Benign lesions of the cervix mimicking neoplasia

Anne-Sophie Van Rompuy

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Overview

- Deep endocervical glands and Nabothian cysts
- Tunnel clusters
- Microglandular hyperplasia
- Mesonephric duct remnants and hyperplasia
- Lobular endocervical glandular hyperplasia
- Diffuse laminar endocervical glandular hyperplasia
- Arias-Stella reaction
- Tubal/tubo-endometrioid metaplasia
- Endometriosis
- Endocervical adenomyoma
- Ectopic prostatic tissue

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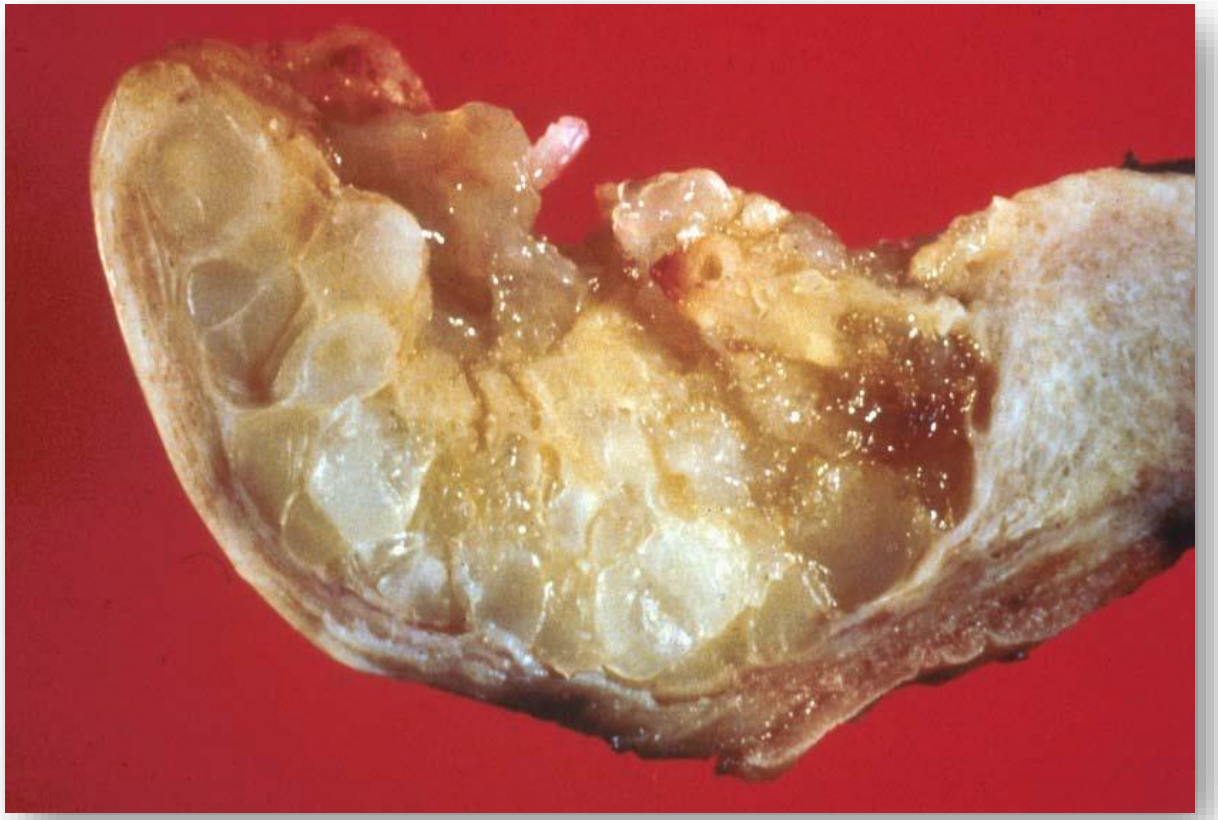
Deep endocervical glands and Nabothian cysts

- Endocervical glands can be **irregulary distributed** in the cervix and extend deep into the outer one-third of the cervical wall.
- May form **large cysts**, creating a mass lesion
- Gross examination: multiple, mucin-filled cysts extending from the mucosa to the deep portion of the wall



Oliva & Tornos, USCAP 2015

Deep endocervical glands and Nabothian cysts

Glands and cysts are relatively uniform in contour, not overly crowded, and lined by a single layer of cytologically benign columnar to flattened epithelium without mitotic activity

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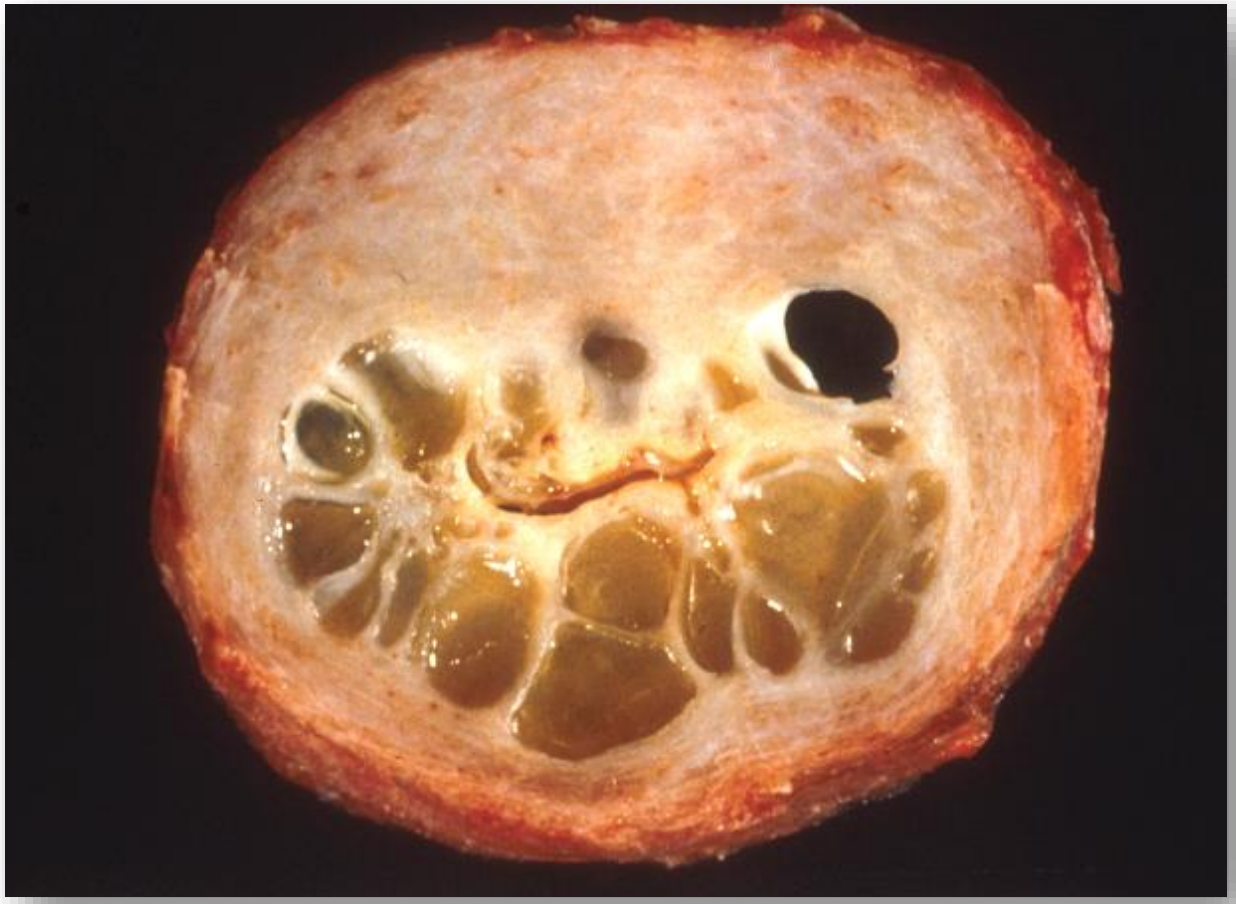
Tunnel clusters

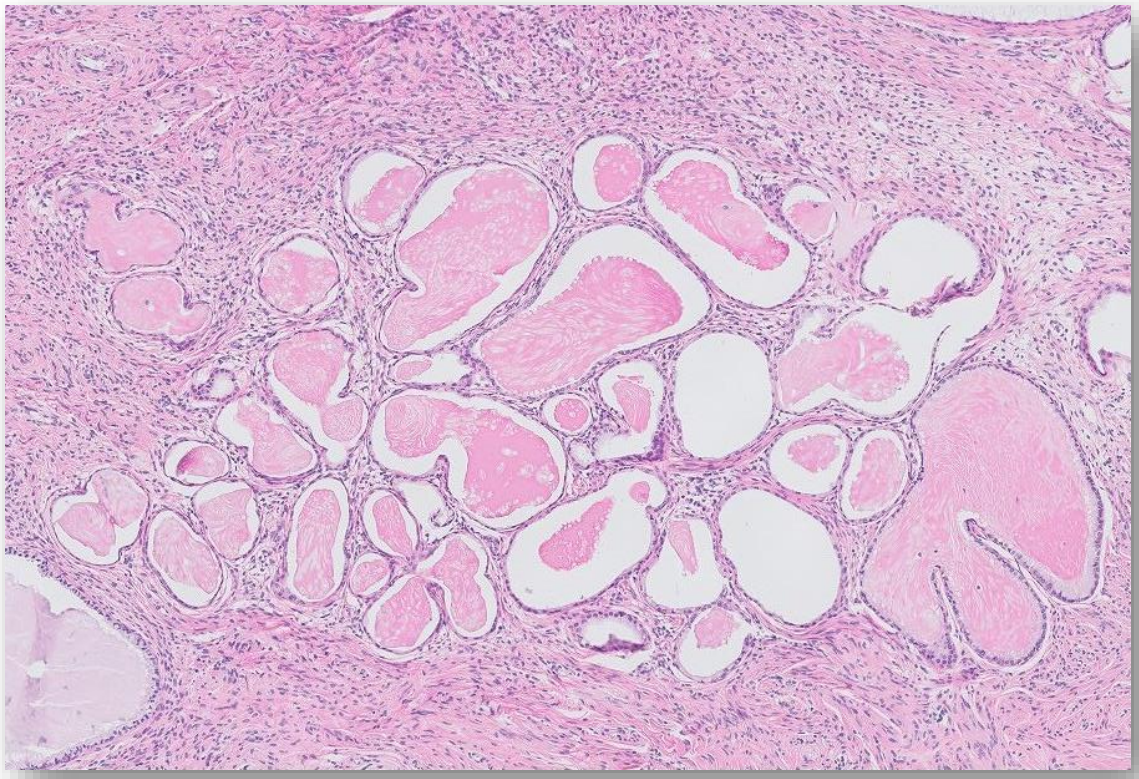
- Occur in **multigravid women**, usually over 30 years of age
- Two types: **type A and type B**. Type B is the most common, can be extensive and macroscopically visible.
- **Multifocal** involvement is common



Oliva & Tornos, USCAP 2015

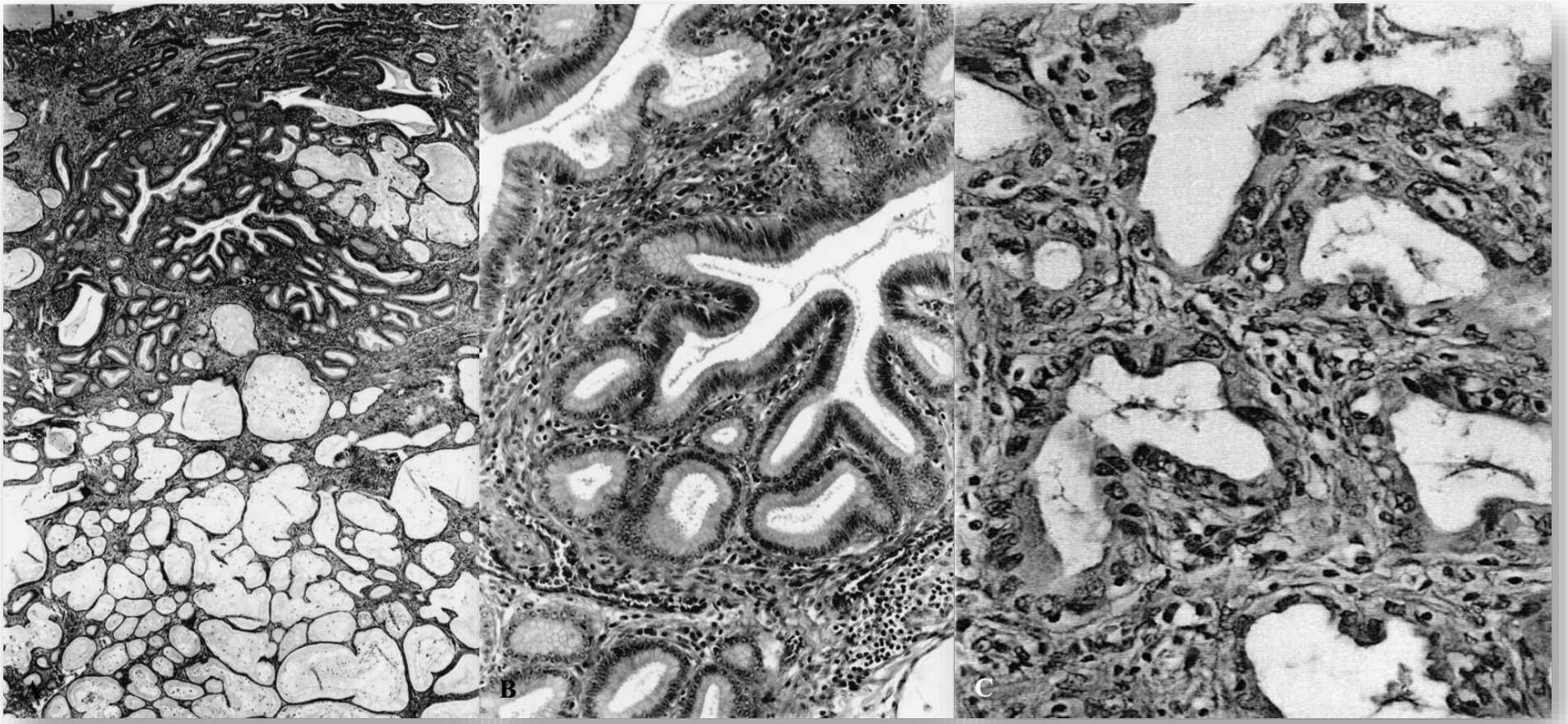
Tunnel clusters: type B

- Closely apposed, simple cystic glands lined by flattened or low cuboidal epithelium that lacks mitotic activity
- Lobular arrangement
- Can expand deeply into the cervical wall mimicking malignancy



Tunnel clusters: type A

- Often **associated** with type **B**
- Well-circumscribed proliferation of oval, round or angulated glands.
- More **irregular, angular** of **pseudo-infiltrative** arrangement
- More **prominent** cells: cuboidal with amphophilic cytoplasm/columnar and mucus secreting. May have enlarged nuclei with small nucleoli



Int J Gynecol Pathol, Vol. 21, No. 4, October 2002. Nucci M

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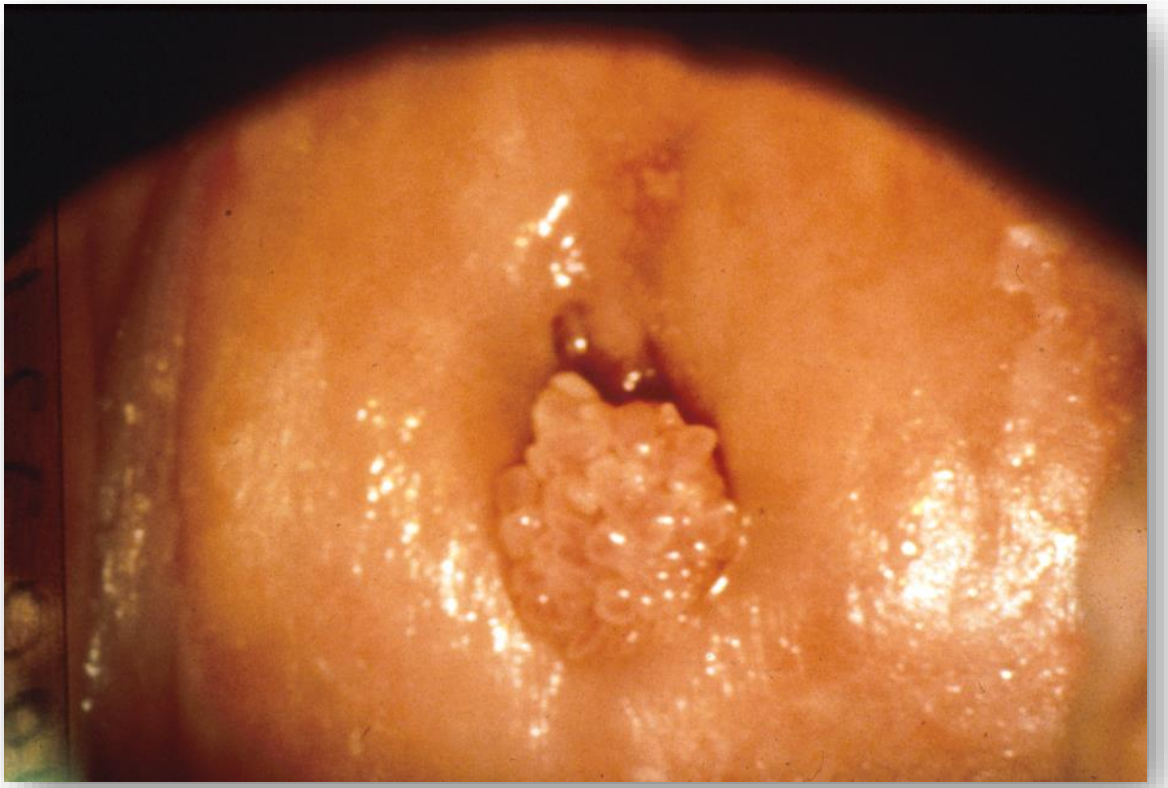
Microglandular hyperplasia

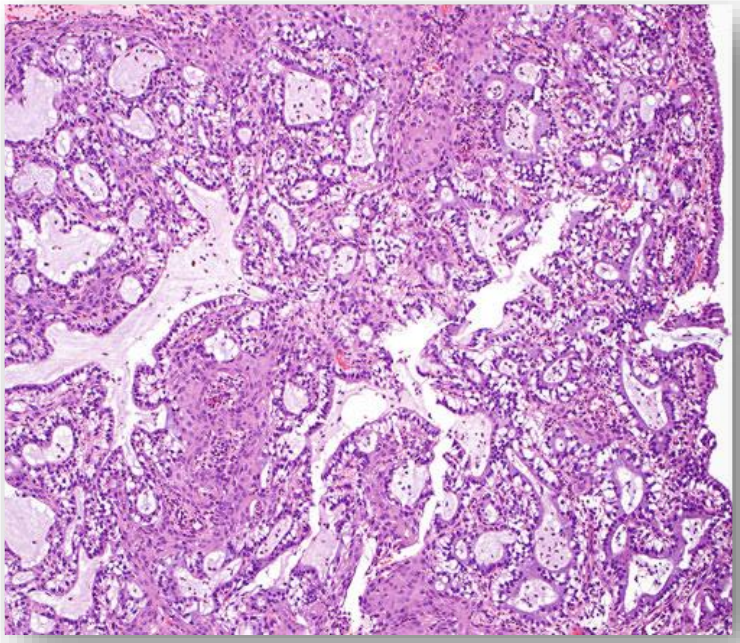
- Can be diagnostically **challenging**, has the potential for misinterpretation as carcinoma
- Mostly **incidental findings**, can produce gross abnormalities in the form of ectropion, polyps or friable, raised areas
- Usually in women of **reproductive age**, but occasionally in post-menopauzal women.
- Apparent association with exposure to **progesterone** in the form of oral contraceptives, Depo-Provera or pregnancy. But can also be found in women without this hormonal background.



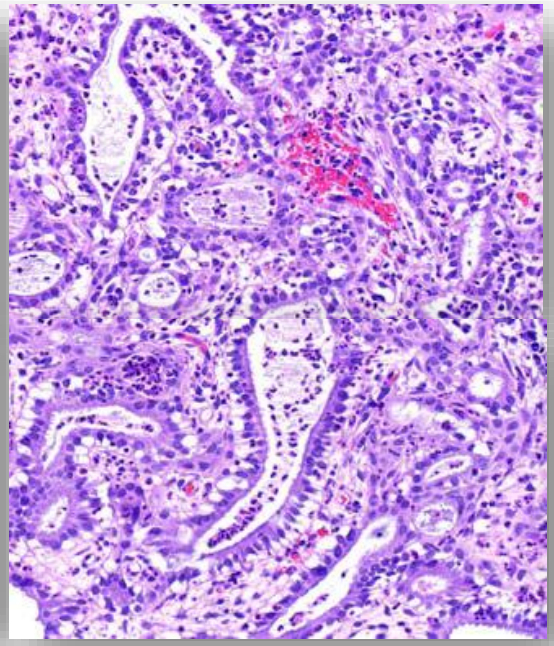
Oliva & Tornos, USCAP 2015

Microglandular hyperplasia

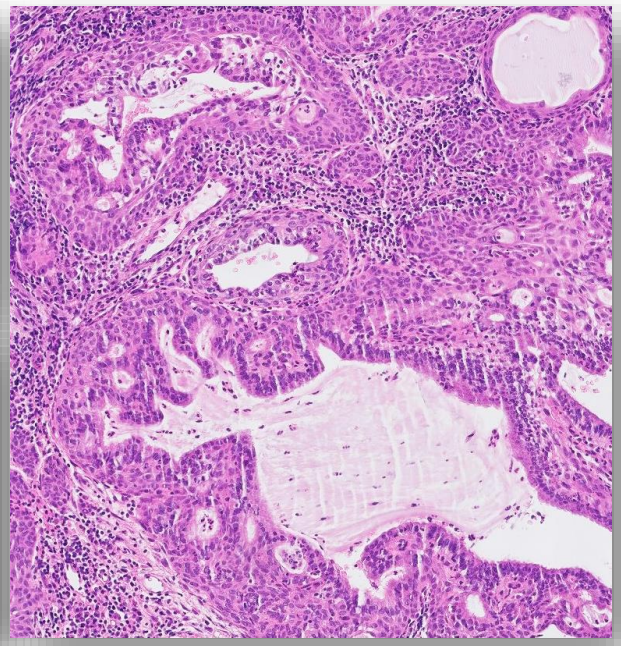
- Unifocal or multifocal
- **Closely packed glands** of variable size and shape, with little intervening stroma
- Epithelial lining is columnar or cuboidal, mucin-producing, and often containing supranuclear or subnuclear **vacuoles**. Usually uniform nuclei, focal atypia can be encountered
- Usually infiltrated by acute and chronic **inflammatory cells**, with neutrophils in the intraglandular mucinous secretions
- Little mitotic activity (< 1 mitosis/10 HPF).
- **Squamous metaplasia** often present



Blaustein, Chapter 4

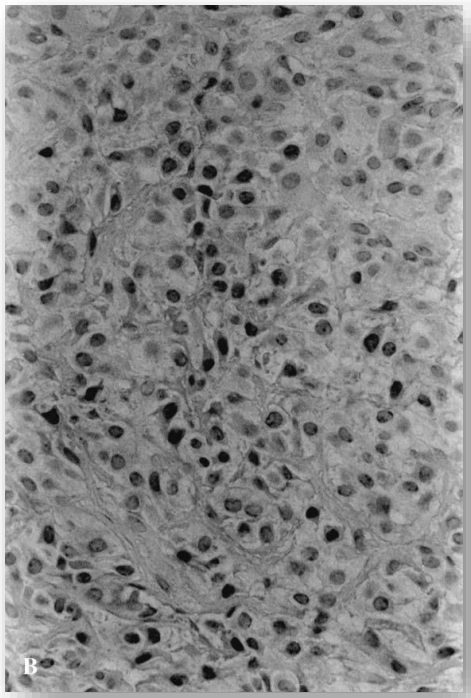


Oliva & Tornos, 2015

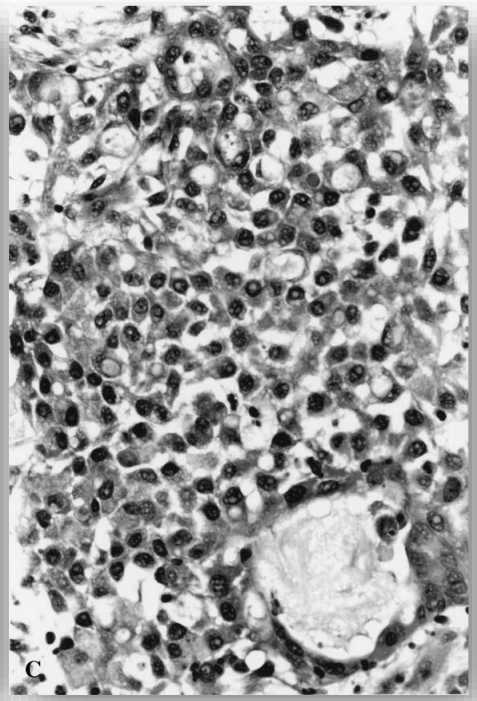


Microglandular hyperplasia

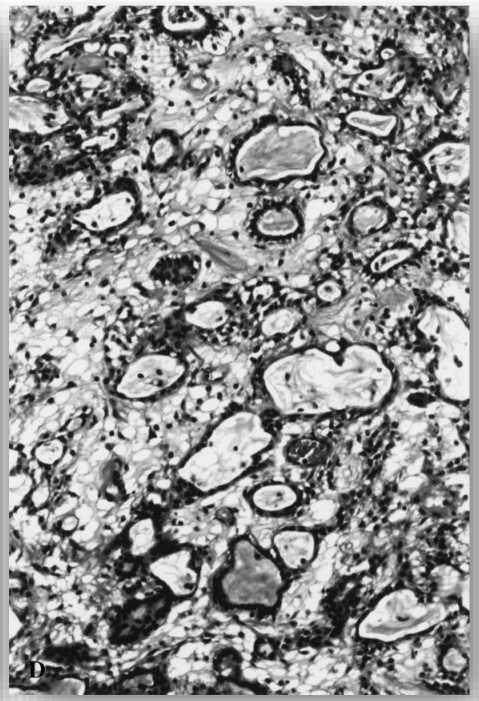
Unusual growth patterns



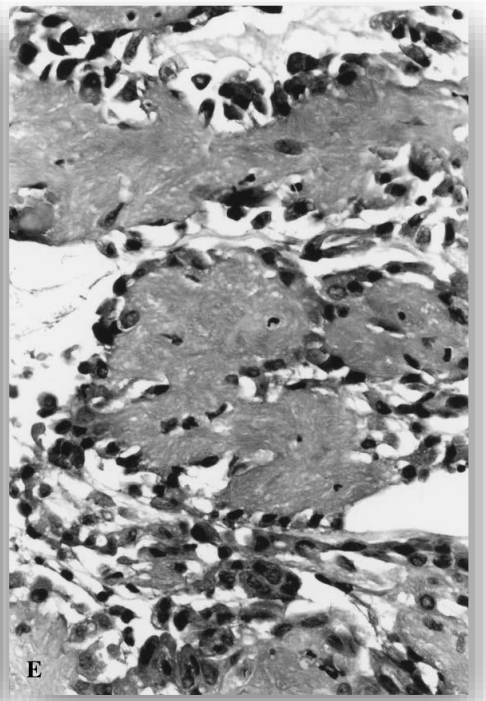
Solid



Signet-ring cells



Pseudoinfiltrative

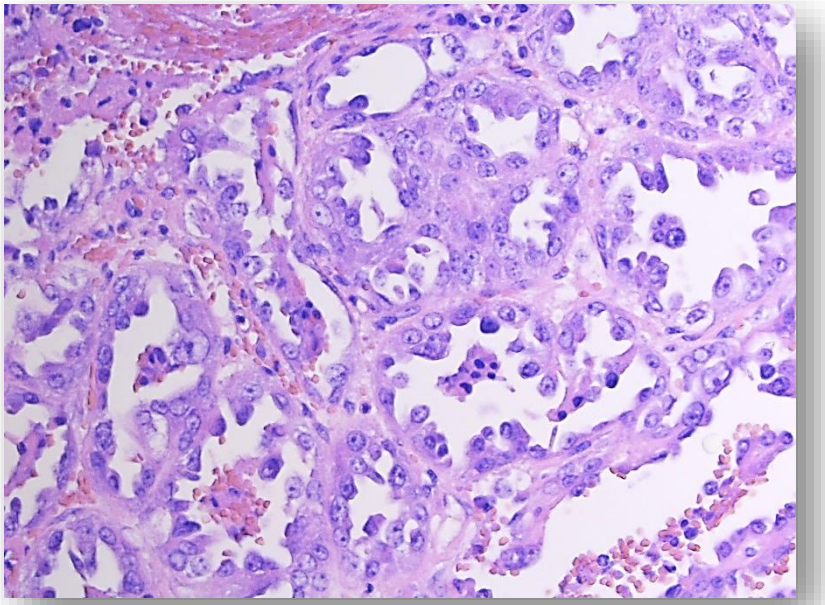


Prominent stromal hyalinization

Int J Gynecol Pathol, Vol. 21, No. 4, October 2002. Nucci M

Microglandular hyperplasia: DD

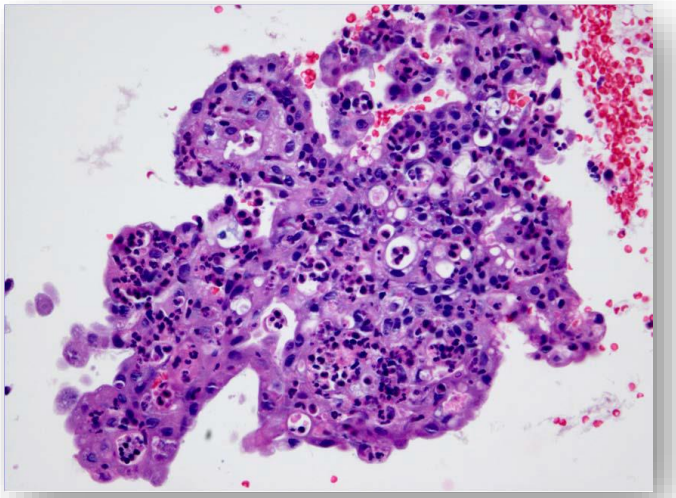
- **Clear cell carcinoma**
  - Cervical mass
  - Infiltrative pattern
  - Pronounced cytologic atypia
  - Papillary growth pattern, hobnailing, sheets of clear cells



- **Endometrioid endometrial adenocarcinoma with microglandular pattern**

→ Features favoring adenocarcinoma:

- Postmenopausal age
- Absence of typical areas of MGH
- Cytologic atypia > than in MGH
- Increased mitotic activity (> 1/10HPFs)
- High Ki-67 index. CAVE inflammatory cells!



Oliva & Tornos, USCAP 2015

Microglandular hyperplasia

The diagnosis of microglandular hyperplasia should be made with caution in a postmenopausal women, particularly if there is cytologic atypia > usual and the morphologic appearance is not typical of microglandular hyperplasia

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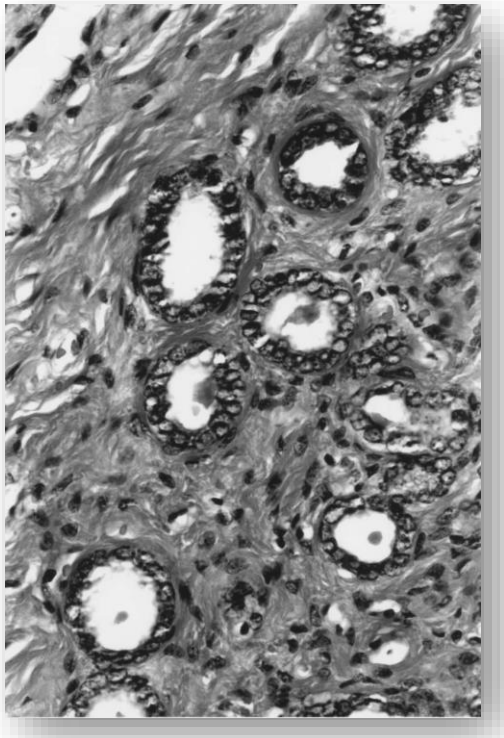
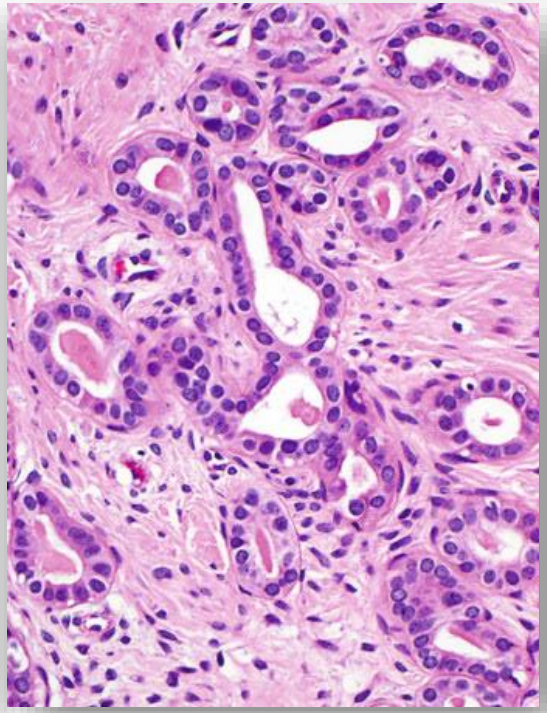
Mesonephric duct remnants and hyperplasia

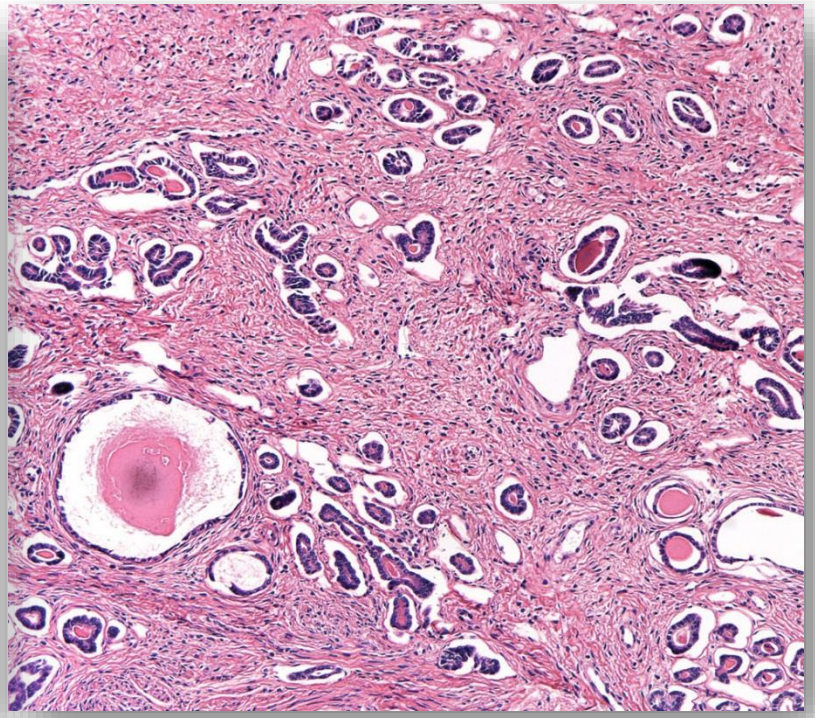
- Vestigial elements of the **mesonephric/wolffian duct**
- Preferentially located in the **lateral walls** of the cervix
- Small **cysts** and/or **tubules** lined by **bland cuboidal** or **low columnar** nonciliated epithelium
- Often a dense **eosinophilic luminal secretion** is present



Nucci, 2002



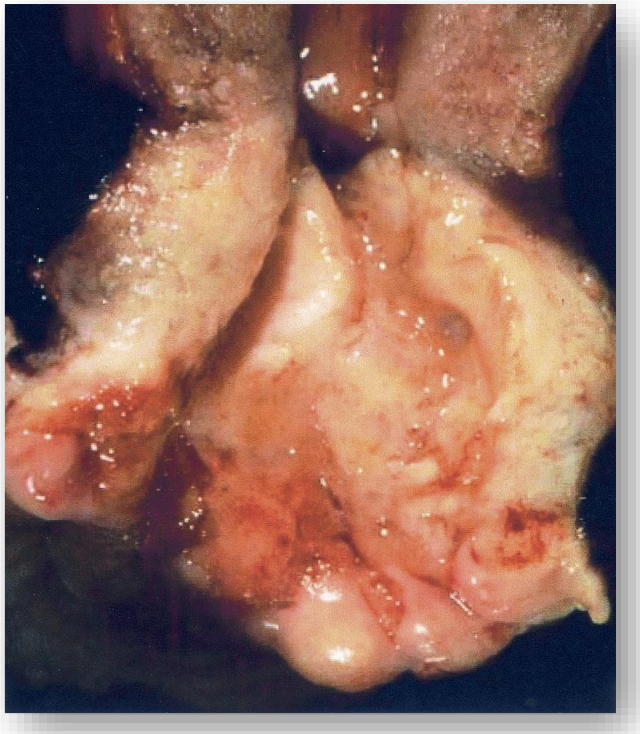
Blaustein, Chapter 4



Soslow & Longacre, chapter 3

Mesonephric hyperplasia

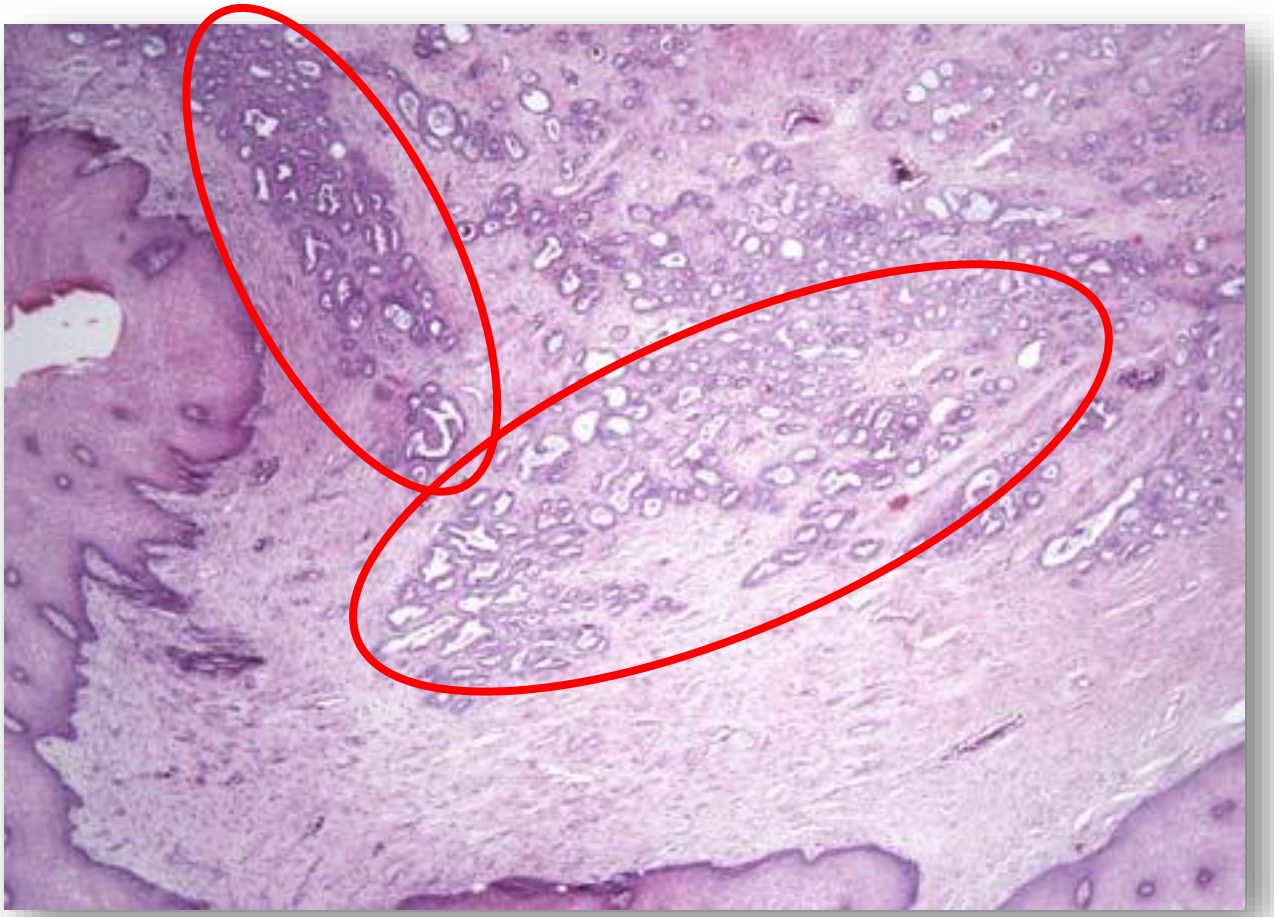
- Proliferation of mesonephric tubules measuring > 6 mm in single dimension
- Typically an incidental finding, rarely mass-forming lesion
- 3 types (no clinical significance)
  - Lobular mesonephric hyperplasia
  - Diffuse mesonephric hyperplasia
  - Mesonephric duct hyperplasia



Int J Gynecol Pathol, Vol. 21, No. 4, October 2002. Nucci M

Lobular mesonephric hyperplasia

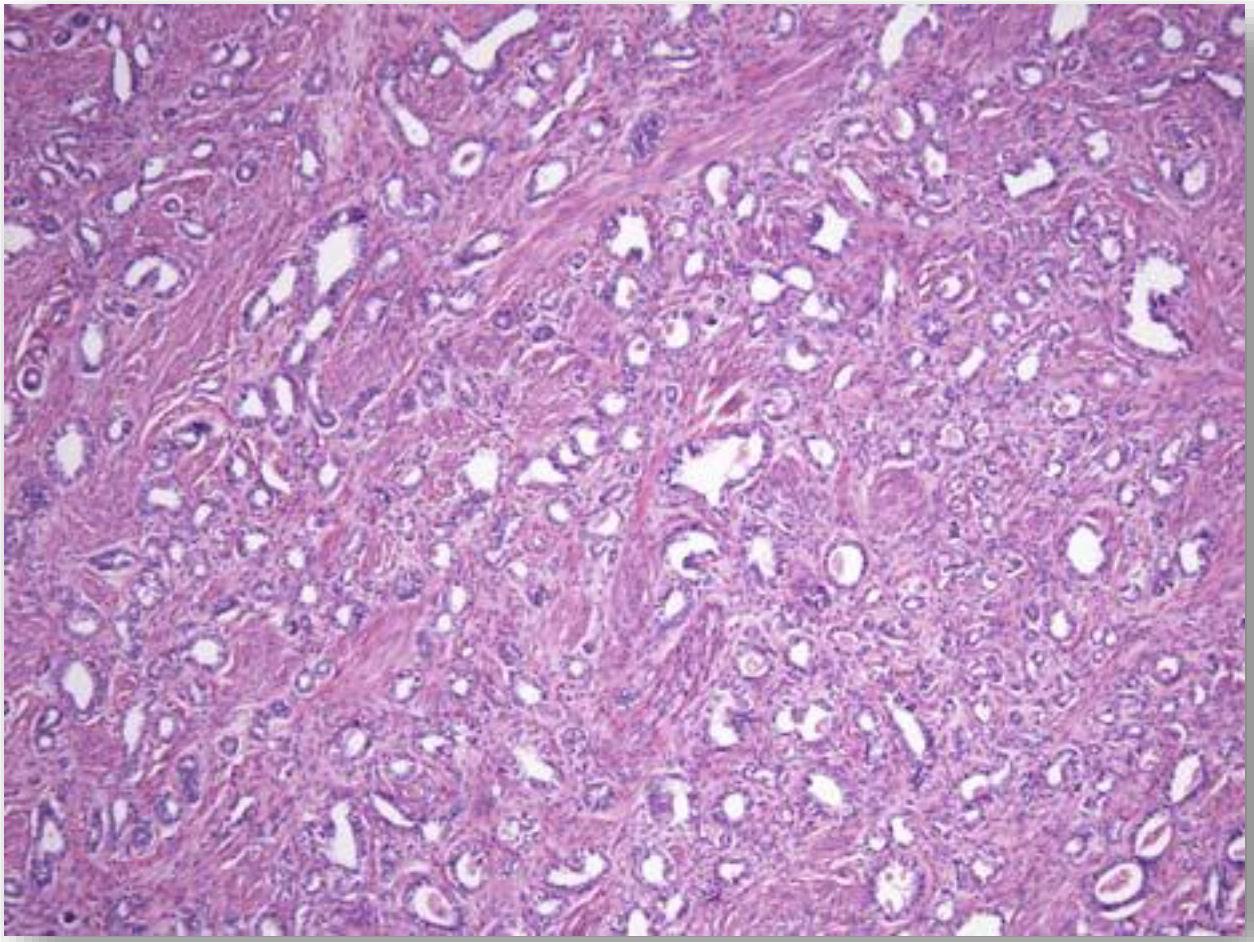
- **Most common** type
- **Lobular** arrangement of small-sized to medium-sized, typically round but occasionally irregularly shaped, tubules separated by varying amount of stroma



Int J Gynecol Pathol, Vol. 33, No. 4, July 2014. Nucci M

Diffuse mesonephric hyperplasia

- **Uniformly** well-spaced, small-sized to medium-sized round to slightly irregular mesonephric tubules separated by stroma.
- The presence of **intervening stroma** is helpful in distinguishing it from mesonephric carcinoma.



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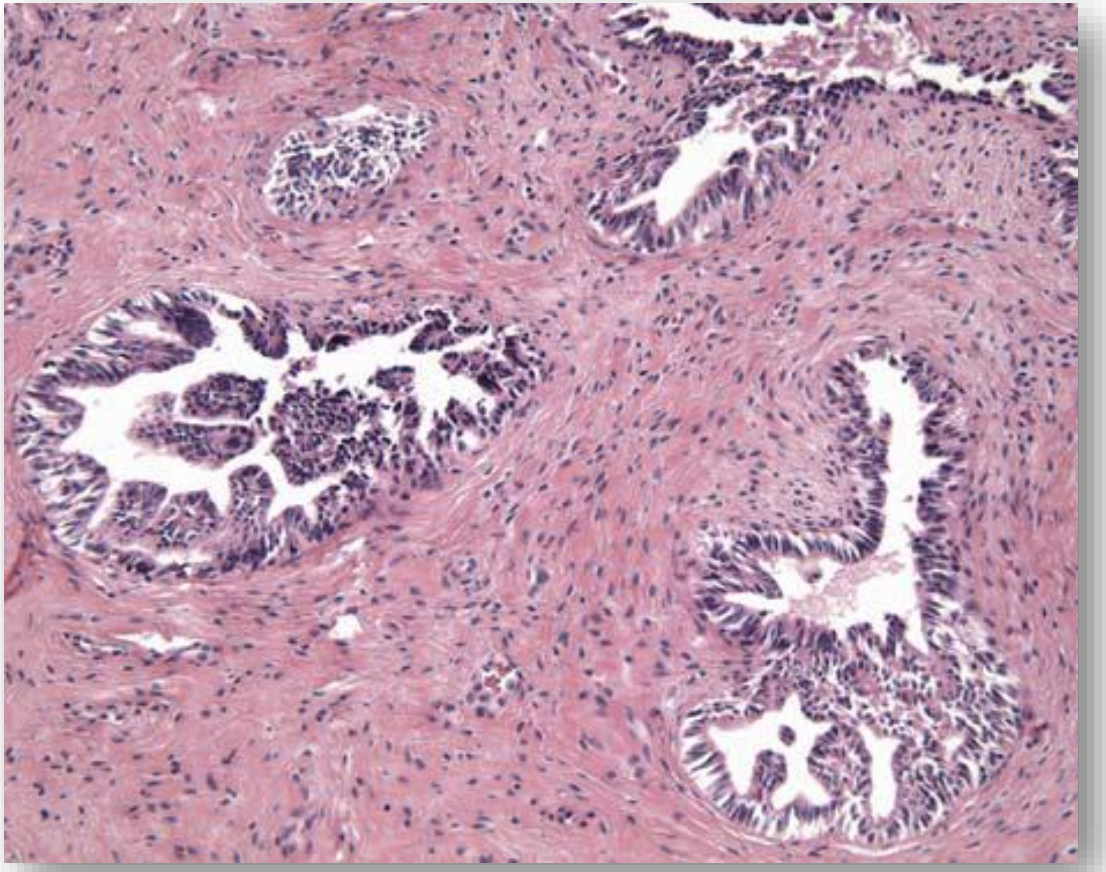
Mesonephric duct hyperplasia

- **Least common** type
- Located beneath normal endocervical glands
- Medium-sized to large-sized duct, often with a **clefted contour**, lined by **hyperplastic-appearing epithelium** with **short papillary intraluminal projections**
- Typically **lacks** the intraluminal **eosinophilic secretions**



Int J Gynecol Pathol, Vol. 33, No. 4, July 2014. Nucci M

Mesonephric duct remnants and hyperplasia

Immunohistochemistry

ER	-
PR	-
PAX8	+
p16	Patchy/focally +
AR	+
CD10	+ (luminal)
GATA 3	+

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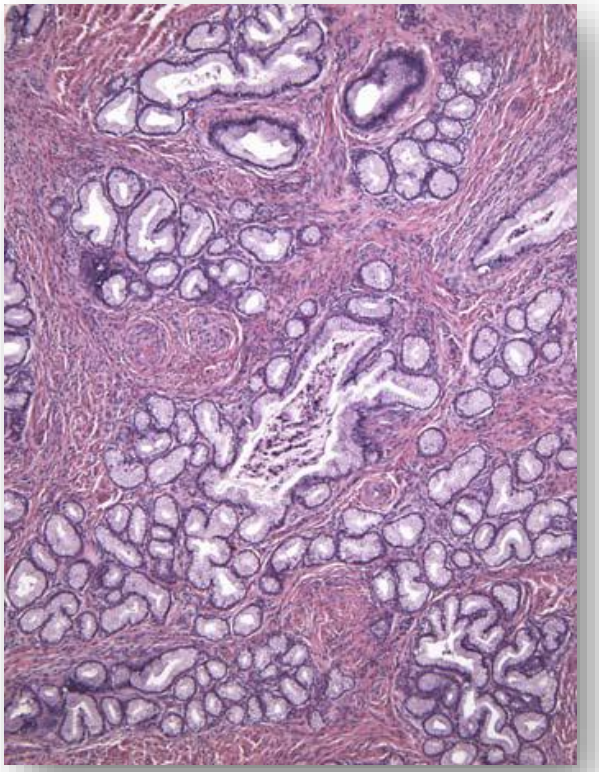
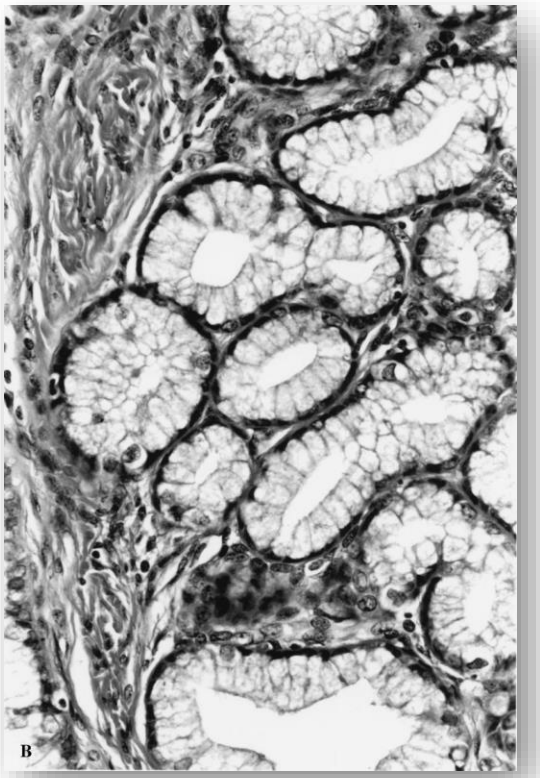
Lobular endocervical glandular hyperplasia (LEGH)

- Reproductive and postmenopausal women
- Usually **incidental** finding, may present with symptoms of watery or mucoid discharge
- **Distinctly lobular proliferation** of small-sized to medium-sized rounded glands often centered around a larger gland
- **Well demarcated** and is usually confined to the **inner half of the cervical wall**
- Single layer of columnar **mucinous epithelium** with **bland**, basally located nuclei (**pyloric gland** metaplasia)
- **No** significant **cytologic atypia** or **mitotic activity**



Nucci, 2014

Oliva & Tornos, USCAP 2015



Nucci, 2002

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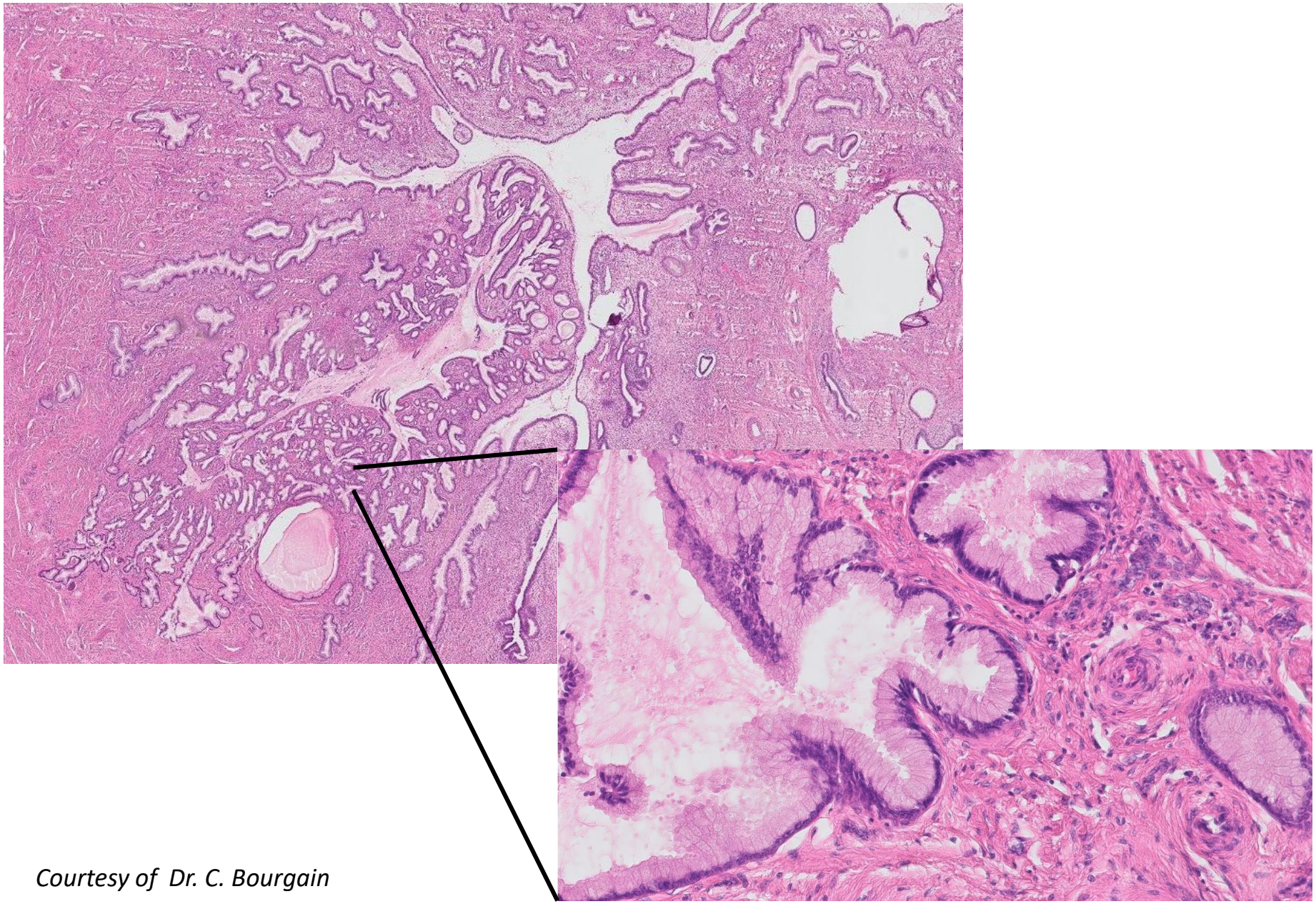

Courtesy of Dr. C. Bourgain

DD mucinous adenocarcinoma gastric-type

	Lobular endocervical glandular hyperplasia	Mucinous adenocarcinoma
Mucinous discharge	+/-	+/-
Mass	-/+	+
Demarcation	Present	Absent
Cervical wall involvement	< 50%	>> 50%
Lobulation	+	-
Cytologic atypia	minimal	Prominent (at least focally)
Stromal response	absent	present

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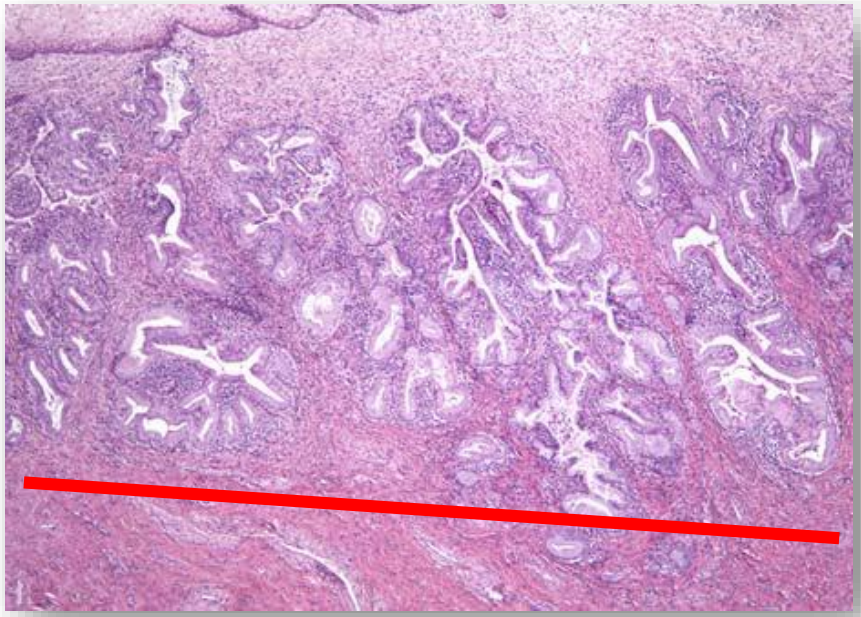
Diffuse laminar endocervical glandular hyperplasia

- Uncommun, mostly **reproductive** women
- Usually **incidental** finding, may present with symptoms of watery or mucoid discharge
- Confined to the **inner third** of the cervical wall
- **Laminar** proliferation of closely-packed glands that appears as a discrete layer that is sharply demarcated from the underlying cervical stroma



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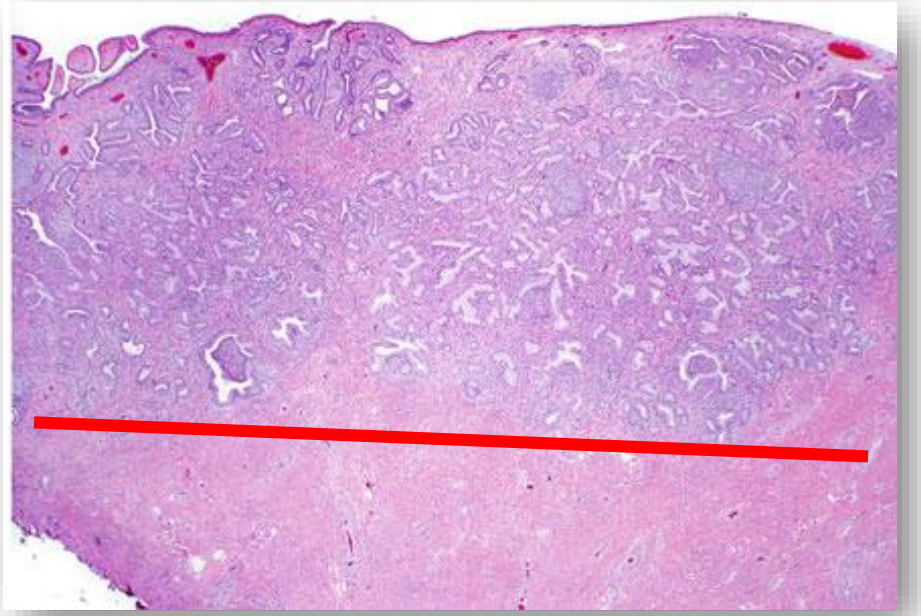
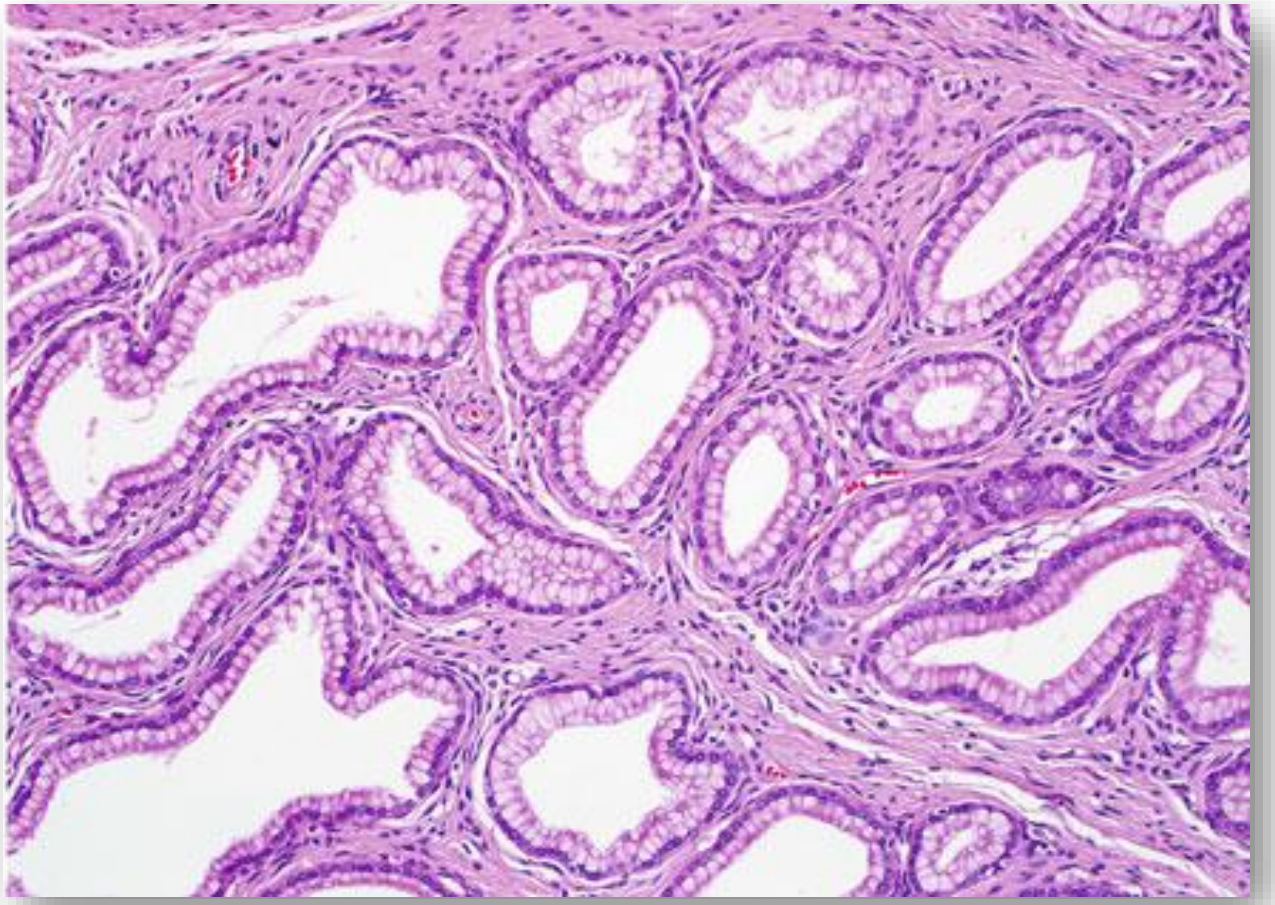


Blaustein, Chapter 4

Diffuse laminar endocervical glandular hyperplasia

- Glands typically have a **round, regular outline**, but irregular, angulated and star-shaped glands frequently occur.
- Lined by tall columnar **mucinous** epithelium with **bland** basally located round nuclei, mitotic activity is uncommon



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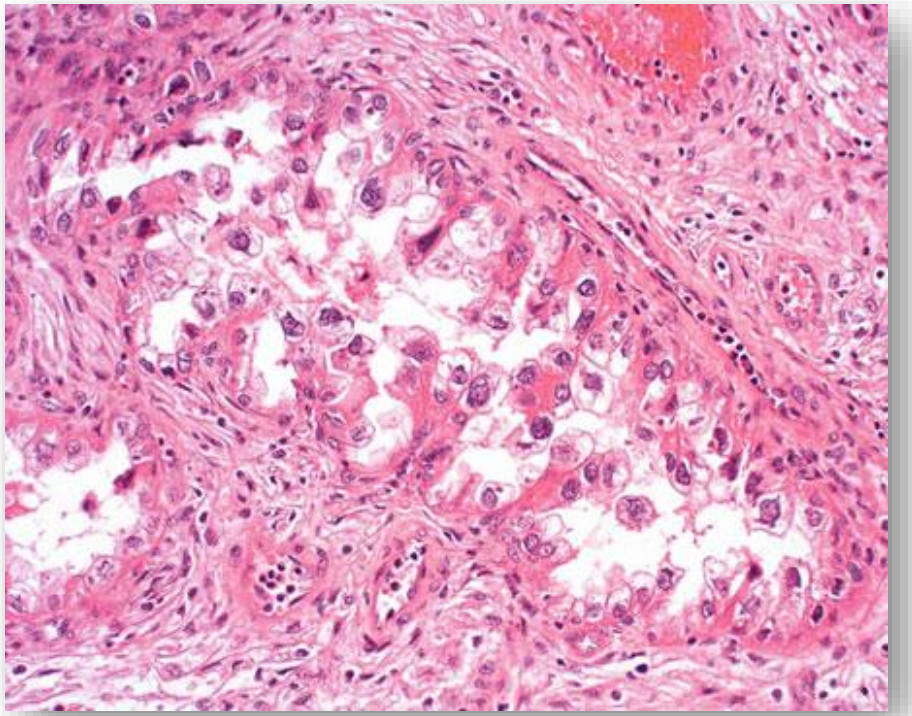
Arias-Stella reaction

- Up to 10% of **gravid** hysterectomy specimens.
- Use of **oral contraceptives**
- Usually focal, superficial glands. Occasionally deep glands, more extensive.
- In endocervical polyp
- Histologic features similar as in the endometrium: **enlarged** cells with abundant vacuolated and/or eosinophilic cytoplasm and **enlarged hyperchromatic nuclei**, smudged nuclear chromatin, **hobnail** appearance. **Mitotic figures** are **very uncommon.**



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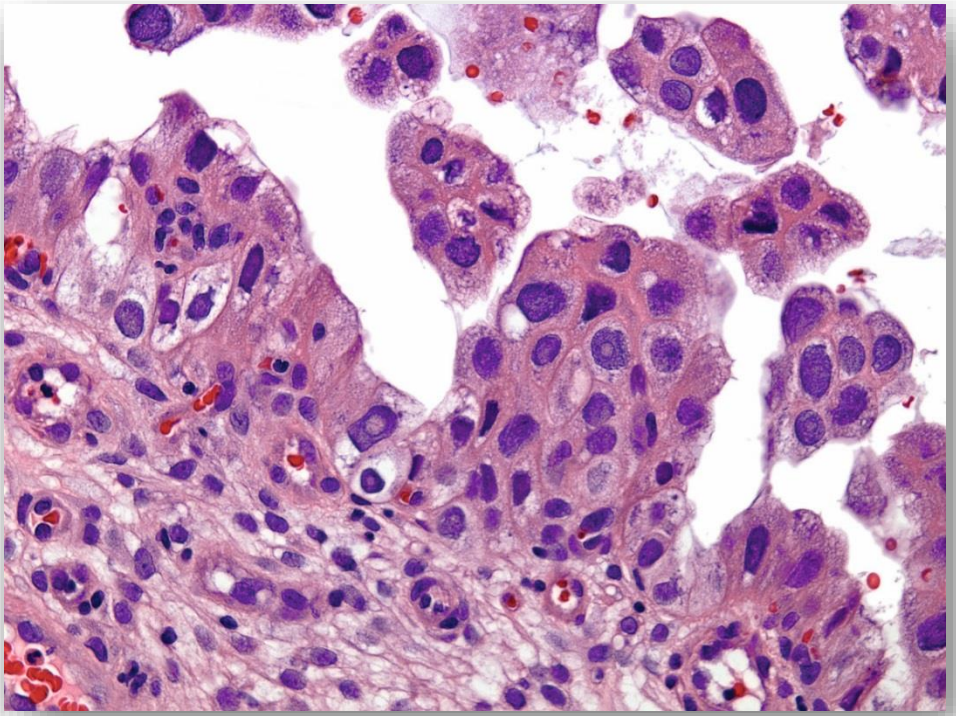
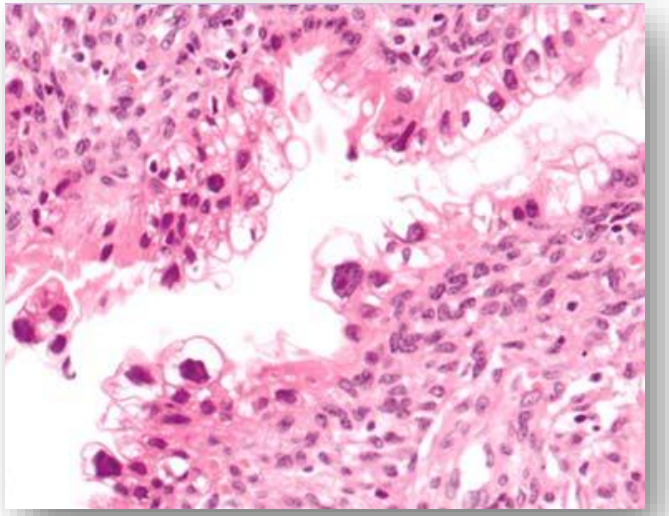
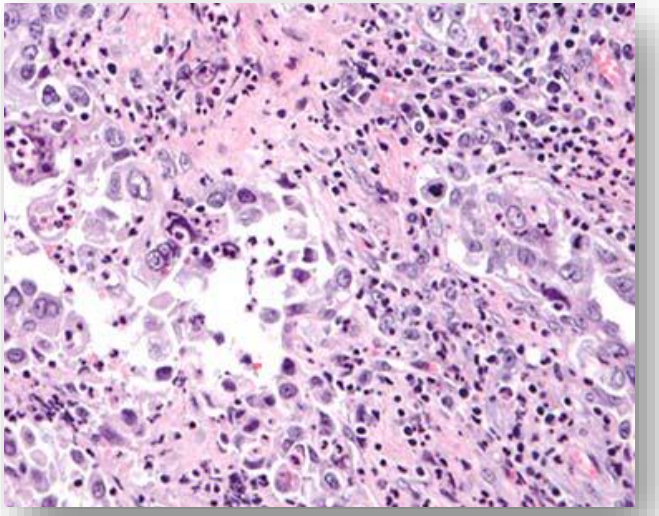


Soslow & Longacre, chapter 18

Arias-Stella reaction DD clear cell carcinoma

	AS	CCC
Pregnancy/OC	+	-
Incidental finding	+	-
Preserved architecture	+	-
Mass forming lesion	-	+
Prominent nuclei	+	-
Mitotic activity	absent	present





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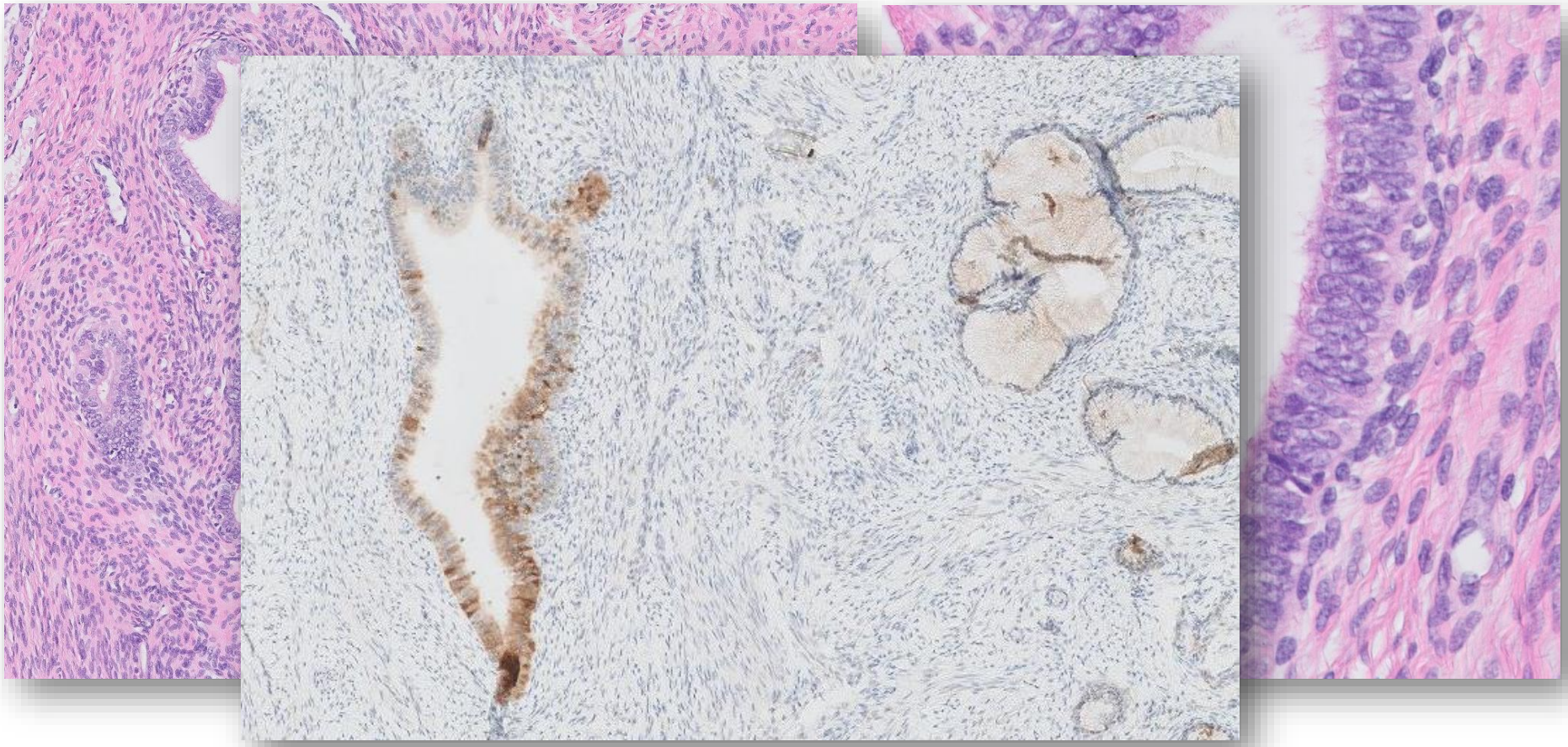
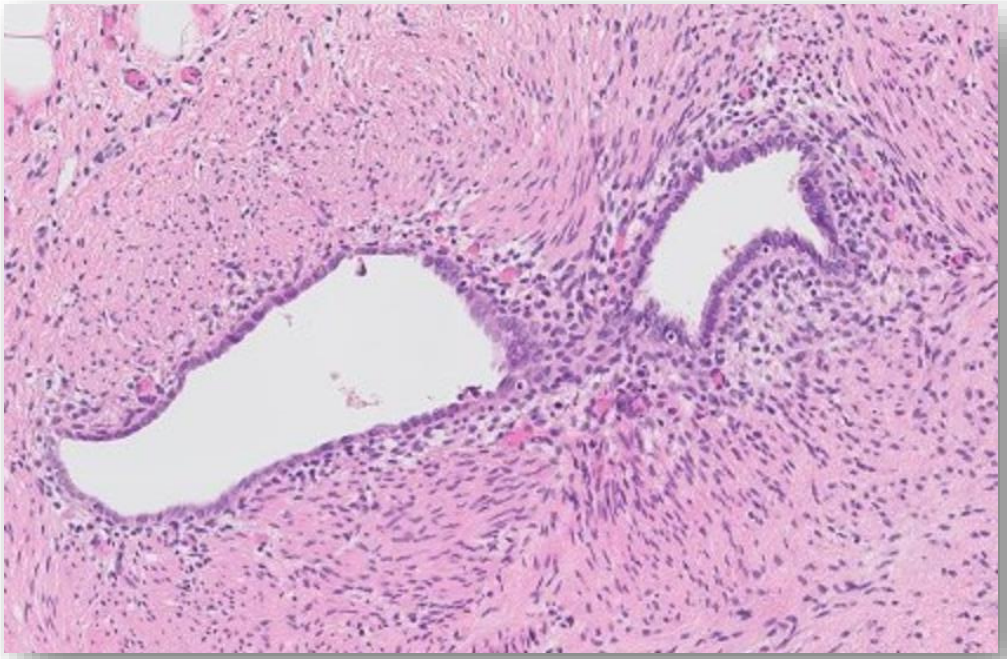
Tubal/tubo-endometrioid metaplasia

- Endocervical glands lined by ciliated cells, tubal type secretory cells, intercalated (peg) cells and reserve cells
- Bland cytological features, sparse mitotic figures
- Pseudostratification
- Secretory features with apical snouts
- DD adenocarcinoma in situ! → **p16**



Endometriosis

- Ectopic **endometrial glands and stroma** resembling proliferative endometrium (pseudostratification, mitosis)
- Usually confined to the superficial third of the cervical wall, occasionally deep
- Frequently develops following **cervical trauma** (cone biopsy, delivery)
- DD endocervical adenocarcinoma (in situ/invasive)
- CAVE! May express high levels of Ki-67 and expression of p16 (patchy)



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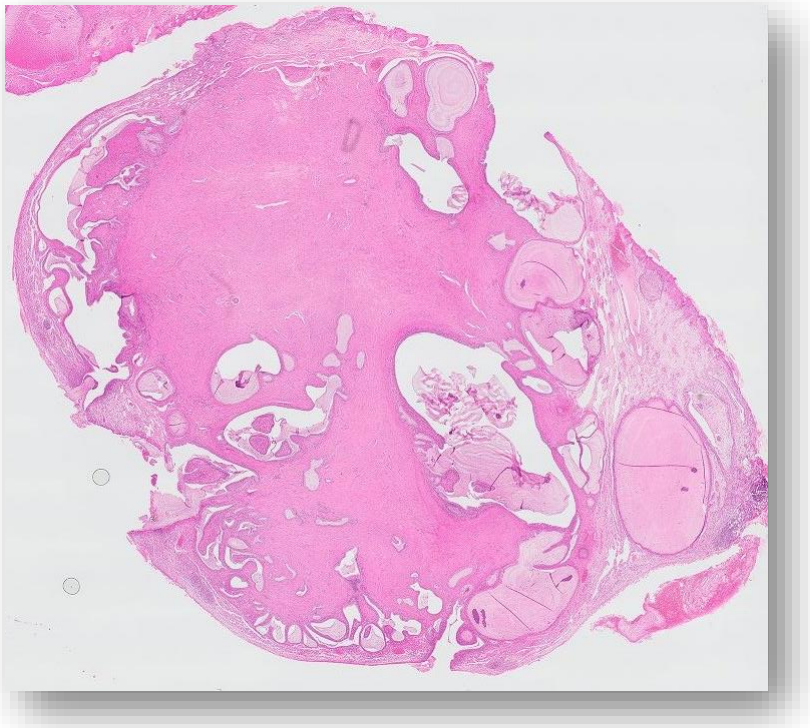
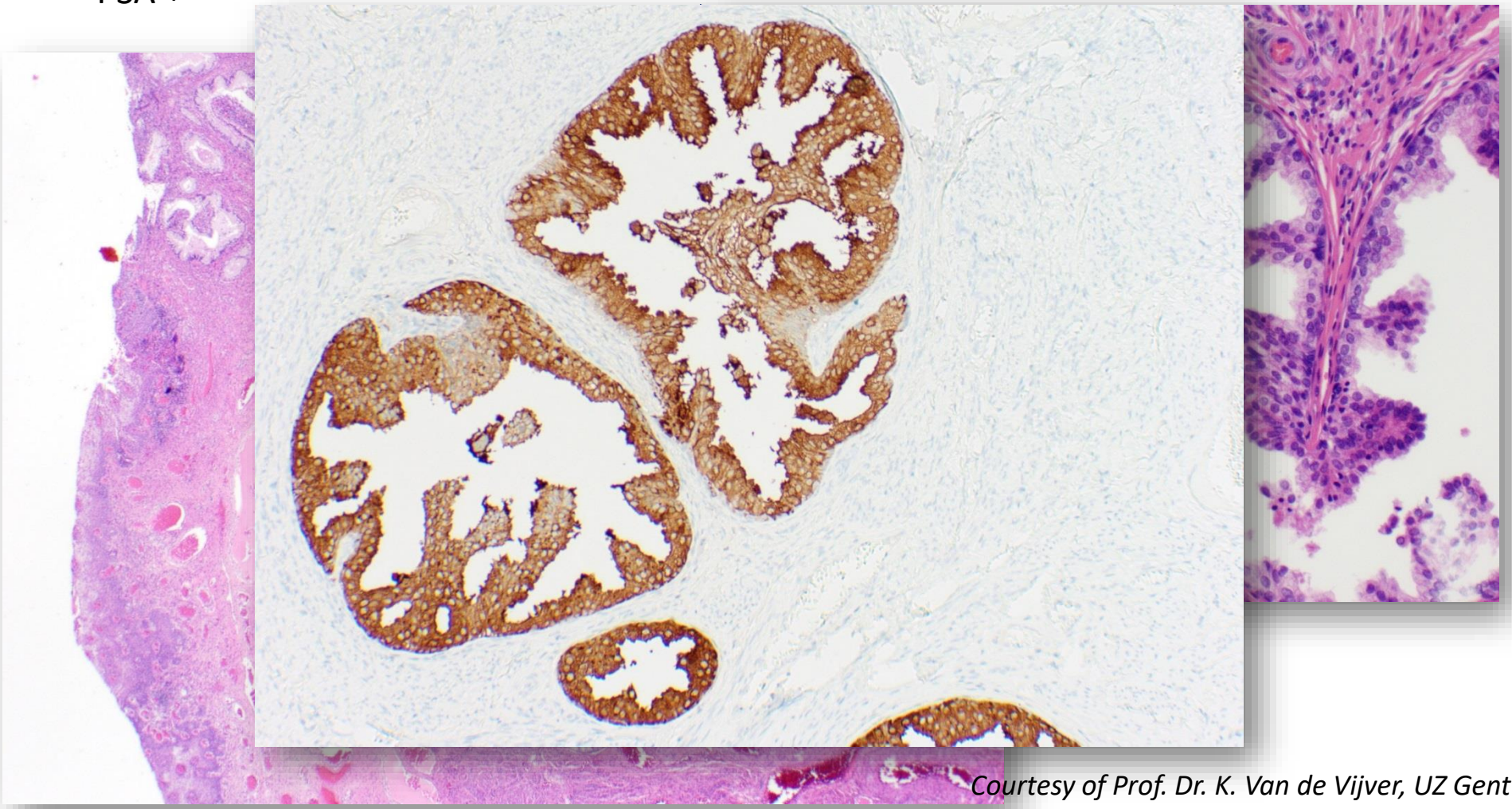
Endocervical adenomyoma

- Rare endocervical counterpart of the adenomyoma of the uterine corpus
- Premenopausal women
- Polypoid lesion, projecting into the endocervical canal
- **Biphasic**: admixture of benign-appearing **endocervical-type glands** and **smooth muscle**
- DD mucinous adenocarcinoma gastric type:
  - Gross circumscription
  - Frequent lobular arrangement of glands
  - Lack of infiltrative pattern
  - Lack of desmoplasia
  - Lack of cytologic atypie



Ectopic prostatic tissue

- Usually incidental finding, rarely cervical mass
- No involvement of the mucosal surface
- Double layer of cells: flattened/cuboidal basal cells and eosinophilic/clear luminal cells
- PSA +



Courtesy of Prof. Dr. K. Van de Vijver, UZ Gent

Take home message

- Be careful with the diagnosis of microglandular hyperplasia in a postmenopausal woman → consider the possibility of endometrioid endometrial adenocarcinoma with microglandular pattern (and ask for more material if necessary…)

- Think about Arias-Stella reaction if you see 'funny looking high grade atypia' and check if the patient is pregnant or is using hormonal therapy


The End