

Glandular lesions in cervical cytology

Margareta Strojan Fležar

Institute of Pathology

Faculty of Medicine University of Ljubljana
Slovenia

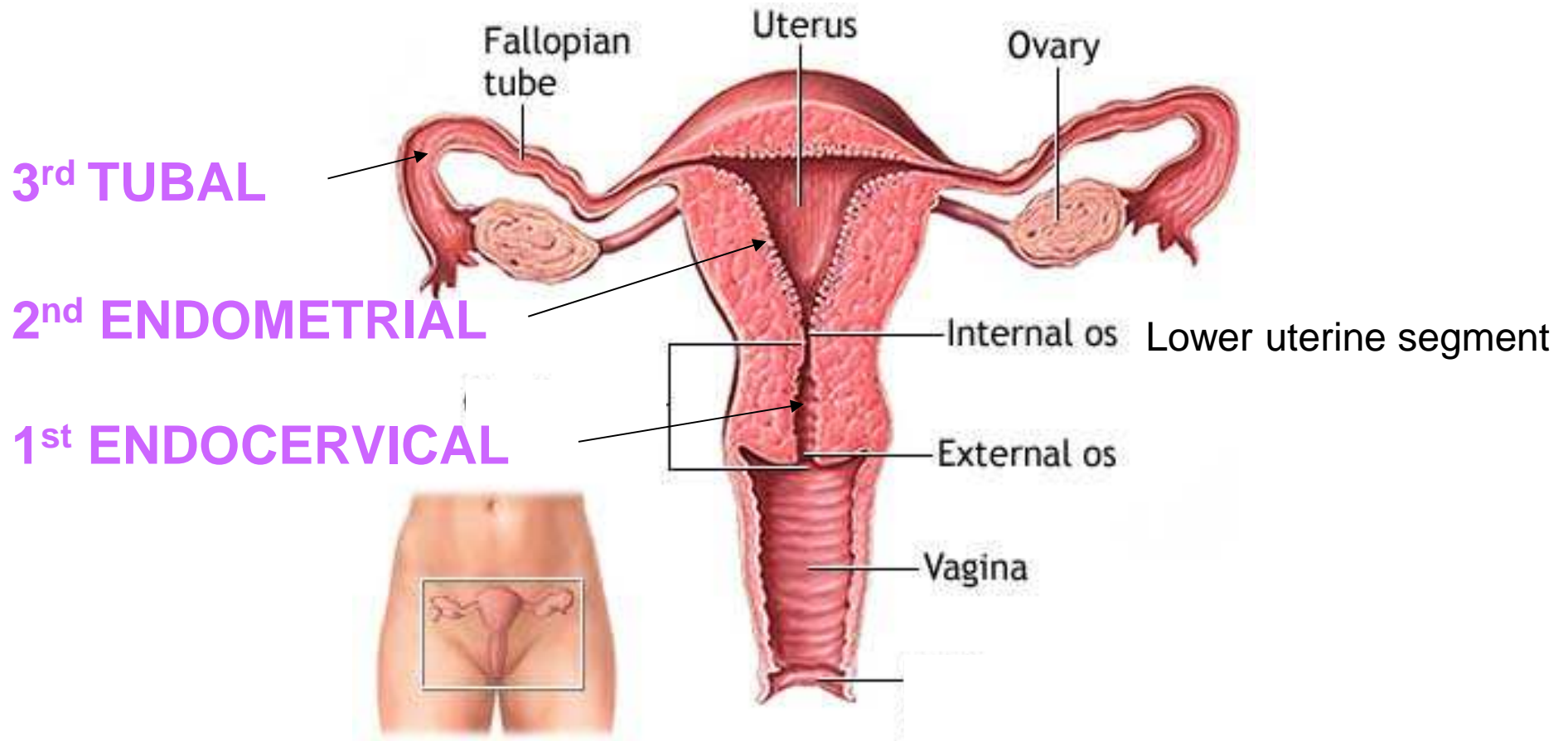


Univerza
v Ljubljani *Medicinska*
fakulteta



2nd PANNONIA CONGRESS OF PATHOLOGY, SIÓFOK, HUNGARY, 17-19 MAY 2012

Glandular cells in cervical smears



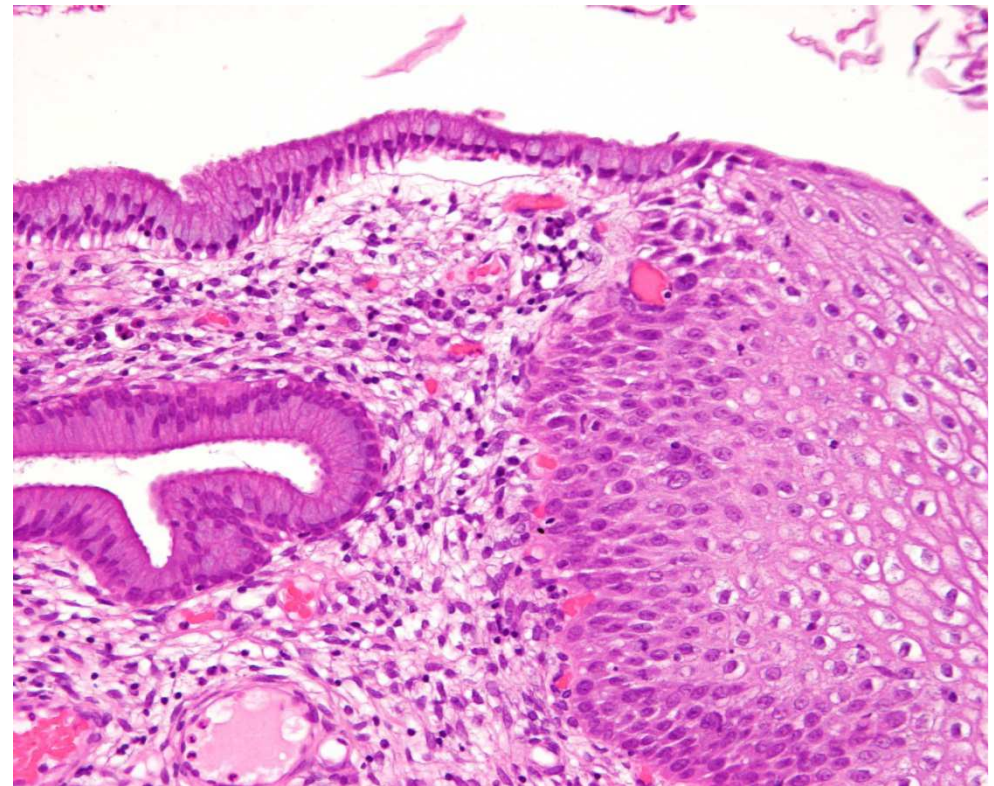
Glandular cells in cervical smears

- Transformation cone
- “junction cone”
- **Endocervical cells key component of Pap test**
- No sq metaplastic/ endocervical cells



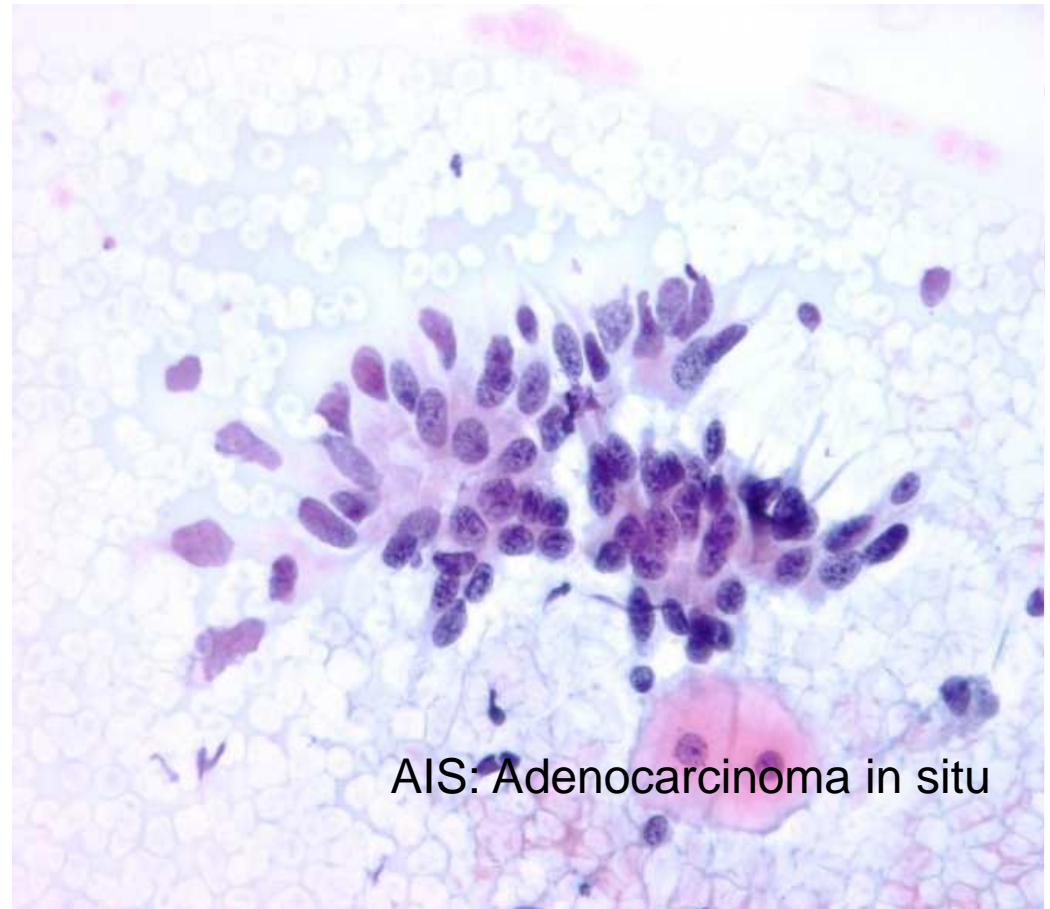
BETHESDA:

- Smear sufficient for evaluation
- – comment about the smear quality!!!



Glandular cells in cervical smears

- Cervical cytology primarily screening test for squamous intraepithelial lesion and squamous cell carcinoma
- Sensitivity for glandular lesions limited by problems with sampling and interpretation
- Rare findings
- ?Brush, ?Bethesda

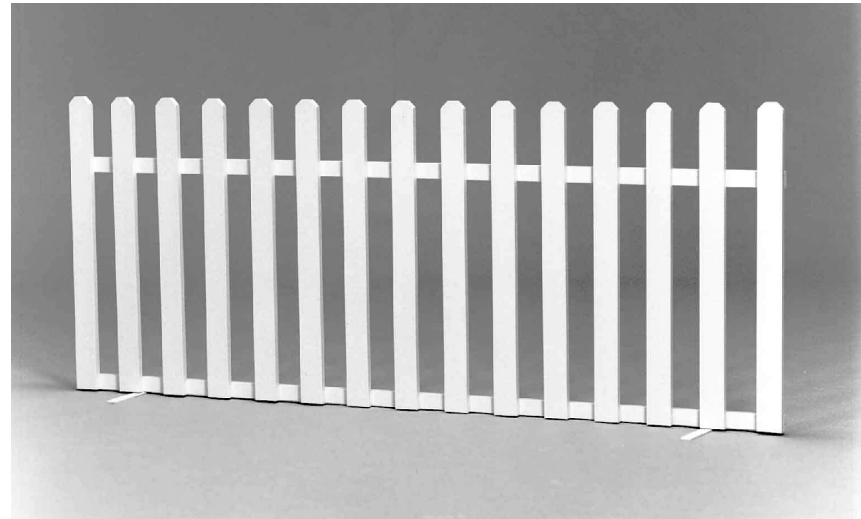


AIS: Adenocarcinoma in situ

Endocervical glandular cells - architecture

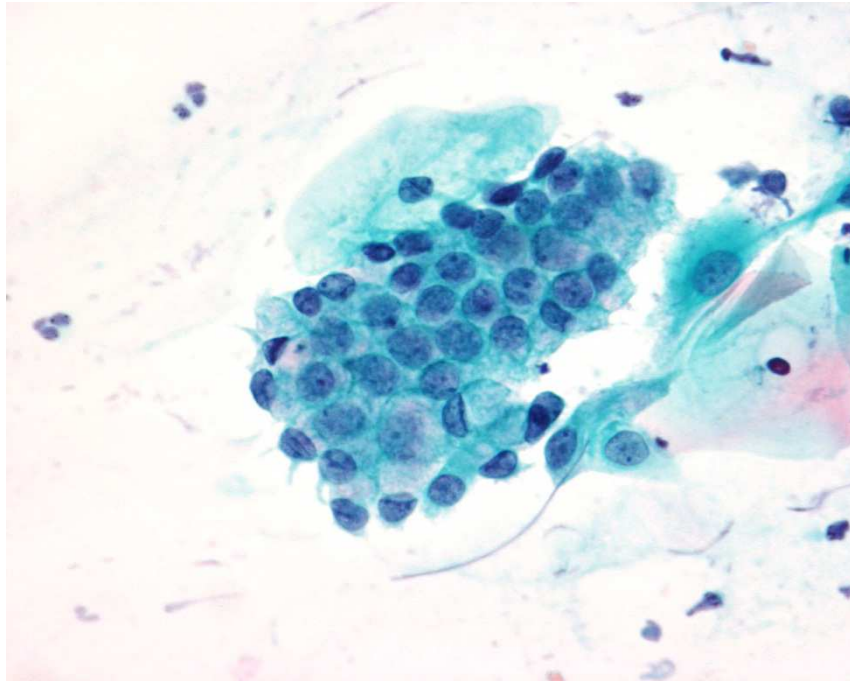


Strips, palisading



(picket fence, palisade)

Endocervical glandular cells - architecture

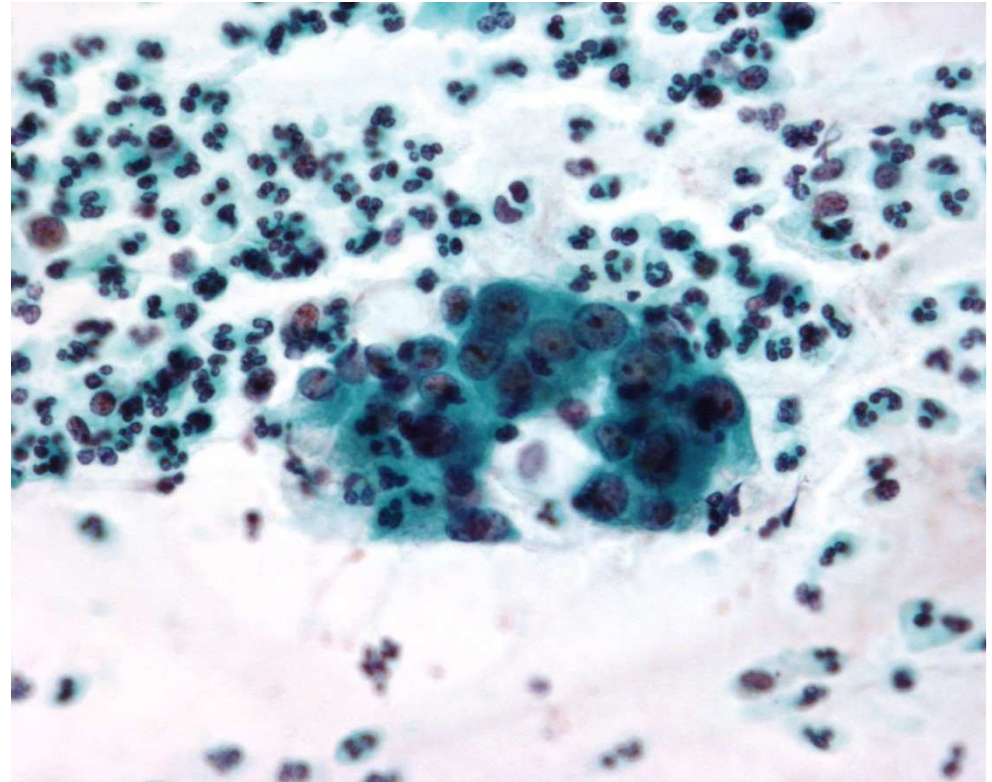


Honeycomb pattern



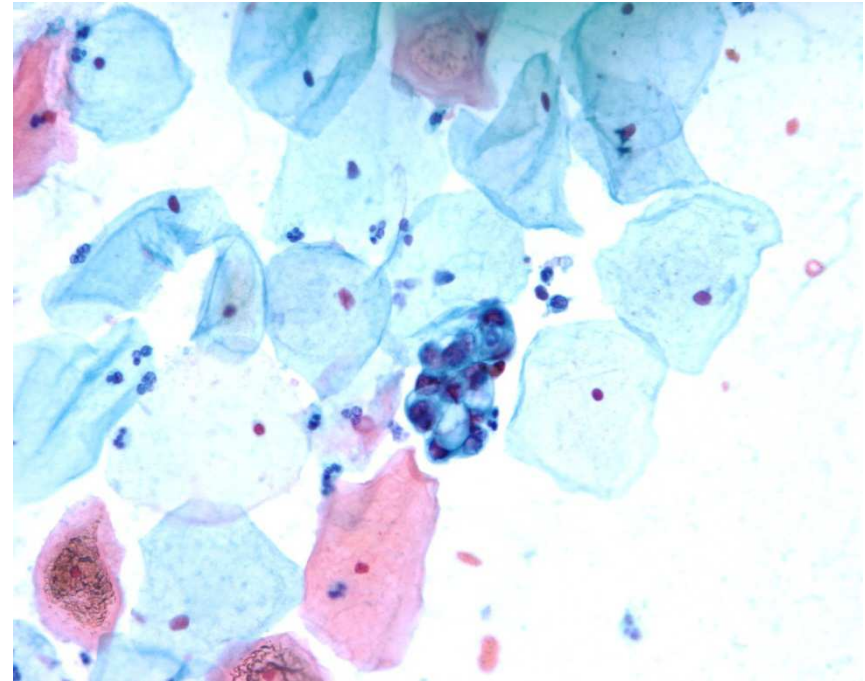
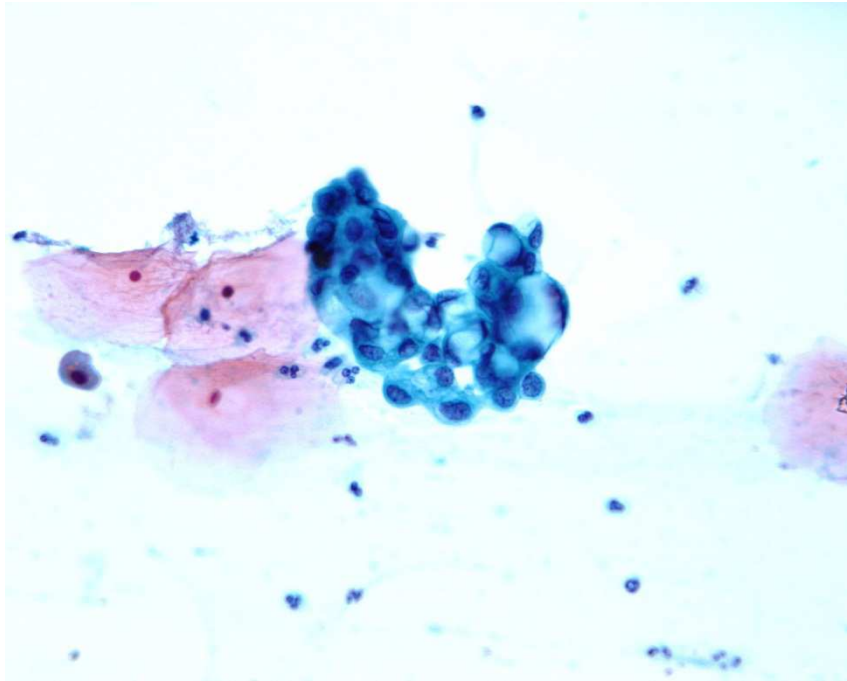
Reactive endocervical cells

- Common
- Hormonal influences
- Inflammation
- Polyps
- DD: neoplastic cells, 3-D groups!!!, elongated nuclei, uneven granular chromatin



BETHESDA: Non-neoplastic changes

Reactive endocervical/endometrial cells with IUD

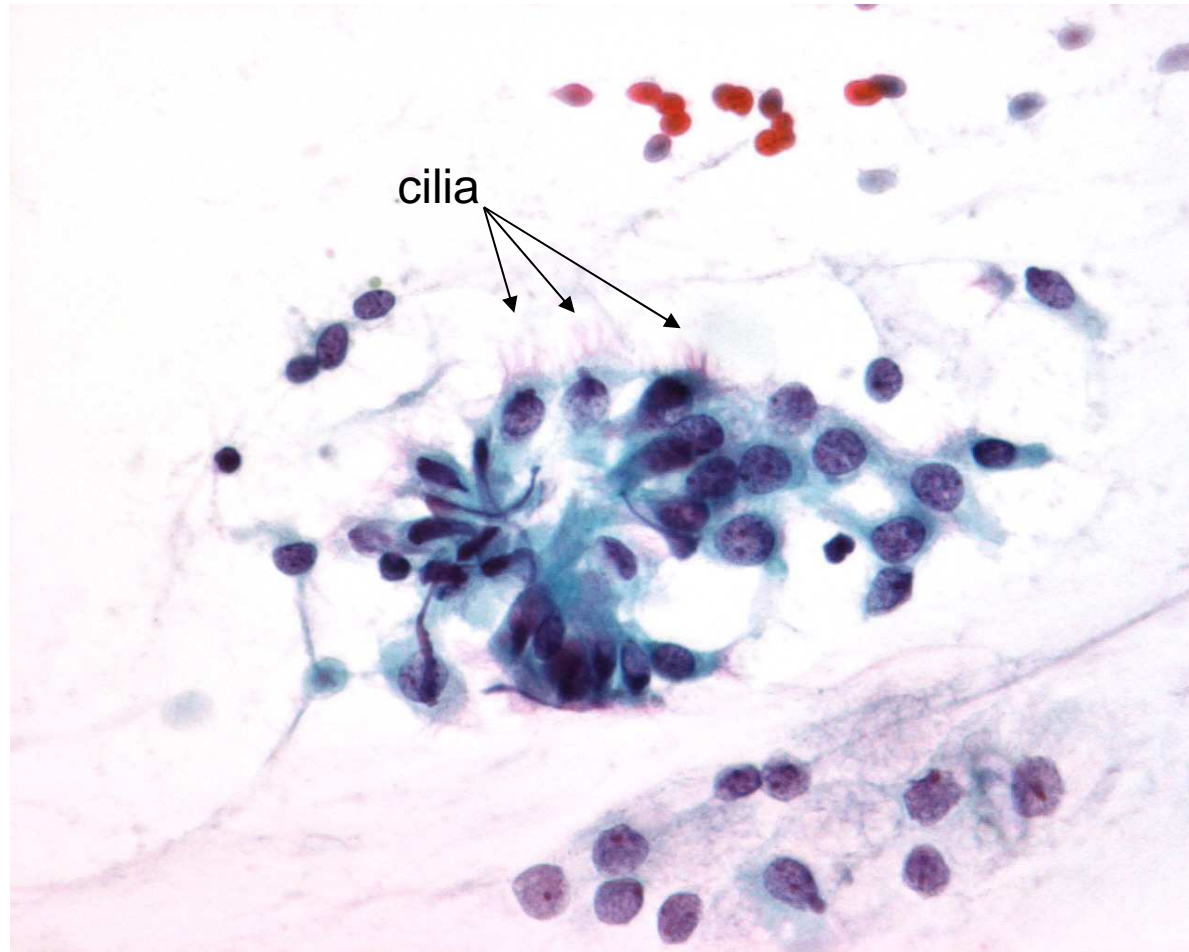


Clinical data!

BETHESDA: Non-neoplastic changes

Tubal metaplasia

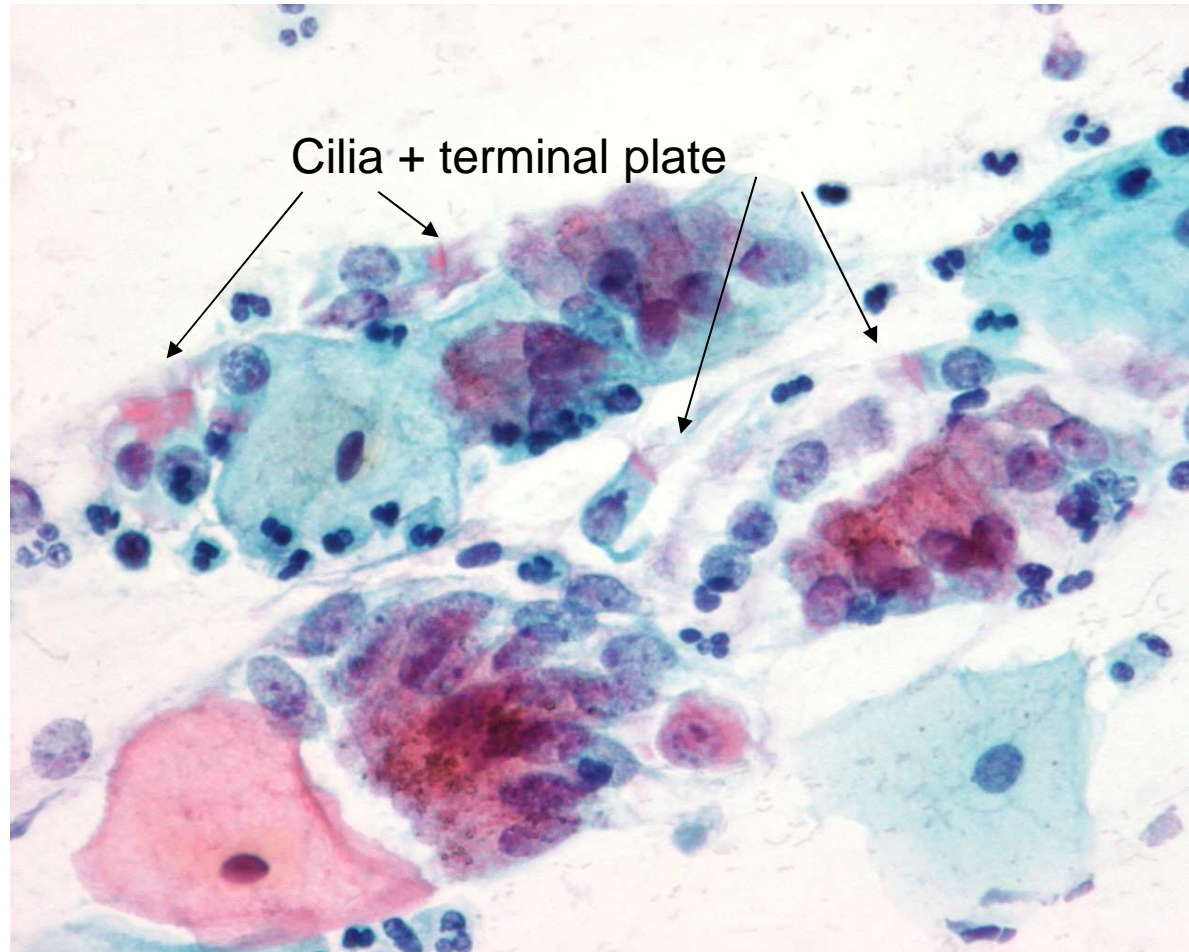
Cilia: when these you divine, it is a fine benign sign! *Richard DeMay*



BETHESDA: Non-neoplastic changes

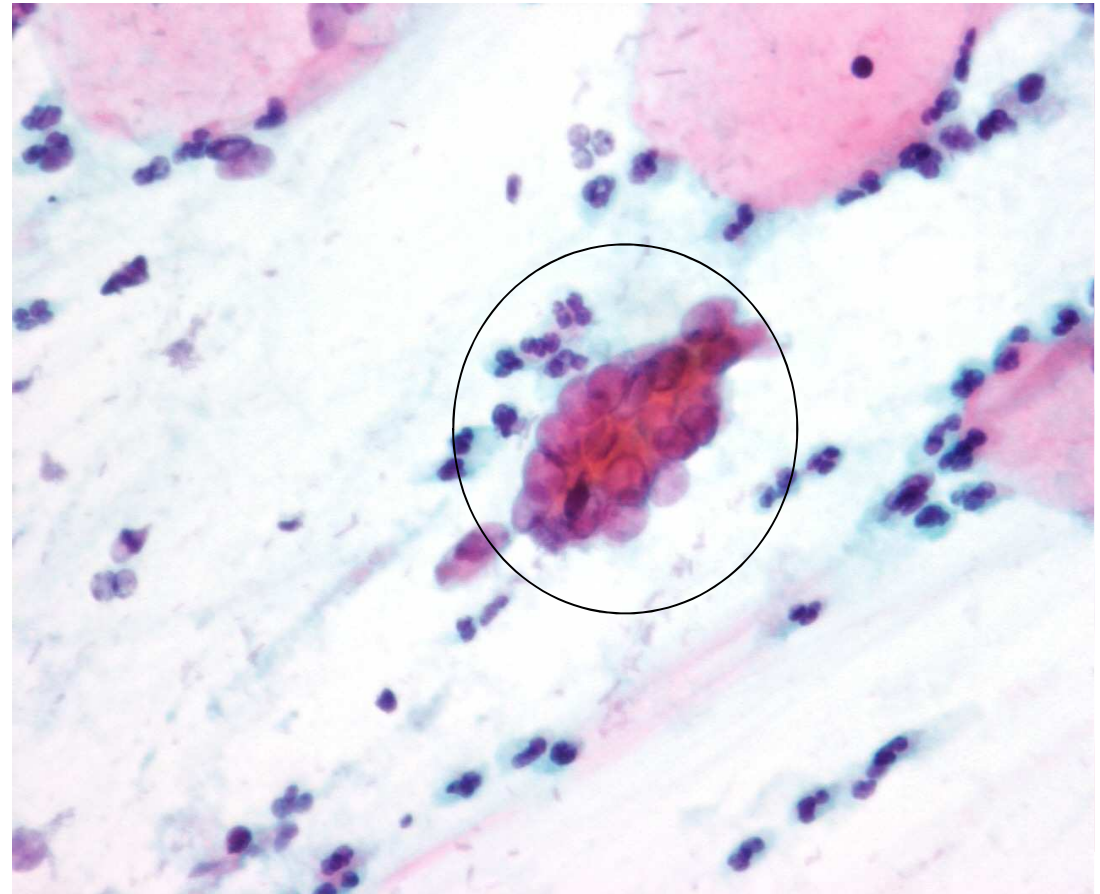
BETHESDA: Non-neoplastic changes

Tubar metaplasia - high endocervical cells?



Endometrial cells - exfoliated

- Exodus: day 6-10
- Glandular and stromal cells
- ?Endometrial pathology: second half of cycle (anovulatory cycle, atrophy, post-partum, post-abortum, instrumentation, IUD, endometriosis, tuboendometr. metaplasia, endometritis, pyometra, leiomyoma, polyp, HRT, OHC, carcinoma (5% PM))
- **Postmenopausal!!!**

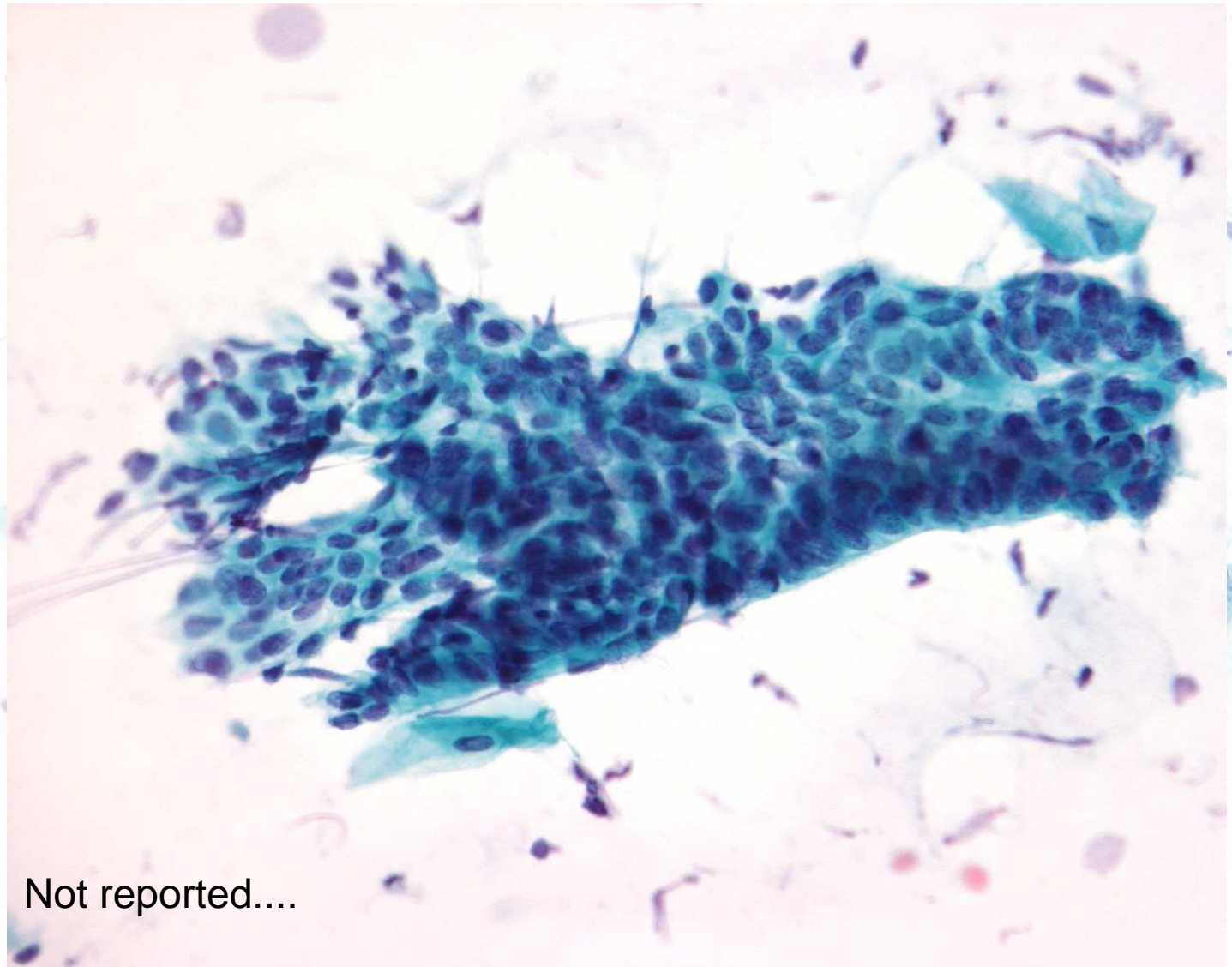


Clinical correlation advised (menstrual history, age)

BETHESDA: Endometrial cells in women ≥ 40 yrs

Endometrial cells in cervical smear

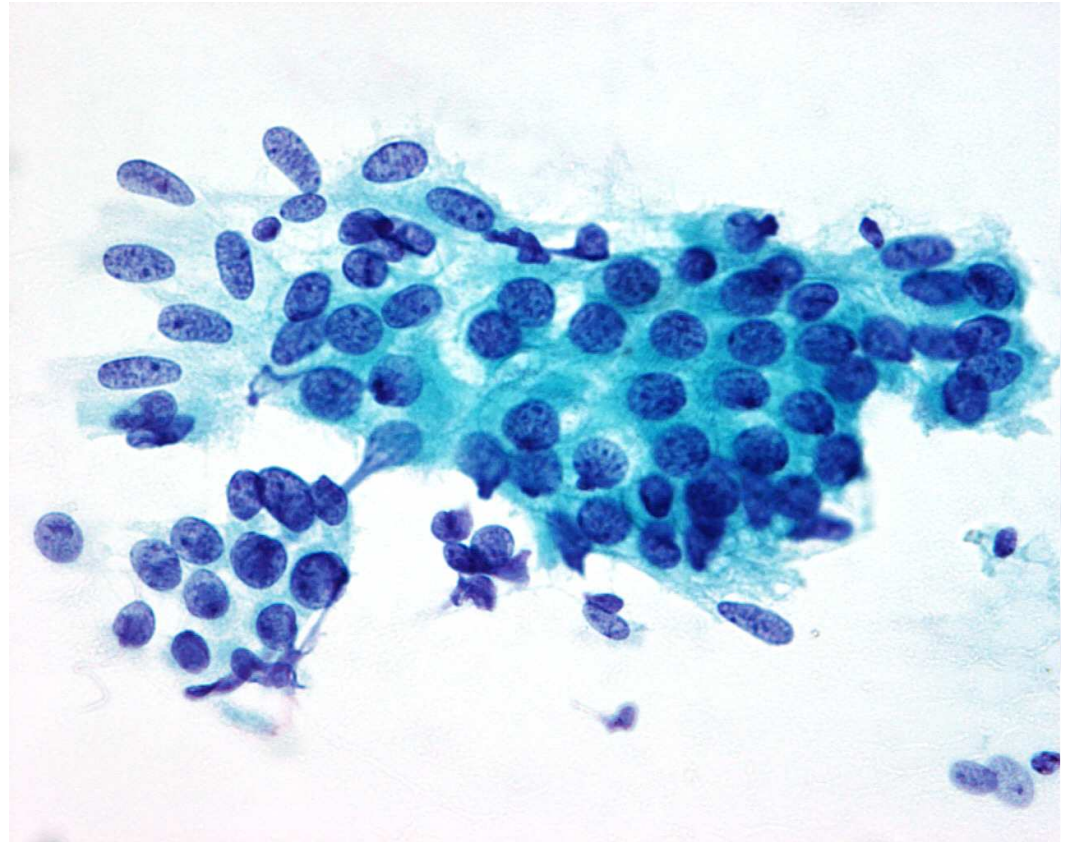
**Direct sampling-abrasia of
the lower uterine segment**



Not reported....

Atypical endocervical cells

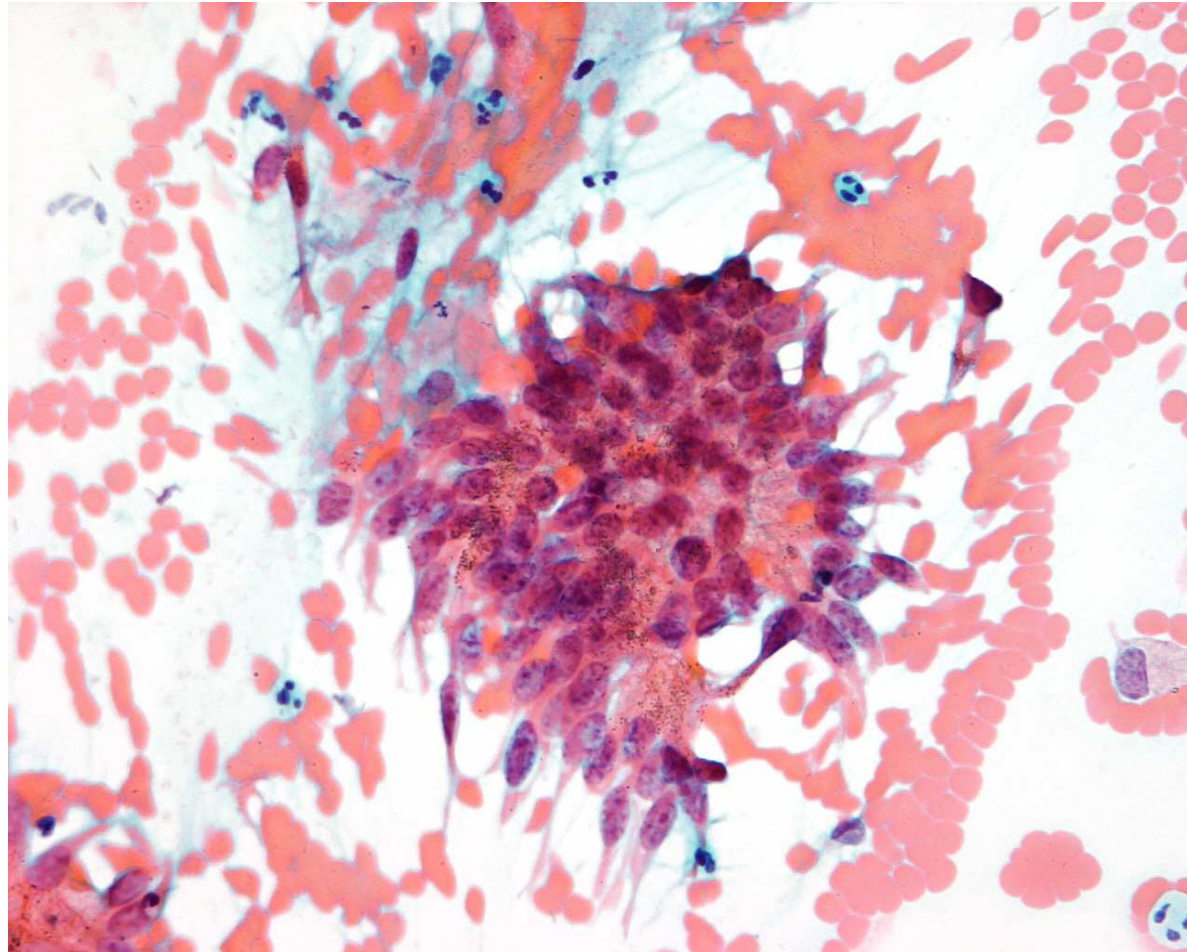
- Benign cellular changes with atypia – mimics of glandular neoplasia
- Inflammation, IUD, RT
- Polyps, microglandular hyperplasia, tubal metaplasia
- HG (squamous) lesions: ~10-50%



DD: tubal metaplasia, cilia?

BETHESDA: Atypical endocervical cells - of unknown significance

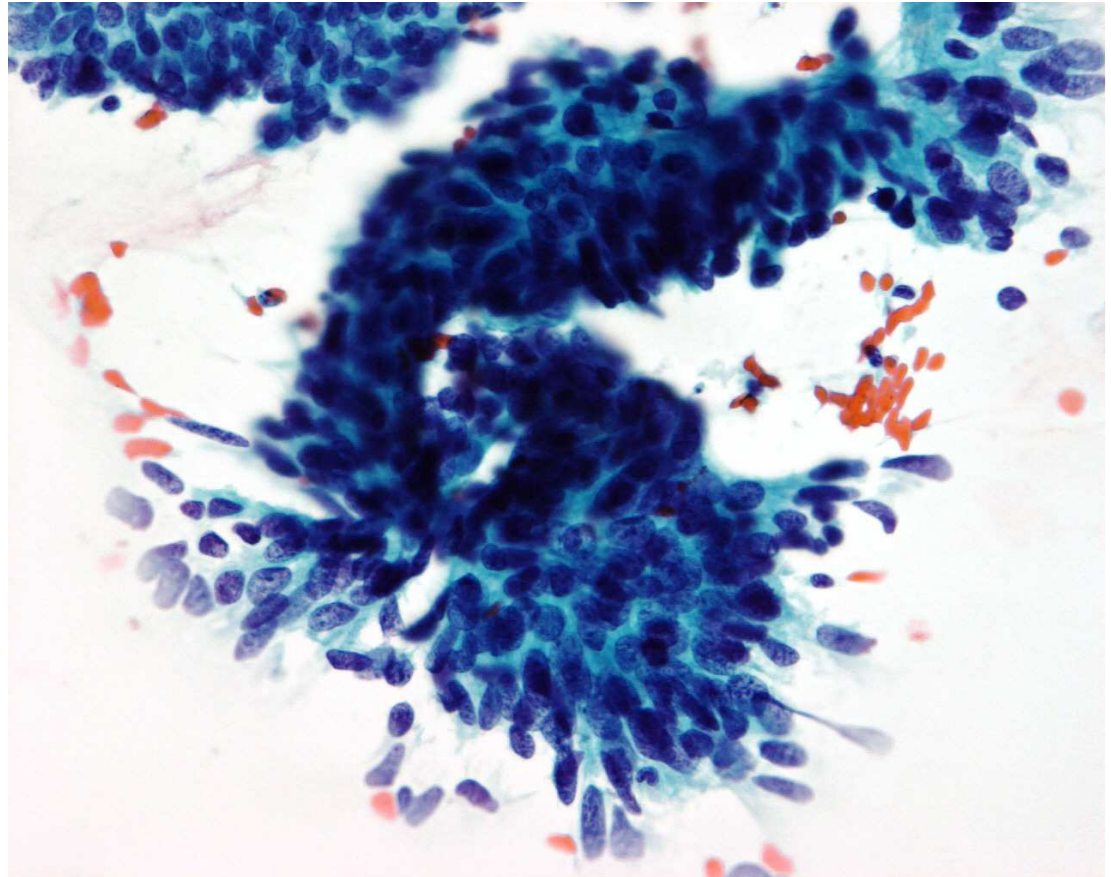
BETHESDA: Atypical glandular cells - favour neoplastic



Histology: CIN 2

Endocervical adenocarcinoma in situ

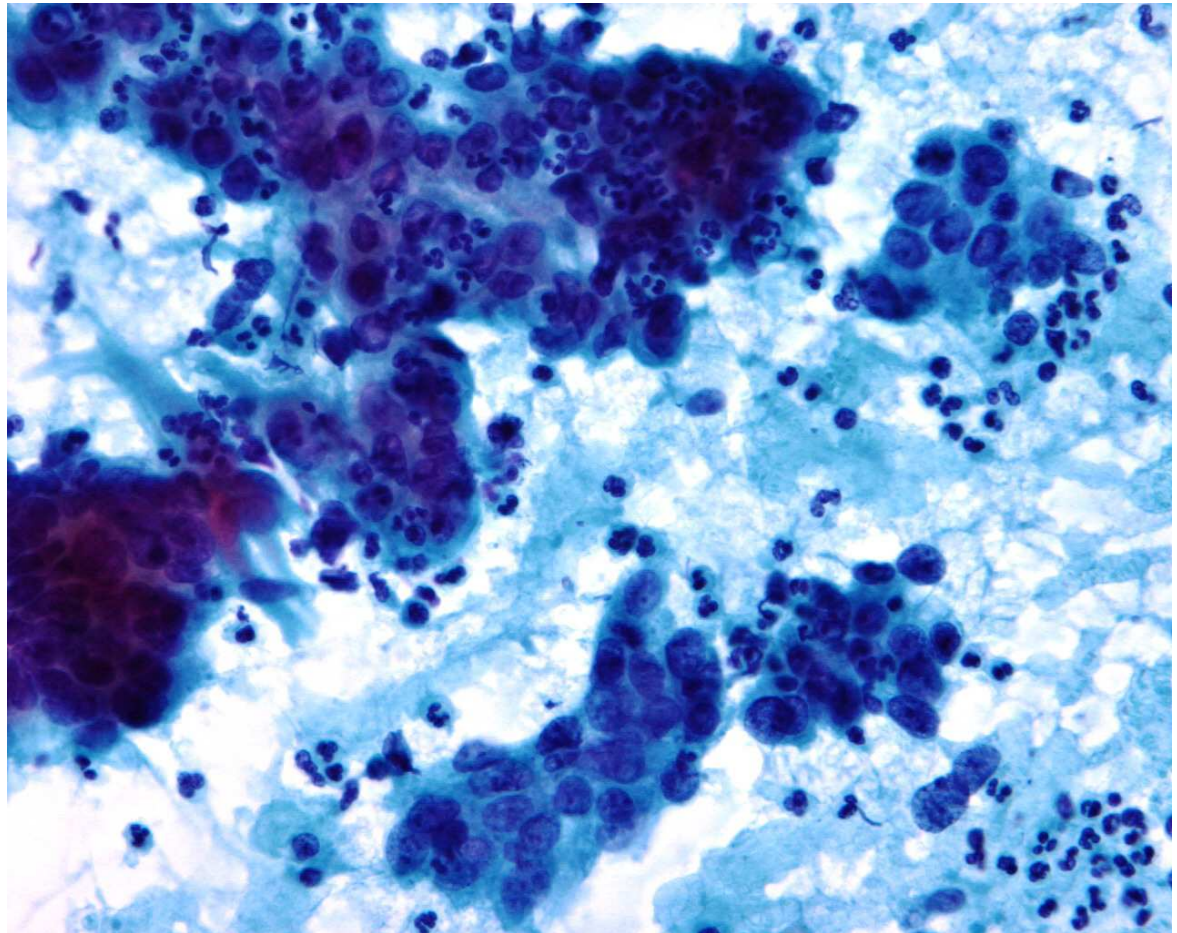
- Loss of honeycomb
- Nuclear crowding, overlap
- Pallisading, feathering
- Nuclei elongated, coarse chromatin



BETHESDA: Endocervical adenocarcinoma in situ

Endocervical adenocarcinoma

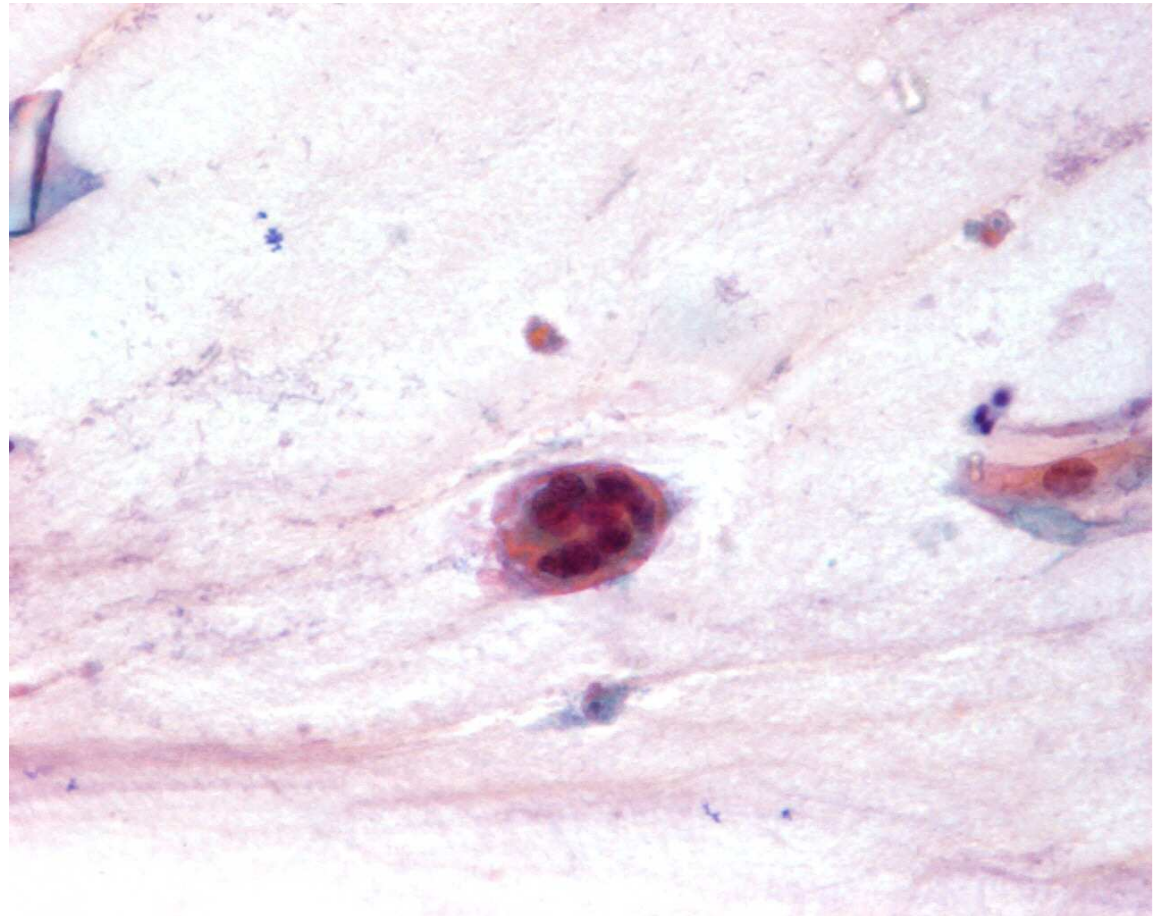
- Different histologic types – cytology?
- Tumor diathesis, nuclear clearing, nucleoli



BETHESDA: Adenocarcinoma - endocervical

Atypical endometrial glandular cells

- Benign/atypical –
↑nuclear size
- Polyp, IUD,
endometritis, endom
hyperplasia, carcinoma

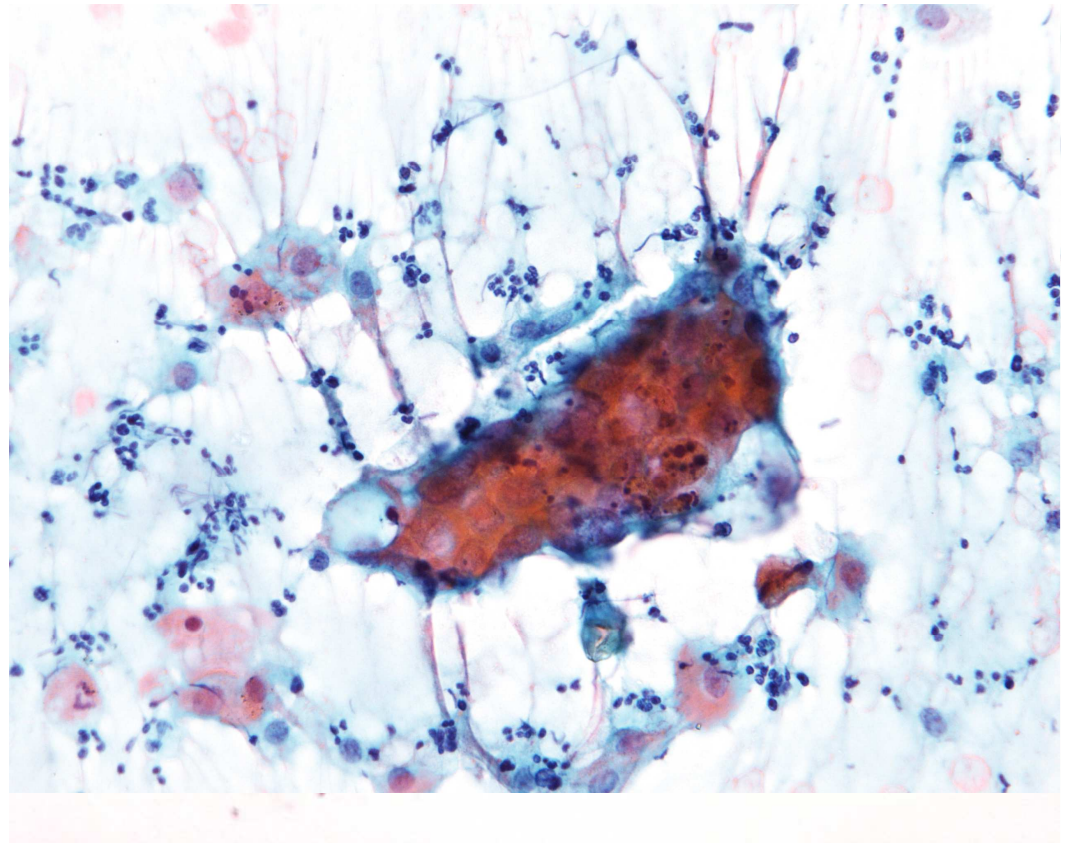


Pap test is not screening procedure for detection of endometrial carcinoma

BETHESDA: Atypical endometrial cells - of unknown significance

Endometrial adenocarcinoma

- Cytology / grade
- Tumor diathesis – finely granular / watery

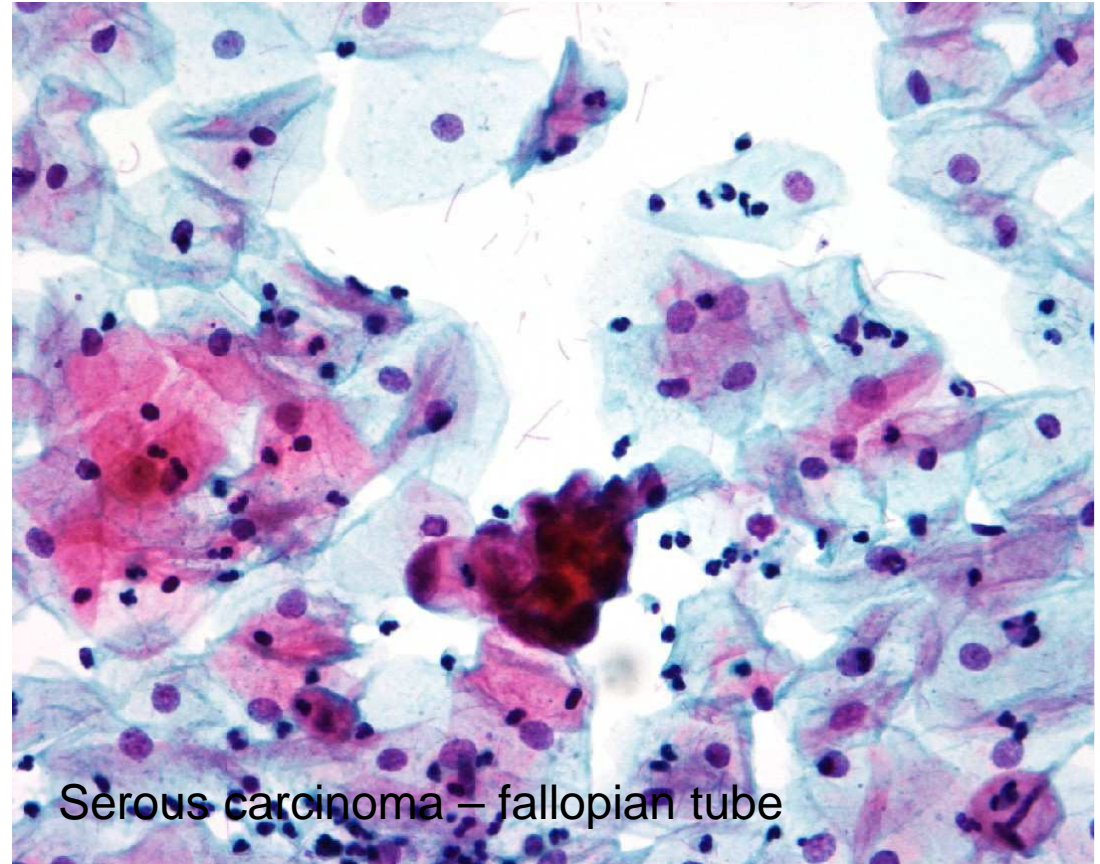


Pap test is not screening procedure for detection of endometrial carcinoma

BETHESDA: Adenocarcinoma - endometrial

Other glandular cells - mlg

- Extruterine adenocarcinoma
 - Ovary
 - Fallopian tube
 - Metastases



BETHESDA: Adenocarcinoma - extrauterine

CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- Major challenge in gynecological cytopathology
- Rare finding: incidence of AGC 0.46%-2.5%
- Limited reproducibility of AGC interpretation
- Significant underlying pathology: 8.2-53% (CIN2/3)
- Non-cervical uterine or adnexal carcinoma



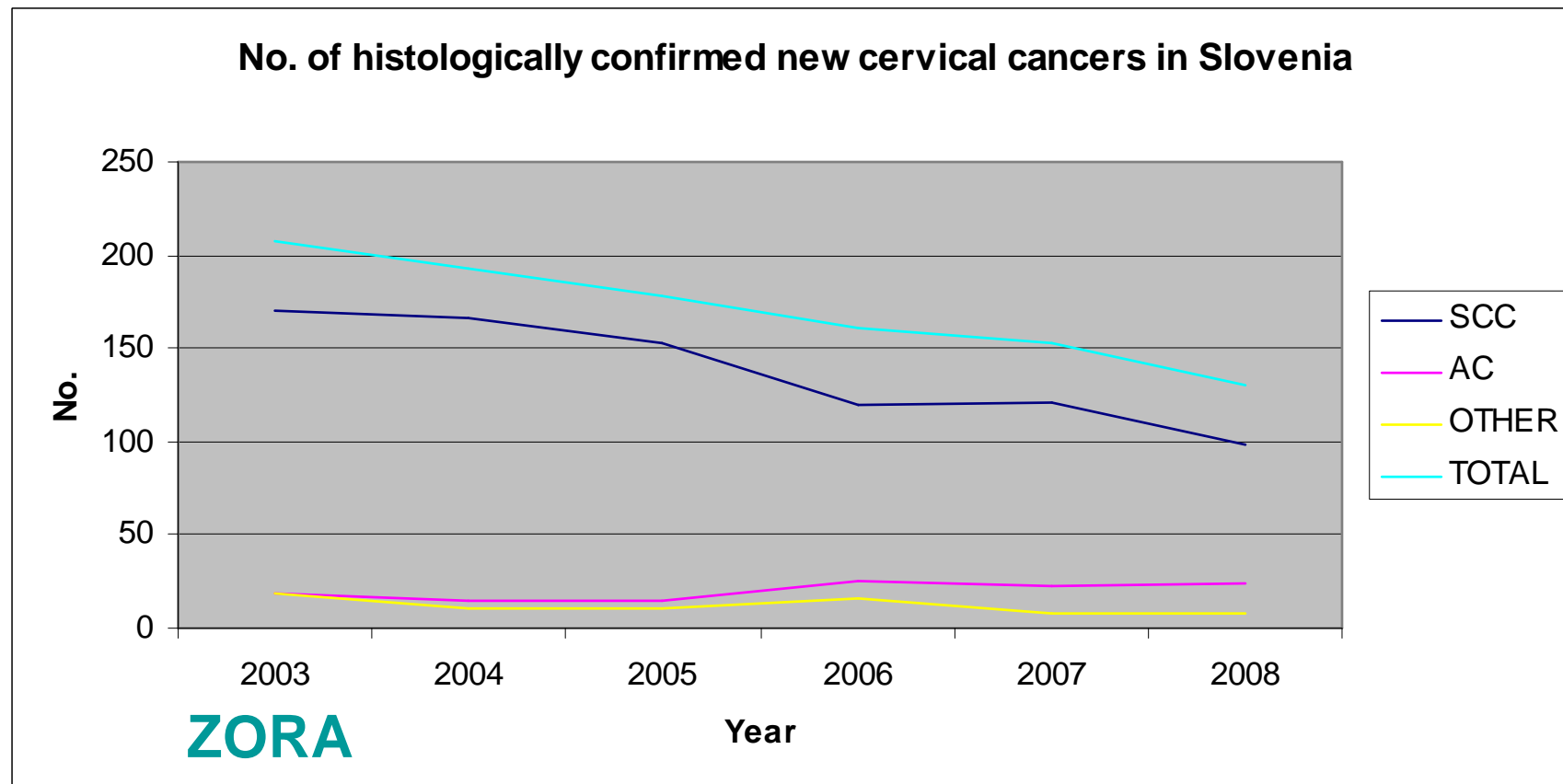
ZORA
slovenian national
cervical screening
program
Zgodnje **O**dkrivanje
pred**RA**kavih
sprememb na
materničnem vratu

<http://www.onko-i.si/zora/>

ZORA

- To decrease incidence and mortality from cervical cancer in Slovenia
- Pilot project 1998 –LJ, 2001 – Izola, Koper, Piran, 2003 – nation-wide
- Aim: to screen at least 70% of women between 20 – 64 years of age every 3 years
- Invitations for non-attenders
- Gynecological examination and the Pap test (conventional: Ayre's spatula and brush)

CERVICAL SCREENING FOR GLANDULAR NEOPLASIA



<http://zora.onko-i.si/>

2003: 210 cases = 20.6

2009: 129 cases = 12.6

↓39%

http://www.onko-i.si/fileadmin/onko/datoteke/dokumenti/LP_2008.pdf

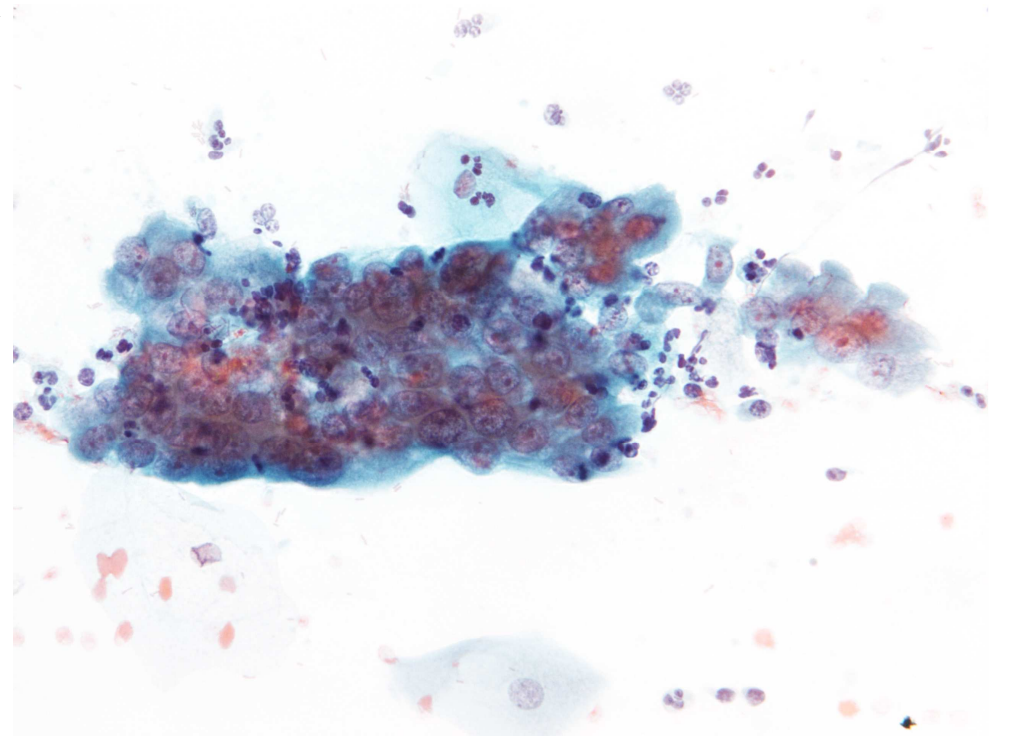
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- IP FM UL 2008: 42.833 cervical smears
- ZORA Registry: 99 (0.23%) cases, different grades of atypical glandular cells
- AGC: 77/99 - 77.8%
- SA-GC/AIS: 12/99 - 12.1%
- Adenocarcinoma (AC): 10/99 - 10.1%



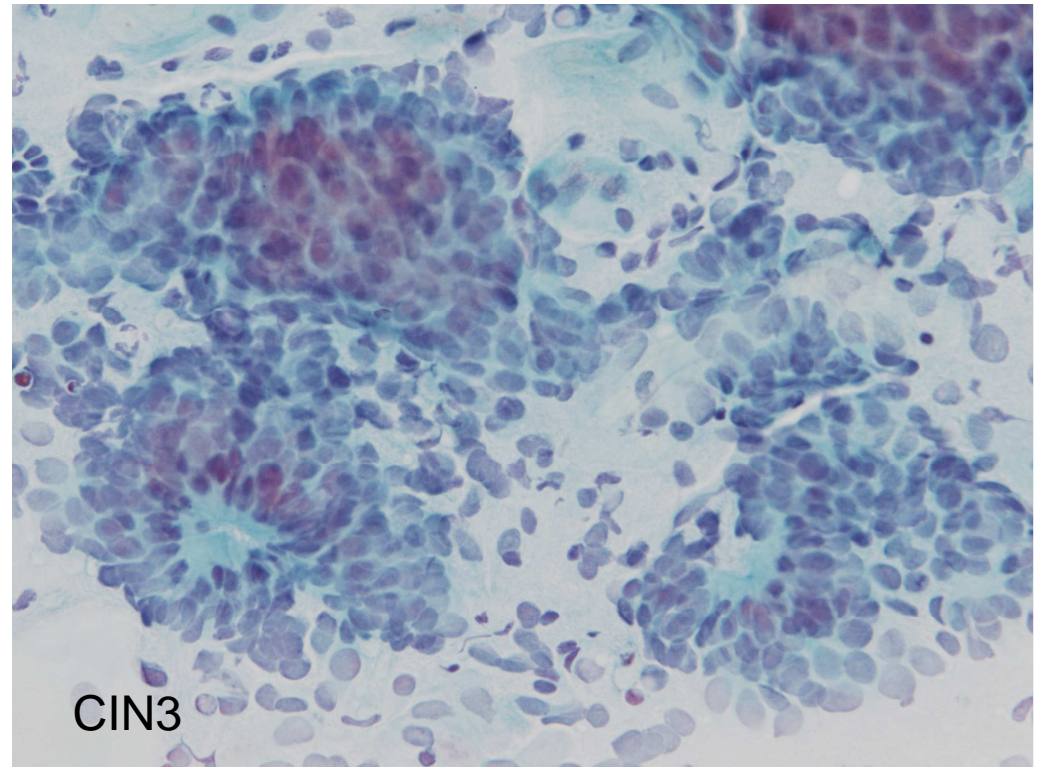
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- HISTOPATHOLOGIC FINDINGS
- In 52/77 (67.5%) **AGC** biopsy not performed
- Follow-up cervical smears (acc. to cytology guidelines)
- All **negative** for neoplasia in 2011



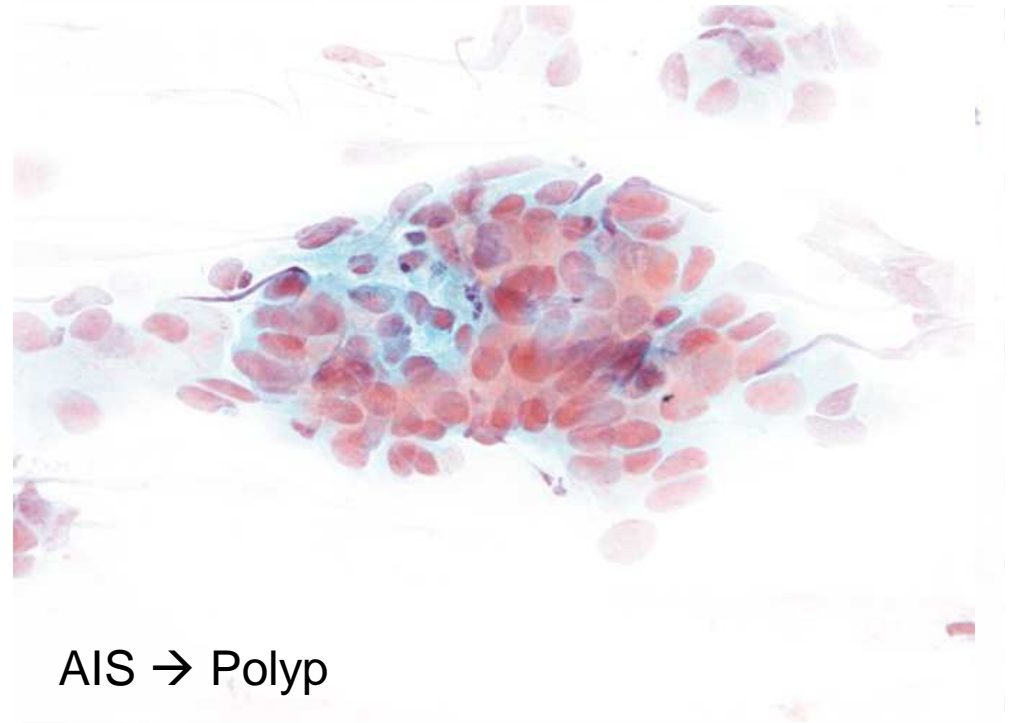
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- HISTOPATHOLOGIC FINDINGS in 32% **AGC**
- **CGIN HG** only in one case (1.3%)
- **CIN** in 12 patients (15.6%), most of them (9 cases, 11.7%) were CIN 2 and CIN3
- **Benign**: 11 (14.3%)
- **EM Adenocarcinoma**: 1 (1.3%)



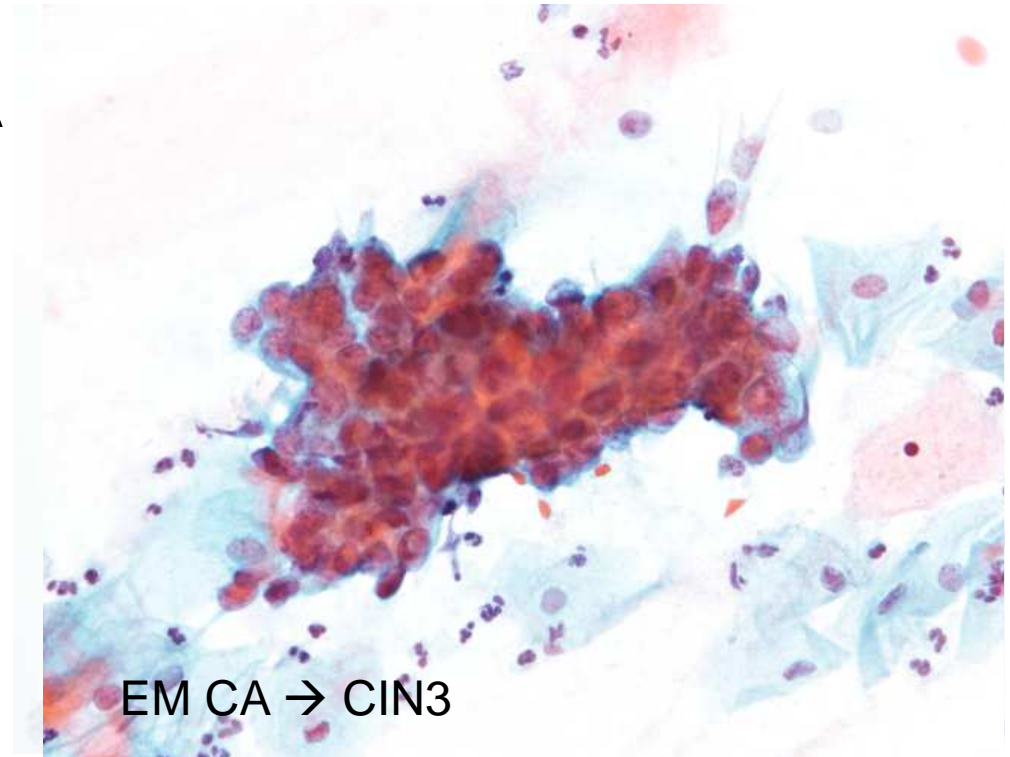
CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- HISTOPATHOLOGIC FINDINGS in **SA-GC /AIS**
- **Adenocarcinoma** (2 EC, 2 EM): 4 patients (33.3%)
- **CIN**: 6 patients (50%, 5/6 CIN 2 and CIN 3)
- **Benign**: 2 (16.7%)



CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

- HISTOPATHOLOGIC FINDINGS in **ADENOCARCINOMA**
- Malignancy confirmed in 7 patients (70%)
- EM ca: 4
- Meta ovarian ca: 2
- SCC: 1
- CIN: 3 cases (30%),
2/3 CIN3



CERVICAL SCREENING FOR GLANDULAR NEOPLASIA

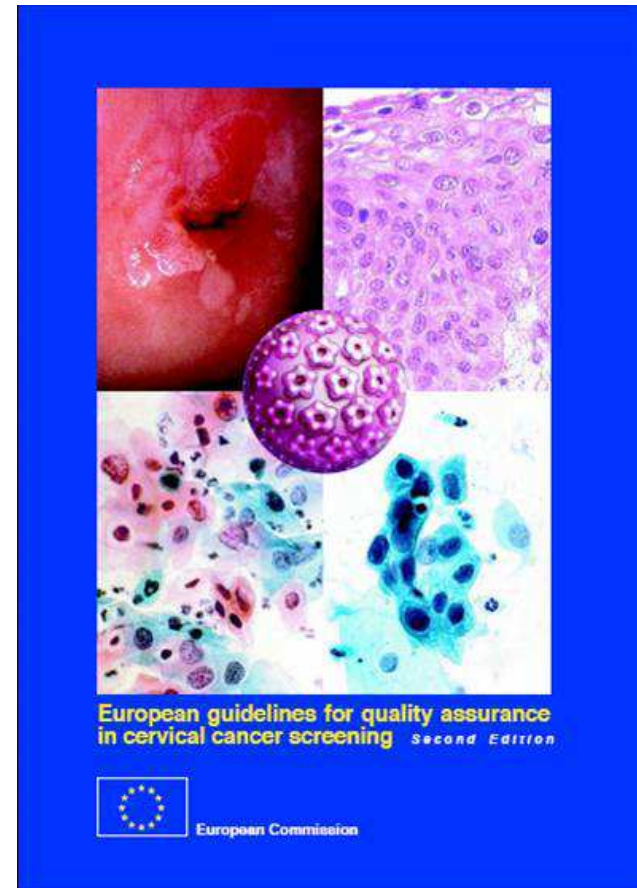
- **ZORA: HPV triage testing** (SLO Oct. 2010)
- Cervical cytology sample in liquid medium
- HPV DNA Hybrid Capture 2 (hc2): HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68
- Indications:
 - Atypical squamous cells NOS (5-12% CIN-VS expected)
 - Atypical glandular (endocervical) cells - NOS
 - LSIL after age 35
 - Follow-up of CIN1
 - Follow-up after TH of CIN

http://zora.onko-i.si/data/2011_Smernice_web.pdf

Rabelo-Santos et al. Cytopathology 2008

CERVICAL CANCER AUDIT

- **Audit** of interval cervical cancers in the context of all the components of the routine screening process
- **Re-screening** of negative or low grade smears before the diagnosis of invasive cancer presents an important part of the audit.



European guidelines for quality assurance in cervical cancer screening. 2nd ed., 2008.

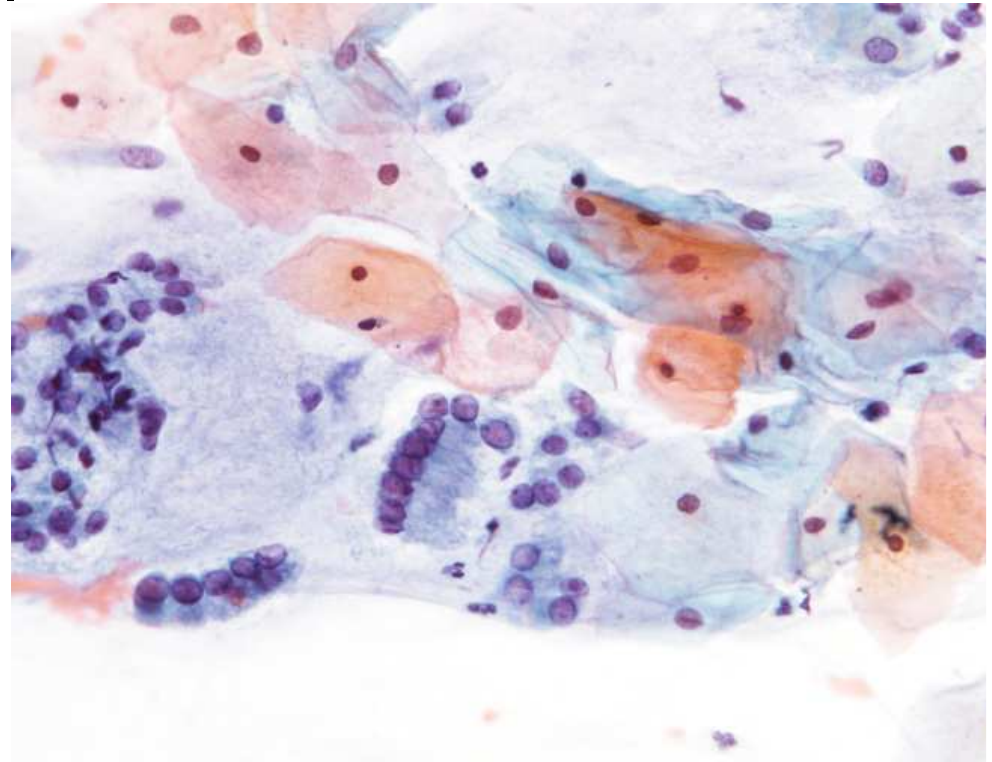
CERVICAL CANCER AUDIT

- Slovenia: only cytopathology part of the audit
- Complete audit of all screening components has not been conducted yet!
- 1st cytology audit 2008 for cervical cancer diagnosed in 2006 : negative or low-grade smears reviewed from 2003 (beginning of ZORA) till 2006



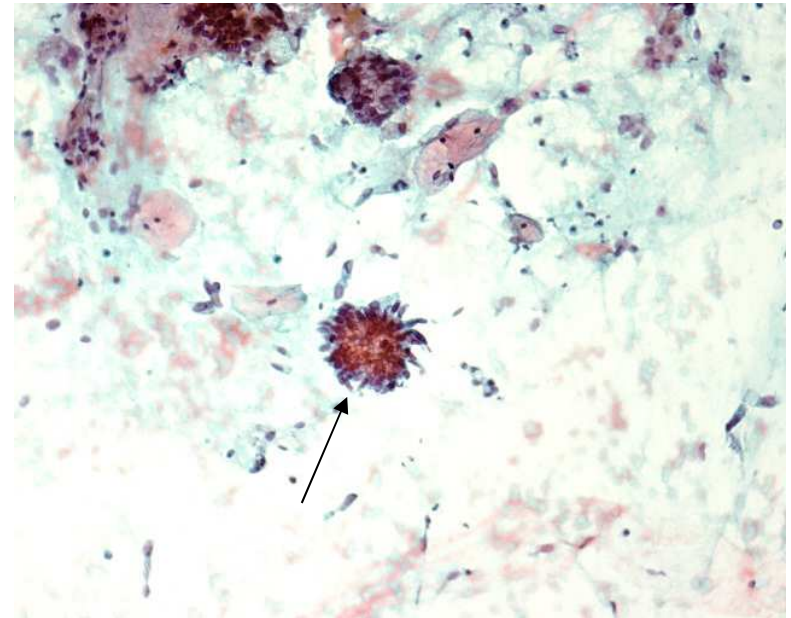
CERVICAL CANCER AUDIT

- Underdiagnosed cervical smears were less likely to be found in endocervical adenocarcinomas compared to squamous cell carcinomas
- Inadequate sampling (EAC in cervical stroma or deeper in the cervical canal)



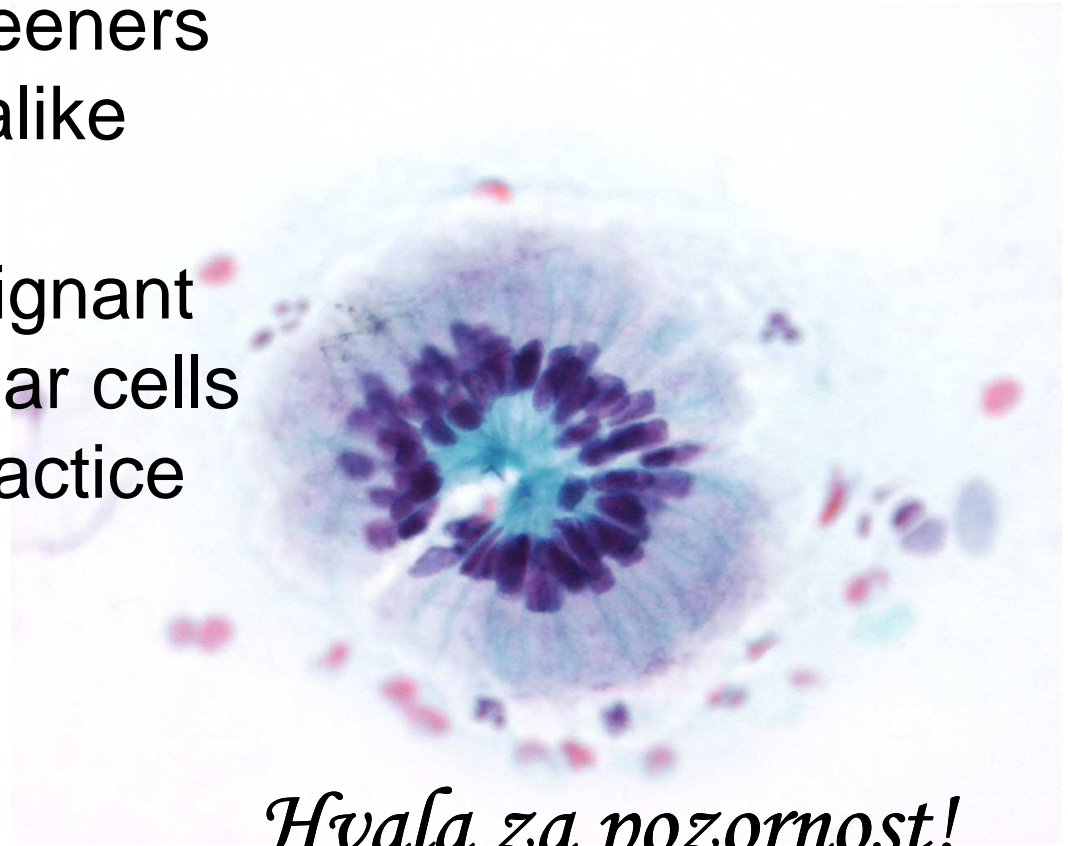
CERVICAL CANCER AUDIT

- Underdiagnosed cases: representative highly atypical glandular cells found on the review but not recognized originally



Glandular lesions in cervical cytology

- Cytotechnologists/screeners and cytopathologists alike very rarely see true premalignant and malignant (endocervical) glandular cells in routine everyday practice
- Continuous medical education in cervical glandular cytology!

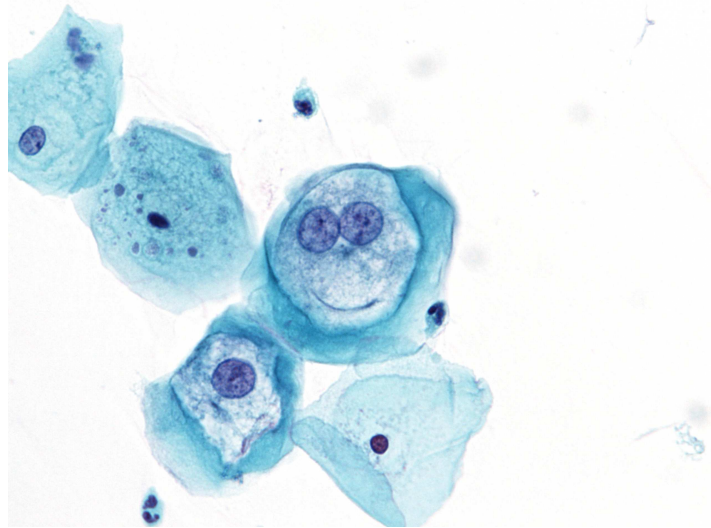


Hvala za pozornost!

XLIIIrd PROFESSOR JANEZ PLEČNIK MEMORIAL MEETING
with International Symposium

Advances in Cytopathology;

Bridge between Clinics and Diagnostic Pathology



December 6-7, 2012

Institute of Pathology, Faculty of Medicine University of Ljubljana,
Korytkova 2, Ljubljana, Slovenia
in cooperation with
Department of Cytopathology, Institute of Oncology Ljubljana, Slovenia