



EMORY
UNIVERSITY
SCHOOL OF
MEDICINE

Department of
Pathology and
Laboratory
Medicine



Georgia Association of Pathology

EMORY

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2020 Virtual Pathology Course

LARA HARIK, MD

ROTATION DIRECTOR,
GENITOURINARY PATHOLOGY

CHAIR, GAP EDUCATION COMMITTEE

Challenging Cases in Surgical Pathology and Hematopathology

Faculty

Saja Asakrah, MD (Lecturer)

Kyle Bradley, MD (**Lecturer**)

Ritu Gupta, MD (Moderator)

Uma Krishnamurti, MD PhD (**Moderator**)

Shiyong Li, MD PhD (**Lecturer**)

Faisal Saeed, MD (**Lecturer**)

Linsheng Zhang, MD PhD (**Lecturer**)

PROGRAM ORGANIZING COMMITTEE



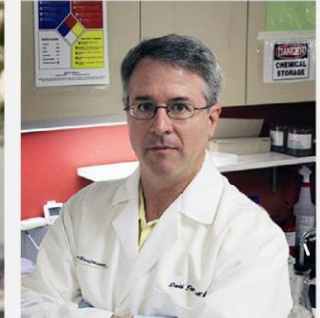
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ASSOCIATE PROFESSOR



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Patrice Smith
COMMUNICATIONS SPEC.

Course Schedule

- 8:00 AM - 9:00 AM: Genitourinary Pathology
- 9:00 AM - 10:00 AM: Gynecological Pathology
- 10:00 AM – 10:30 AM: Break
- 10:30 AM - 12:30 PM: Hematopathology
- 12:30 PM - 1:00 PM: Separate Zoom Continued Discussion and Chat
 - Surgical Pathology
 - Hematopathology



Lara Harik, MD



@LaraHarikMD

- Disclosures

- Winship Invest Prostate Cancer Research Grant: 2020-2021

- Background

- **Rotation Director** of GU Pathology
- Board Member and Chair of the Education Committee of the **Georgia Association of Pathology**

A histological section of the bladder stained with hematoxylin and eosin (H&E). The image displays numerous glandular structures of varying sizes, some with prominent nuclei and others appearing more atrophic. The glands are embedded in a dense, cellular stroma. The overall appearance is characteristic of glandular lesions in the bladder, such as those seen in prostatic adenocarcinoma or bladder adenocarcinoma. The glands are lined by a layer of epithelial cells, and the surrounding stroma contains many small, dark-staining nuclei, likely representing inflammatory cells or tumor cells.

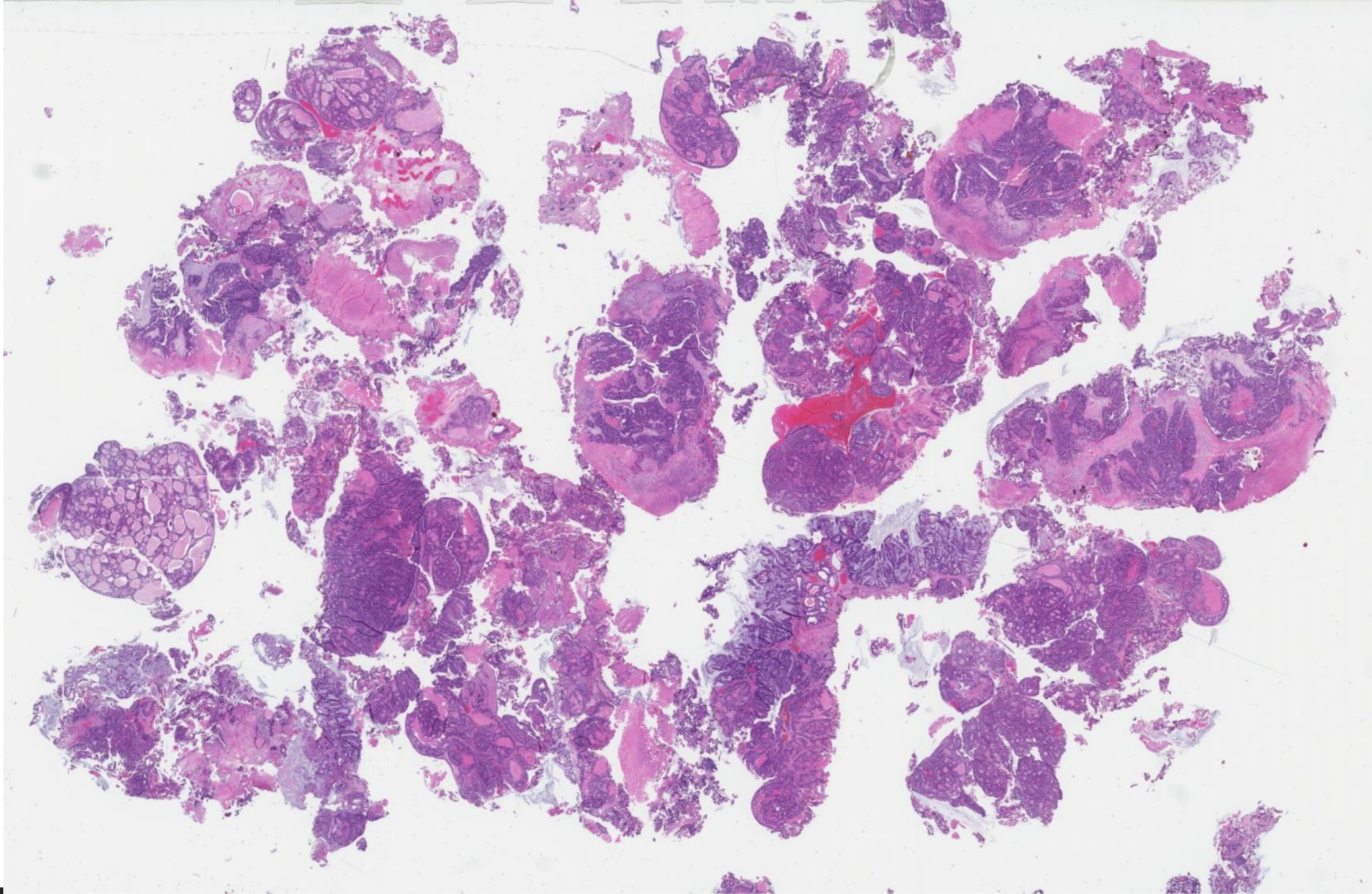
Glandular Lesions of the Bladder

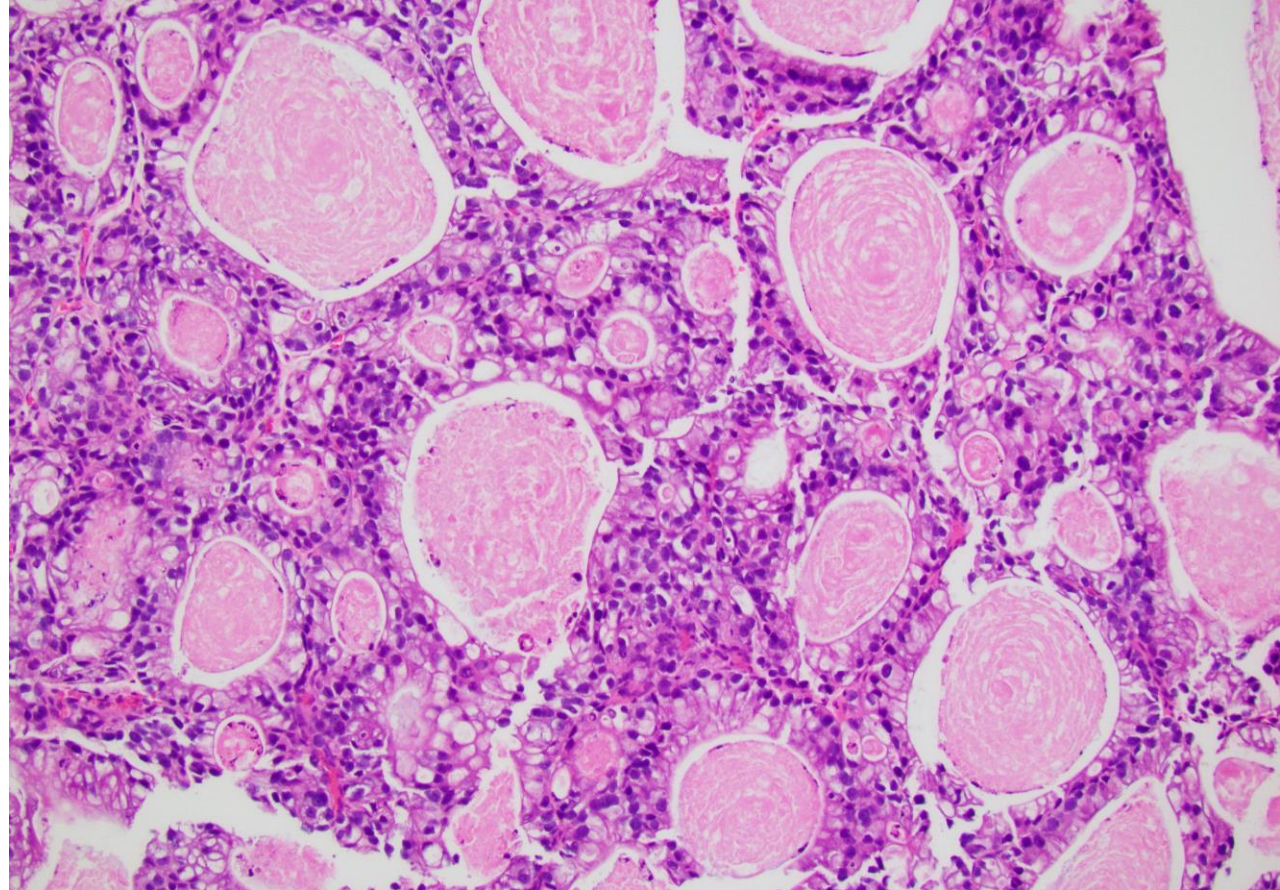
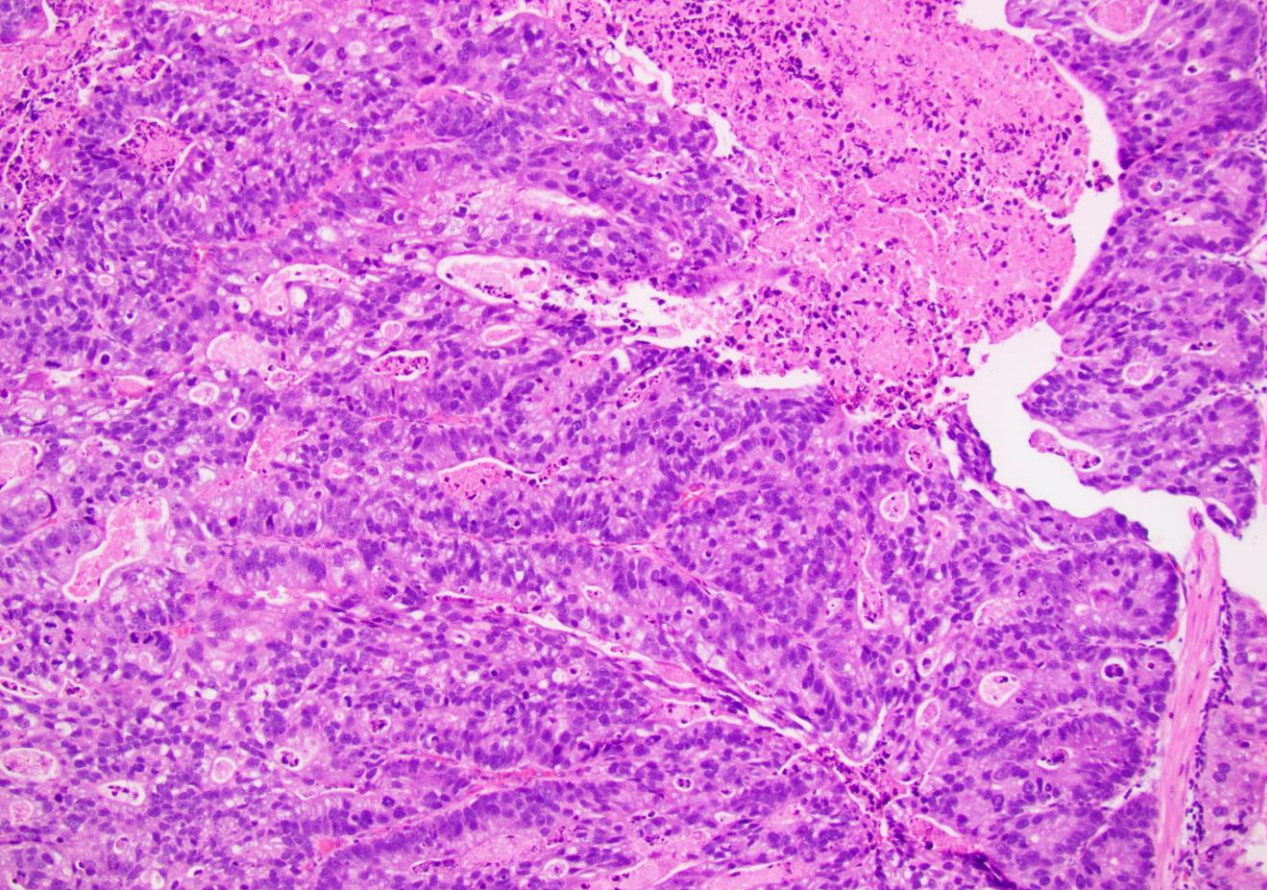
Case 1

68 year old male presenting to the urologist for **hematuria**

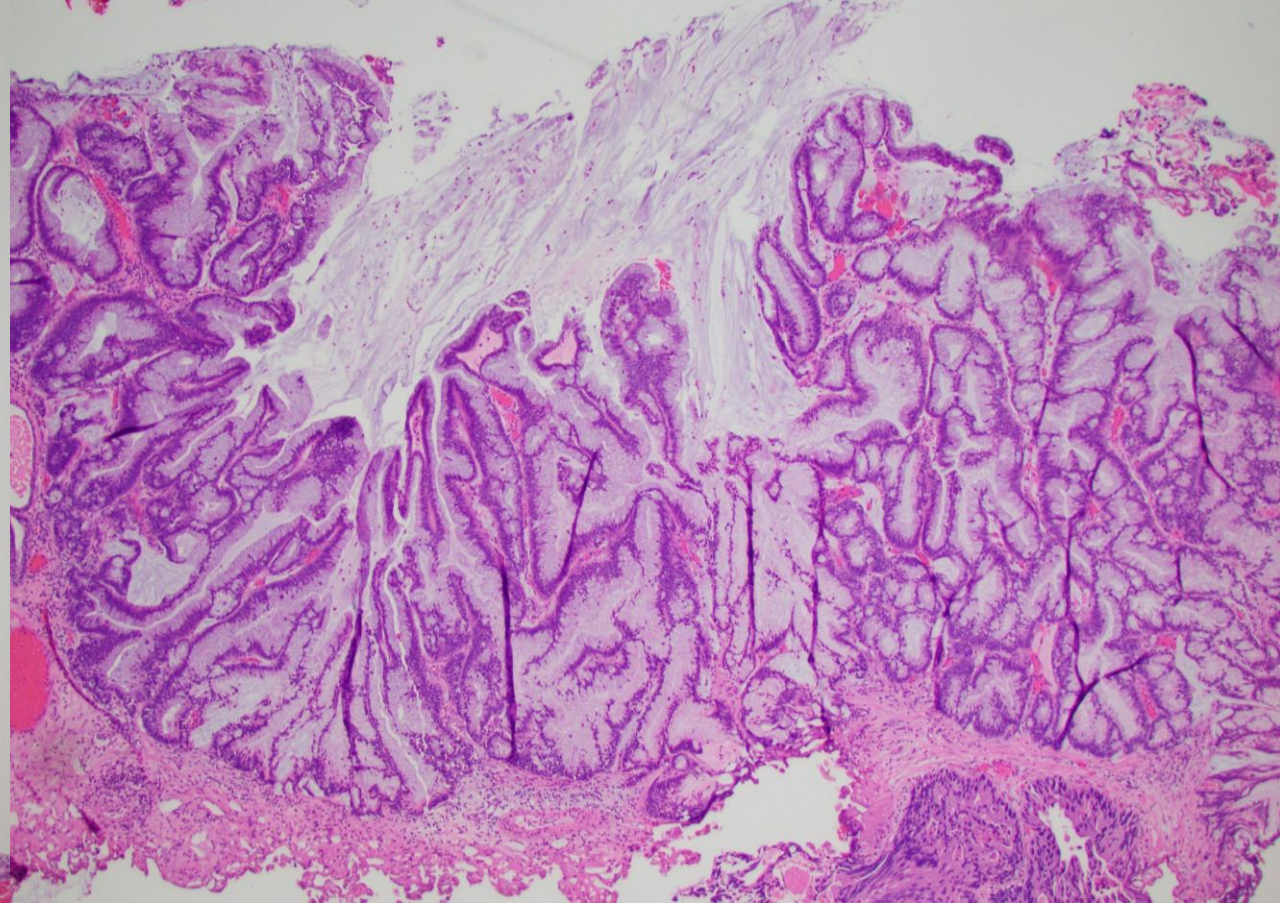
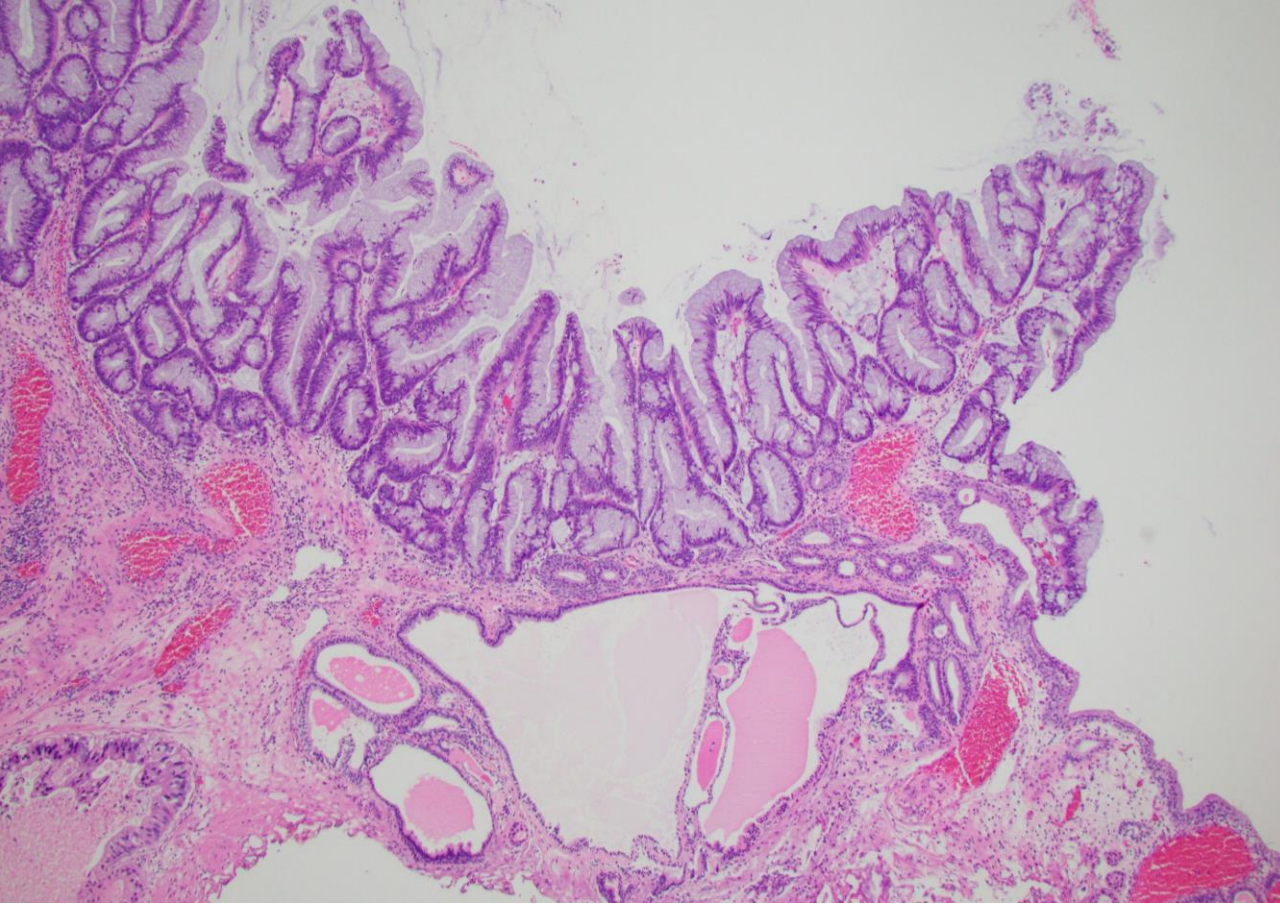
He has hypertension and is otherwise healthy.

He has a **family history** of **breast carcinoma** and **colon carcinoma**.



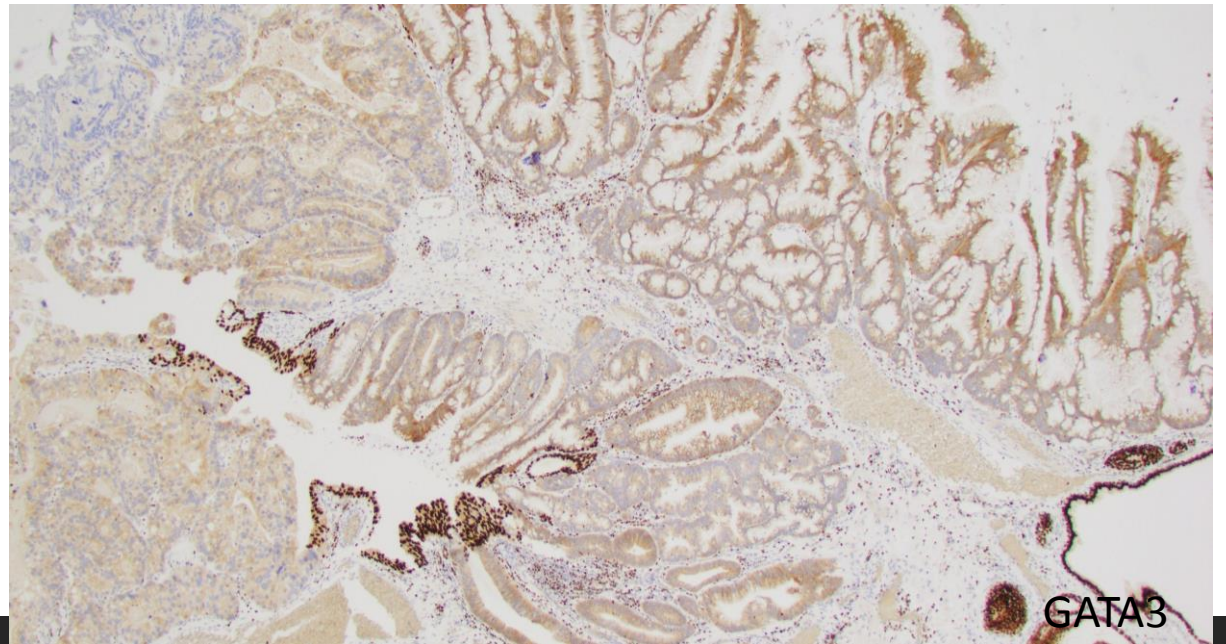
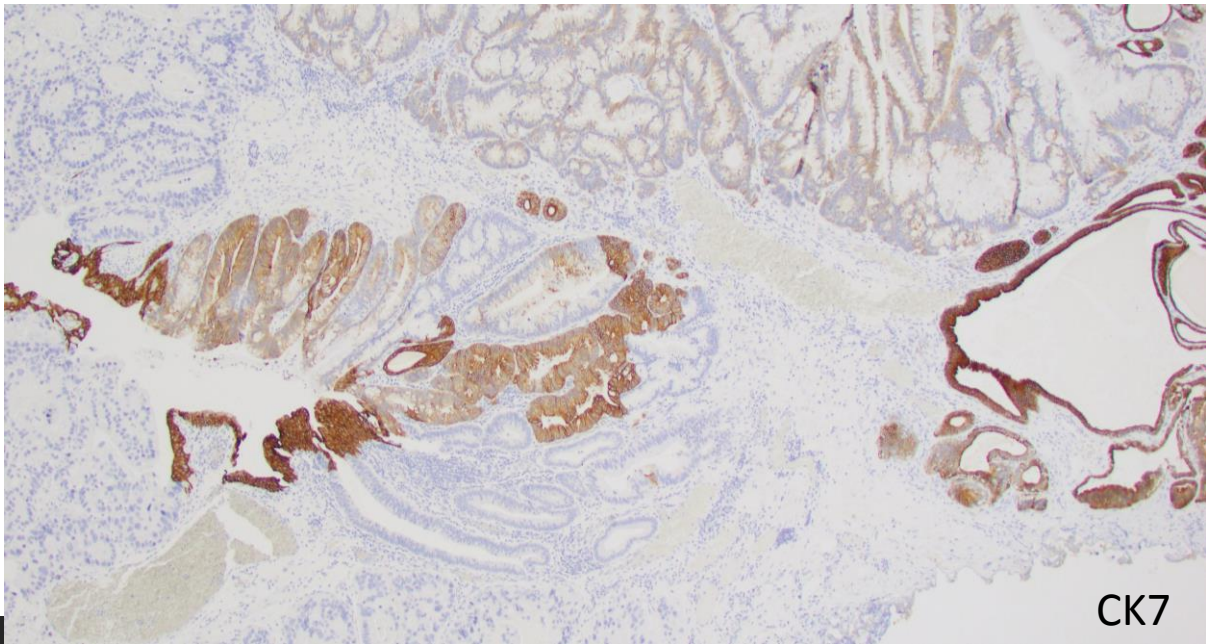
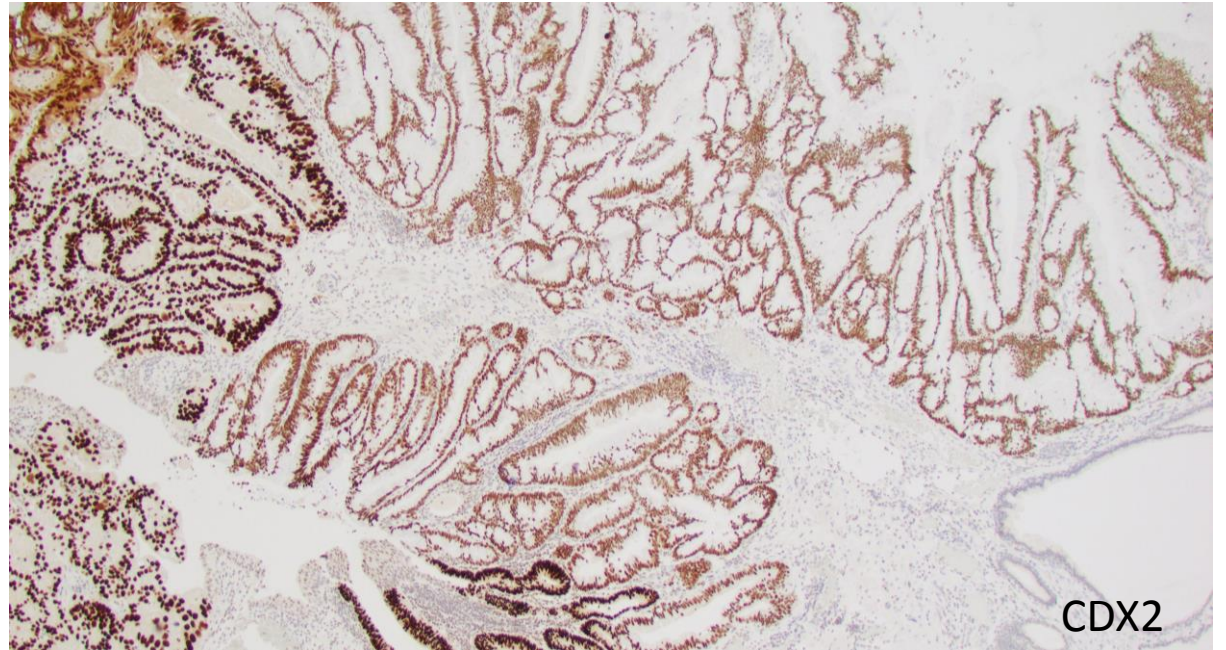
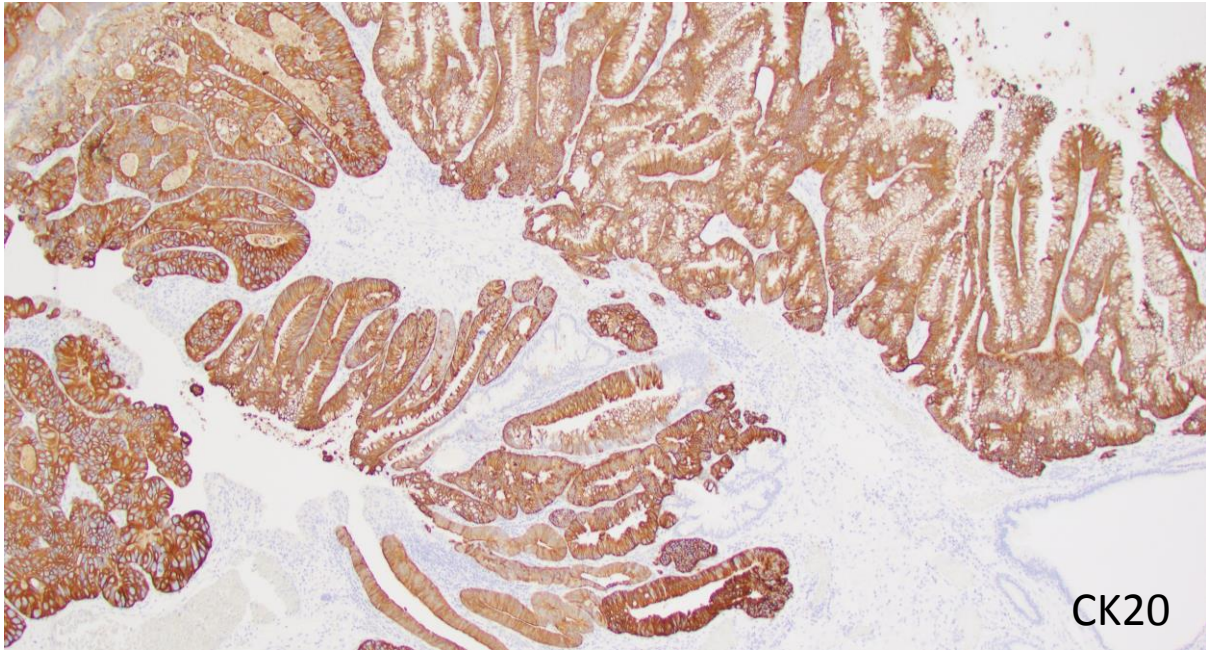


Adenocarcinoma



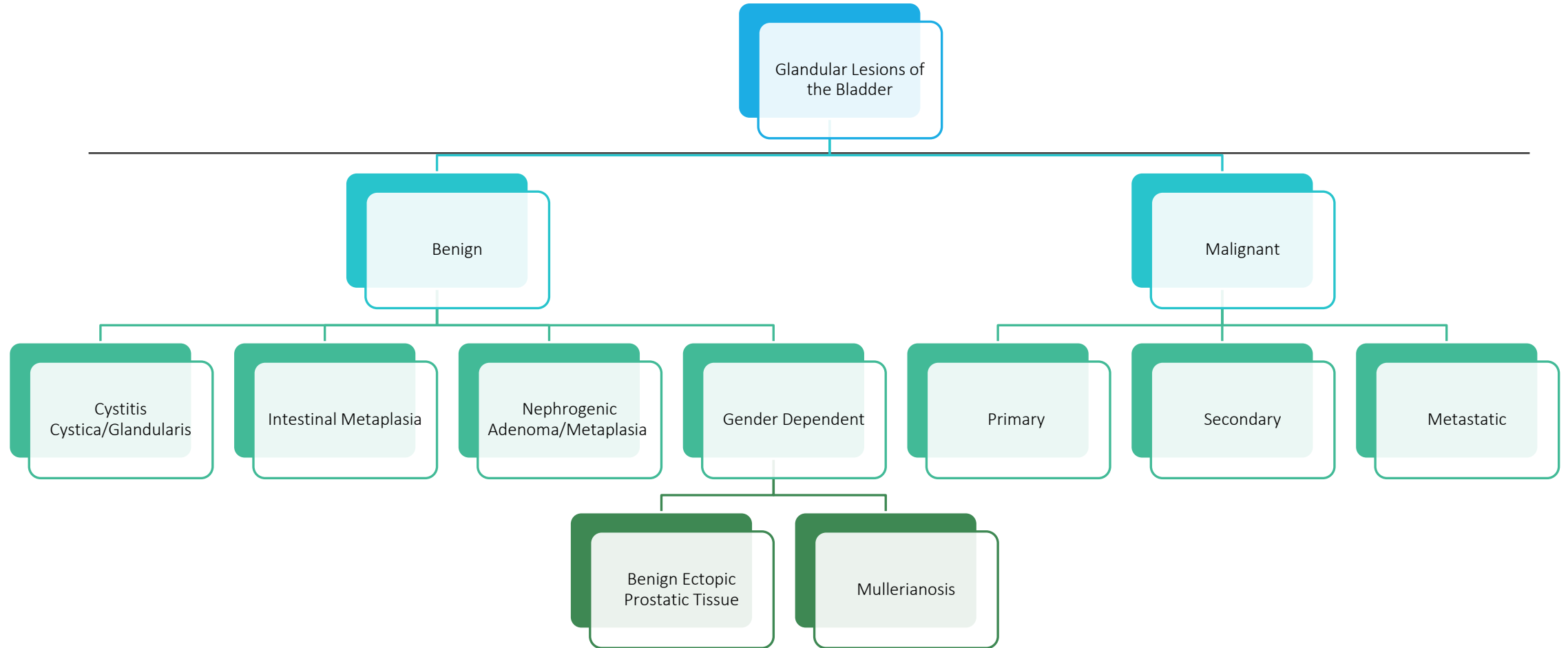
Background

Cystitis Cystica Glandularis, Intestinal Metaplasia and Adenomatous change



Primary Adenocarcinoma of Urinary Bladder

BACKGROUND INTESTINAL METAPLASIA AND ADENOMATOUS
EPITHELIUM



Malignant Glandular Lesions

Primary

Pure Adenocarcinoma

Urothelial Carcinoma
with glandular
differentiation

Secondary

Prostatic/Gynecologic

Colorectal

Metastatic

Breast/Stomach

Other

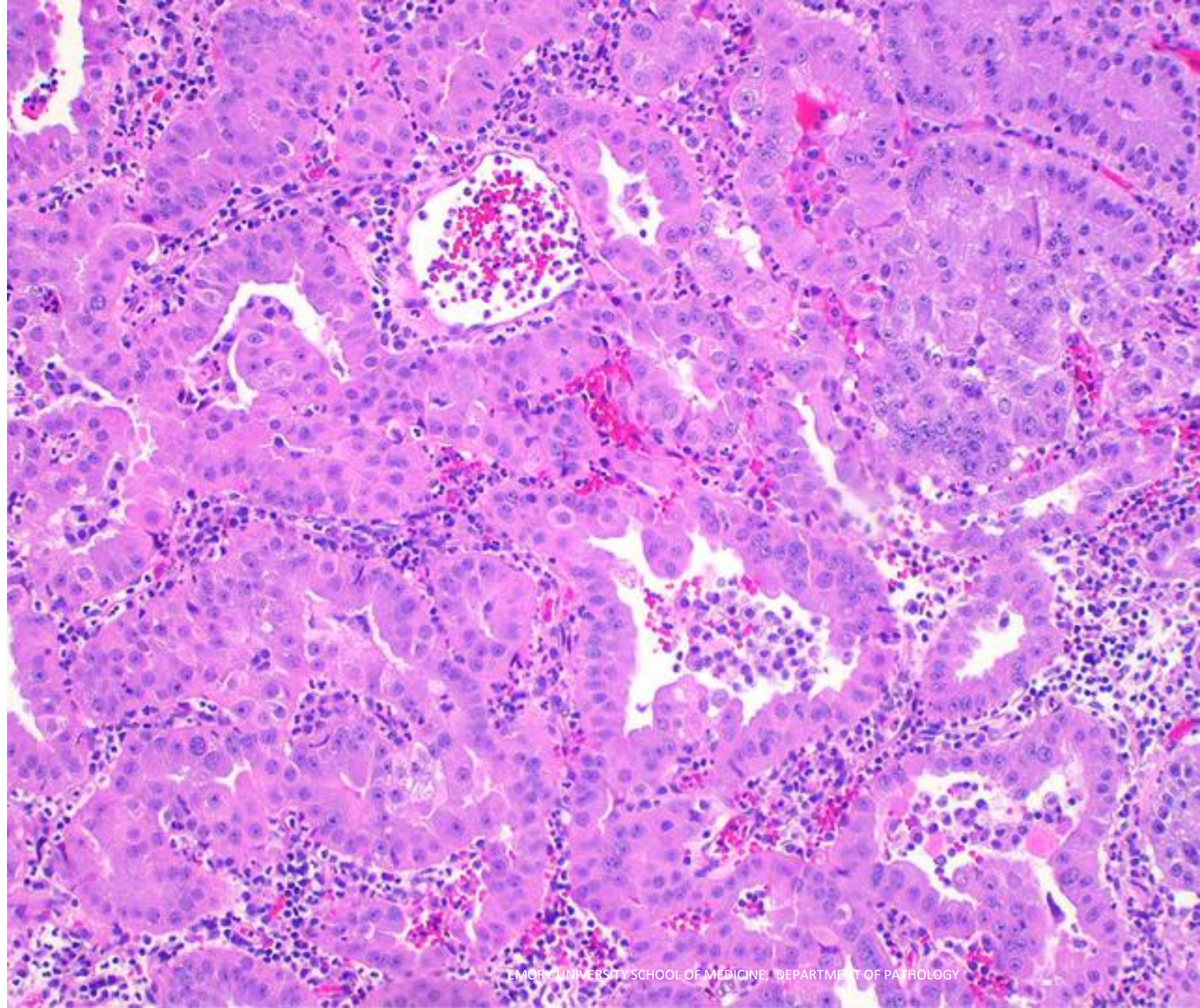
Primary Invasive Adenocarcinoma

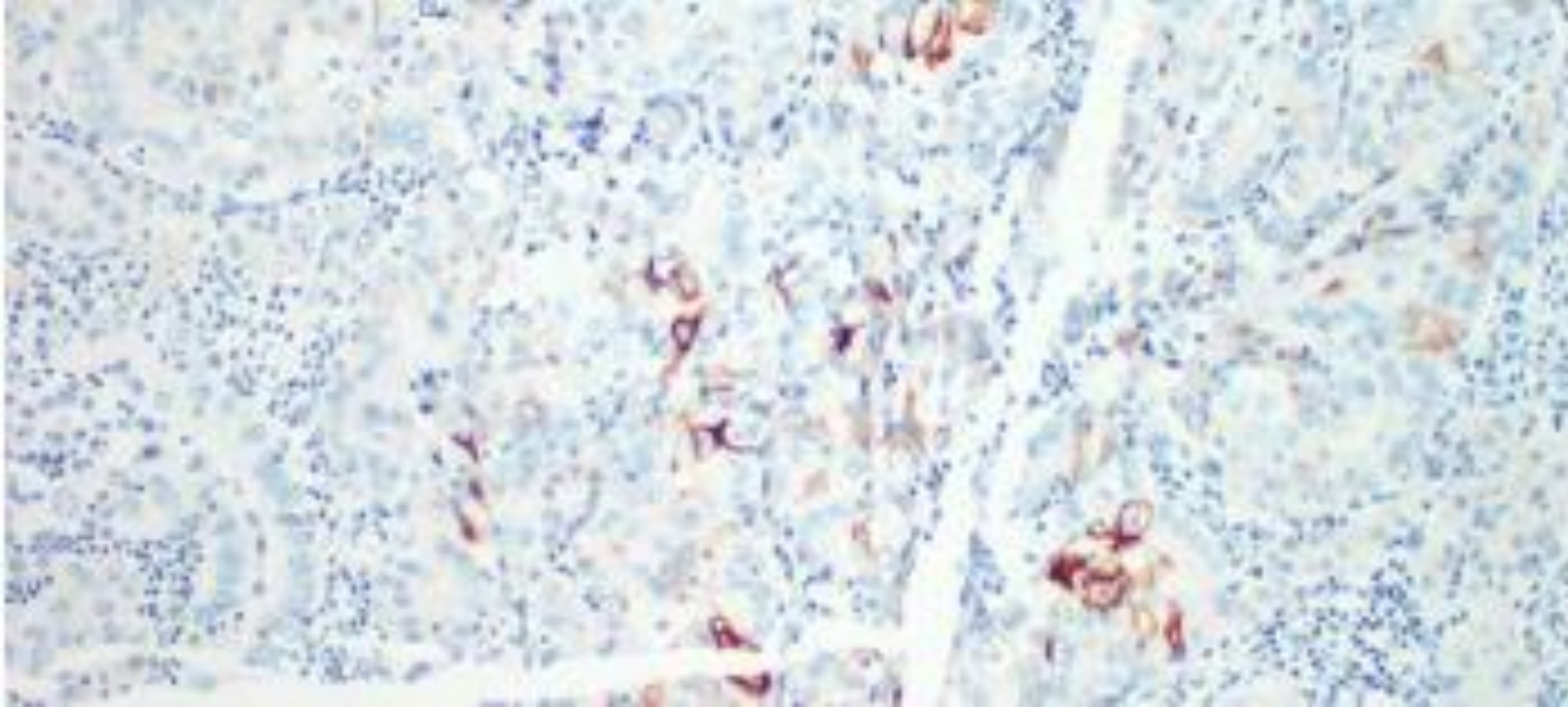
Rare tumors <5%

Risk Factors: Bladder extrophy, chronic inflammation, irritation and urachal remnants (dome) are risk factors

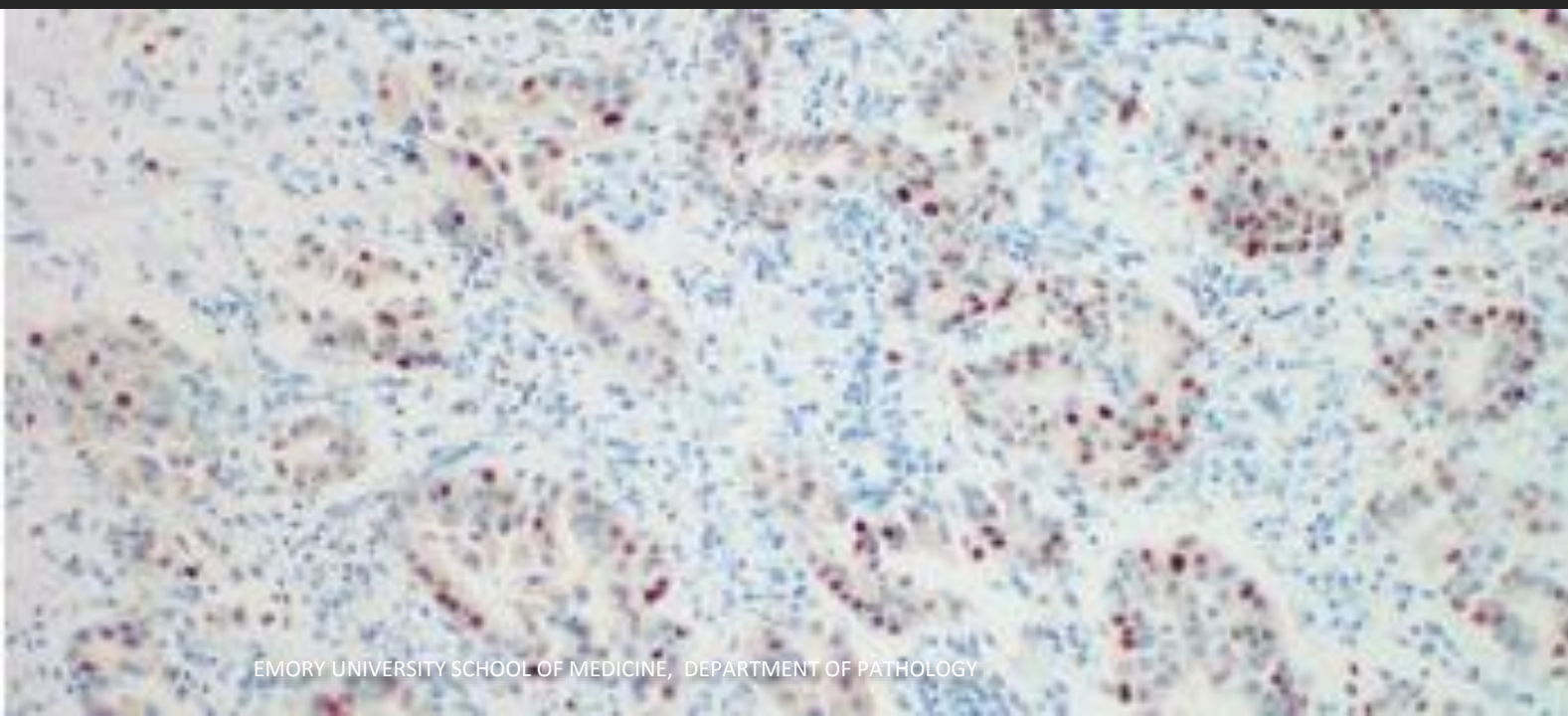
Can present at high stages: Prognosis depends on stage.

Distinction between primary and secondary tumors could be difficult





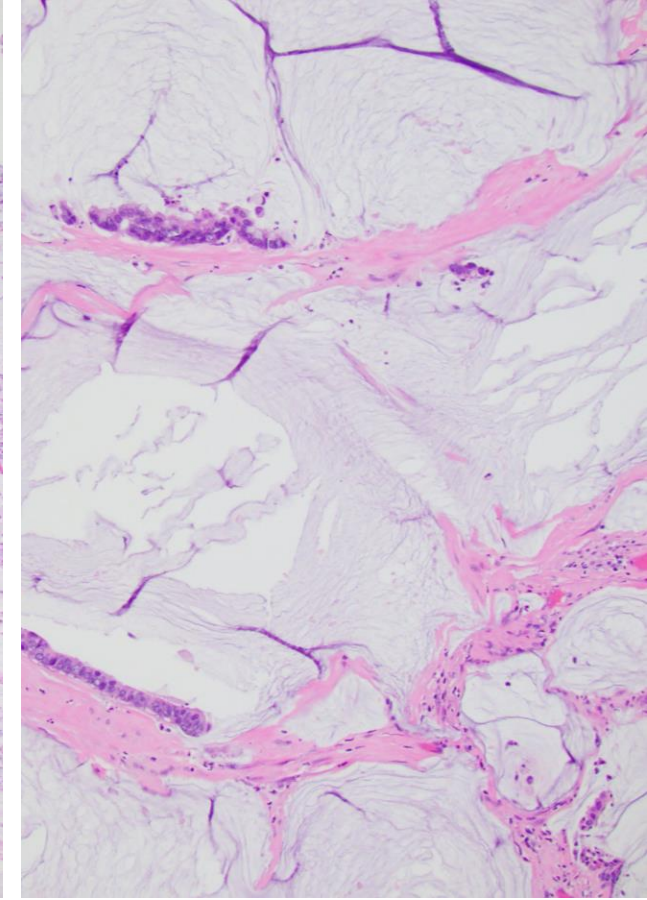
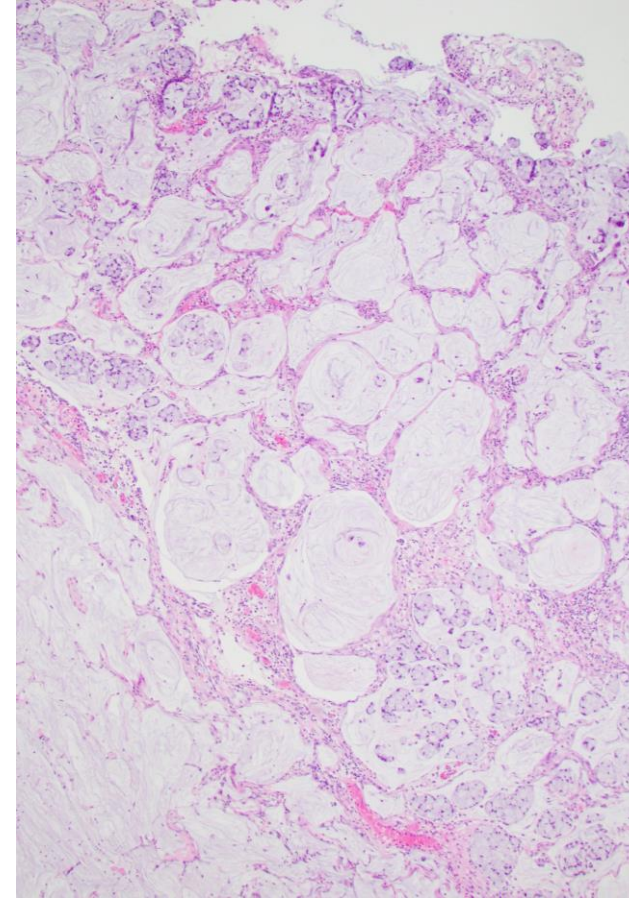
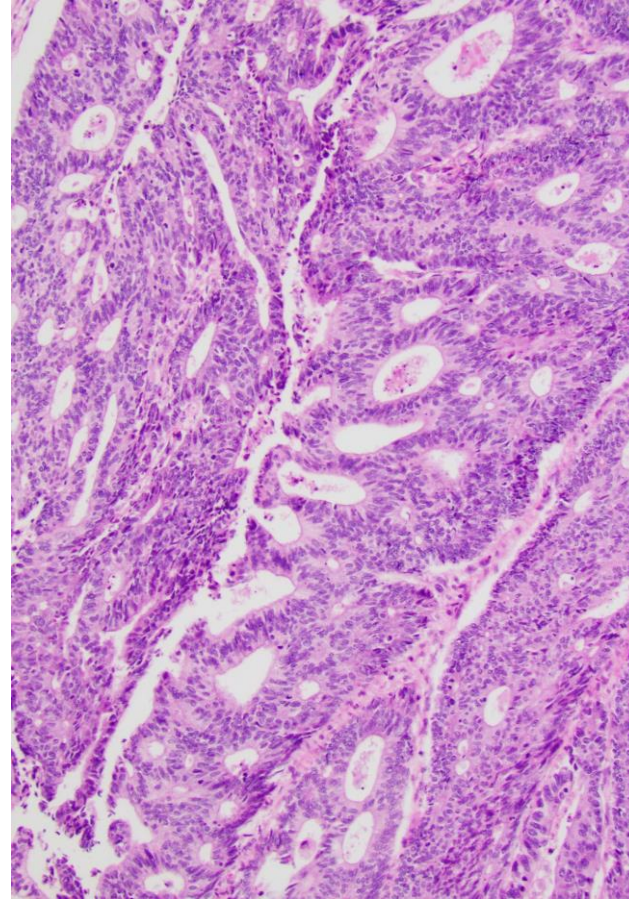
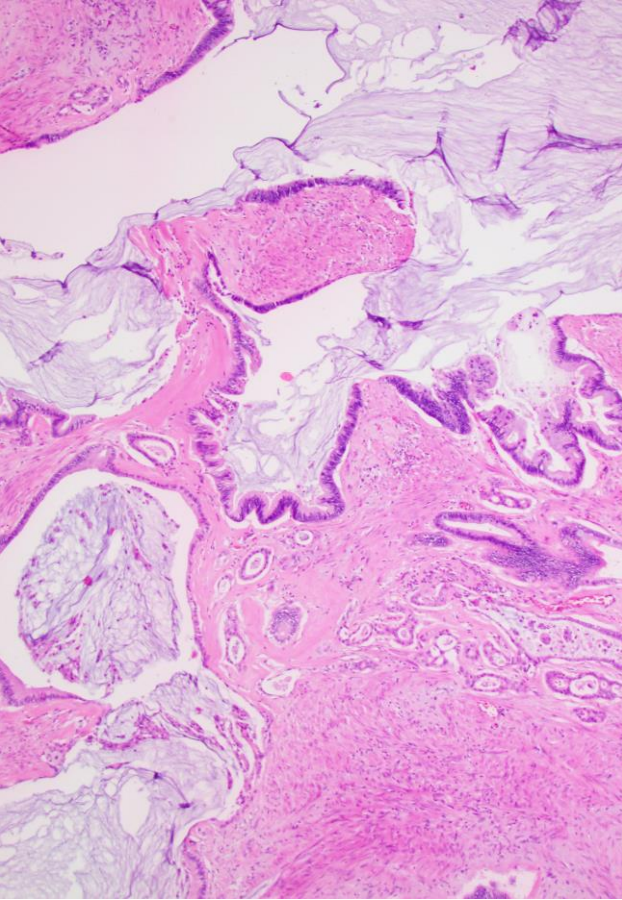
HMWCK



p63

A high-magnification histological micrograph of urothelial carcinoma. The image shows a dense population of malignant urothelial cells with hyperchromatic, pleomorphic nuclei and prominent nucleoli. The cells are arranged in a disorganized, infiltrative pattern, forming irregular nests and cords. Several areas exhibit pseudoglandular spaces, which are irregular, non-epithelial-lined cavities that resemble glandular lumens. The surrounding stroma is desmoplastic, with increased collagen deposition and scattered inflammatory cells. The overall architecture is highly cellular and lacks the normal layered structure of the urothelium.

Urothelial Carcinoma with Pseudoglandular Spaces

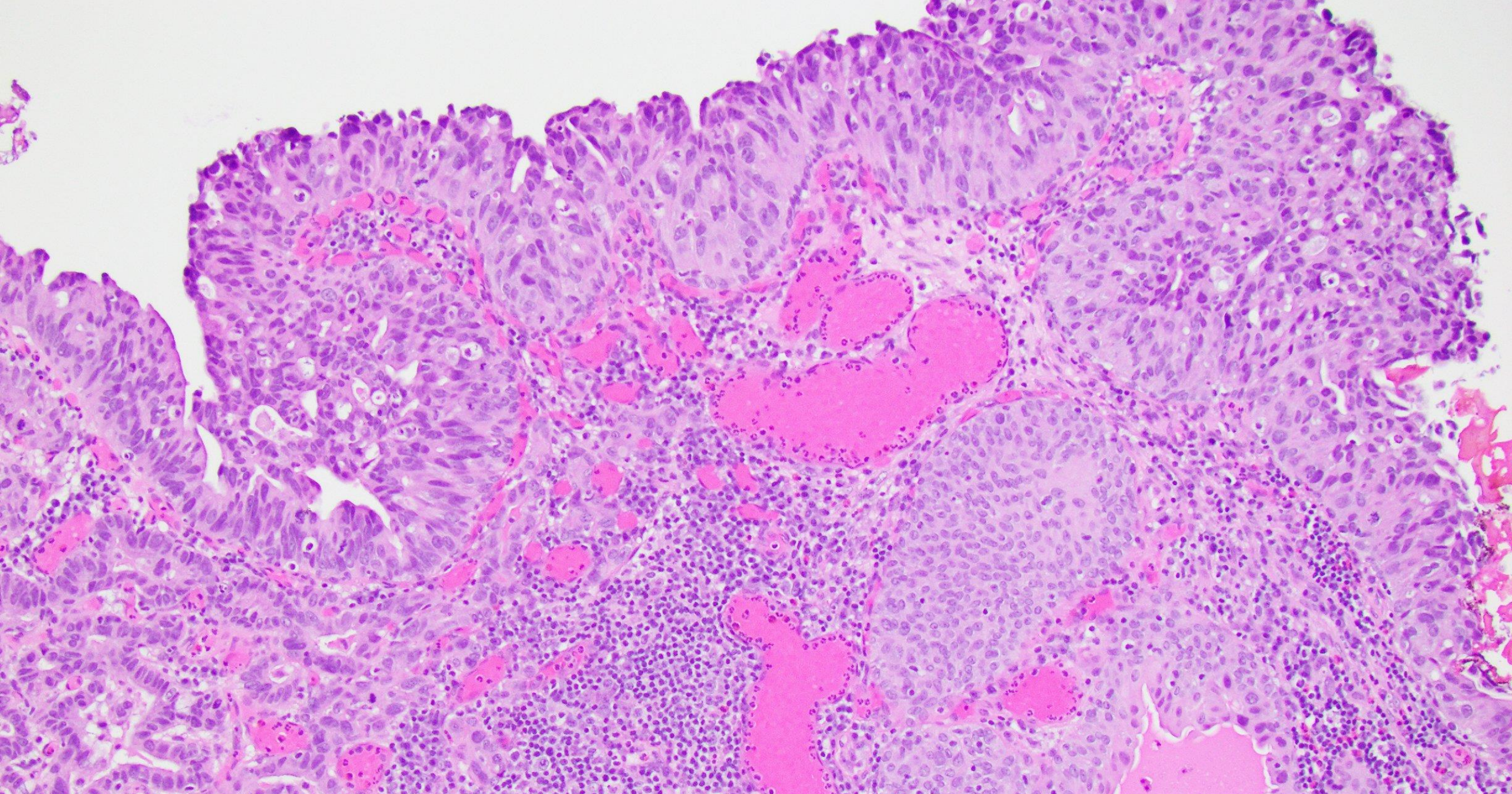


Invasive Adenocarcinoma with Mucinous Features

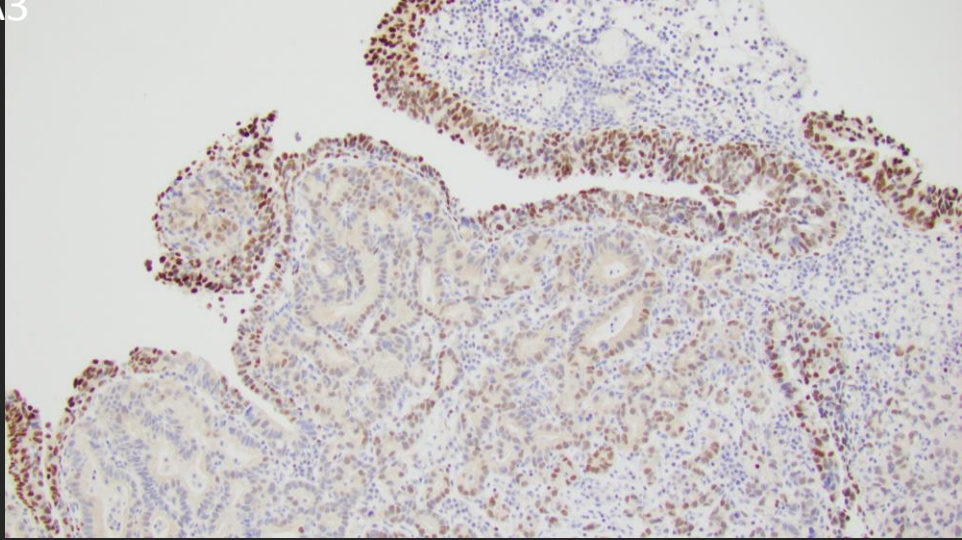
Urothelial Carcinoma with Glandular Differentiation

Defined as glandular divergent differentiation in the setting of urothelial carcinoma

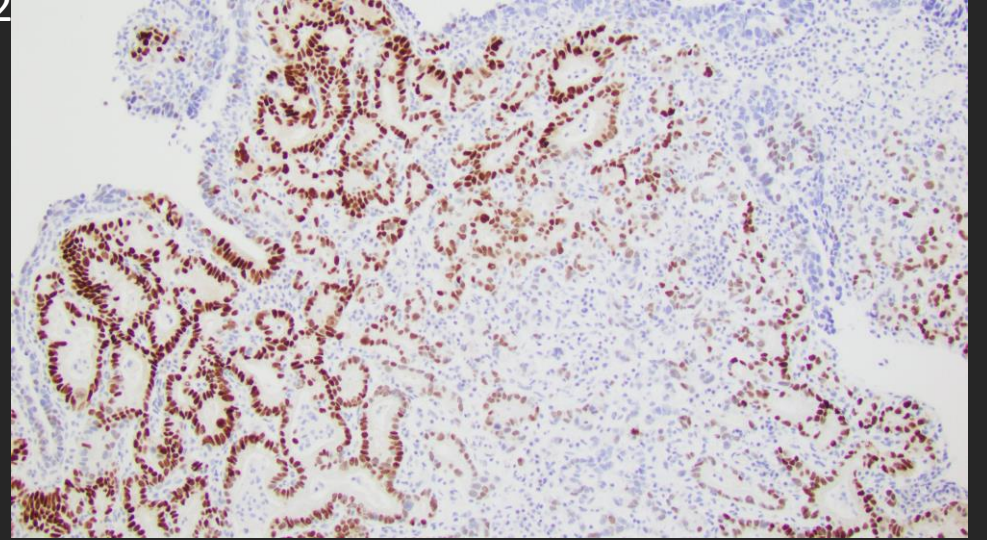
- Non-invasive (CIS or papillary) and/ or invasive urothelial carcinoma



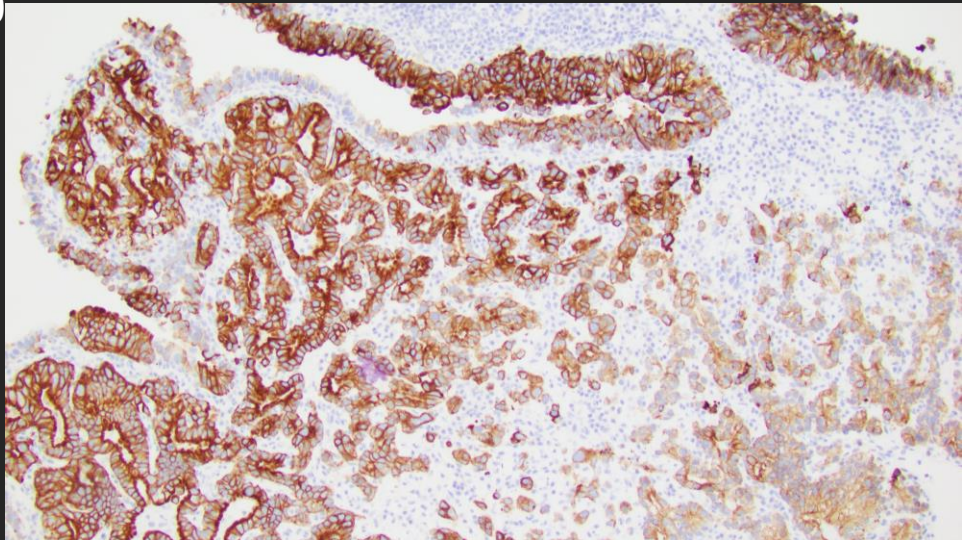
GATA3



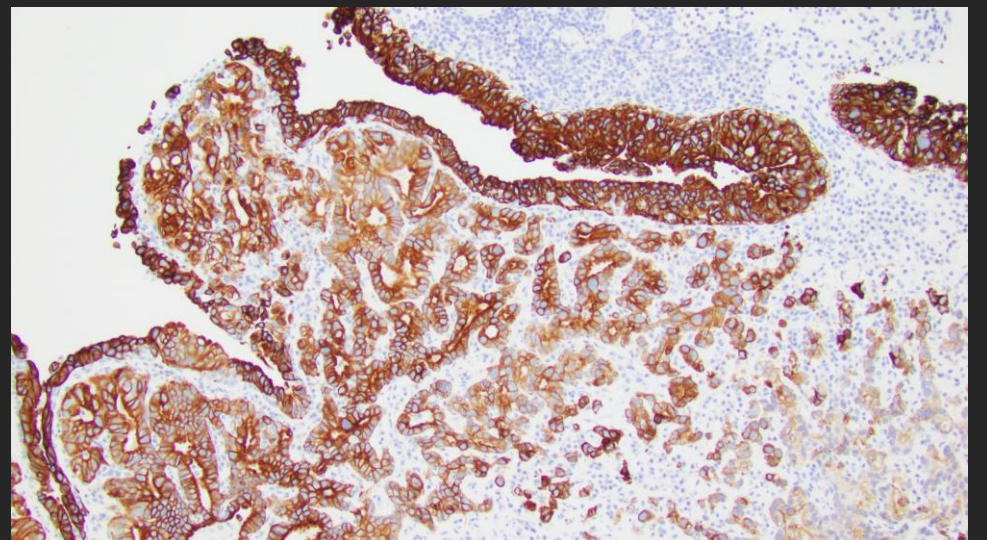
CDX2

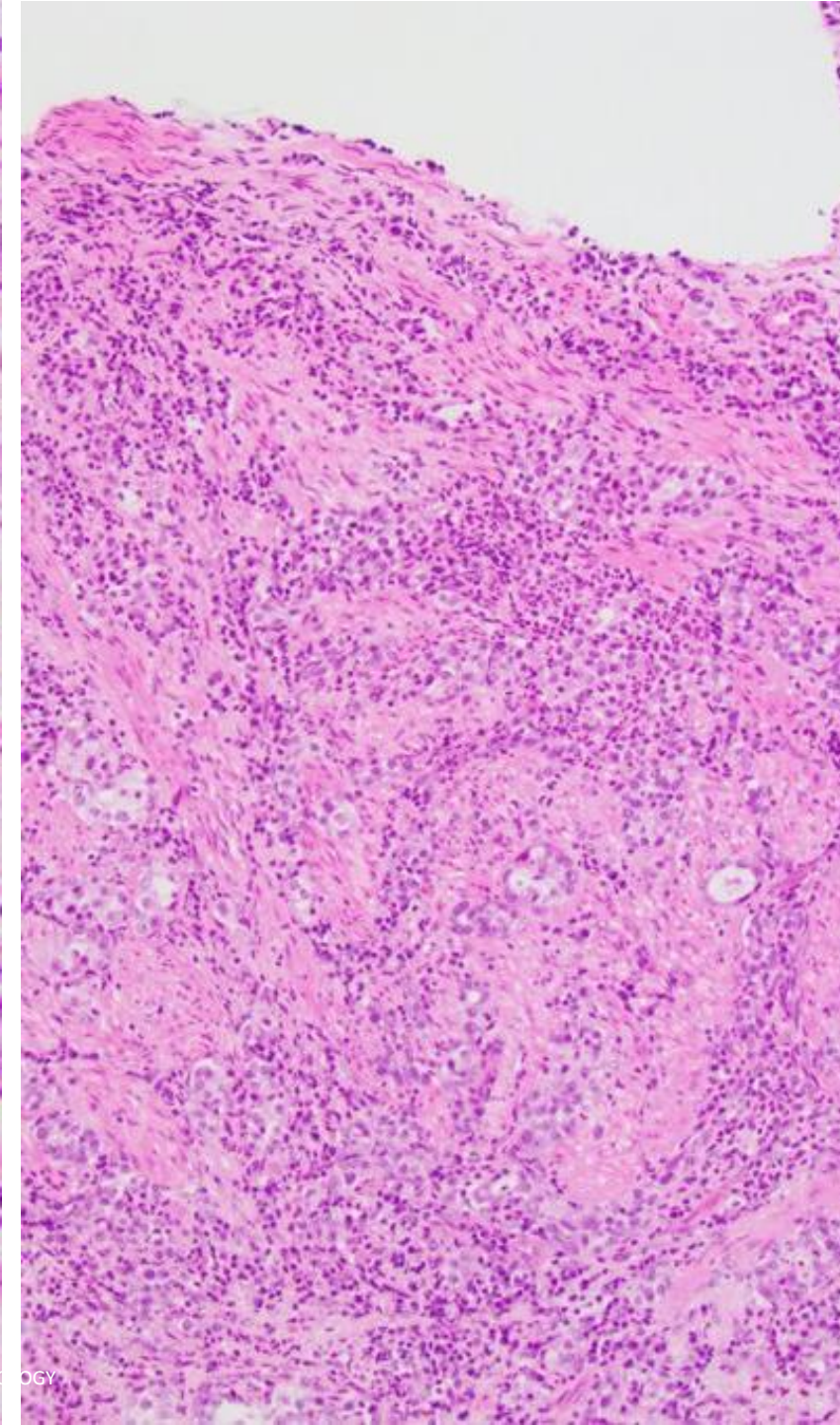
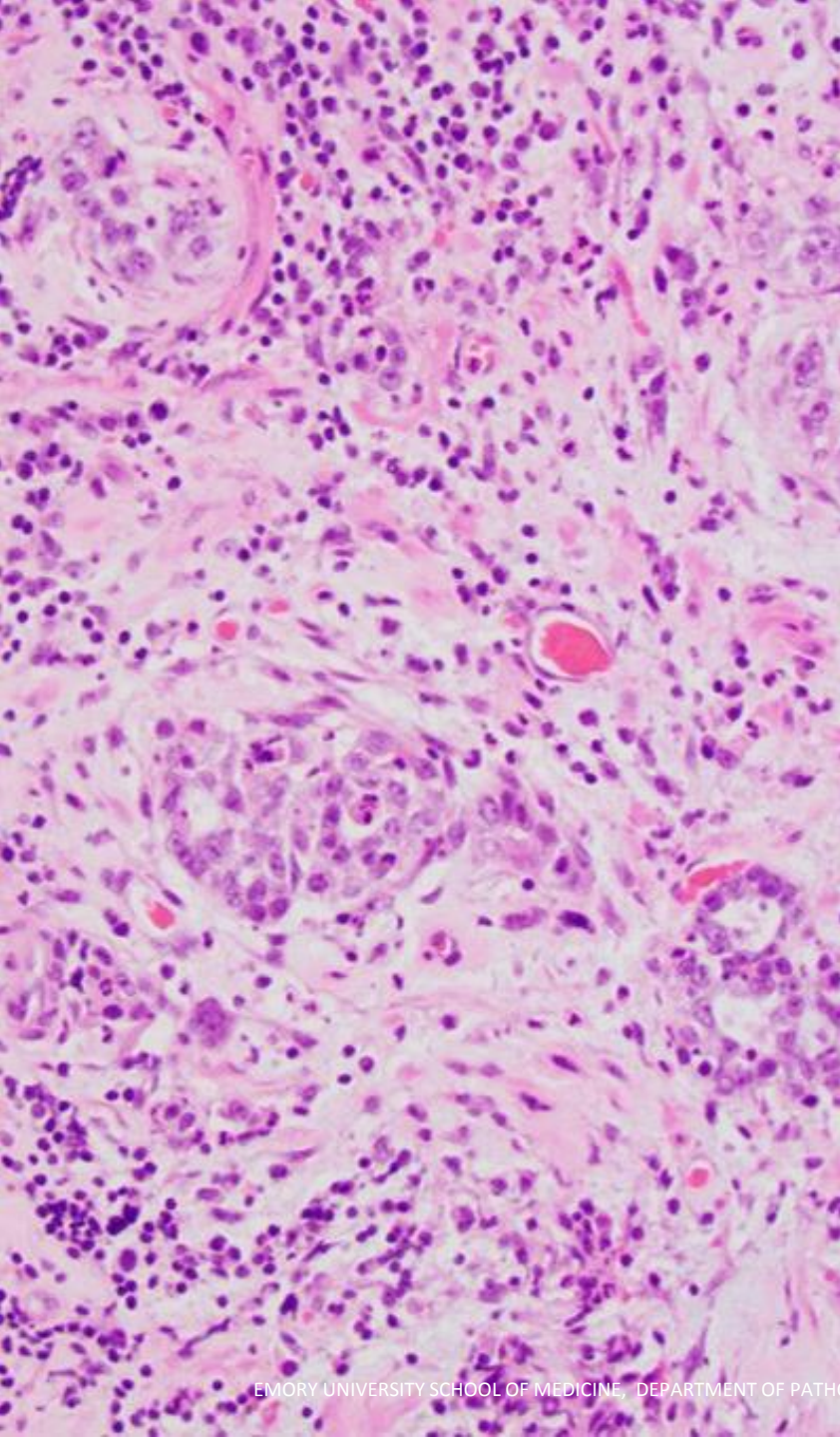


CK20



CK7





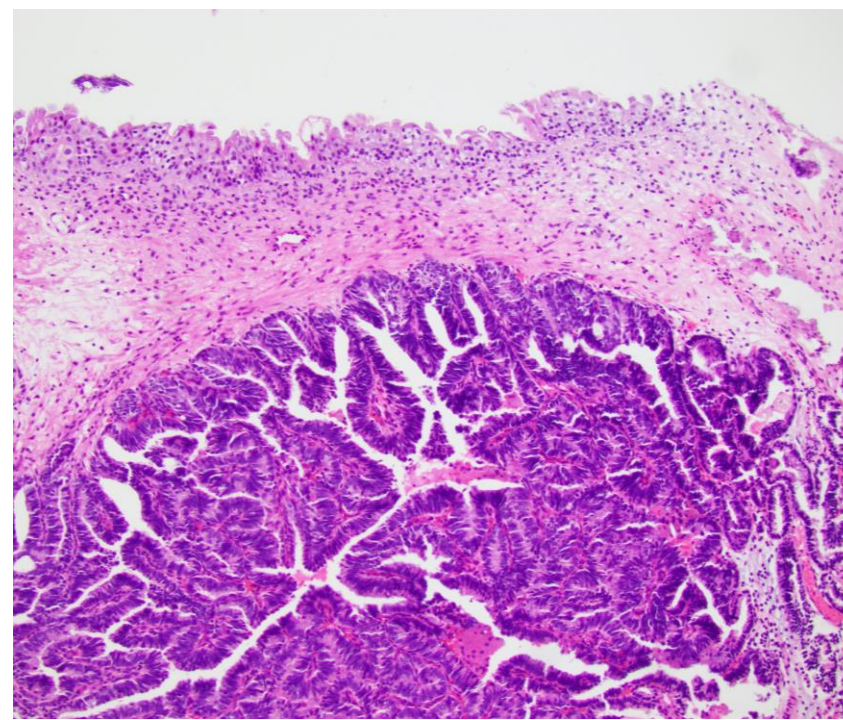
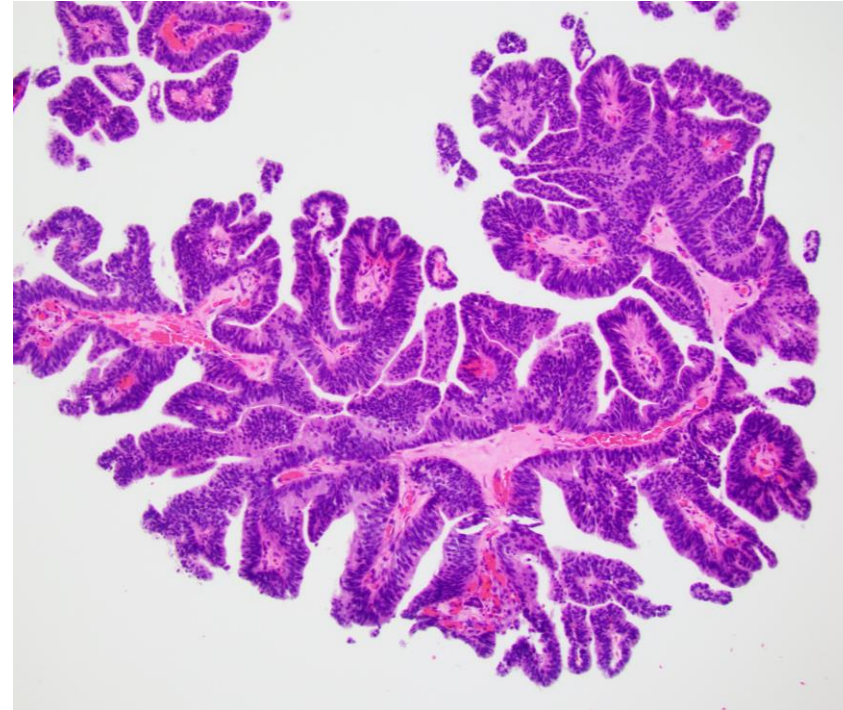
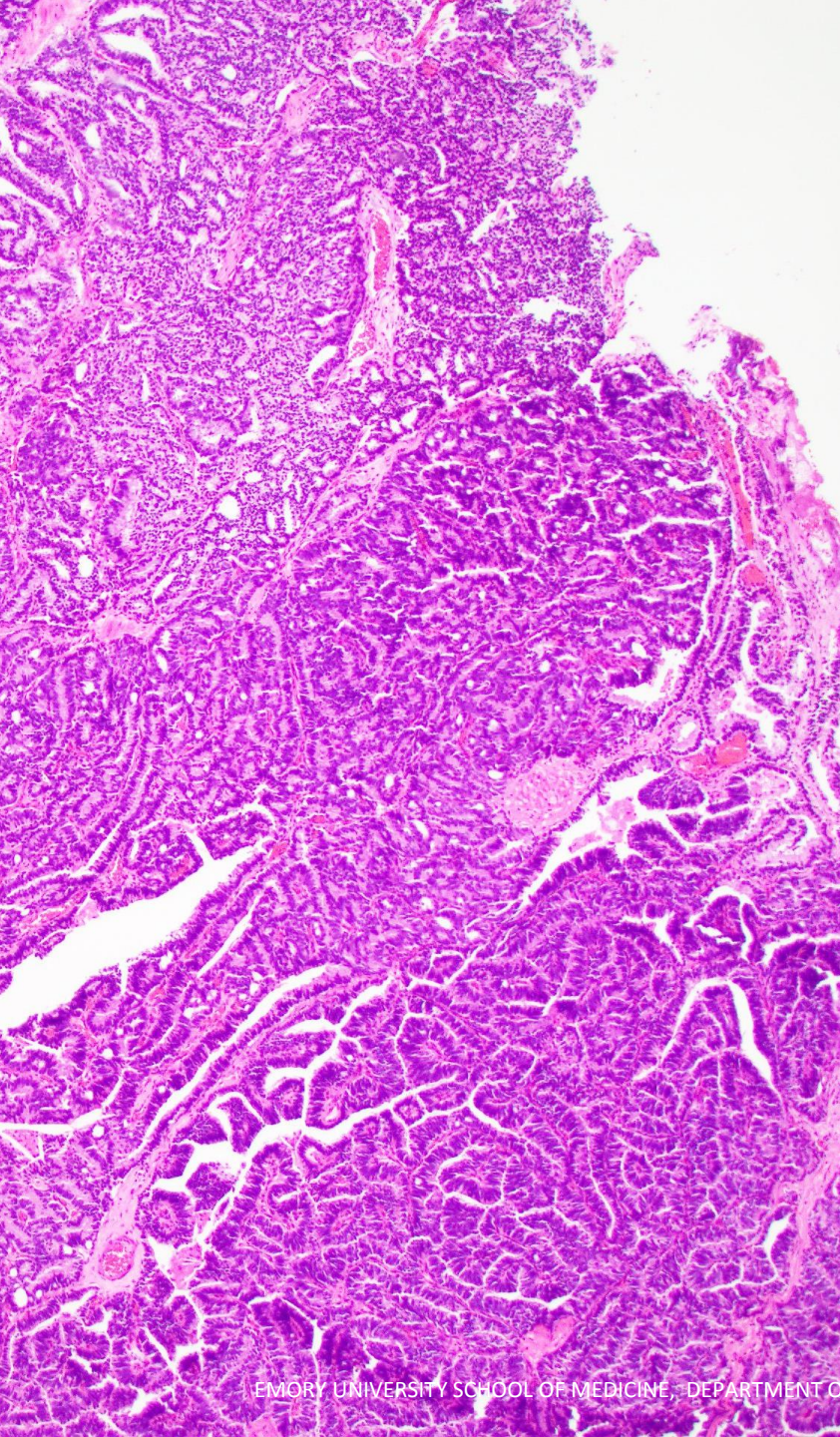
Clear Cell Carcinoma

Very Rare

More common in urethra with female predominance

Thought to be of Mullerian origin

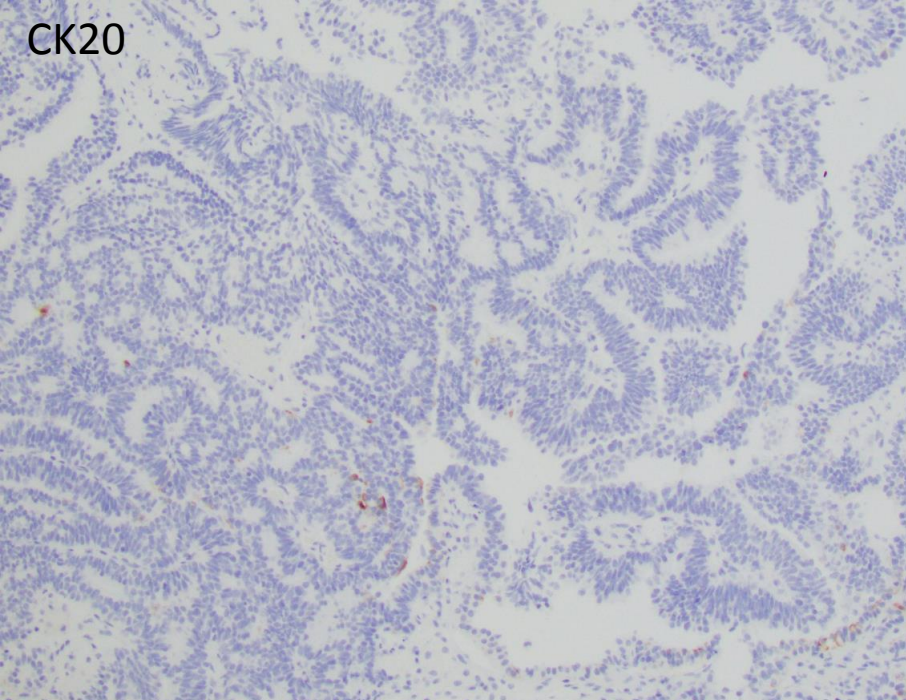
CK, CA125, PAX2 and 8, Napsin, HNF1 β : positive



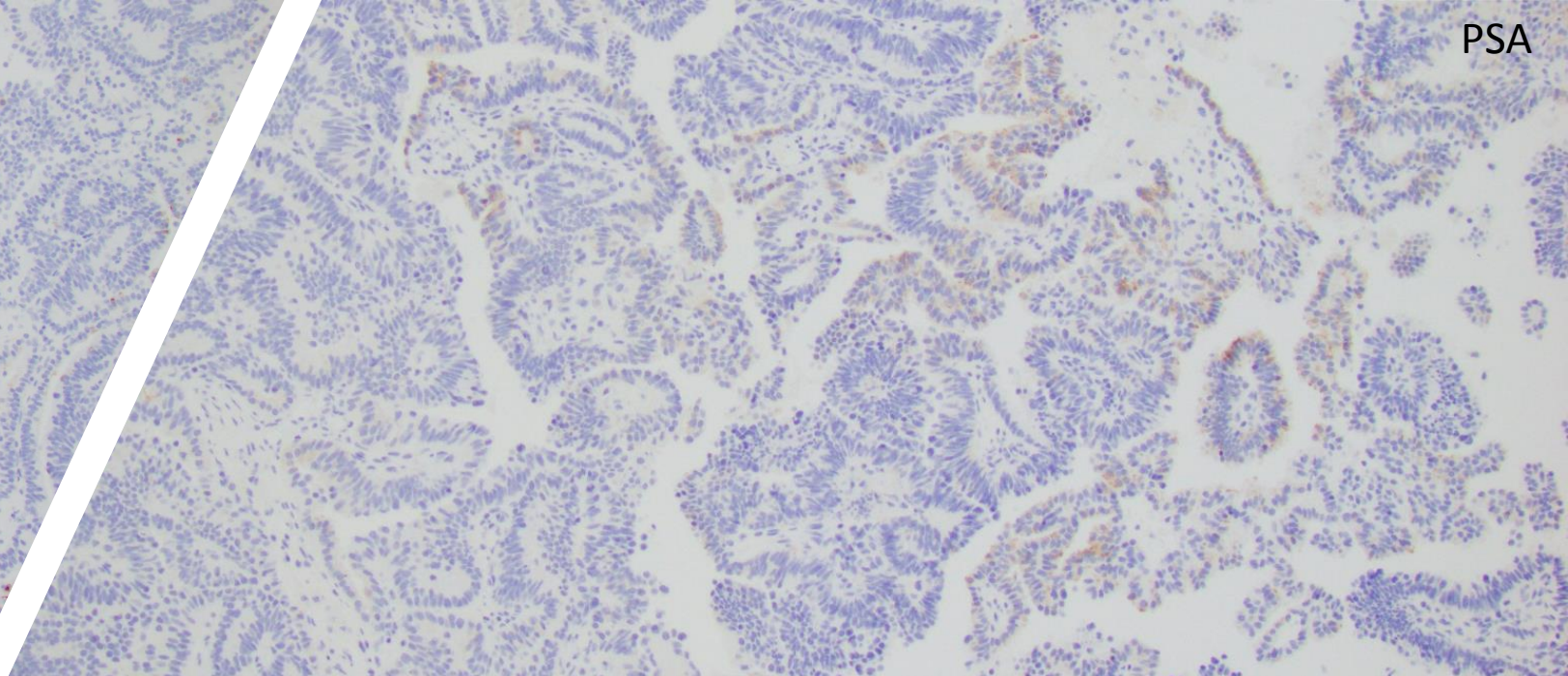
Secondary
Adenocarcinoma

Prostatic
Adenocarcinoma

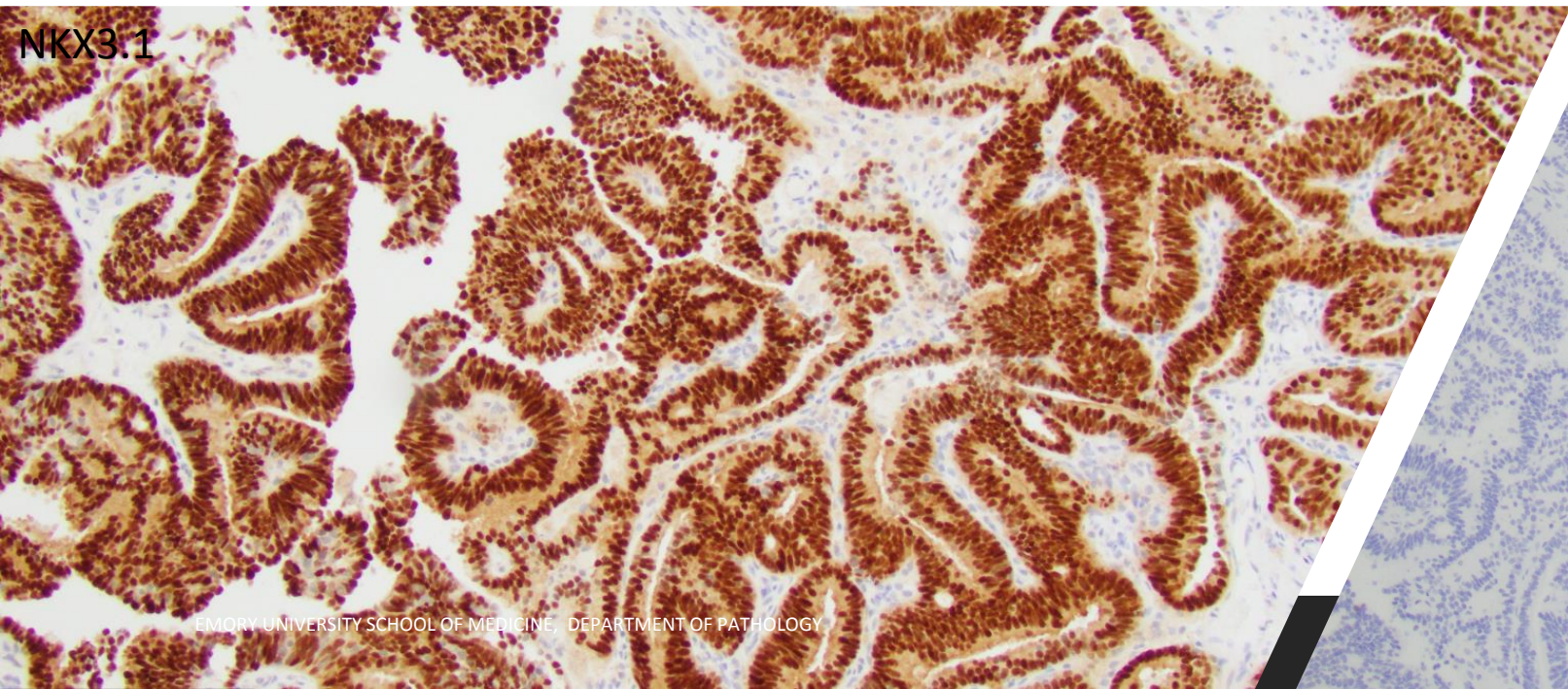
CK20



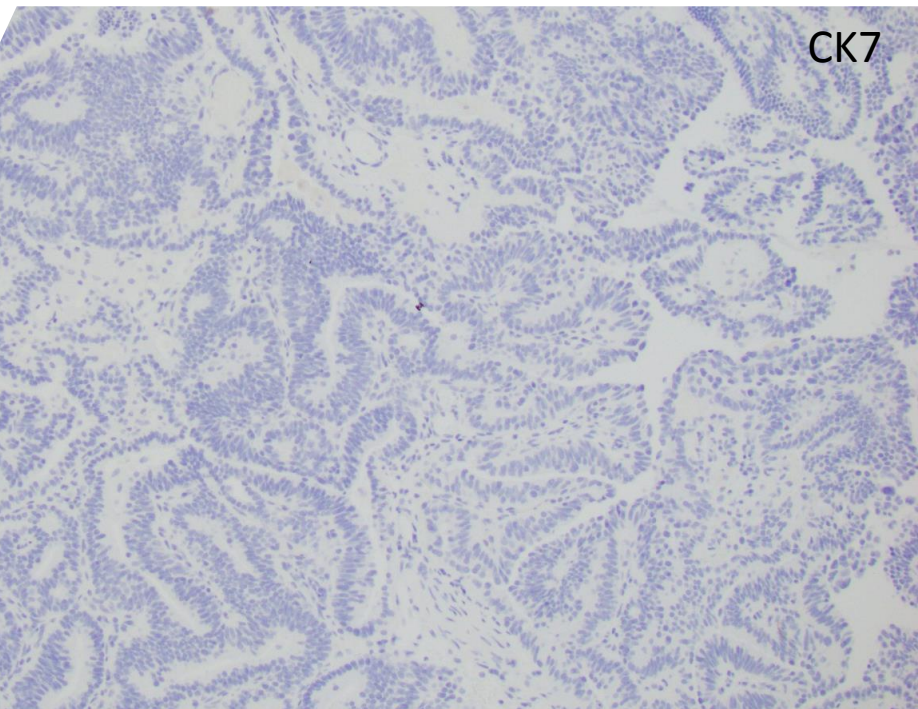
PSA

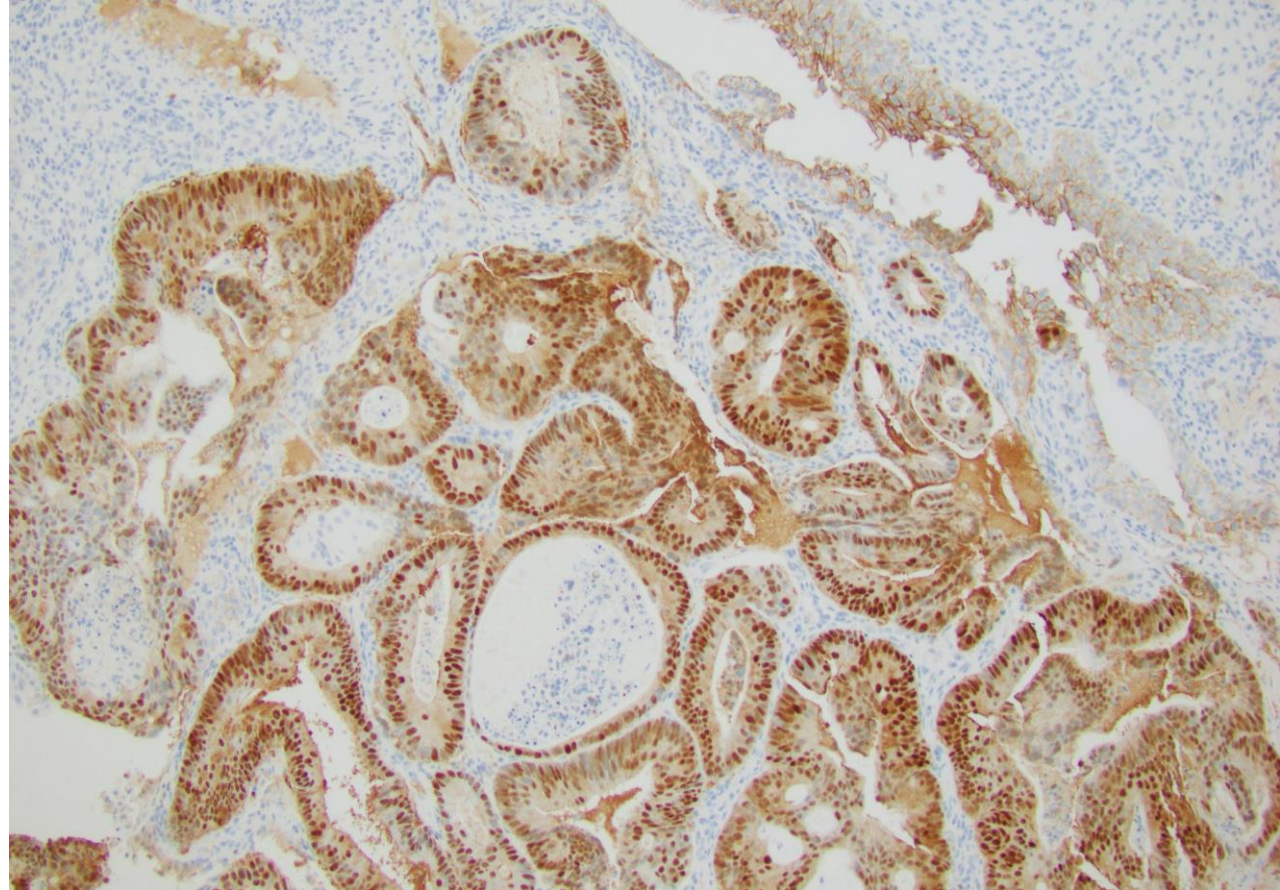
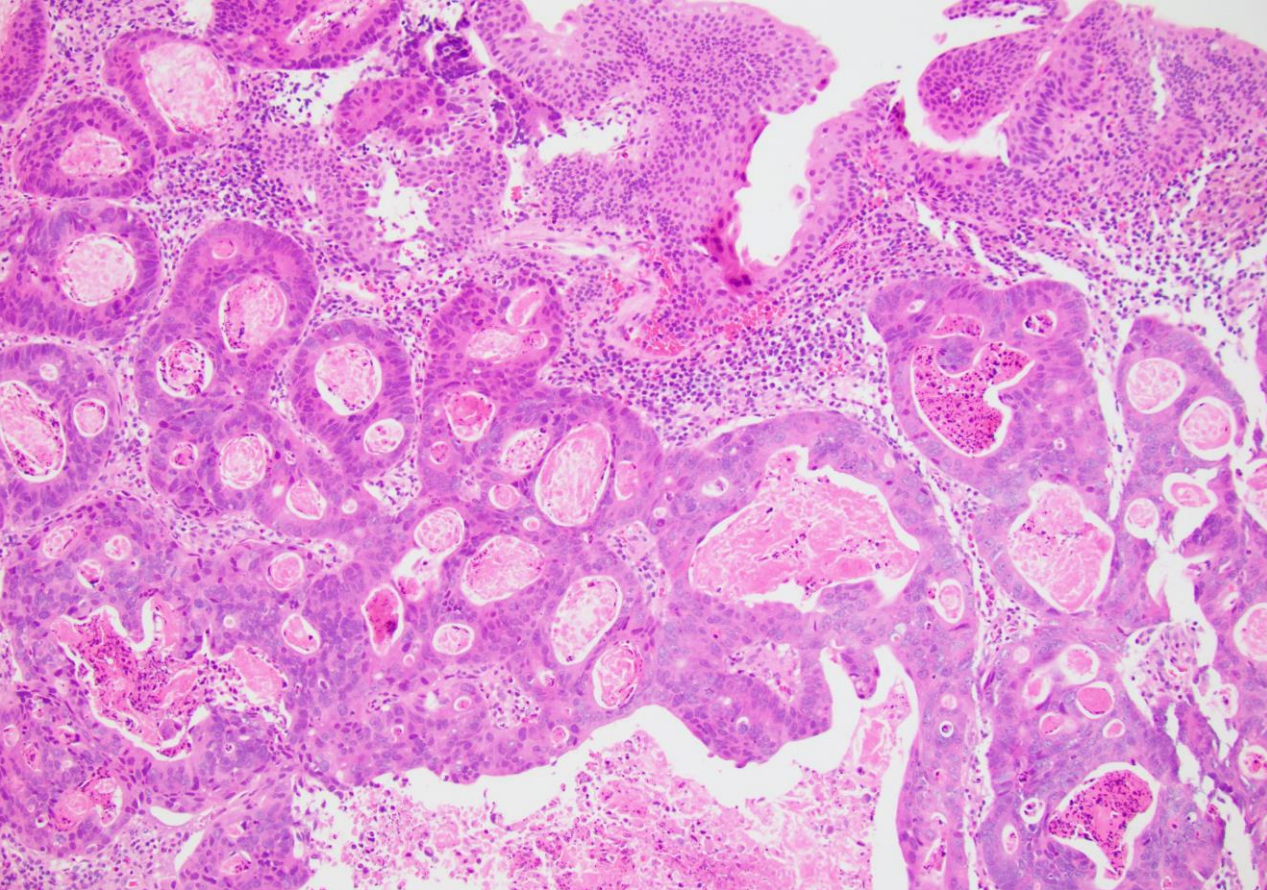


NKX3.1



CK7





Secondary Adenocarcinoma:

Colorectal Adenocarcinoma

Helpful Immunohistochemical Panels: Adenocarcinoma with Enteric Differentiation

	<u>Bladder</u>	<u>Colon</u>
CK7 ⁺ /CK20 ⁻	Around 40%	Less than 1%
β-catenin	Cytoplasm	Nuclear
P63/p40/Gata3	+ / -	Usually Negative

Helpful Immunohistochemical Panels:

Prostate

- NKX3.1, PSA, PSAP, Prostein, CK7/CK20
- Clinical / Serum PSA Level

Gynecologic

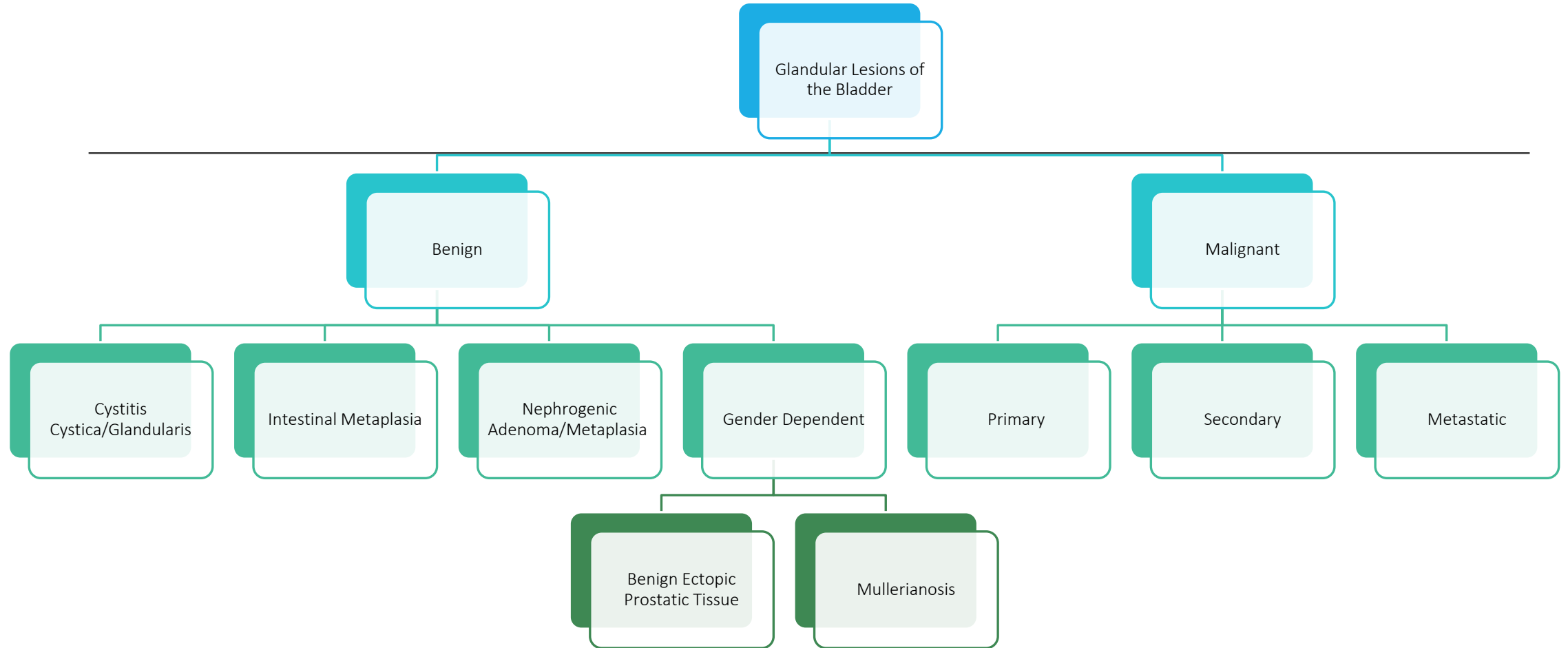
- General: PAX8
- Endocervical: P16, HPV ISH
- Endometrial: ER, PR
- Ovarian Serous: WT1, p53
- Clinical

Breast

- GCDFP15, Mammaglobin, ER, PR
- Clinical

Stomach

- ? SATB2 (negative in Gastric)
- Clinical



Cystitis Cystica/ Cystitis Glandularis

Benign lesions

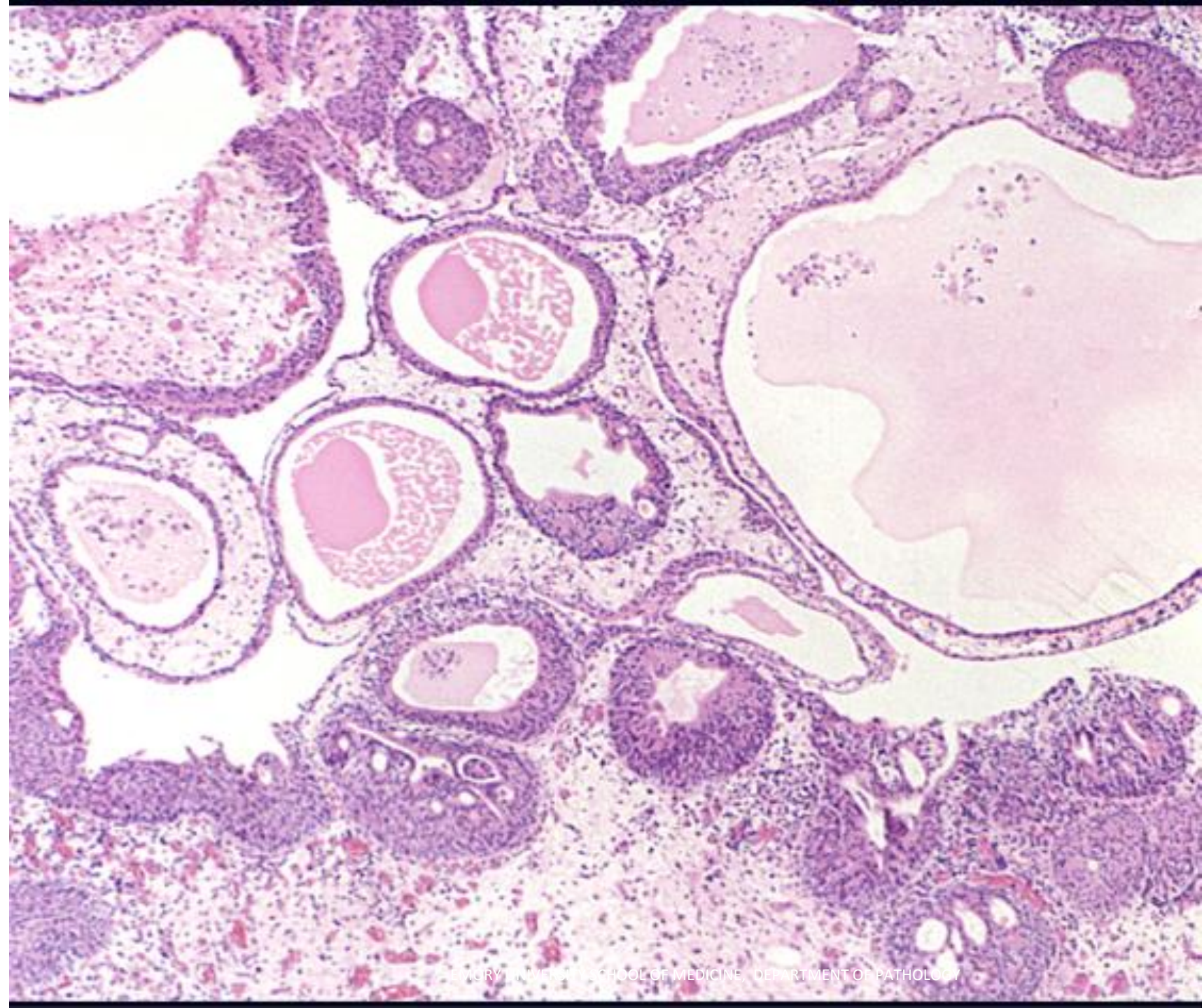
Cystitis Cystica: dilatation of Von
Brunn nests

Cystitis Glandularis: Columnar lining
on top

Up to 60% of autopsy bladders

Reactive process

No evidence of pre-
neoplastic potential



Intestinal Metaplasia

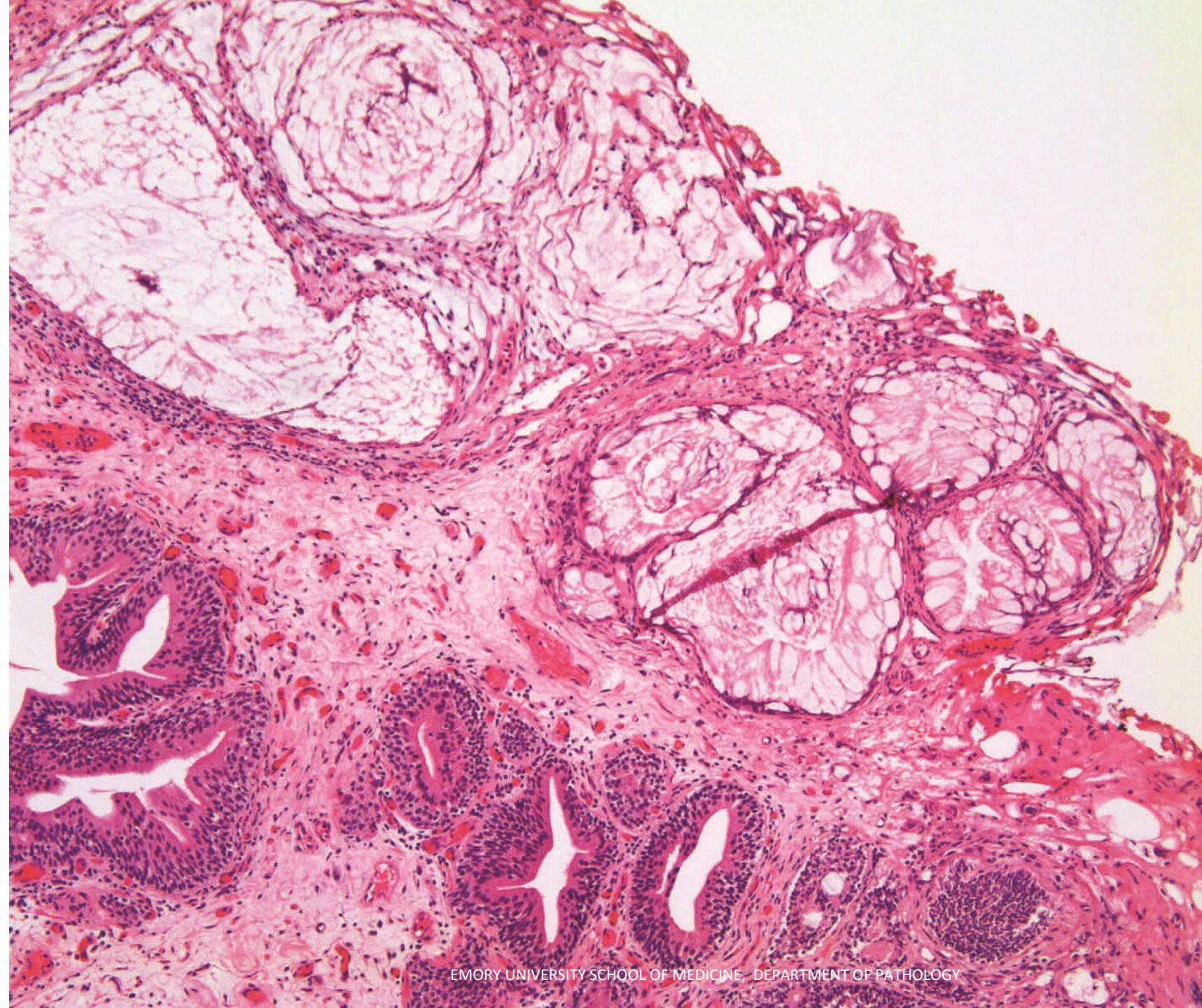
Setting of Cystitis Glandularis

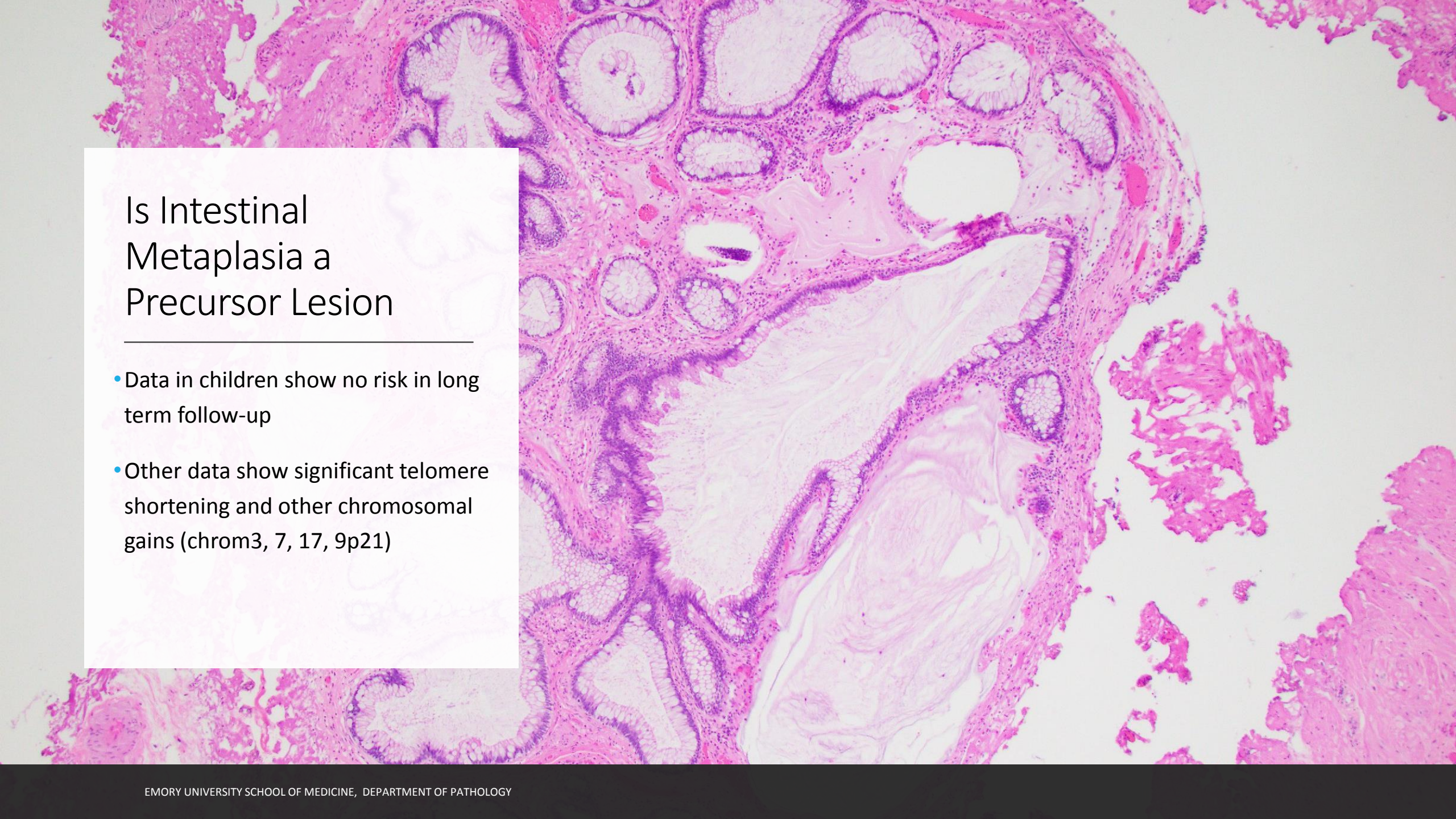
Focal or extensive

Presence of goblet cells

No atypia, no increase in mitoses,
no infiltration, no necrosis, no
complex arborizing architecture

Mucin extravasation can be a pitfall




A histological section of intestinal tissue stained with hematoxylin and eosin (H&E). The image shows a transition from normal intestinal crypts with goblet cells to areas of intestinal metaplasia, where the normal columnar epithelium is replaced by a more disorganized, glandular structure. The metaplastic area is characterized by a loss of the normal crypt architecture and the presence of irregular, glandular structures with varying degrees of cellular atypia.

Is Intestinal Metaplasia a Precursor Lesion

- Data in children show no risk in long term follow-up
- Other data show significant telomere shortening and other chromosomal gains (chrom3, 7, 17, 9p21)

Adenoma and Villous Adenoma

A histological slide showing a transition from a tubular adenoma on the left to a villous adenoma on the right. The tubular adenoma consists of irregular, crowded glandular structures with hyperplastic, columnar epithelium. The villous adenoma is characterized by a dense, branching network of finger-like villi, each lined by a single layer of columnar epithelial cells. The overall architecture is highly disorganized, and the glands are closely packed together. The background stroma is fibrous and contains scattered inflammatory cells.

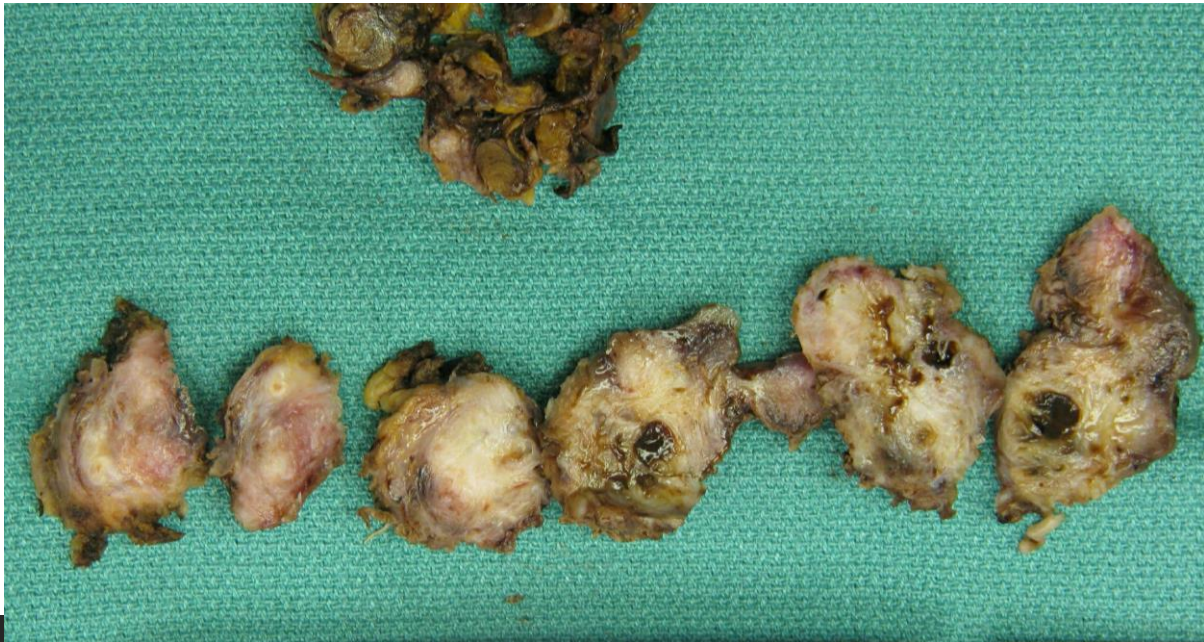
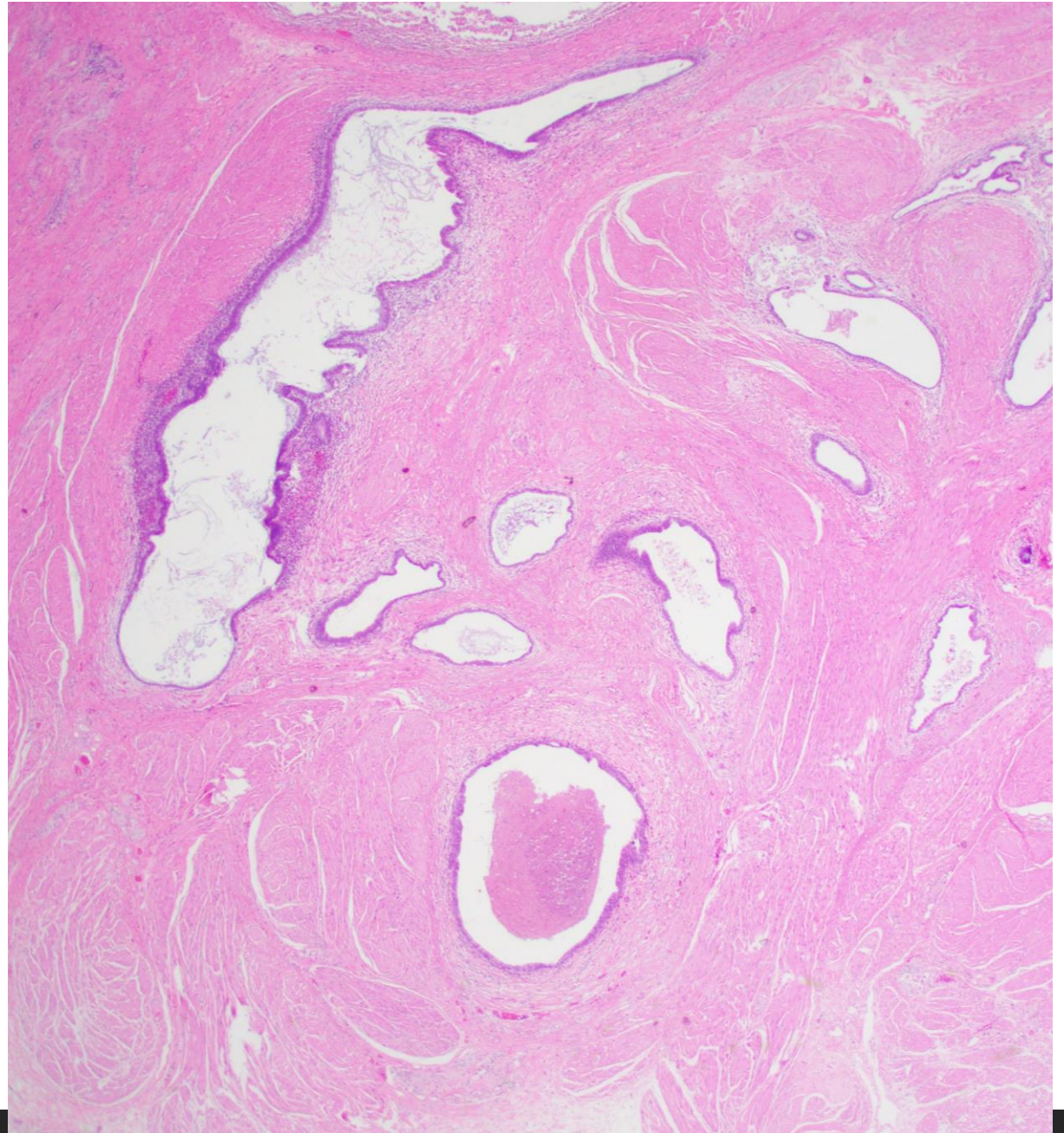
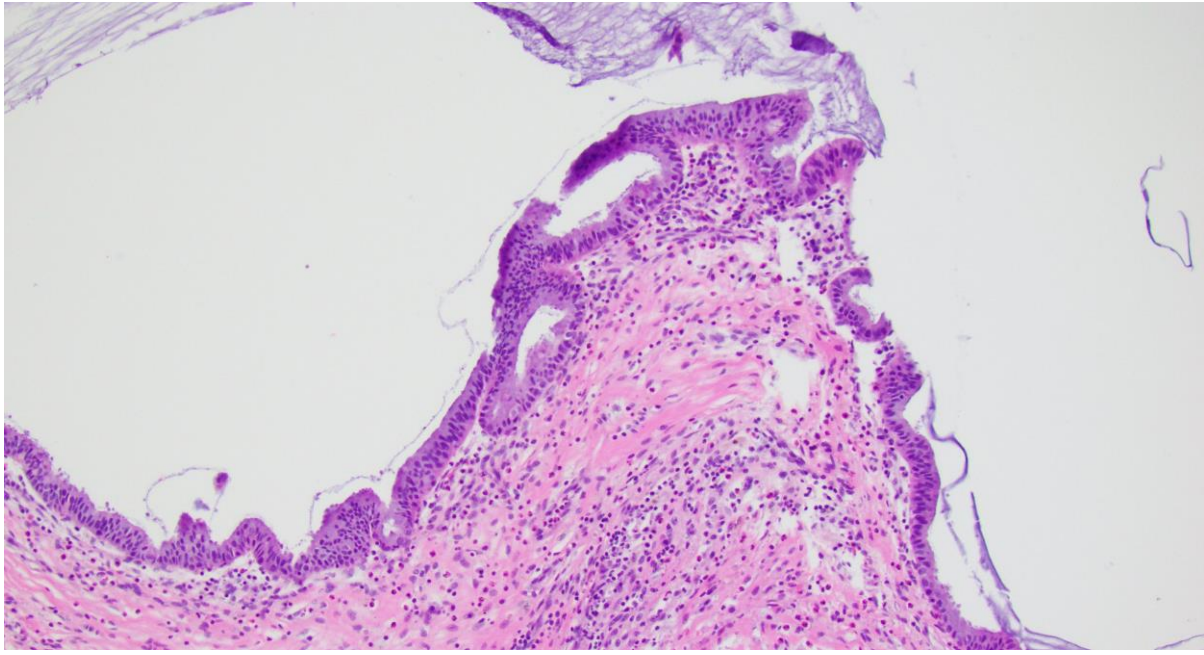
A histological section of the uterus stained with hematoxylin and eosin (H&E). The image shows the endometrial lining at the top, followed by the myometrium. Several cross-sections of endometrial glands are visible, some containing red-stained secretions. The overall architecture is consistent with a normal or hyperplastic endometrium.

Gender Dependent: Mullerianosis

Endometriosis

Endosalpingiosis

Endocervicosis



Nephrogenic Adenoma/ Metaplasia

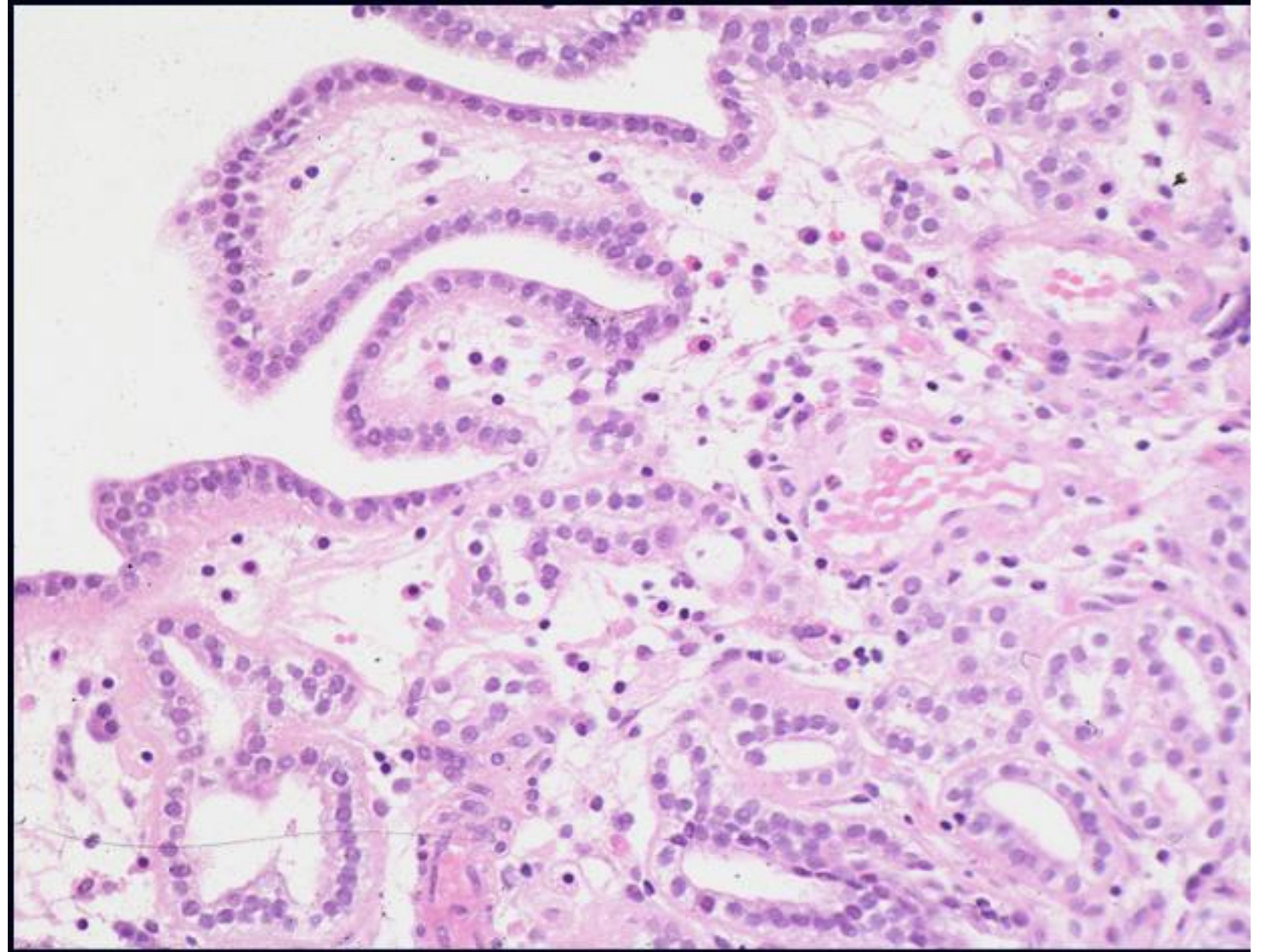
Benign Lesion

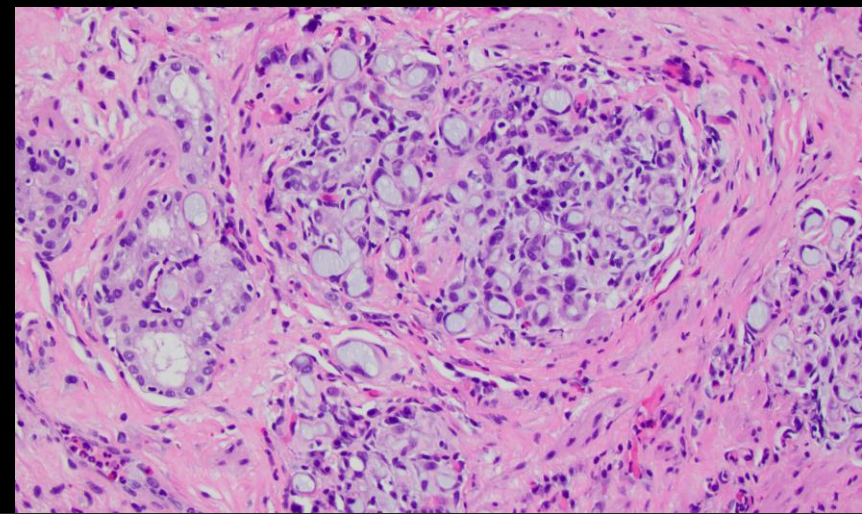
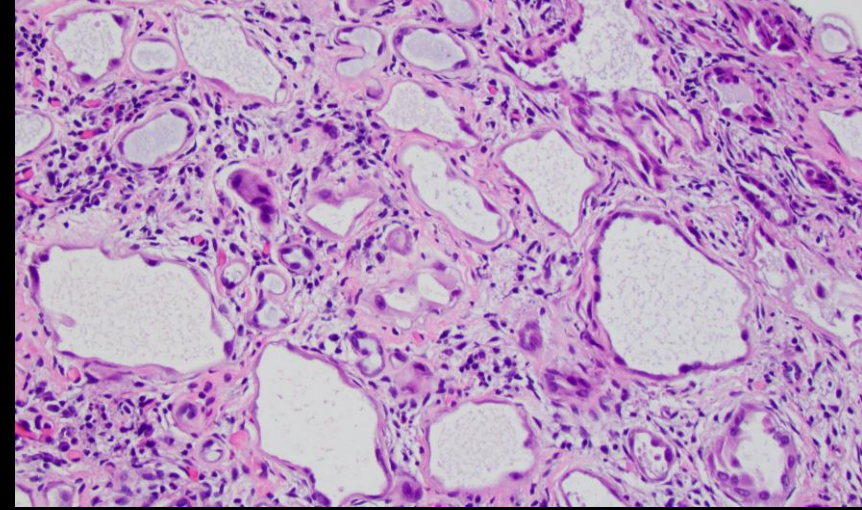
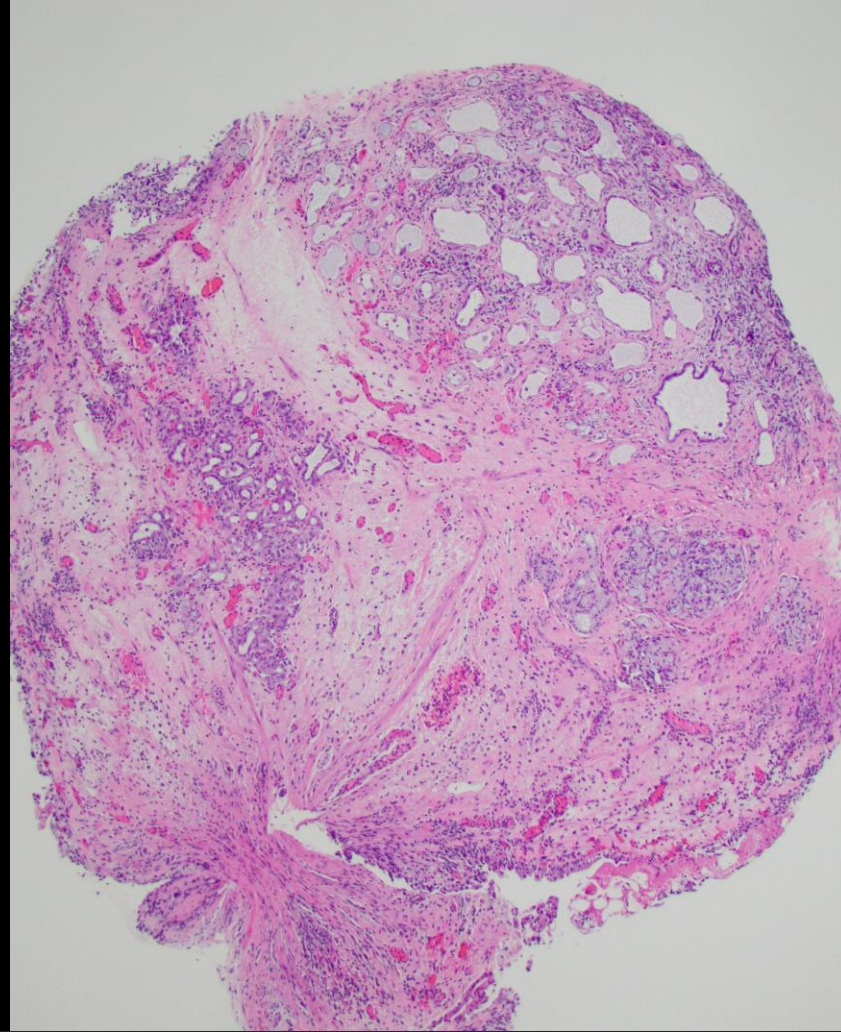
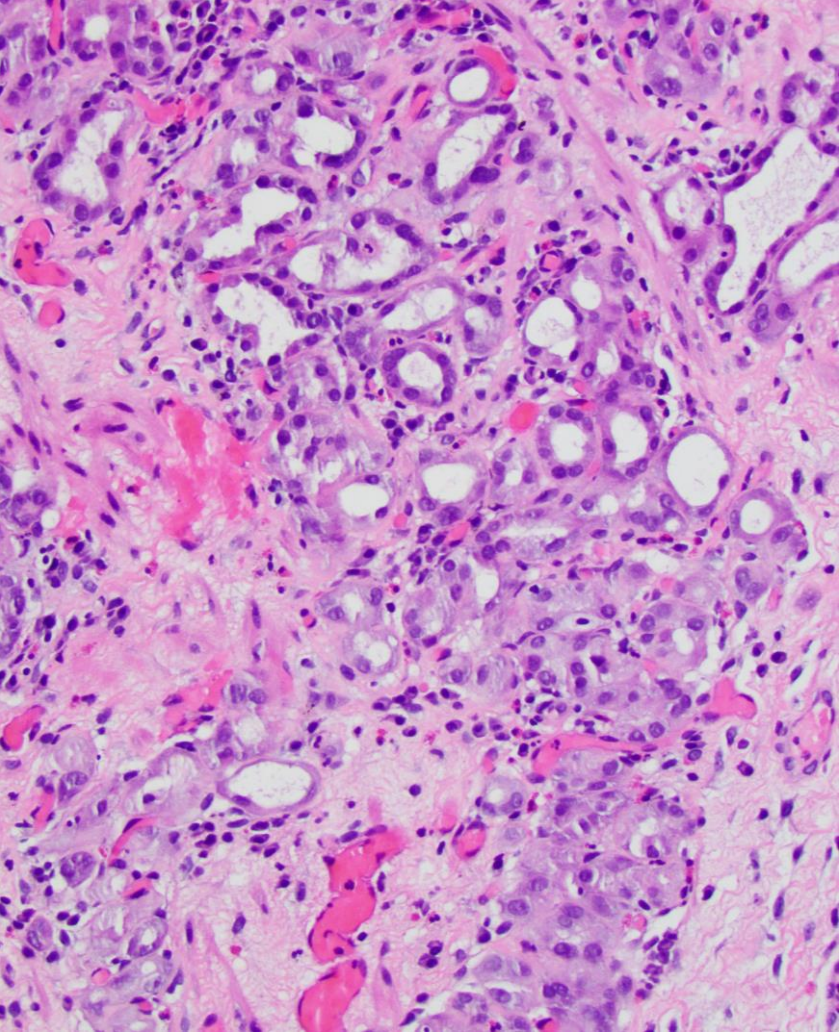
Papillary, Cystic, Glandular

No atypia, necrosis, mitosis, infiltrative
pattern

Prior injury/instrumentation

PAX8 positive





Nephrogenic adenoma/metaplasia

Summary of Glandular Lesions

Wide variety of benign and malignant lesions

Adenocarcinoma and Urothelial Carcinoma with glandular differentiation have poor prognosis

Adenocarcinoma of the bladder can have different histologic appearances and the immunoprofile is not specific

Think about secondary adenocarcinoma and if needed perform stains to exclude the possibility



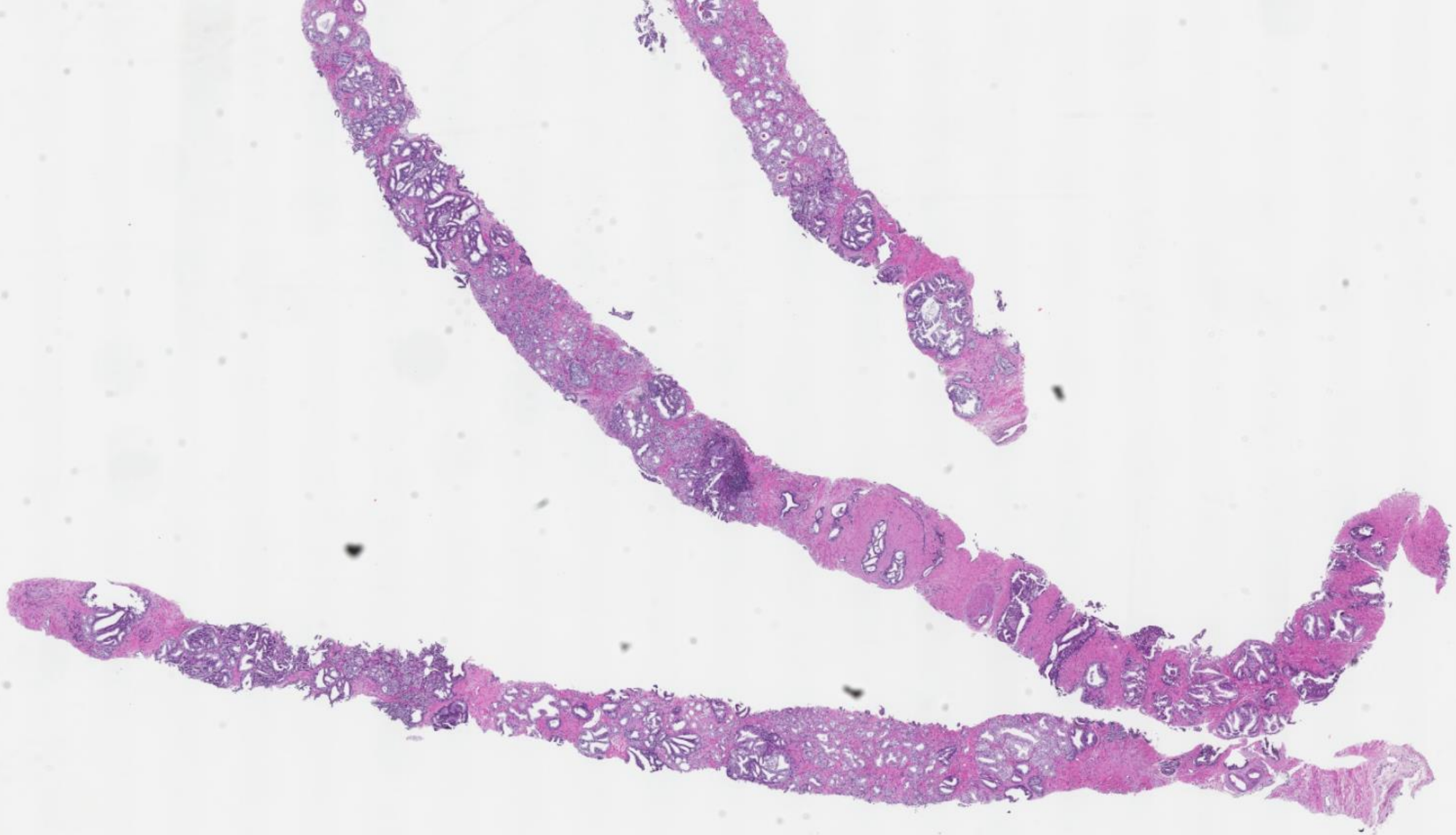
Updates in Grading of Prostatic Adenocarcinoma

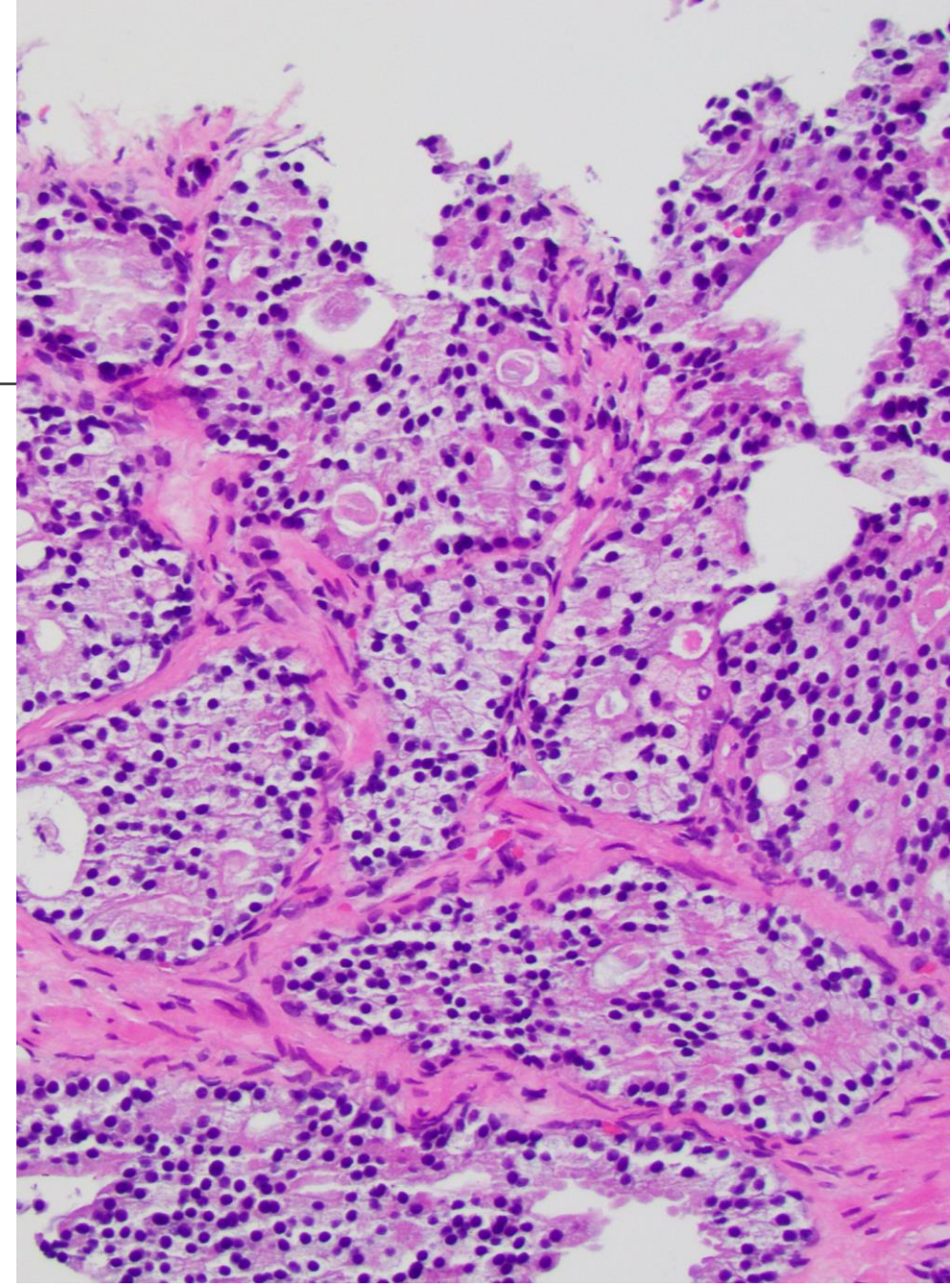
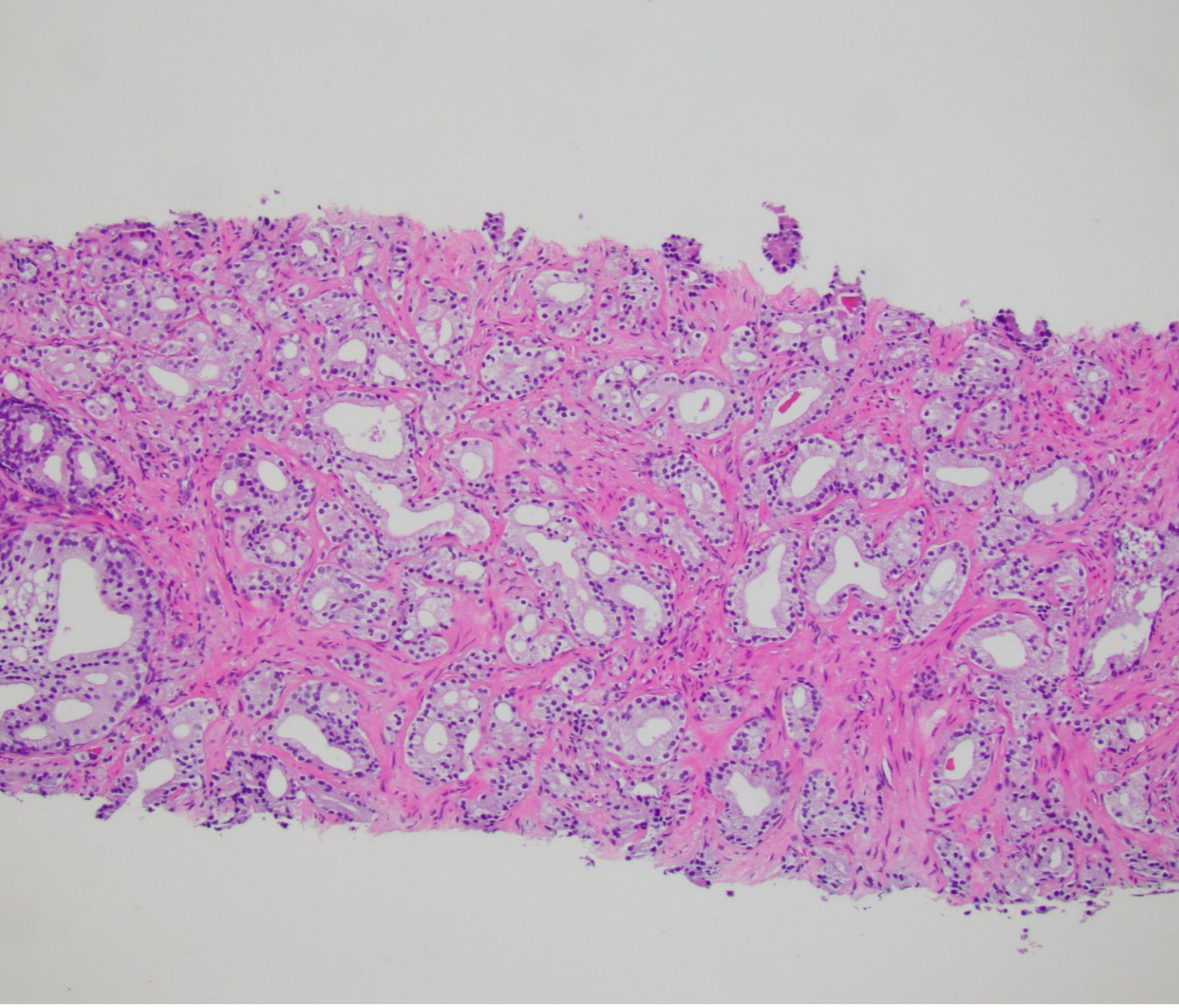
Case 2

75 year old male with an **elevated PSA of 5.97 ng/ml**

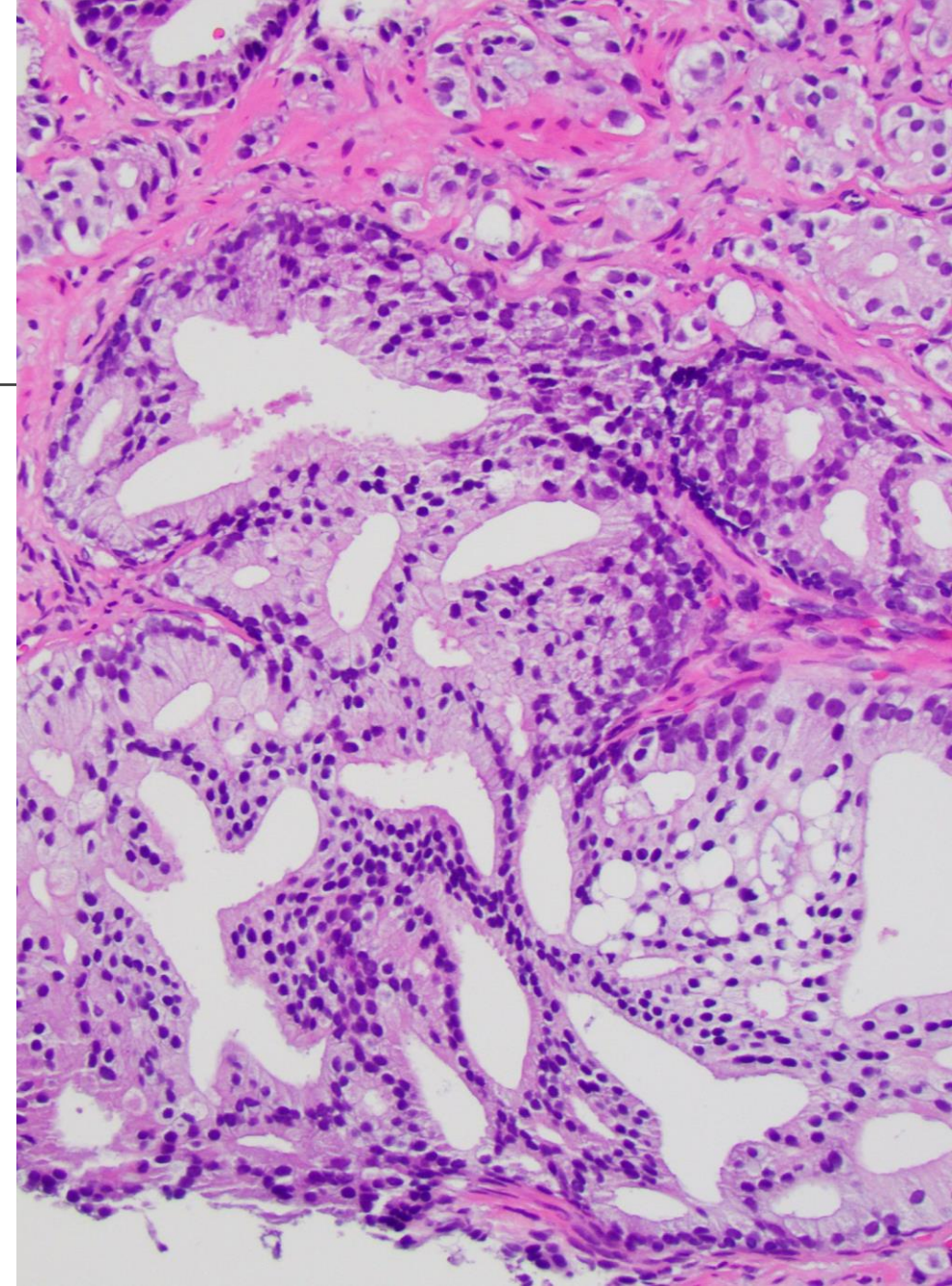
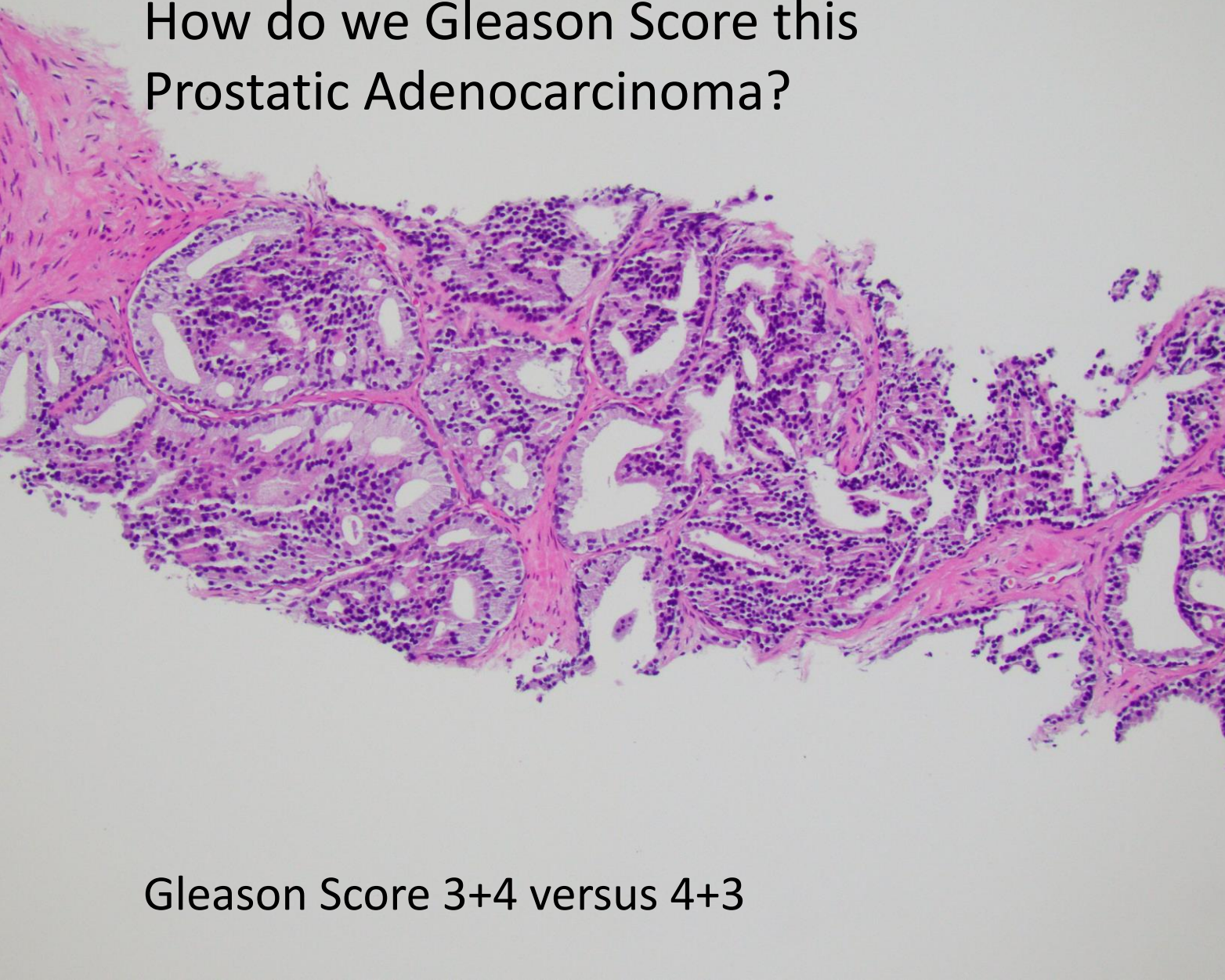
He has a history of chronic renal disease and hypertension.

No family history of carcinoma.





How do we Gleason Score this
Prostatic Adenocarcinoma?



Gleason Score 3+4 versus 4+3

The 2019 International Society of Urological Pathology (ISUP) Consensus Conference on Grading of Prostatic Carcinoma

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Andrew J. Evans, MD,§ Glen Kristiansen, MD,|| Charlotte F. Kweldam, MD,* Geert Litjens, PhD,¶
Jesse K. McKenney, MD,# Jonathan Melamed, MD,** Nicholas Mottet, MD,††‡‡
Gladell P. Paner, MD,§§ Hemamali Samaratunga, FRCPA,|||| Ivo G. Schoots, MD,¶¶
Jeffry P. Simko, MD,### Toyonori Tsuzuki, MD,*** Murali Varma, MD,†††
Anne Y. Warren, MD, FRCPath,‡‡‡ Thomas M. Wheeler, MD,§§§
Sean R. Williamson, MD,||||| ISUP Grading Workshop Panel Members,
and Kenneth A. Iczkowski, MD,¶¶¶*

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The 2019 Genitourinary Pathology Society (GUPS) White Paper on Contemporary Grading of Prostate Cancer

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Giovanna A. Giannico, MD; Jennifer B. Gordetsky, MD; Charles C. Guo, MD; Donna E. Hansel, MD, PhD;
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Rodolfo Montironi, MD; George J. Netto, MD; Jane K. Nguyen, MD, PhD; Adeboye O. Osunkoya, MD; Anil Parwani, MD;
Brian D. Robinson, MD; Mark A. Rubin, MD; Rajal B. Shah, MD; Jeffrey S. So, MD; Hiroyuki Takahashi, MD, PhD;
Fabio Tavora, MD, PhD; Maria S. Tretiakova, MD, PhD; Lawrence True, MD; Sara E. Wobker, MD; Ximing J. Yang, MD, PhD;
Ming Zhou MD, PhD; Debra L. Zynger, MD; Kiril Trpkov, MD*

ISUP: Include IDC in GS
GUPS: Do not include IDC in GS

Is the glass full
or empty?



Intraductal Carcinoma of the Prostate

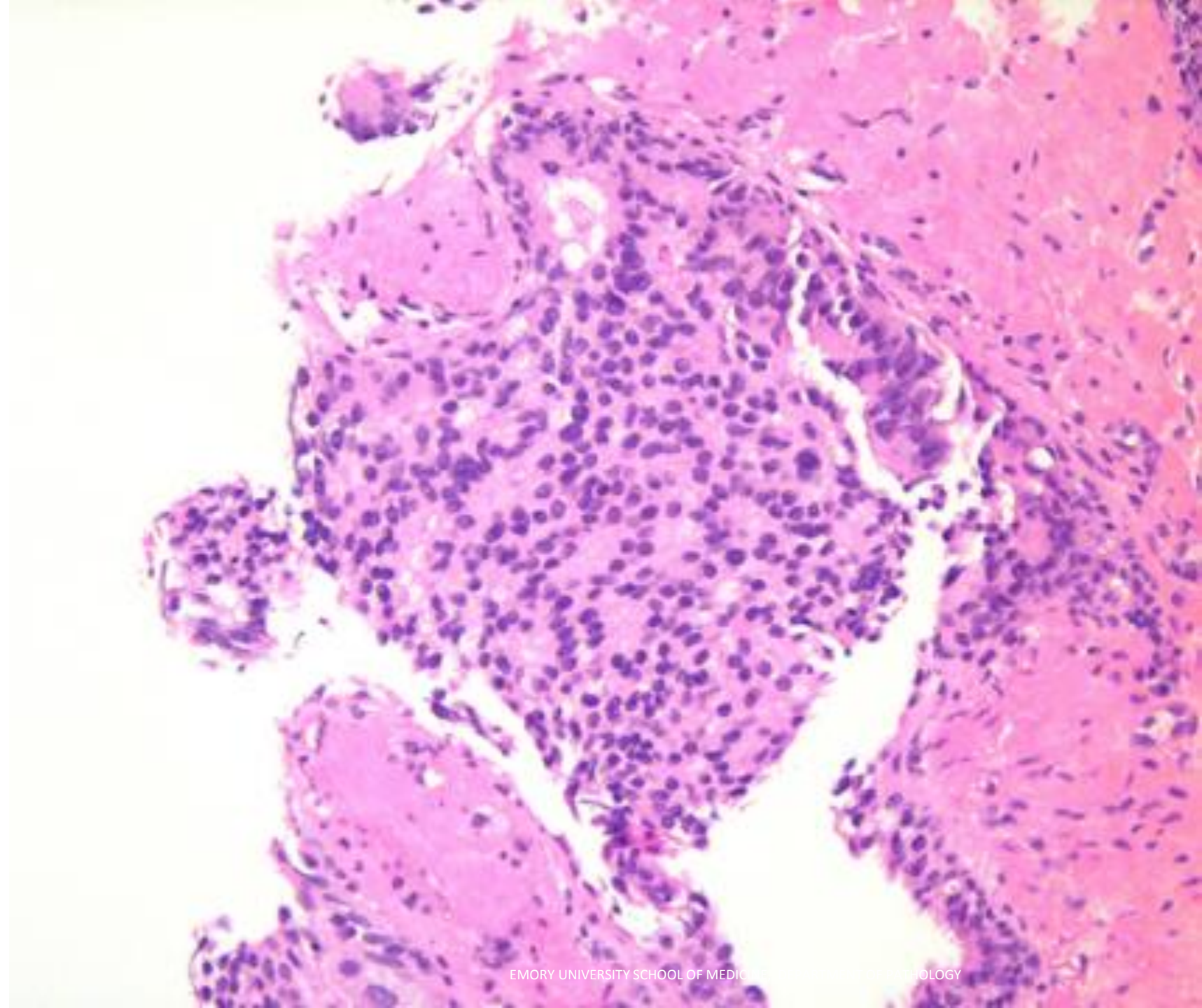
Overall incidence of IDC is lower than 3%

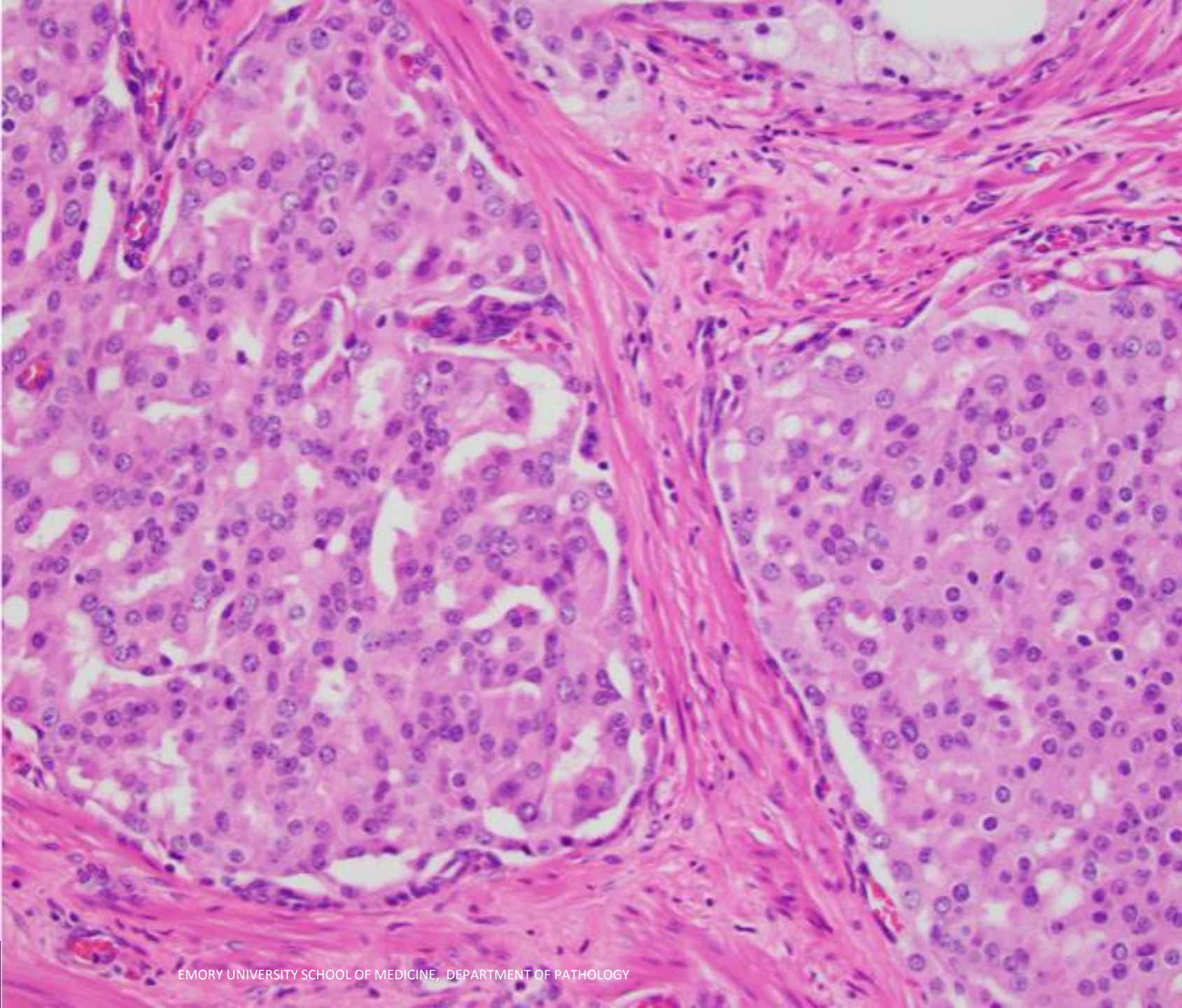
Isolated IDC in needle core biopsies (without concomitant invasive cancer) is between 0.06%--0.3%.

Studies call for aggressive treatment of IDC-P on biopsy, even in the absence of documented infiltrating cancer

In situ carcinoma or retrograde involvement of invasive carcinoma

Frequently associated with high-grade/score cancer and poor prognostic parameters at radical prostatectomy.





Intraductal Carcinoma: Diagnostic Criteria

Three major histologic patterns:

Dense solid/cribriform atypical
proliferation within ducts/ glands

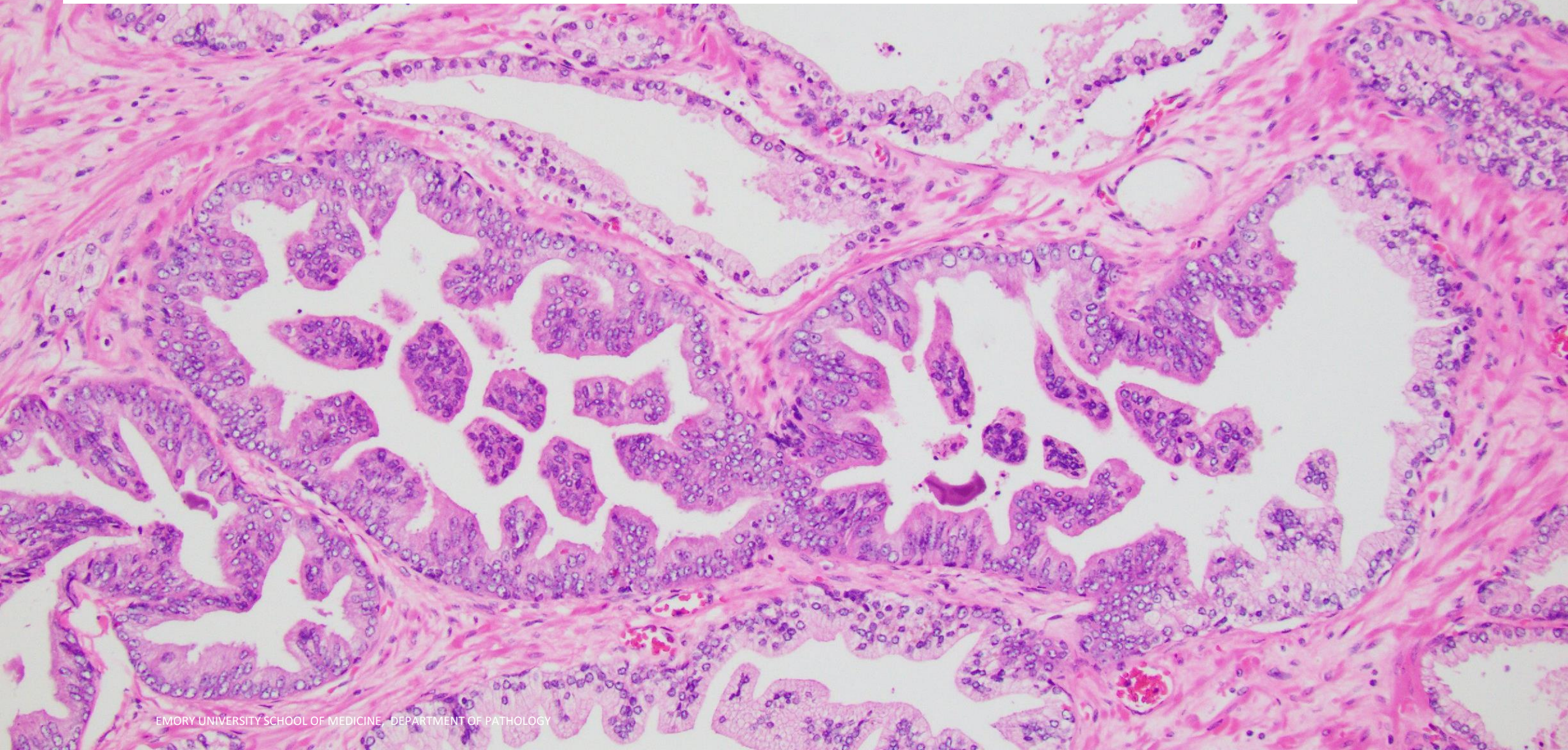
Loose cribriform/ micropapillary
growth with:

Marked nuclear atypia

≥ 6 times normal

Necrosis

Atypical Intraductal Proliferation



Intraductal Carcinoma of the Prostate

What We All Agree On

Clinically relevant
on needle biopsies/
TURP

Should always be
mentioned

- (Bx
and Prostatectomies)

If Intraductal
carcinoma is the
only lesion: Do not
grade it

Associated
with Poor Prognosis
when present
with GS6/GG1

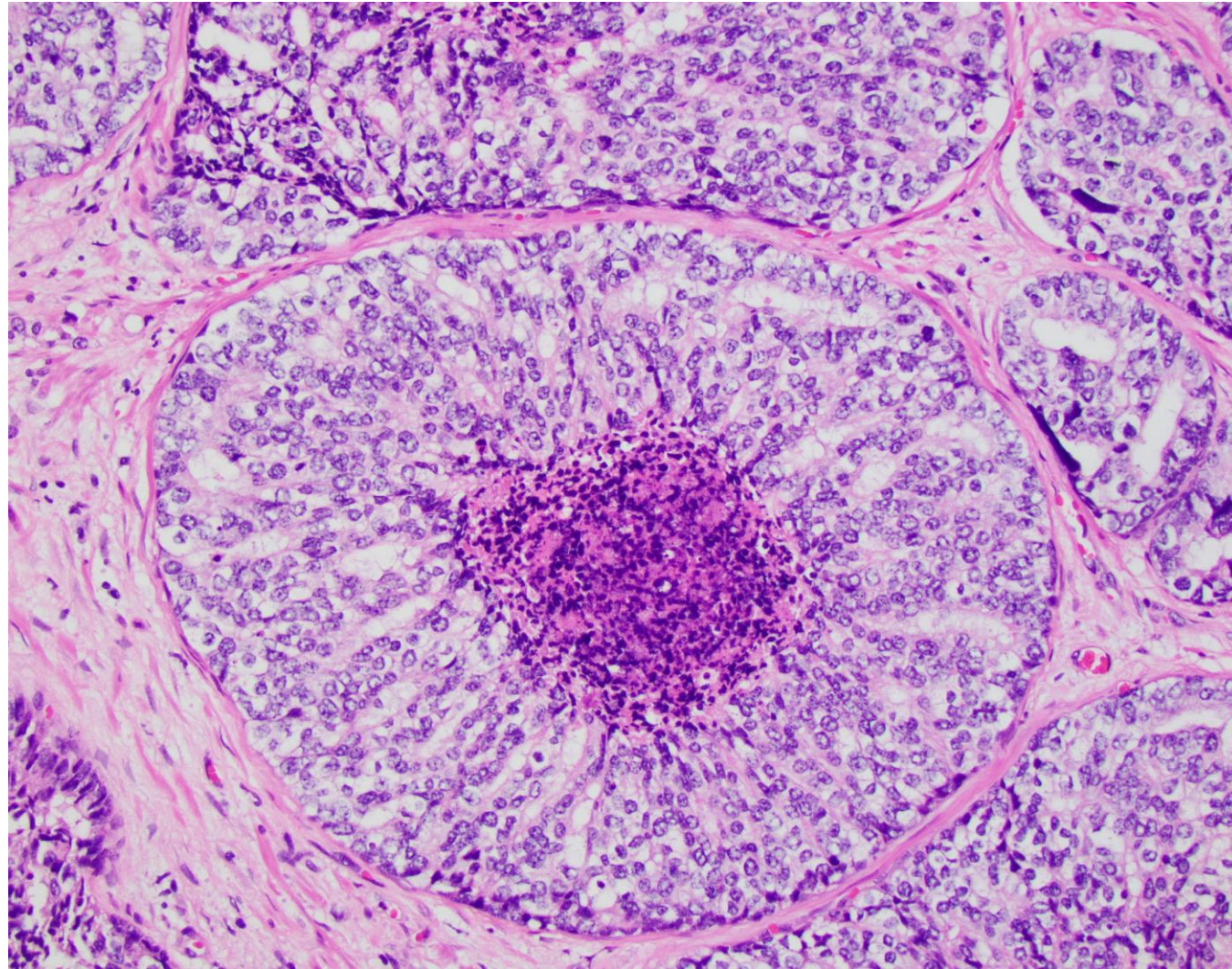
Intraductal Carcinoma of the Prostate

What is Debated

Should we
perform PIN3 to
exclude IDC

- When it changes the GS/GG

Lesions which upgrade
upgrade to pattern 5
e.g. comedo necrosis?
necrosis?

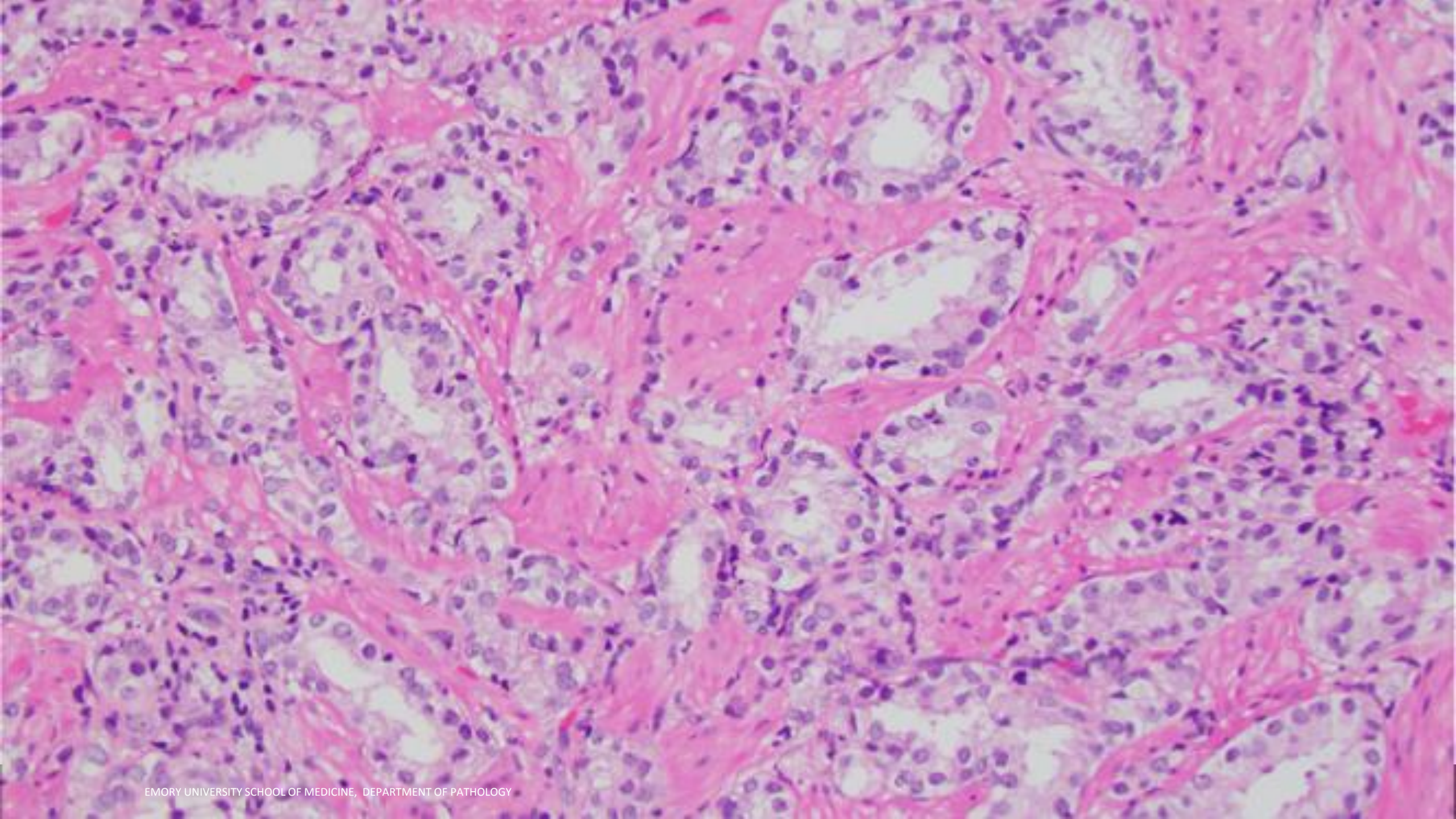


Reporting Percentage of Gleason Grade 4

Percentage Pattern 4 should be recorded for Gleason score 7 (Grade Group 2 and 3):

3+3 versus 3+4

3+4 versus 4+3



Defining Minor/Tertiary Pattern

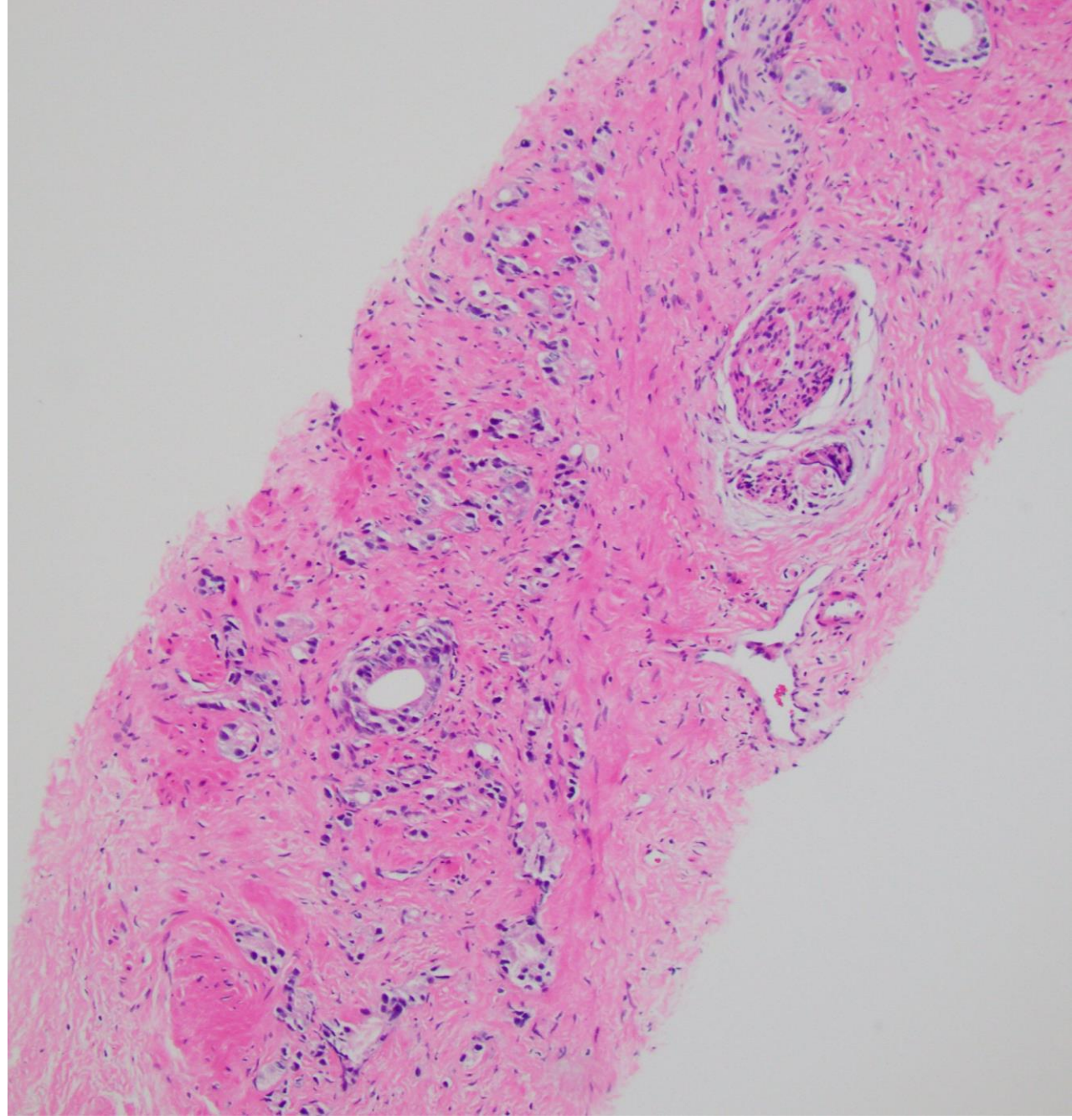
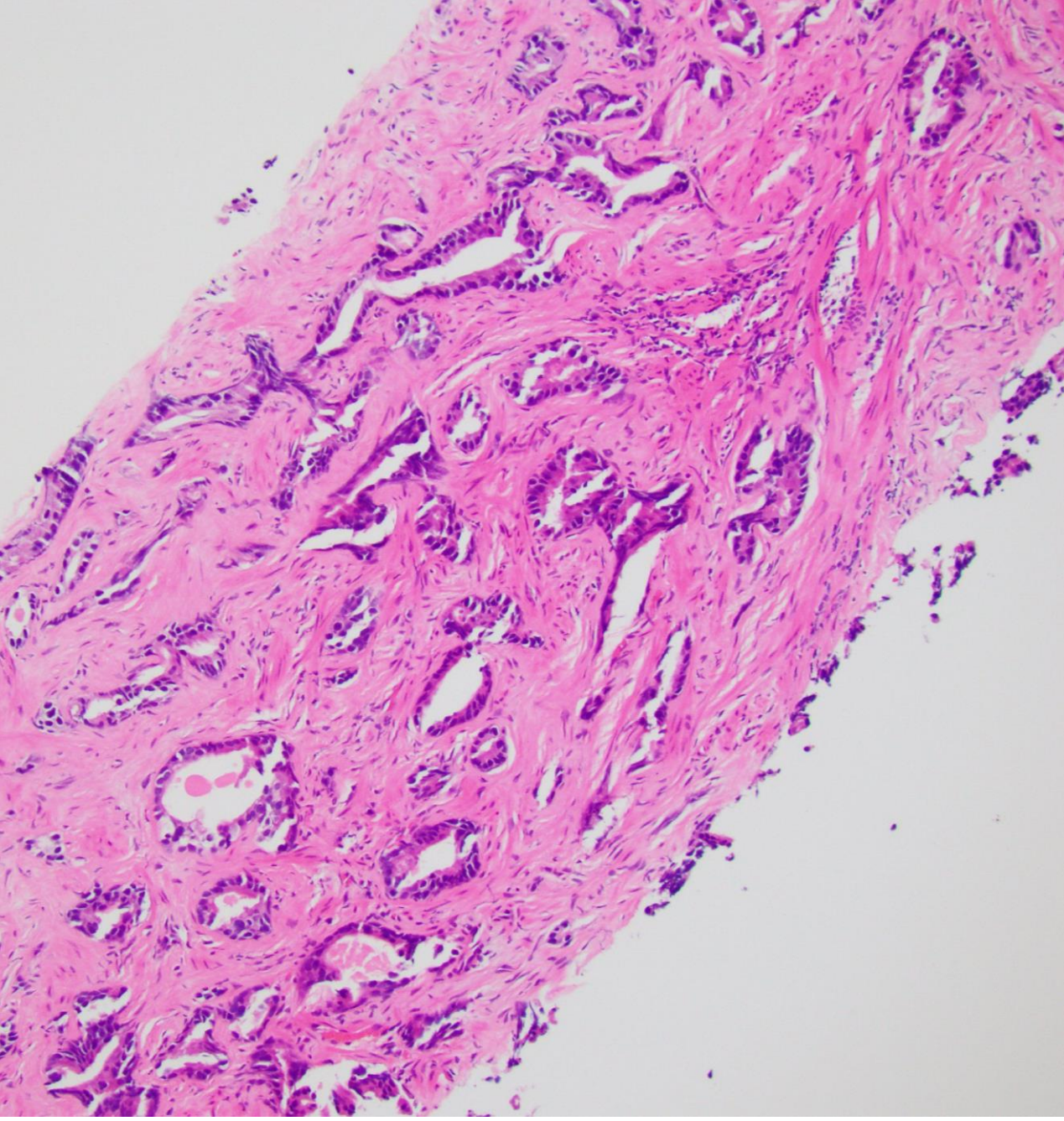
Higher grade pattern (4 or 5), which represents <5% of tumor volume.

Needle core Biopsy:

- Minor / Tertiary pattern is incorporated into Gleason score
- Gleason Score (most common+highest)

Radical prostatectomy:

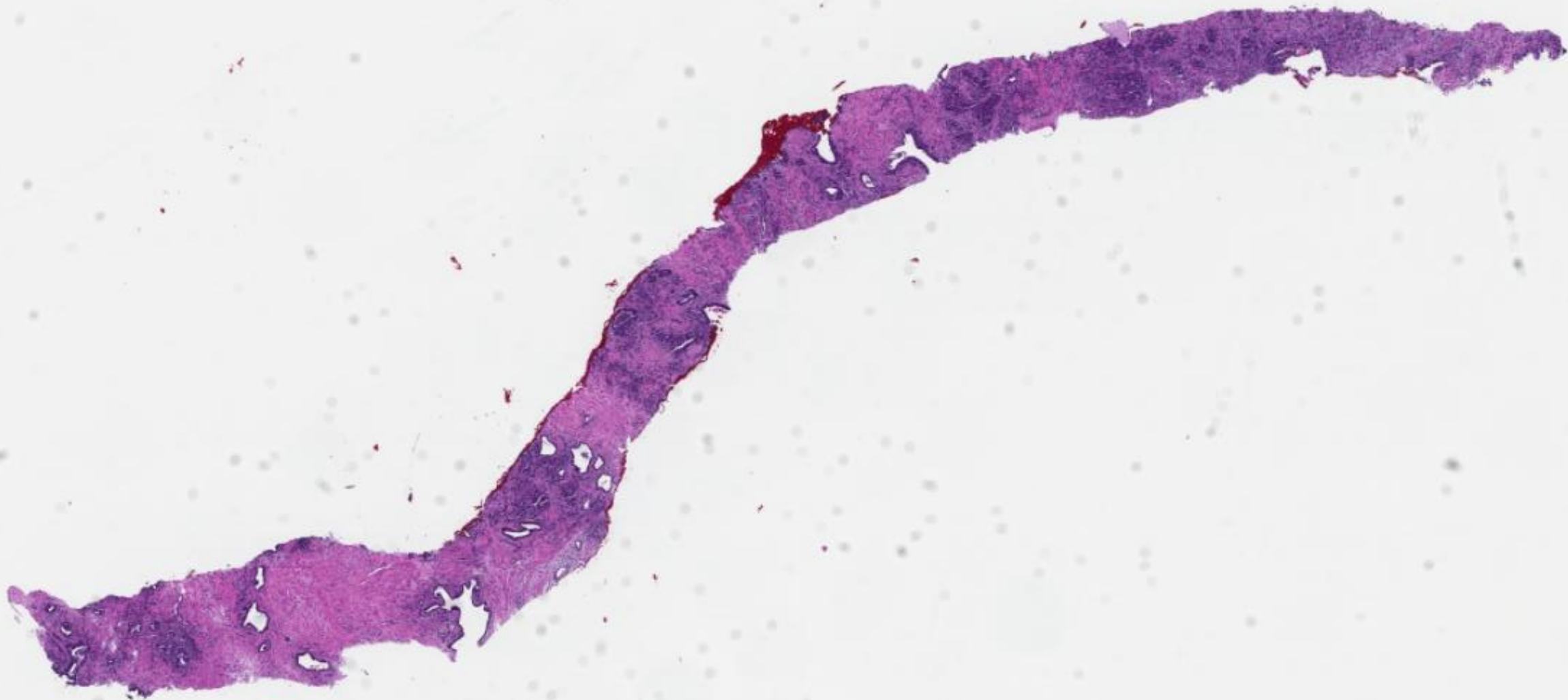
- Gleason Score (most common+second most common $\geq 5\%$)
- Minor / Tertiary highest Grade pattern $\leq 5\%$

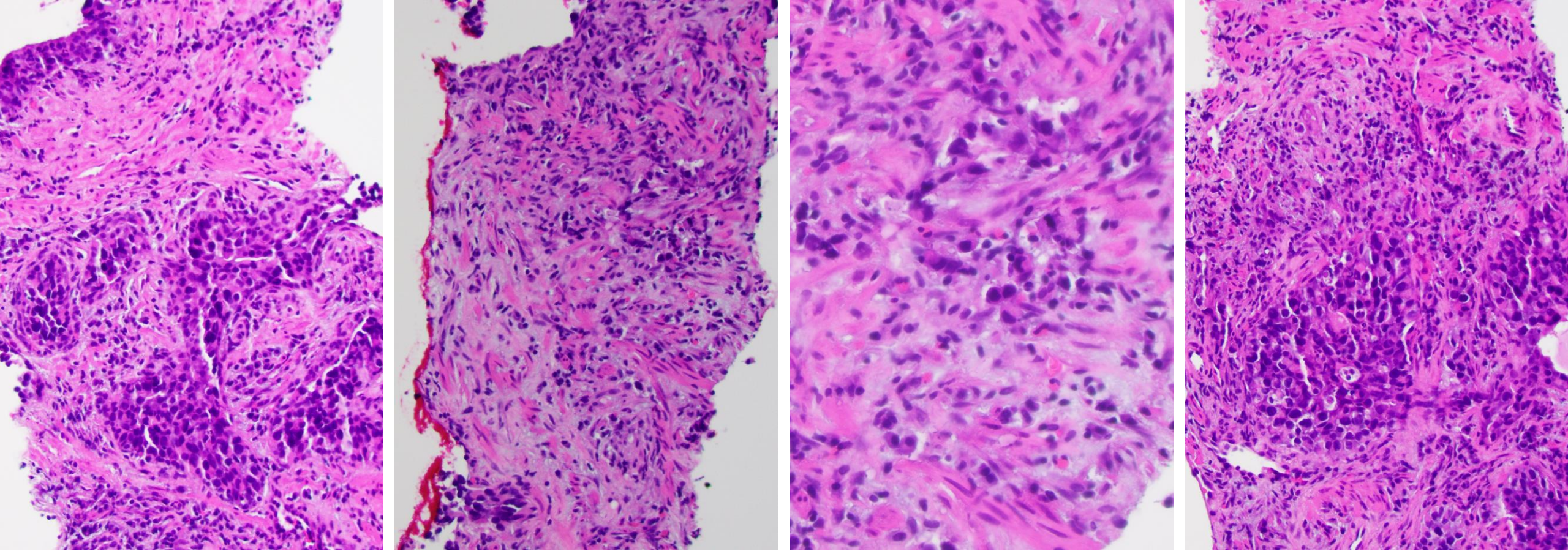


Case 3

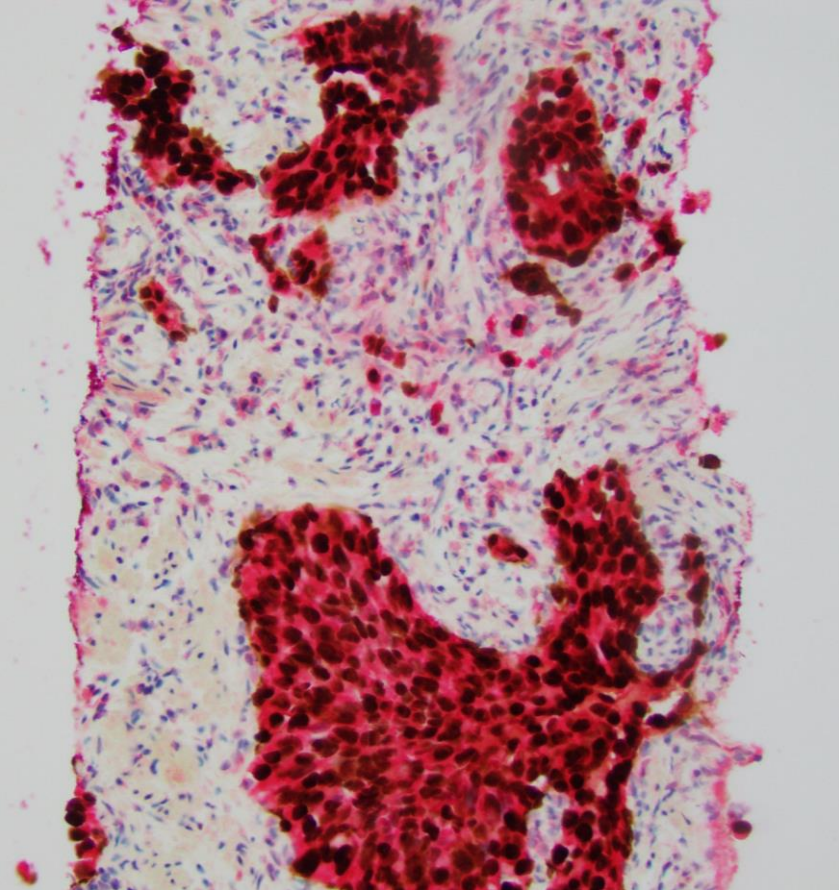
51 year old male, previously healthy, with **lower urinary tract symptoms**, including frequency and urgency up to every 15 minutes.
PSA was 5.1

Family history of skin cancer in the mother.

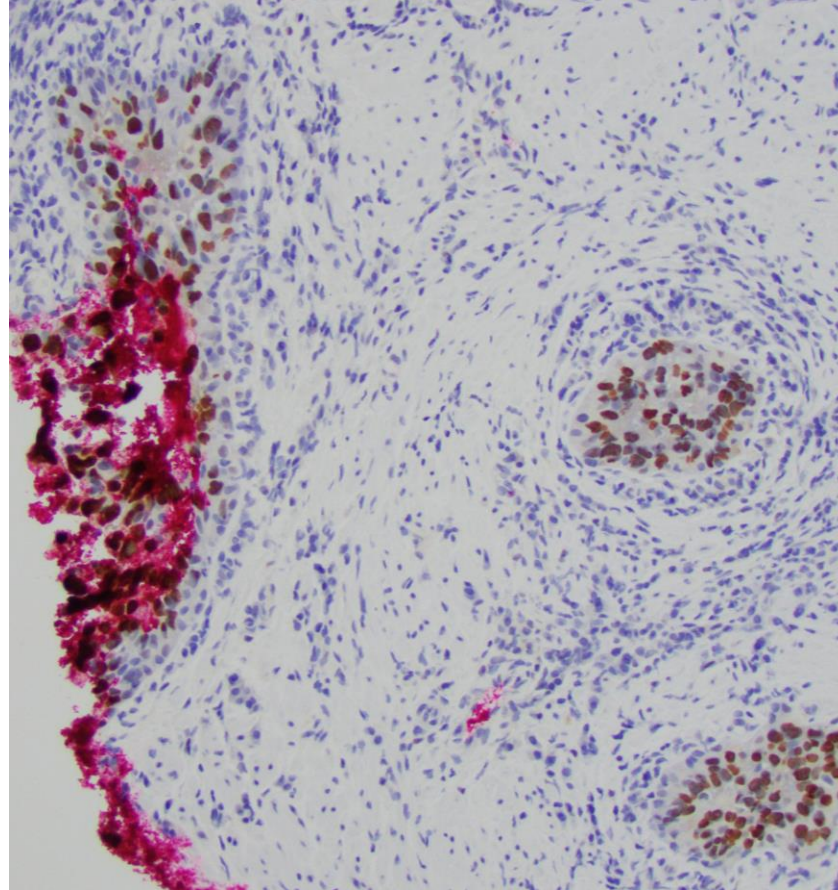




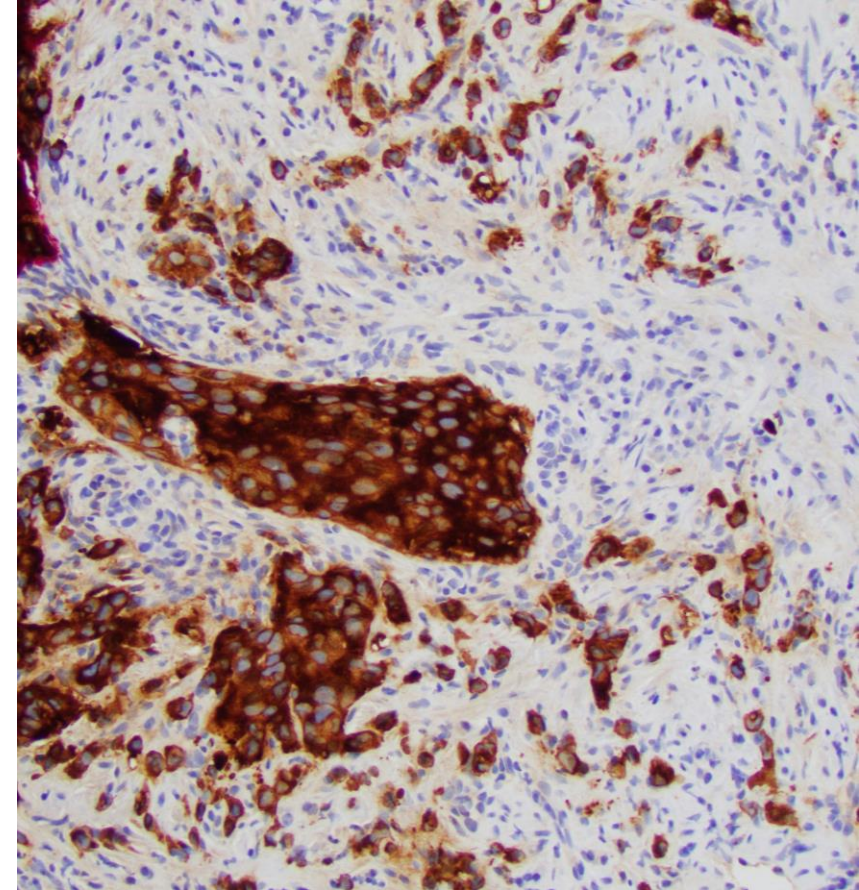
How will you grade this lesion?



PIN3 cocktail



GATA3



CK OSCAR

Plasmacytoid Urothelial Carcinoma Involving the Prostate

Summary of Prostatic Grading Update

Intraductal carcinoma

- Intraductal carcinoma of the prostate should always be mentioned
- Intraductal carcinoma without invasive carcinoma is not graded.
- Perform PIN3 if the amount of possible IDC changes the GS/GG or invoked a Gleason Pattern 5
- Associated with high GG and stage

Report the percentage of Gleason Pattern 4 in GG2 and GG3

Minor tertiary Pattern are reported only on radical prostatectomy

- High grade pattern $\leq 5\%$



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