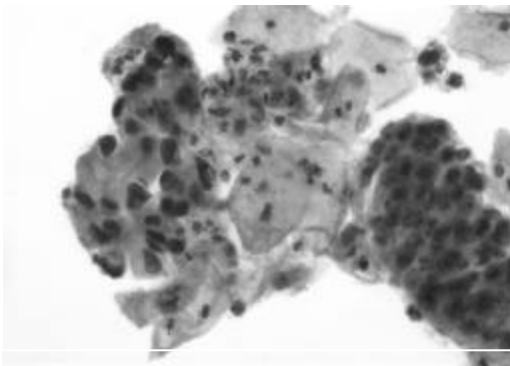


## Clinical Pathologic Correlations – Case Four

Richard W. Lieberman, M.D.  
<http://gynonc.path.med.umich.edu>

### Case 4 — Part I

- 44 y.o. G3 P3 referred with abnormal PAP
- atypical glandular cells of undetermined significance (AGUS). See comment.
- Comment:
  - “a metastatic adenocarcinoma cannot be excluded”



### Case 4 – AGUS PAP

#### Your thoughts...

- risk factors
- cervical
- endometrial
- ***metastatic!?***

## Case 4 – AGUS PAP

- PMH
  - no prior abnl PAP
    - regular exams
  - no known h/o HPV
  - + Hypertension
  - + menorrhagia
- PSH
  - C/S x3
- FH
  - father – +breast CA
  - brother – +melanoma

**Next?**

## First Office Visit...

- Exam
  - slightly obese
  - normal breast exam
  - no lymphadenopathy
- Pelvic
  - TNS uterus
  - no cervical enlargement
  - no adnexal mass
  - guaiac negative stool
- Colposcopy
  - no lesions of the cervix, vagina, or vulva
- ECC
- Endometrial Biopsy

## Pathology — Part I

- ECC
  - fragments of benign endocervical glands and squamous epithelium
- Endometrial biopsy
  - Non-hyperplastic secretory endometrium

## Case 4 — Additional Workup

- Labs
- Radiographic Studies
- Review the cytology

*What would you do?*

## Case 4 — Additional Workup

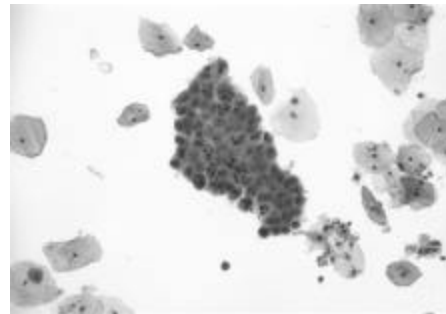
- Review of original cytology
  - AGUS... agreed
- “not worried about metastatic adenocarcinoma”
- source of “atypia”?
  - indeterminate
- CA-125 <35
- CXR – negative
- XMG – negative
- CT abdomen/pelvis
  - slightly enlarged uterus
  - no significant abnormalities

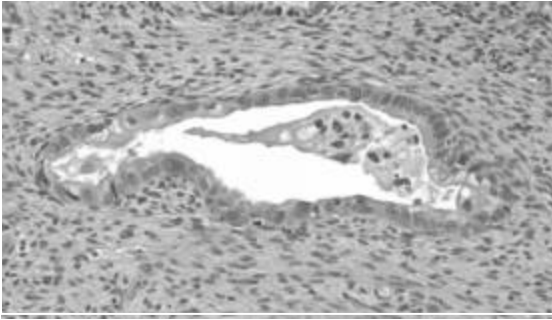
## What is the next step?

1. repeat cytology in...
    - 3 months...
    - 6 months...
  2. cone biopsy
    - not a LEEP
  3. D&C
- } 2&3

## Second Office Visit... 3 months

- Exam
  - unchanged
- Pelvic
  - PAP repeated
- Colposcopy
  - no lesions of the cervix, vagina, or vulva
  - ECC repeated



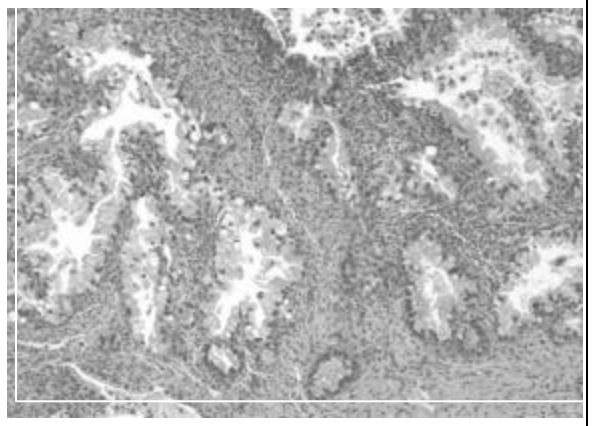


## Case 4 – Diagnosis

- ECC
  - highly suspicious for Müllerian (mucinous) type endocervical adenocarcinoma

## Next?

- A diagnostic procedure is scheduled
- Cold knife conization
  - Not a LEEP
  - With ECC and endometrial curettage



## Diagnosis — Part II

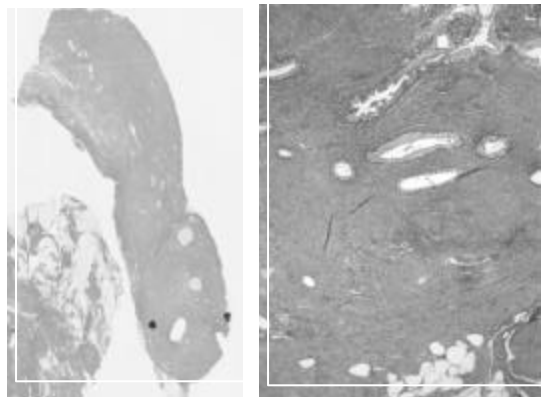
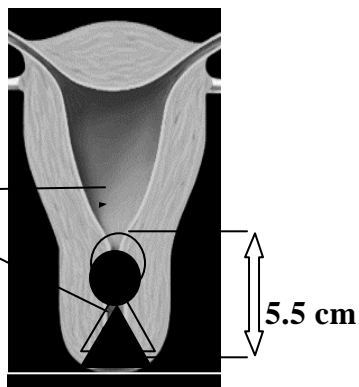
- cone biopsy
  - moderately-well differentiated mucinous adenocarcinoma with superficial invasion. Endocervical margins positive.
- endometrial curettage
  - fragments of mucinous adenocarcinoma
- endocervical curettage
  - fragments of mucinous adenocarcinoma. Hypermucinous endocervical glands

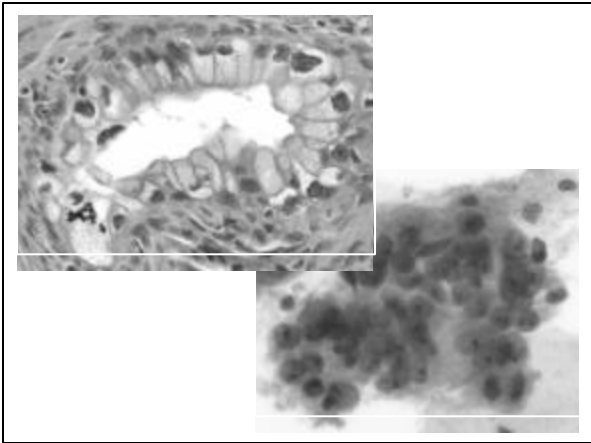
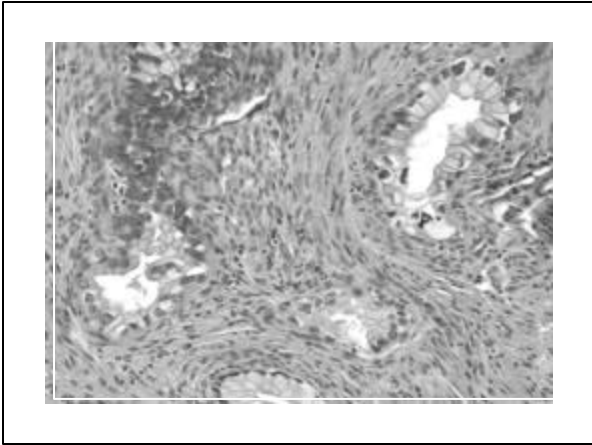
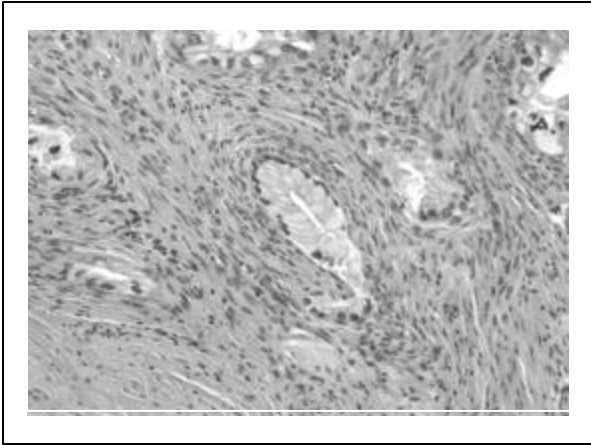
## Radical Hysterectomy

- no gross photo available
- gross description
  - 1.3 x 1 cm hemorrhagic area at upper endocervix
  - cervix 5.5cm in length

### Gross Depiction of Tumor

- false negative:
  - Embx sample
- ECC sampling





Follow-up: Stage IB Mucinous Adenocarcinoma of the Cervix

- Adjunctive pelvic irradiation
- NED at 3 years

## AGUS: Issues to Consider

- what are *usual* findings with AGUS?
  - false negative initial evaluation
    - what do you do?
- what *is* appropriate management?
  - Bethesda 2001 recommendations

<http://bethesda2001.cancer.gov>

## Outcomes of AGUS\*

Qualifier	Neg	SIL	AIS	ECCa	EmCa
Reactive (n=442)	75	22	1.4	0	1.6
NOS (n=960)	65	26	2	2	5
Neoplastic (n=421)	20	18	48	12	2

\* % of patients

All AGUS – 10 % with carcinoma (AIS, ECCa, & EmCa)

## Clinical Management of AGUS

- colposcopy
- endocervical sampling
- possible endometrial biopsy or curettage

**Refs:**  
 Oncology 1999; 13:550-574  
 Am J Obstet Gynecol 2000; 182:1278-82

## Bethesda System 2001

- AGC (atypical glandular cells)
  - atypical glandular cells, NOS
  - atypical glandular cells, favor neoplasia
  - atypical endocervical cells, NOS
  - atypical endocervical cells, favor neoplasia
  - atypical endocervical cells, probably AIS
  - atypical endometrial cells
  - adenocarcinoma in situ (AIS)
  - AGC (any of the above) with squamous abnormality

AGC, “favor reactive” replaced by NOS  
 NCI Bethesda System 2001

## AGC Recommendation

- All women with AGC
  - colposcopy
  - endocervical sampling
  - repeat cytology not acceptable

NCI Bethesda System 2001

## AGC Qualifiers That Increase Risk

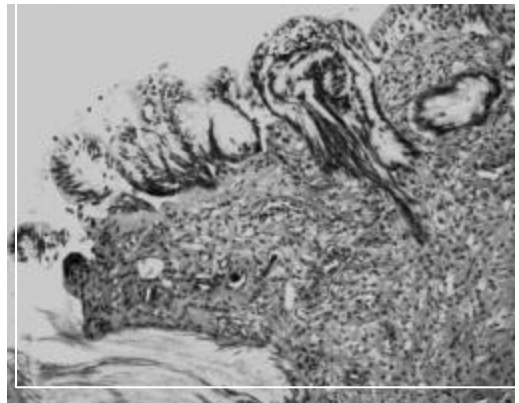
- favor neoplasia
- probable AIS
- AIS
  
- Recommendation\*
  - diagnostic cervical excisional procedure
    - cold knife conization

\*unless invasive cancer on exam, biopsy or ECC

NCI Bethesda System 2001

## Why not LEEP?

Thermal cautery effect renders the endocervical glandular epithelium at the margin... ***uninterpretable!***



## AGC – Increased Risk of Endometrial Neoplasia

- atypical endometrial cells
- age  $\geq$  35
- unexplained vaginal bleeding with AGC at any age
  
- Recommendation
  - endometrial sampling (pipelle or D&C)

NCI Bethesda System 2001

## AGC – Negative Initial Evaluation

- AGC, glandular or endocervical, NOS
  - repeat PAP every 4-6 months
  - continue for 3-4 negative cytologies
- AGC, favor neoplasia, AIS or carcinoma
  - diagnostic cervical excision (CKC)
    - if negative, consult with cytopathologist

NCI Bethesda System 2001

## Negative Colposcopy, ECC, EMC, and CKC

- Recommendation
  - pelvic ultrasound
  - abdominal-pelvic CT scan
    - look for non-gynecologic source
  - review of cytology
    - original pathologist and second opinion

## Case Presentation & AGUS Dilemma: Summary

- uncommon diagnosis
  - limited literature
- "qualifiers"
  - assist in projecting outcome
  - "favor neoplasia" et. al. with high probability for disease
- Bethesda 2001 with consensus recommendations

<http://bethesda2001.cancer.gov>

Please avoid LEEP!