma

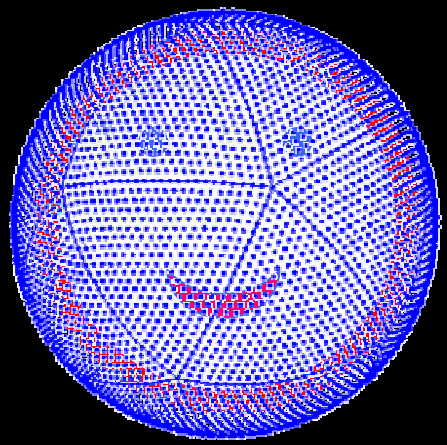
Cervical cancer

- The most common cancer in women in most developing countries
- ~ 500,000 deaths per year worldwide
  - 80% in developing countries
- Incidence related to:

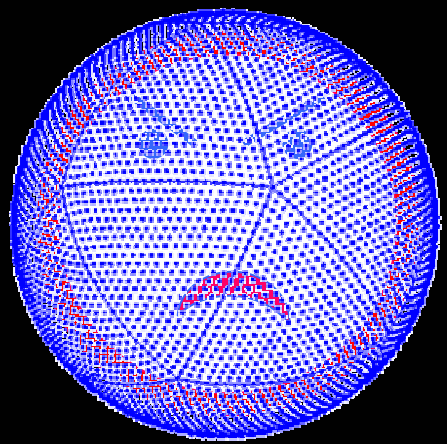
HPV


Human
Papilloma
Virus

Circular double-stranded DNA, 8 kilobases, 70 documented types

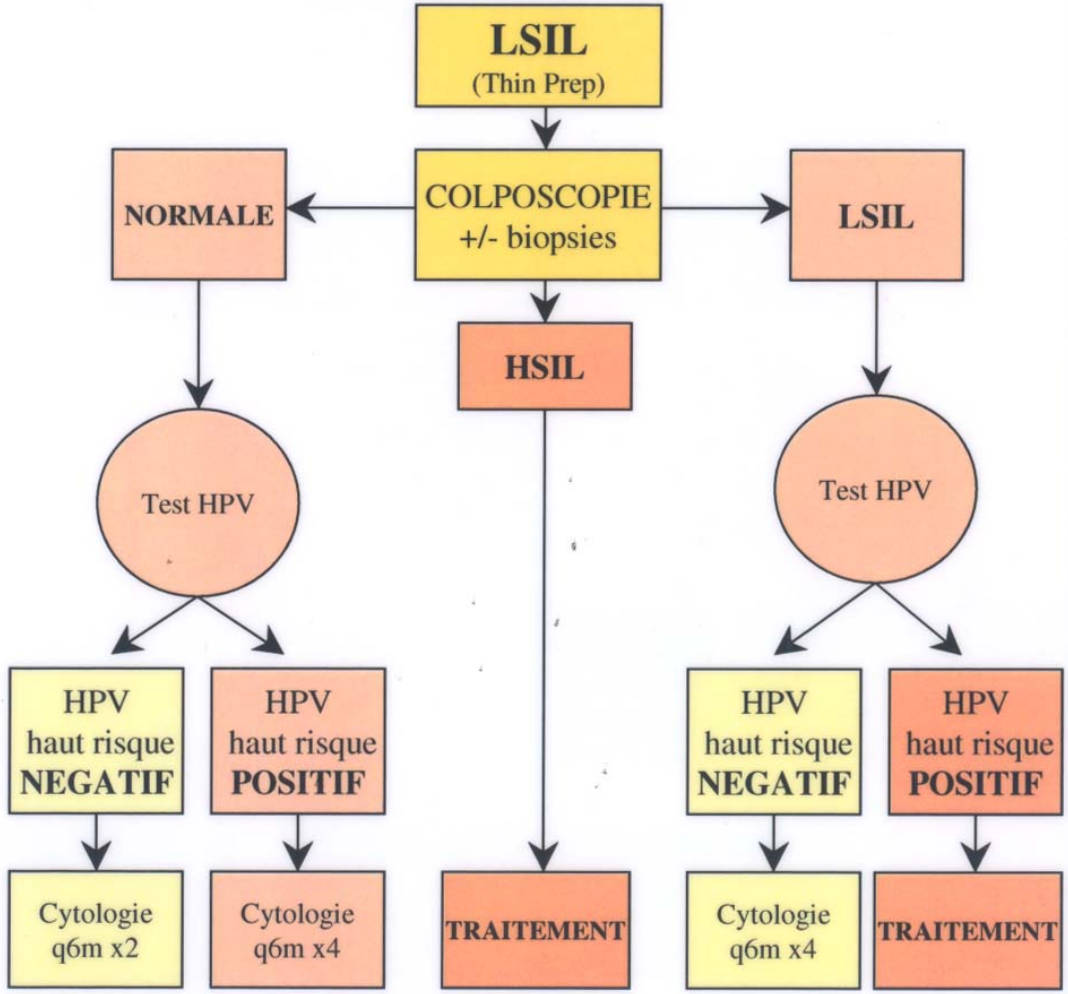


Types 53, 54, 55, 70



Types 6, 11, 16, 18, 31, 33,35, 39, 66

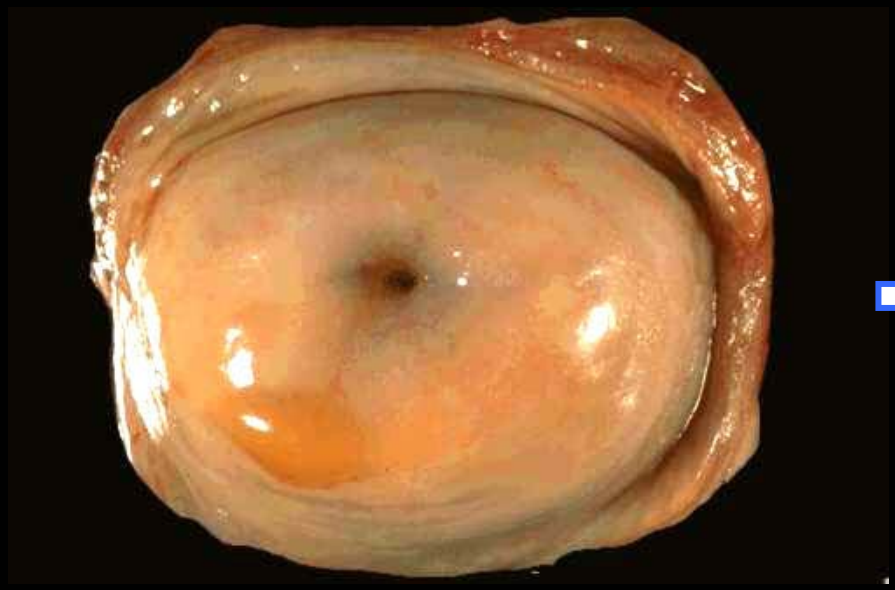
LSIL
prise en charge des patientes en utilisant le test HPV



Dr S. Diebold Berger, Dr E. Mégevand, Dr J. Weintraub, conférence du 4 octobre 2001. Adapté de Bethesda 2001, ASCCP 2001, étude ALTS 2001.

Preneoplastic lesions of the cervix
Classification Systems

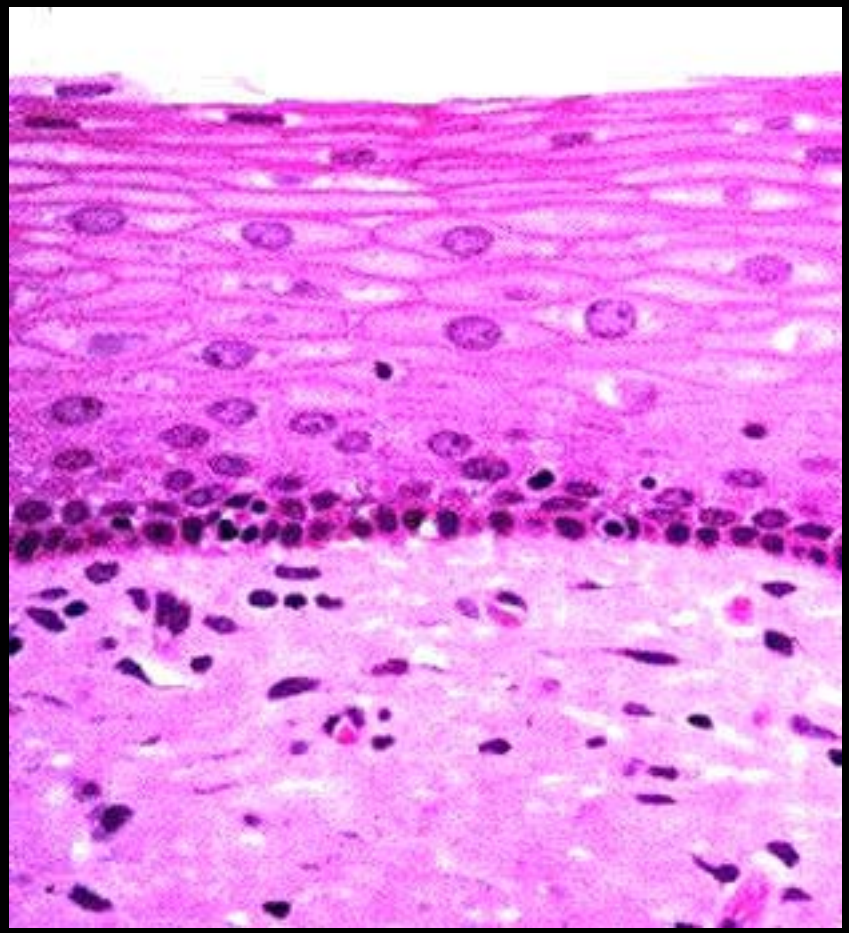
WHO Traditional	CIN	Bethesda
Mild dysplasia	CIN 1	L SIL
Moderate dysplasia	CIN 2	H SIL
Severe dysplasia	CIN 3	H SIL
Carcinoma in situ	CIN 3	H SIL

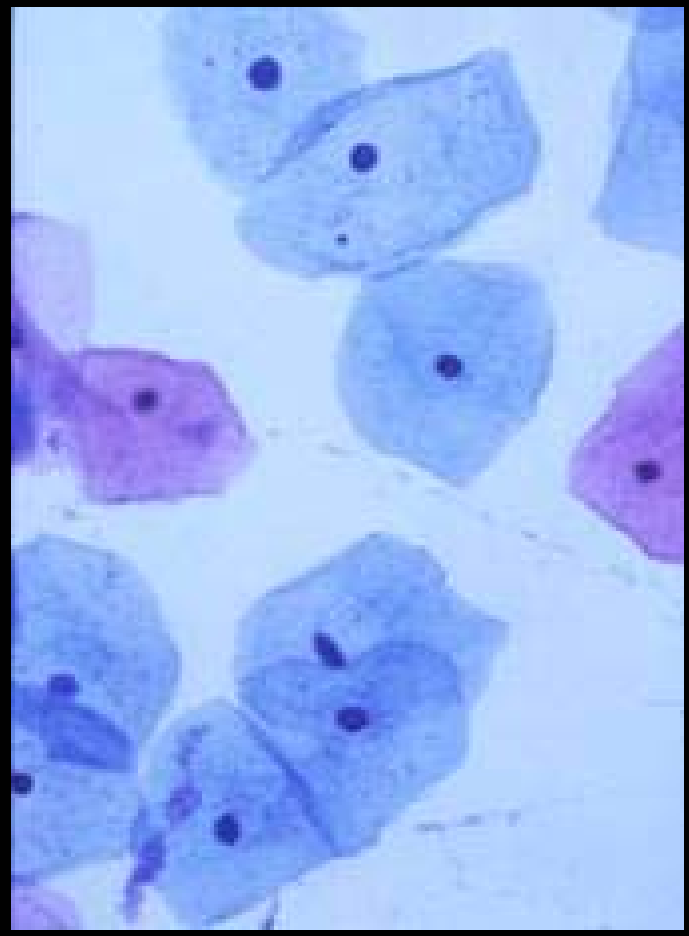


Cervical cancer after the "Pap test"

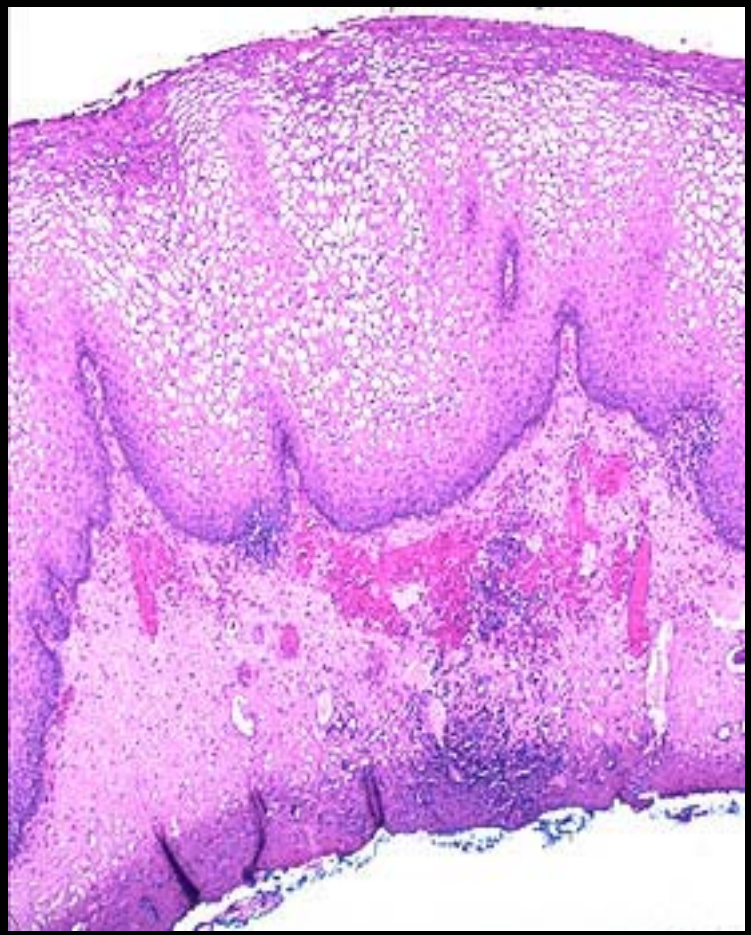
- USA: 1973 to 1994: from 14.2 to 7.8/100.000
- UK: 26% decrease 1995 – 2000
- UK: screening prevents ~2,000 – 4,000 cases/year
- USA: 50% of deaths occur in women who never had a Pap test

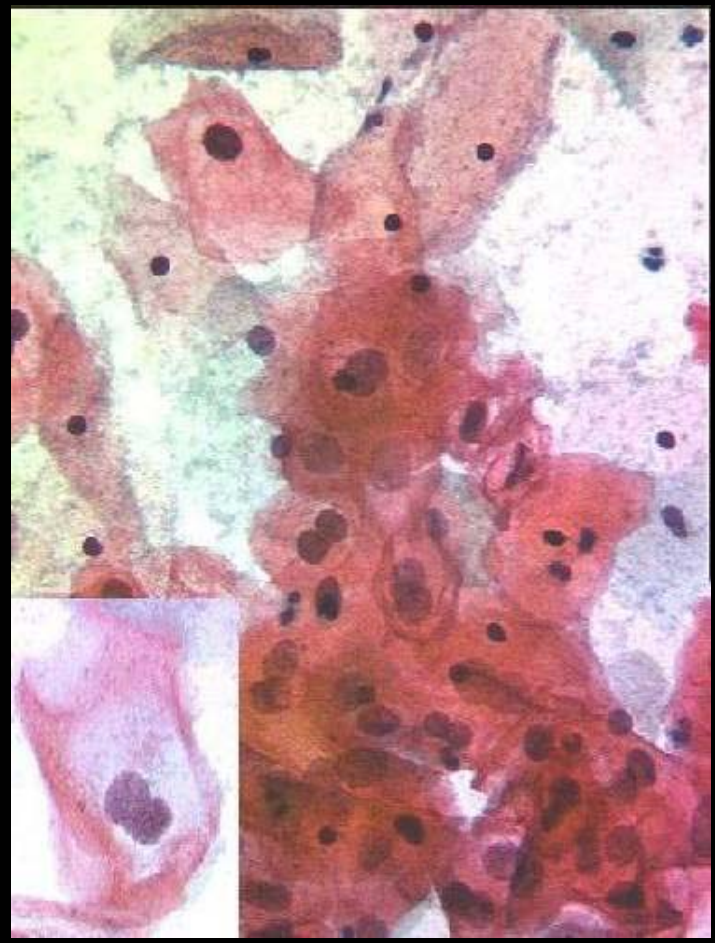
Normal



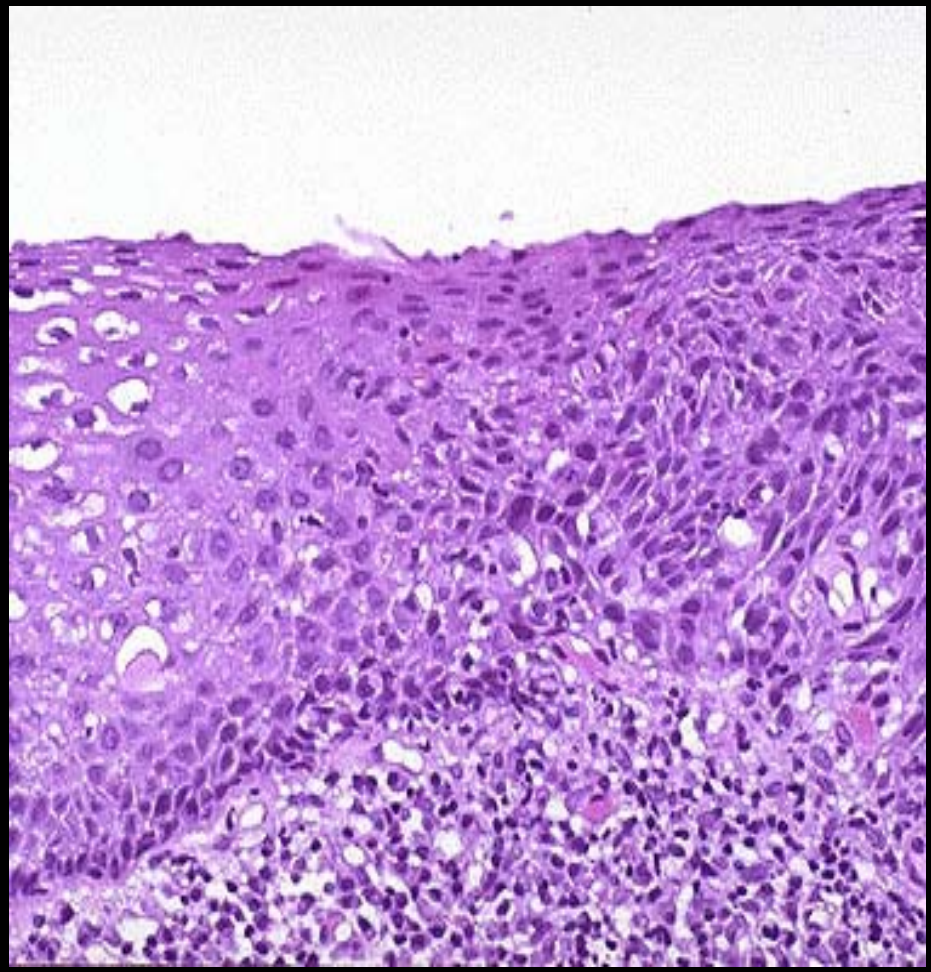


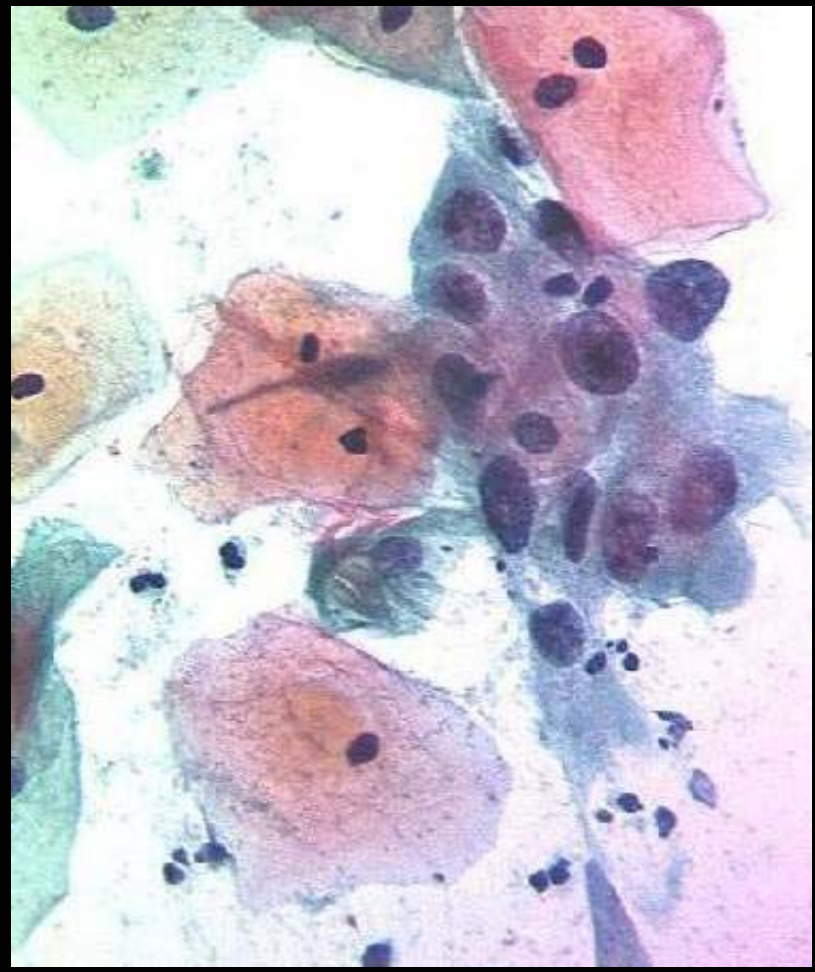
HPV - Mild dysplasia



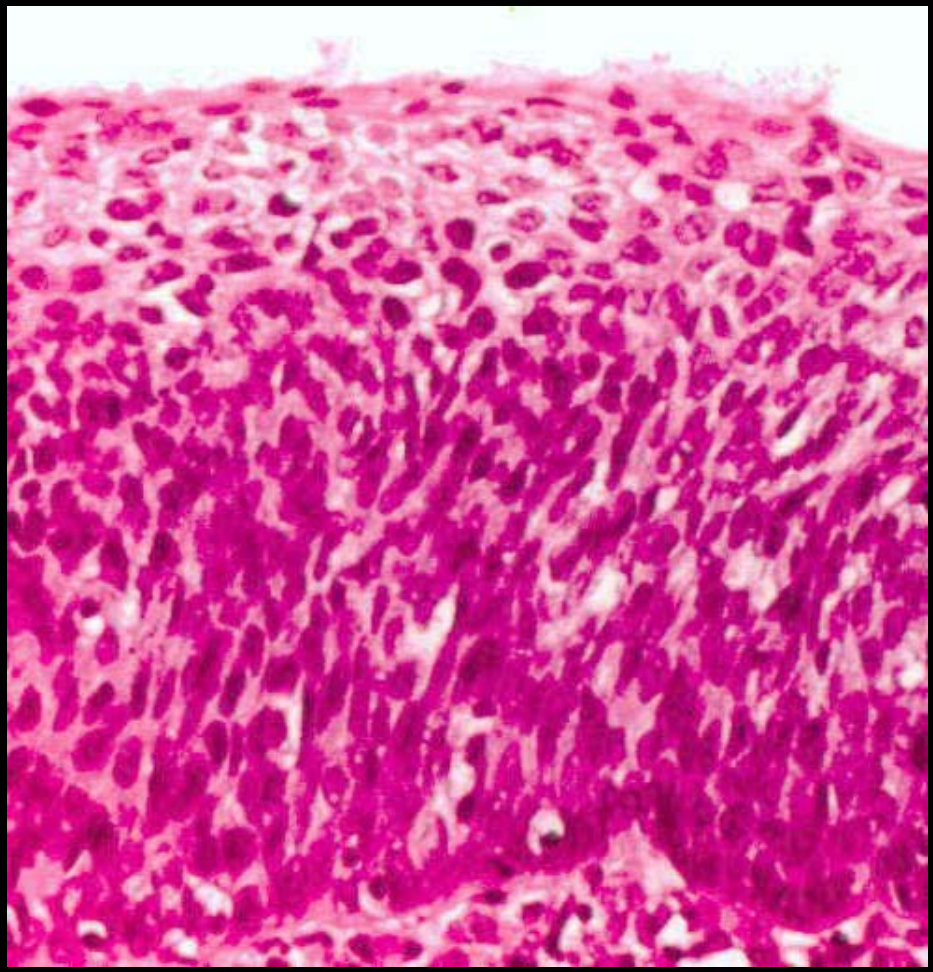


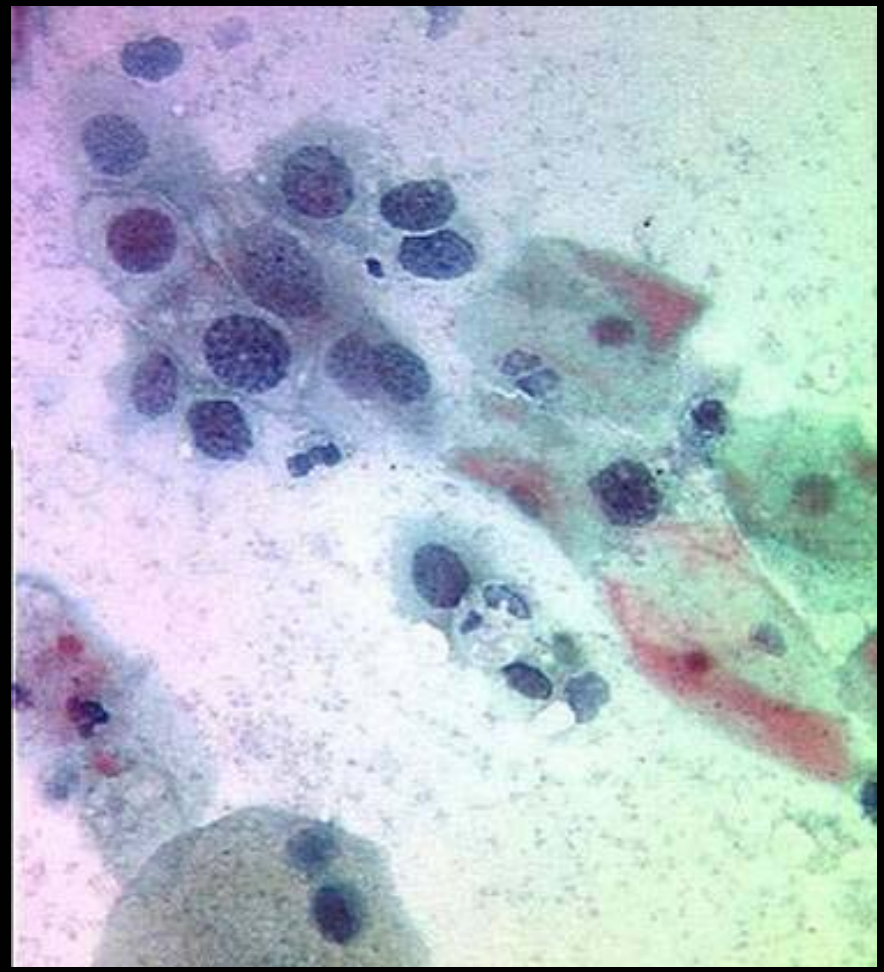
Moderate dysplasia



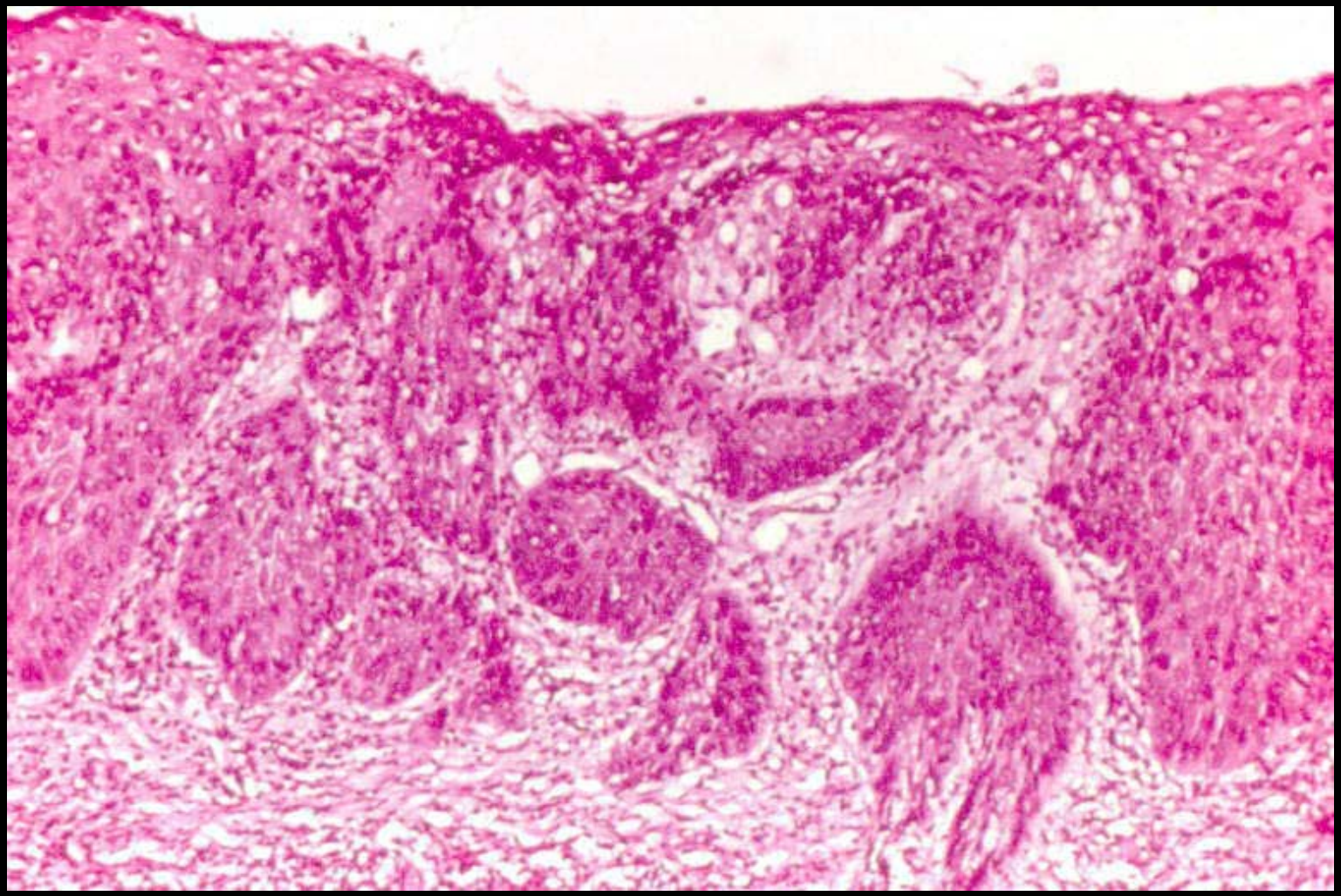


Severe dysplasia

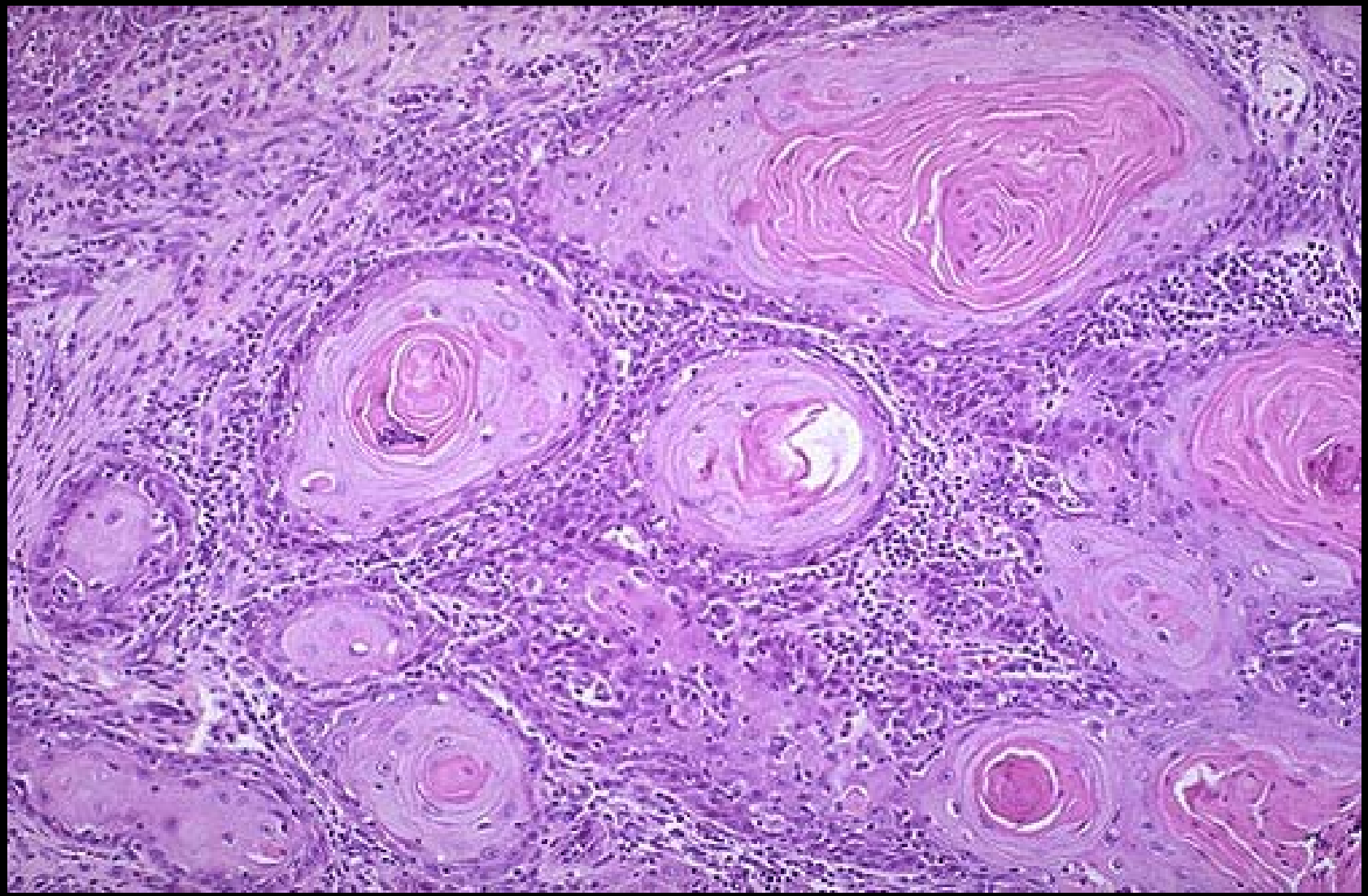




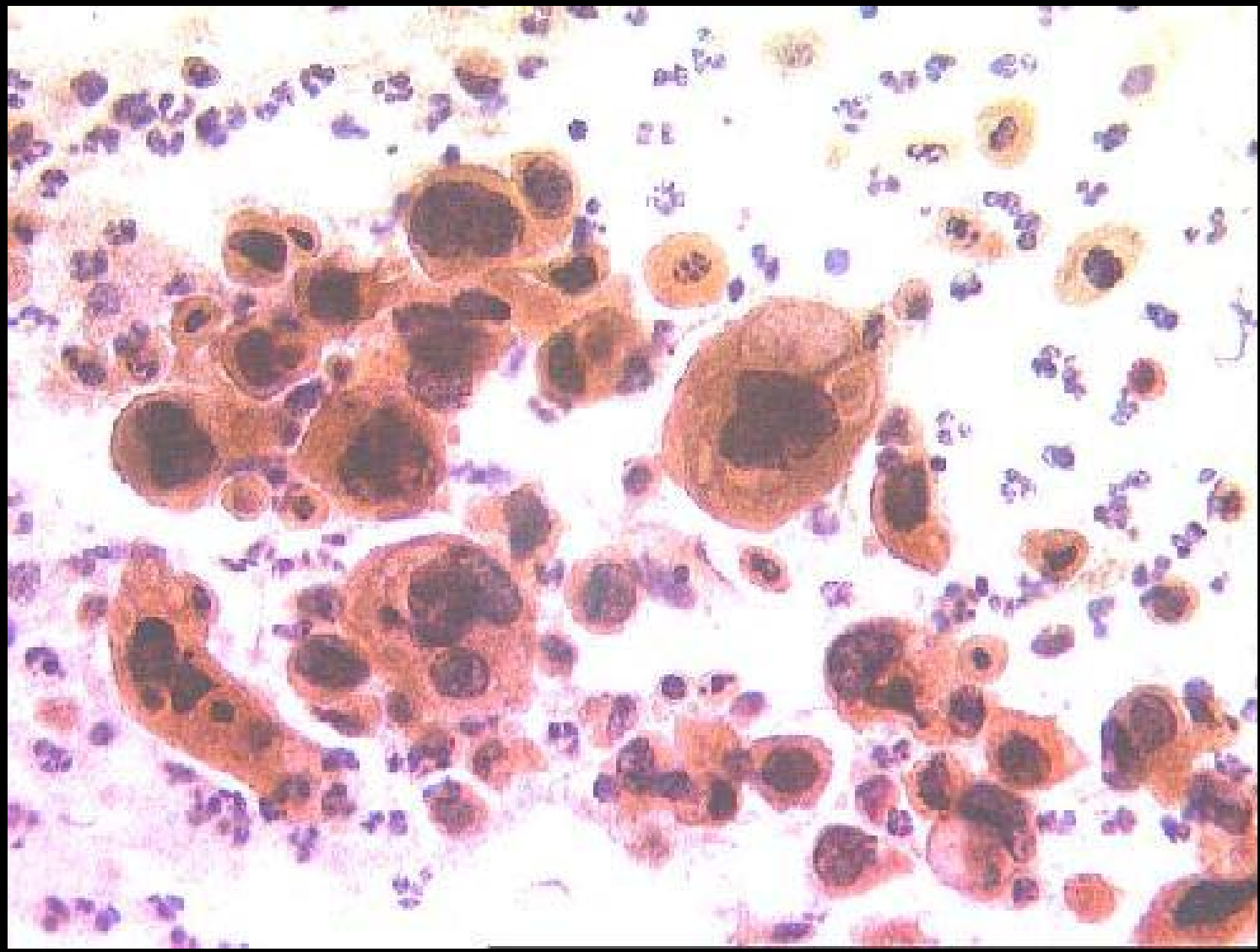
Carcinoma



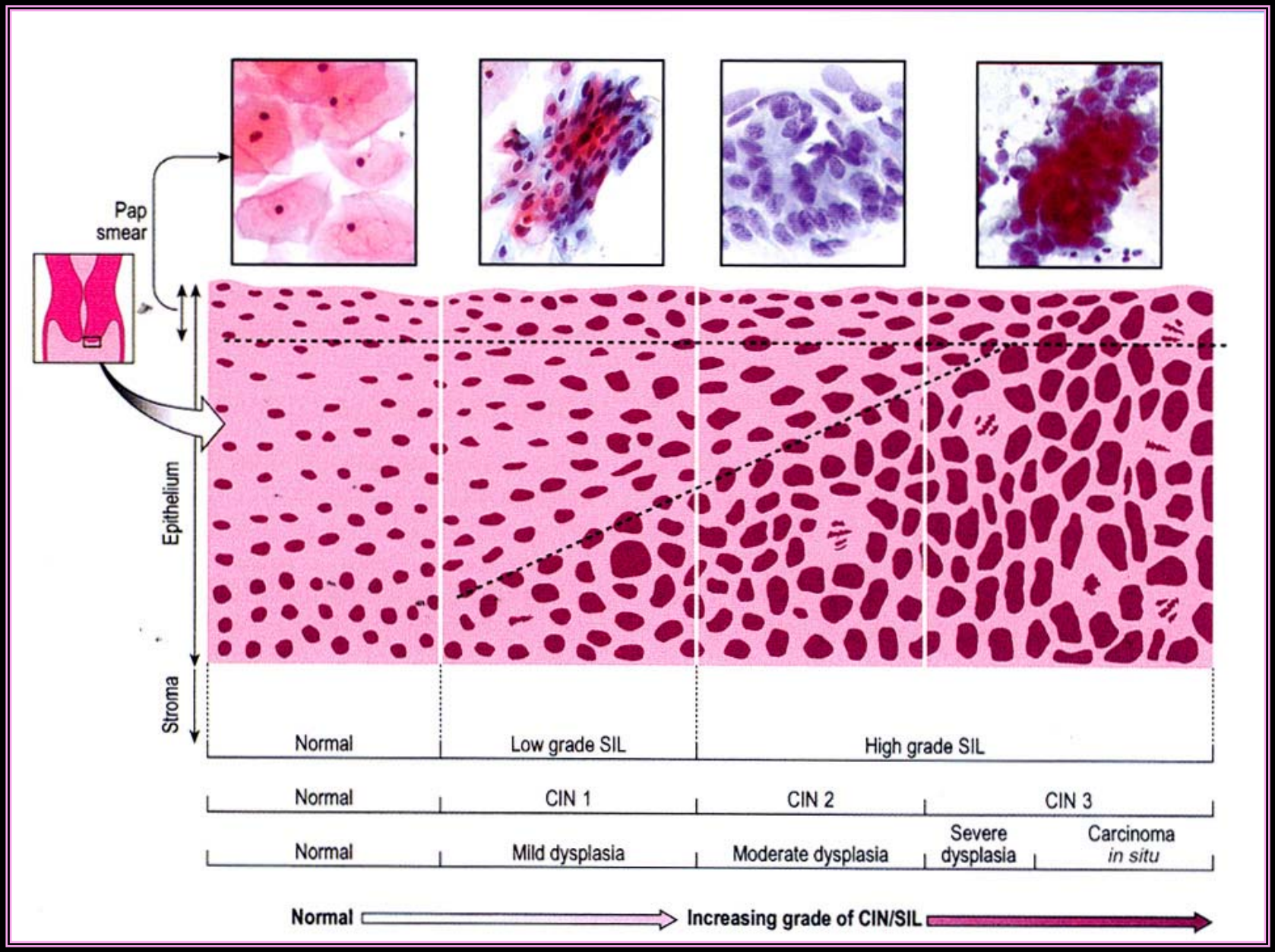
Invasive carcinoma



Invasive carcinoma



Visual Analogue Scales



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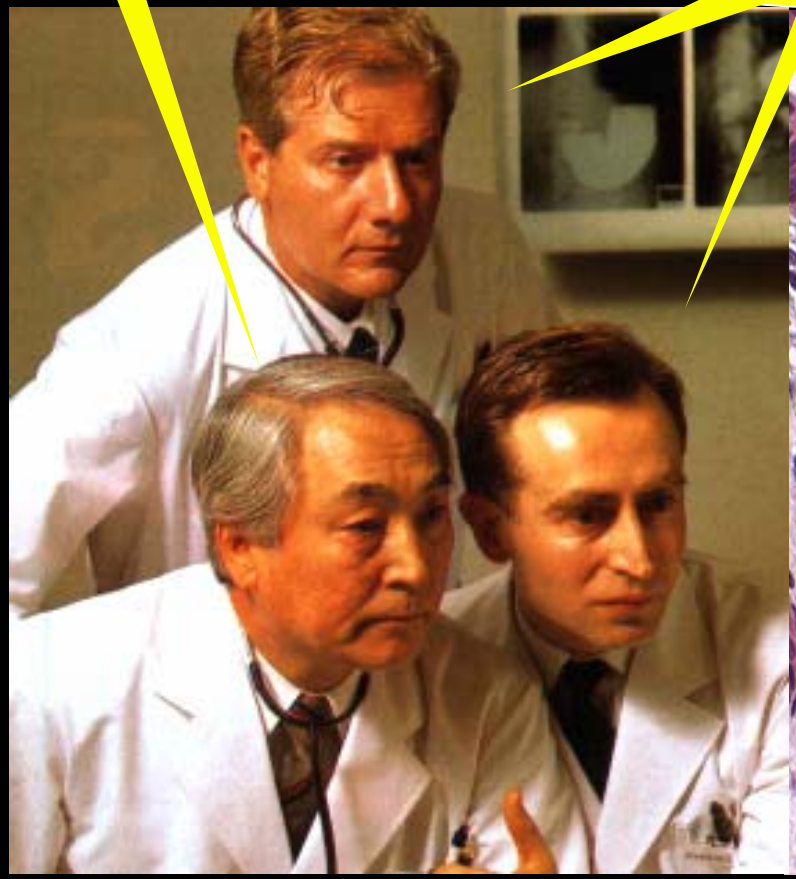
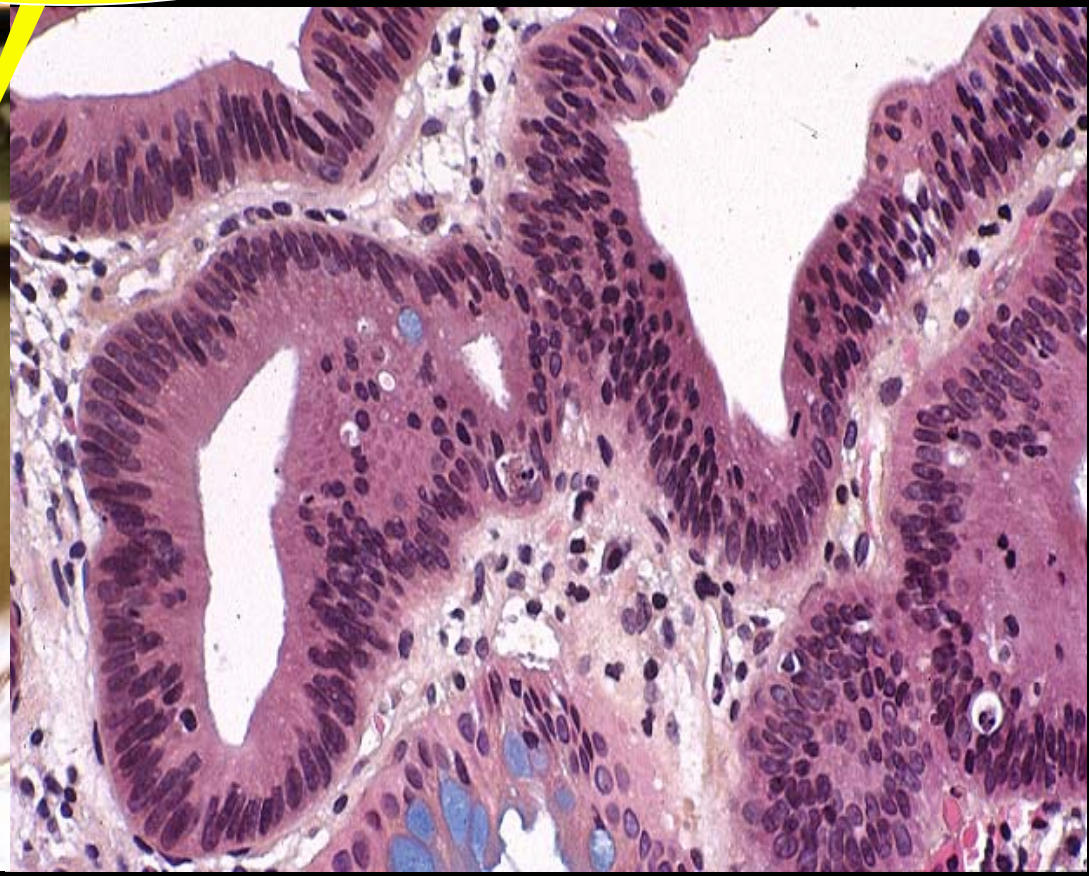
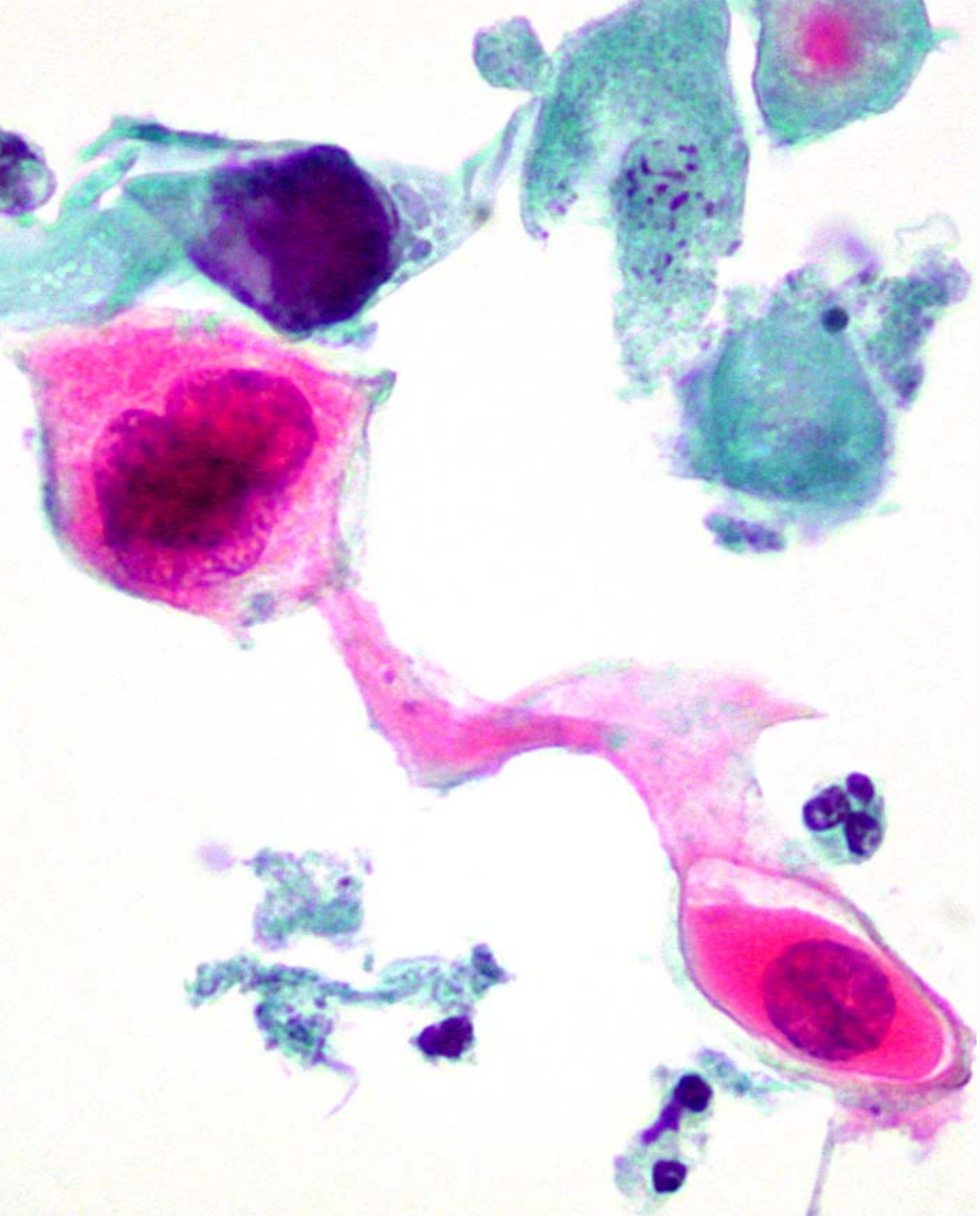
These two guys are hopeless, they should learn to agree...



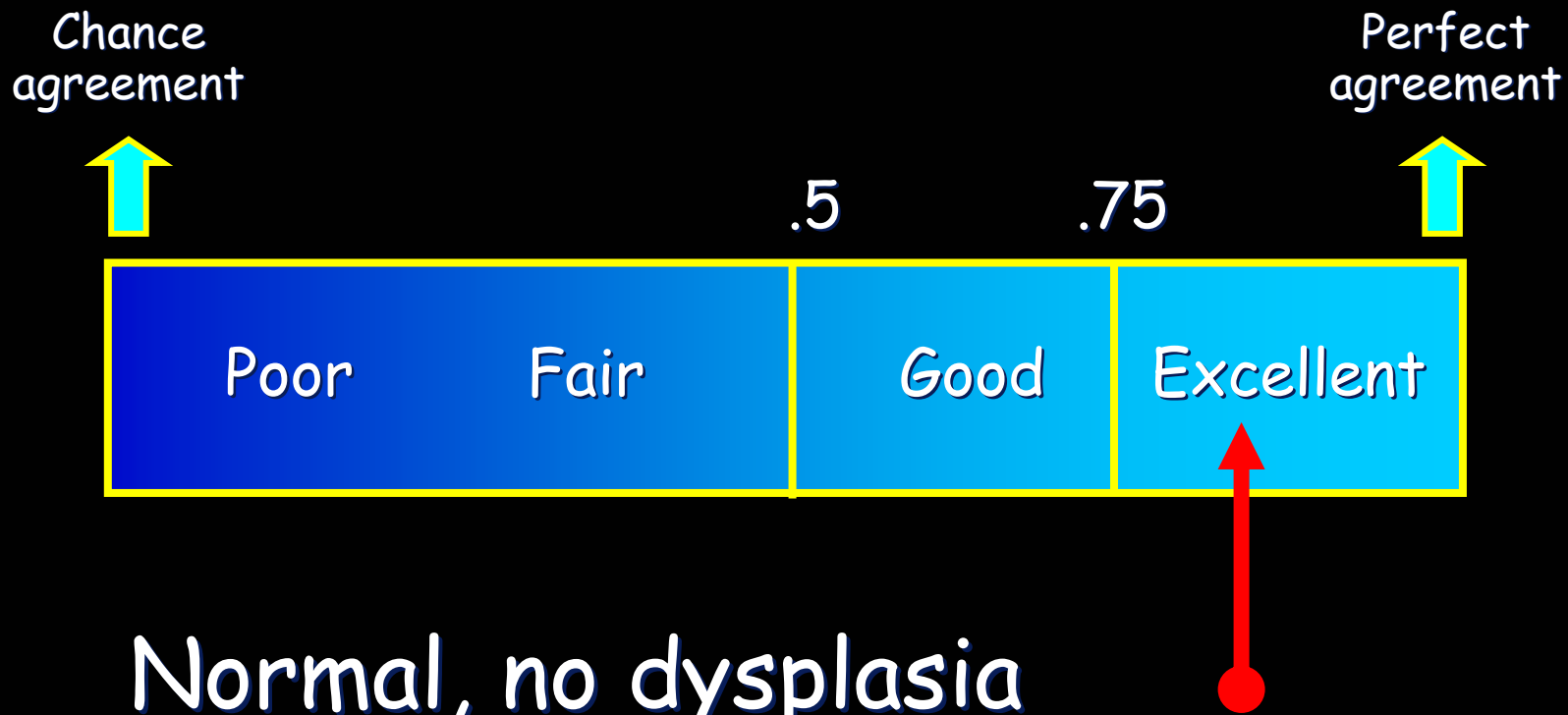




Who can recognize dysplasia and cancer?

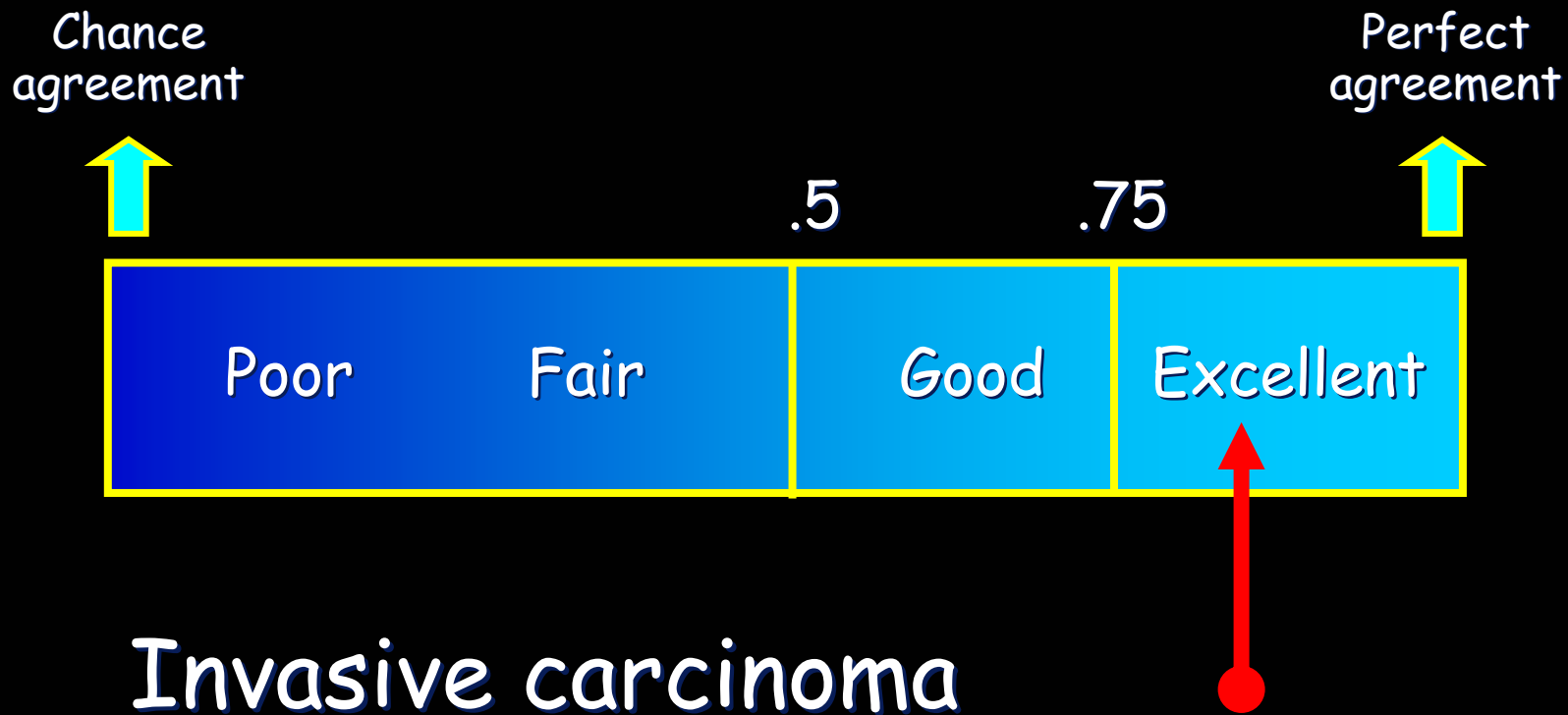
Kappa statistics

Performance of a group of cytologists

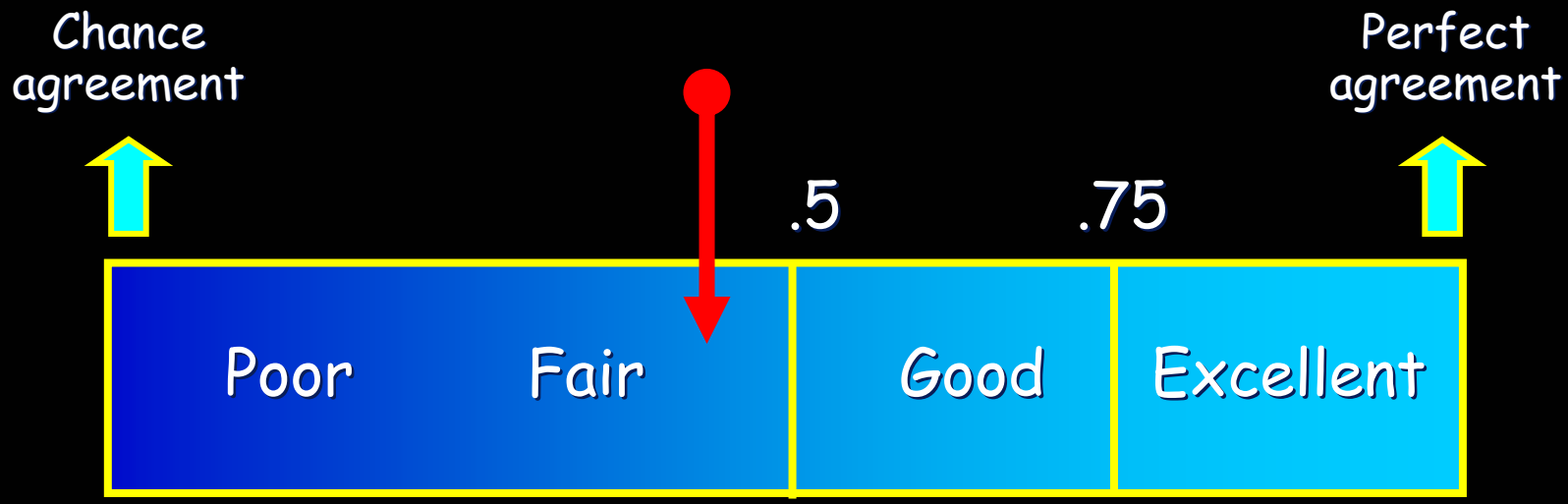


Normal, no dysplasia

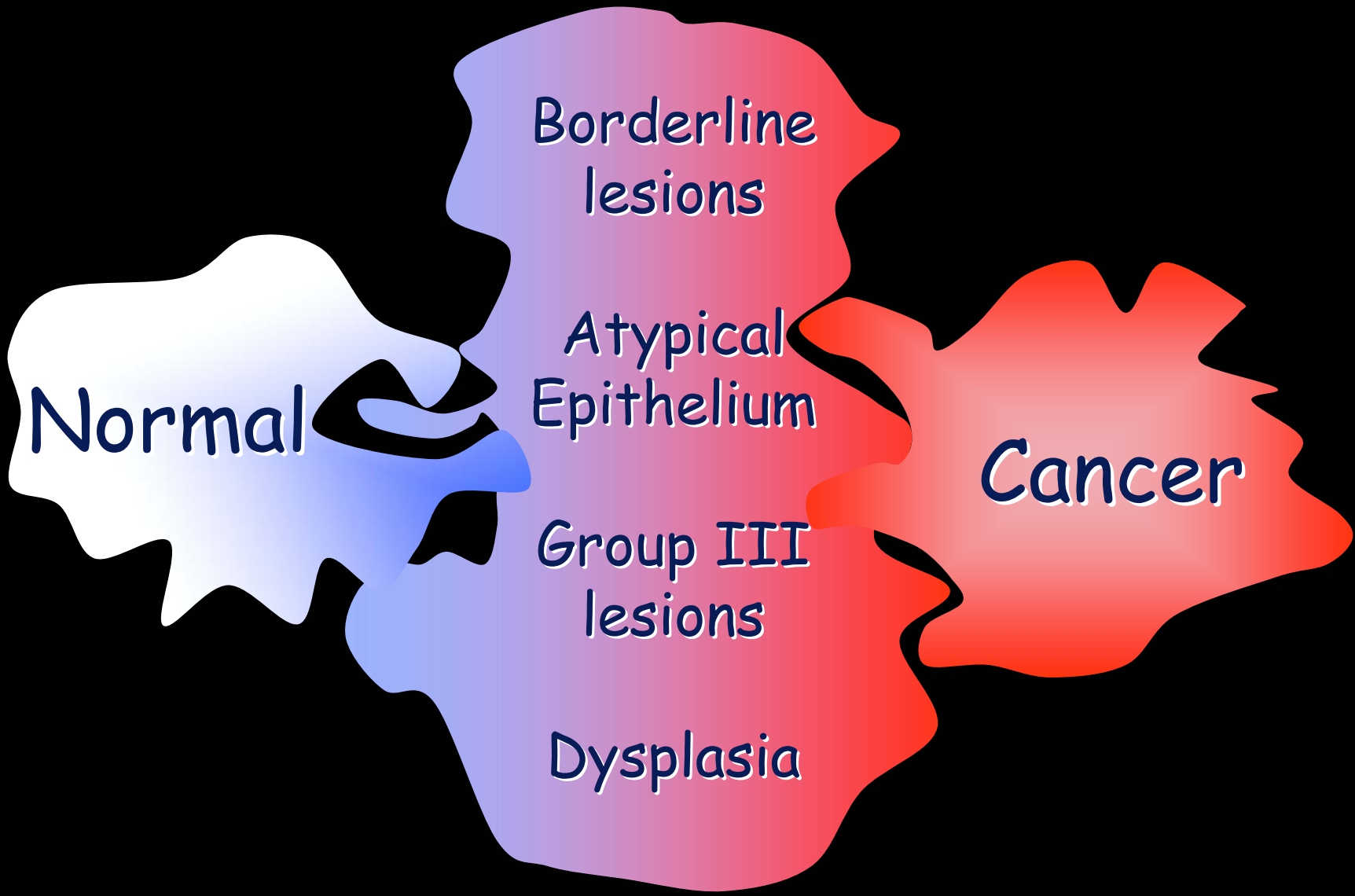
Performance of a group of cytologists



Performance of a group of cytologists



Dysplasia (particularly low-grade)


Normal
Borderline lesions
Atypical Epithelium
Group III lesions
Dysplasia
Cancer

Major problems in histological and cytological assessment

- Distinction between non-dysplastic and dysplastic phenotype
- Grading of dysplasia and correlation with cancer risk
- Distinction between high-grade dysplasia and early invasive gastric cancer

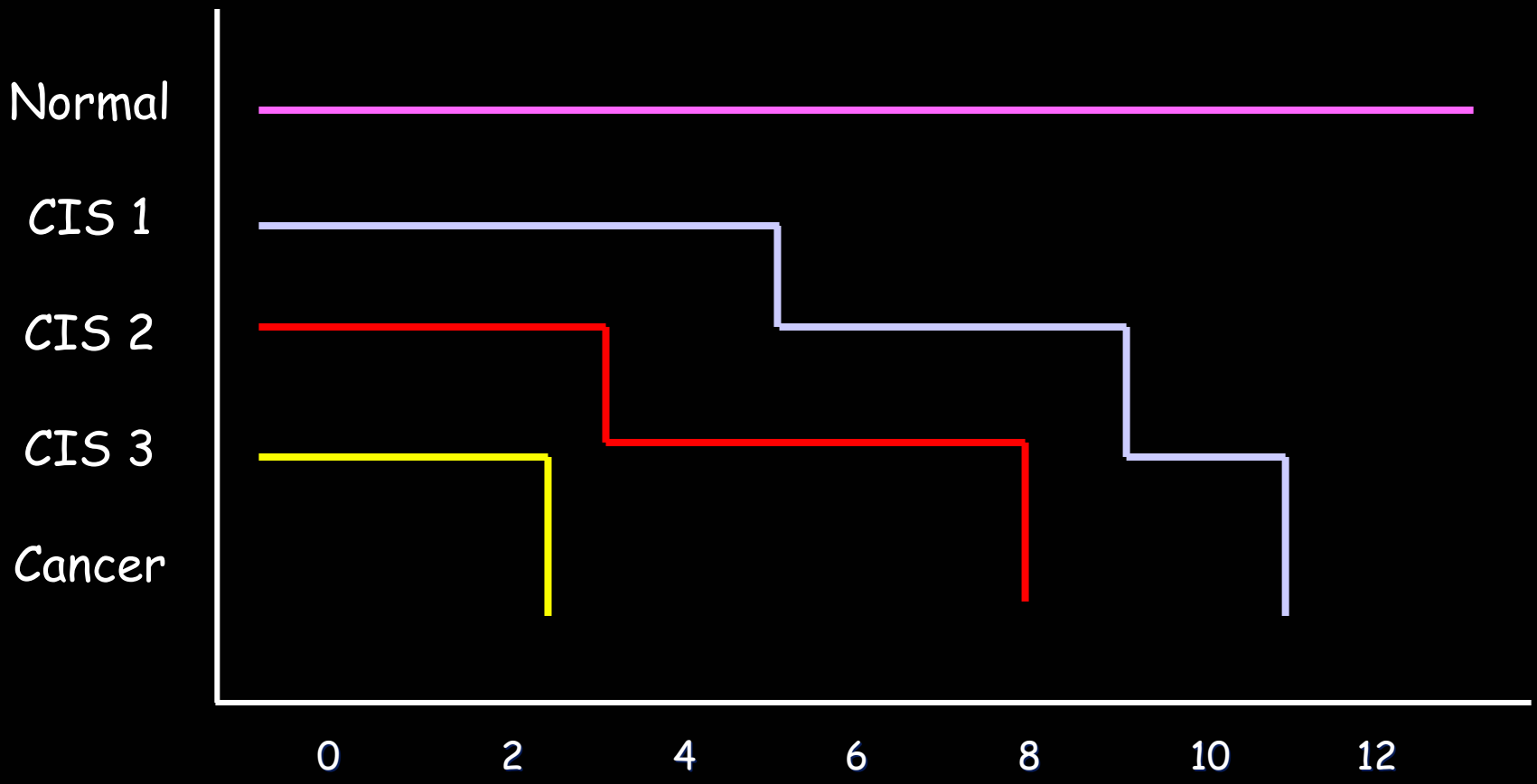
Study A: patients

- Four groups of 100 women each followed up yearly for 12 years
  - Group 1: normal PAP
  - Group 2: mild dysplasia/koilocytosis
  - Group 3: moderate dysplasia
  - Group 4: severe dysplasia
- End point: invasive carcinoma

Study A: methods

- Patients followed by Research Nurse Florence Picky
- All PAP smears examined by famous cytopathologist Dr. Smartcell
- All histopathology reviewed by Prof. Goodeyes, an expert in uterine cancer
- All slides reviewed by a group of experts at the end of the study

Study A: results



Study A: conclusions

- Patients with a normal PAP smear do not develop cancer within 12 years
- 11% of CIN 1 progress to CIN 3
- 22% of CIN 2 progress to CIN 3
- > 12% of CIN 3 develop invasive carcinoma
- CIN 1 regresses more often than CIN 2, and more than CIN 3

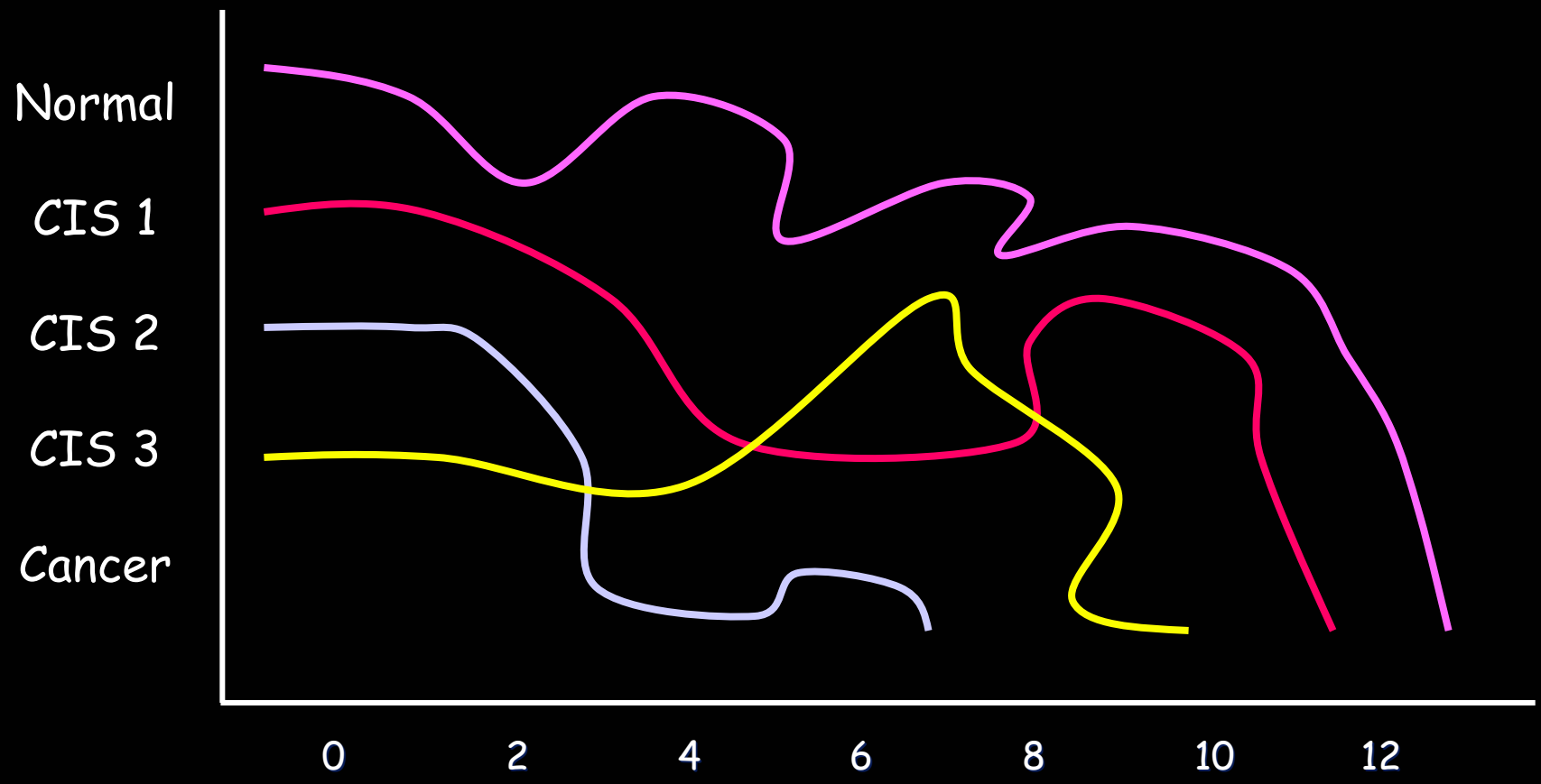
Study B: patients

- Four groups of 100 women each followed up yearly for 12 years
  - Group 1: normal PAP
  - Group 2: mild dysplasia/koilocytosis
  - Group 3: moderate dysplasia
  - Group 4: severe dysplasia
- End point: invasive carcinoma

Study B: methods

- Patients told to come once a year
- PAP smears examined by different cytopathologists
- Histopathology diagnosis at three local hospitals
- Slides not reviewed at the end of the study

Study B: results



Study B: conclusions

- More patients with CIN 1 progress to cancer than those with CIN 3
- Normal patients develop cancer more often than CIN patients
- Regression very common in patients with CIN 3, less common in CIN 1

These results are internally invalid

Lessons learned

- The design of a study is the most important key to its success

Beware of the pitfalls!

Study B: pitfalls

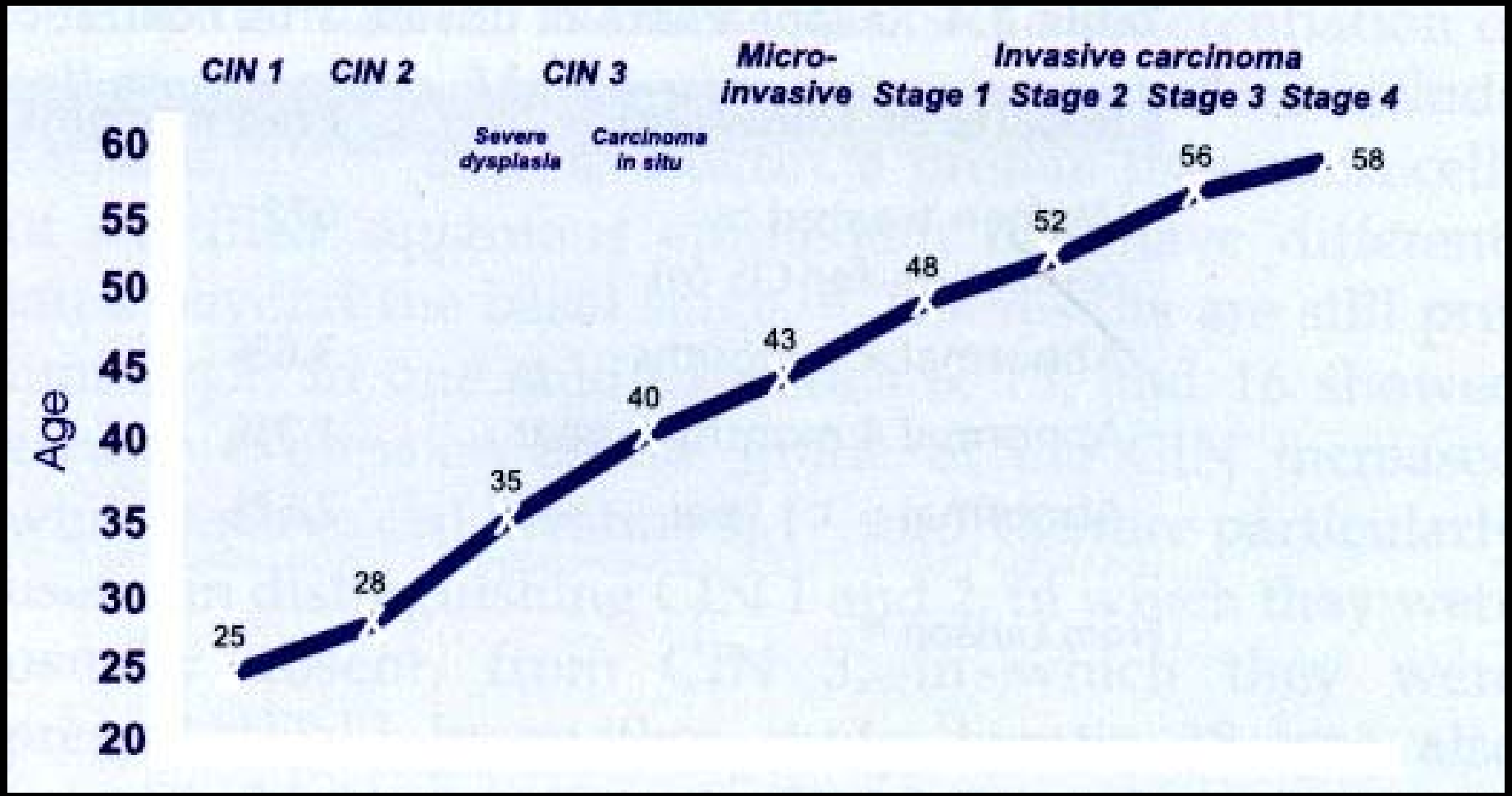
- Patients told to come once a year
- PAP smears examined by different cytopathologists
- Histopathology diagnosis at three local hospitals
- Slides not reviewed at the end of the study

Meta-analysis

Table 7.3 Natural history of CIN. A meta-analysis

	Regress	Persist	Progress to CIS	Progress to invasion
HPV lacking CIN	80%	15%	5%	0%
CIN 1	57%	32%	11%	1%
CIN 2	43%	35%	22%	5%
CIN 3	32%	< 56%	–	> 12%

Age of occurrence



Conclusions

Cytology is a valuable method to screen for and prevent cervical cancer

Before programs are designed and implemented, a thorough knowledge of local conditions is indispensable

Important studies in many populations remain to be performed

A clinical study is a community effort: investigators, patients, health authorities, statisticians, consultants, must be involved form the planning stage

Additional Information

http://www.cytopathology.org/
American Society of Cytopathology

http://pathology2.jhu.edu/cytopath/
Johns Hopkins Cytopathology

http://crsg.ubc.kun.nl/thesaurus/
Internet Thesaurus of Cytopathology

DPC - Cytologie
HUG