Prostate Tumors

Acinar Adenocarcinoma   *(The most common/default type of "Prostate Cancer")*

An invasive adenocarcinoma consisting of neoplastic prostatic epithelial cells with secretory differentiation arranged in a variety of patterns, typically without basal cells.

Most common cancer in men and second leading cause of cancer death in the U.S.A.

Prevalence is <u>strongly correlated with age</u> (older = higher prevalence)
Majority are **multifocal**, often with 2-3 separate tumors in each prostate.
Most commonly located in **posterior/posterolateral peripheral** gland.
Early tumors are often asymptomatic. Locally advanced prostate cancer mimics BPH with urinary symptoms. Bone very common site of metastasis → bone pain and pathologic fractures.

Morphology: Always use *multiple* features (there is no single feature to Dx!)

Nuclear Features:
- Prominent nucleoli
- Nuclear enlargement
- Nuclear hyperchromasia
- Mitotic figures
- Apoptotic bodies

Cytoplasmic features:
- Amphophilic cytoplasm
- Sharp luminal borders

Luminal contents:
- Blue-tinged mucin
- Pink amorphous secretions
- Crystalloids

Architecture:
- Crowded small glands
- Linear row of atypical glands spanning the width of a core
- Small glands on both sides of a benign gland
- Haphazard, infiltrative pattern
- Confluent or Cribriform glands
- Single cells

Absent basal cell layer (can highlight with IHC, as fibroblasts may mimic basal cells)
Usually lack desmoplastic stroma. When present, often associated with high-grade carcinoma.
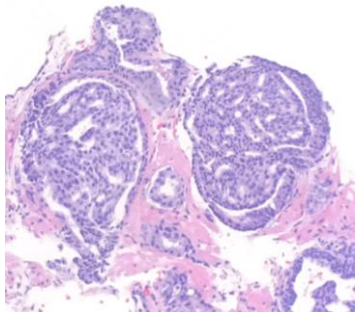
Findings more common in <u>benign</u> glands:
- Atrophic cytoplasm
- Merging with benign glands
- Corpora amylacea
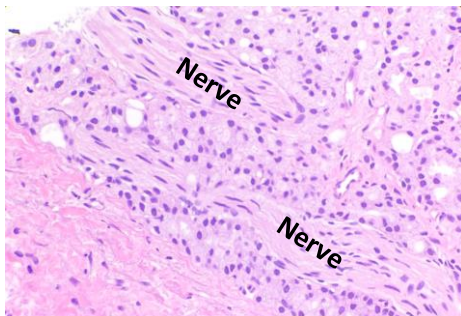- Inflammation
- Lipofuscin
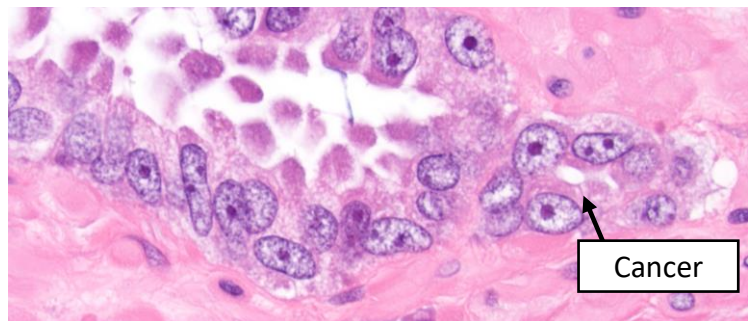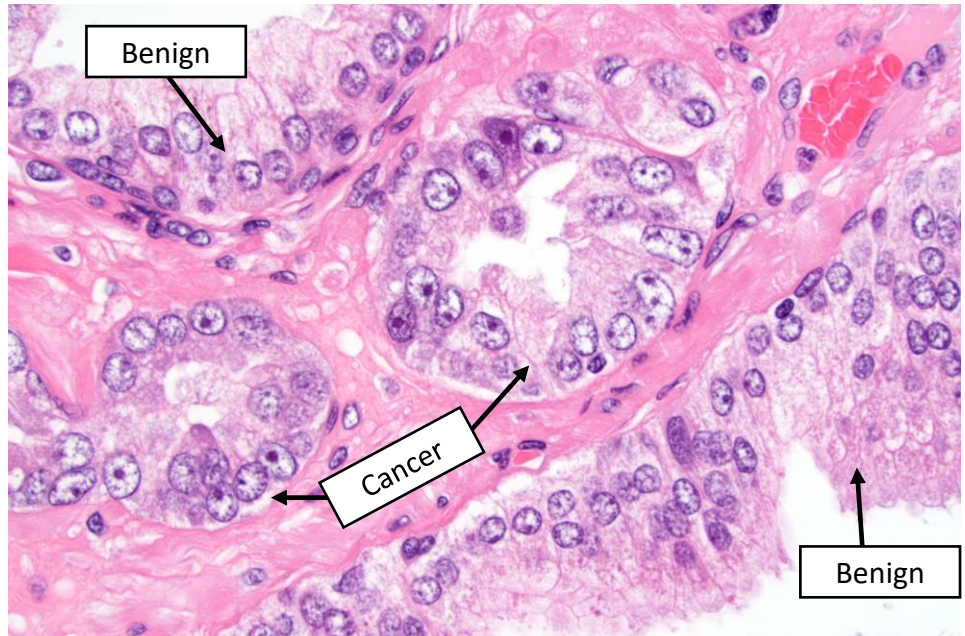
Features *Specific* To Malignancy

Glomerulations
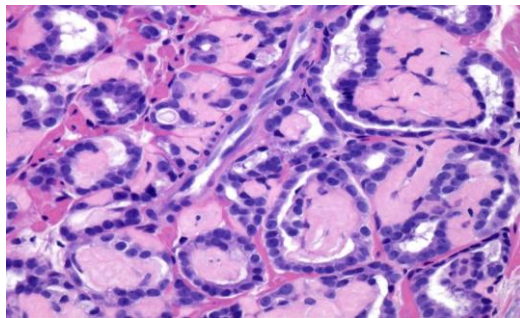Cribriform formations attached only to one edge of the surrounding gland

Perineural Invasion
To Dx malignancy, tumor must *completely* encircle nerve. (Benign glands may abut, but not encircle)

Nerve

Nerve

Mucinous Fibroplasia
(Collagenous micronodules)
Dense nodules of collagen (hyalinized mucin) surrounded and encased by epithelium

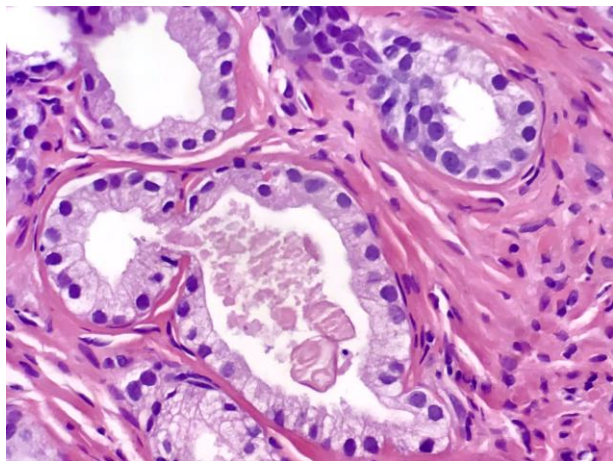# Specific Variants

(Same prognosis, unless otherwise mentioned)

Atrophic variant
Cytoplasmic volume loss (like atrophy), Often absent nuclear enlargement and nucleoli→ mimicking benign atrophy!
Luckily, conventional carcinoma often present nearby.
Can be sporadic or after therapy.
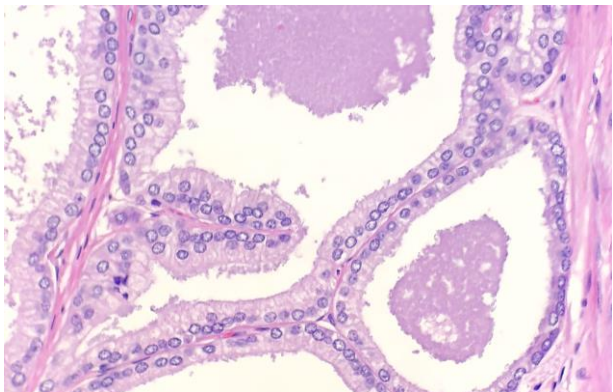Often Gleason pattern 3 (small infiltrative glands)

Pseudohyperplastic variant
Simulates luminal cell hyperplasia→ papillary infoldings, luminal undulations, and branching.
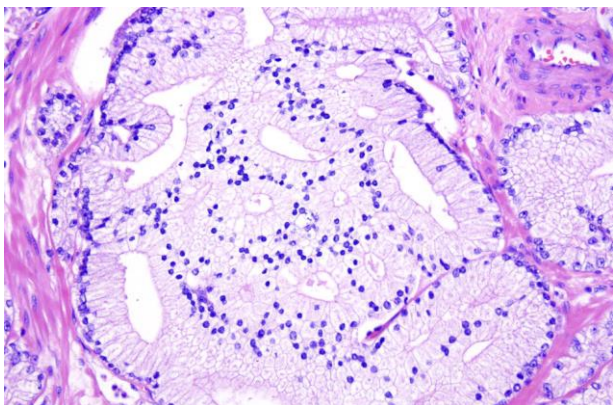Round nuclei, not pseudo stratified, with prominent nucleoli.
Often relatively pure and well-circumscribed.

Foamy gland variant
Abundant foamy/xanthomatous cytoplasm and small, pyknotic nuclei
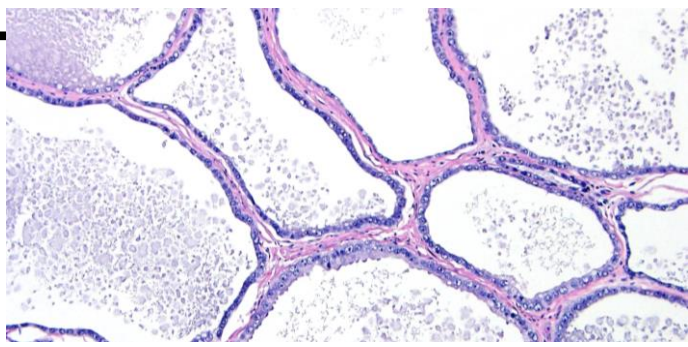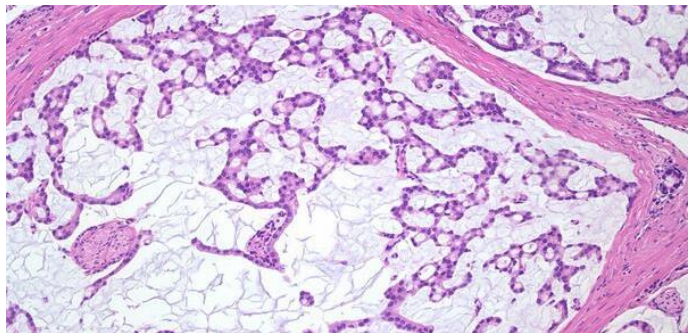Usually combined with usual type (rare to be pure)

Microcystic variant
<u>Large, dilated round glands with flattened luminal cells</u>→ mimic benign atrophy.


Mucinous (colloid) variant
<u>≥25% of tumor has extracellular mucin pools</u>
Can only be Dx'd on prostatectomy (on Bx say "mucinous features")
Mentally subtract mucin for grading.


Signet ring-like variant
<u>≥25% of tumor is composed of infiltrative **single** cells with large **vacuoles**</u> (that do not actually contain mucin). Gleason pattern 5.
Poor prognosis. Must consider GI metastasis.

Notably, vacuoles can be seen in any grade prostatic cancer (vacuoles ≠ Signet ring-like)!
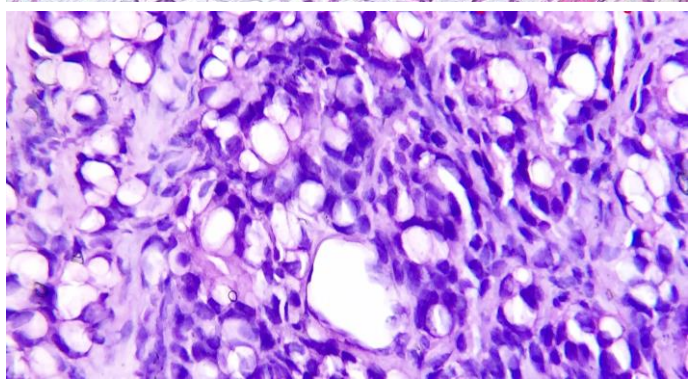
Sarcomatoid variant (Carcinosarcoma)
Biphasic with both epithelial and mesenchymal differentiation. Poor prognosis.
Can see various heterologous elements.
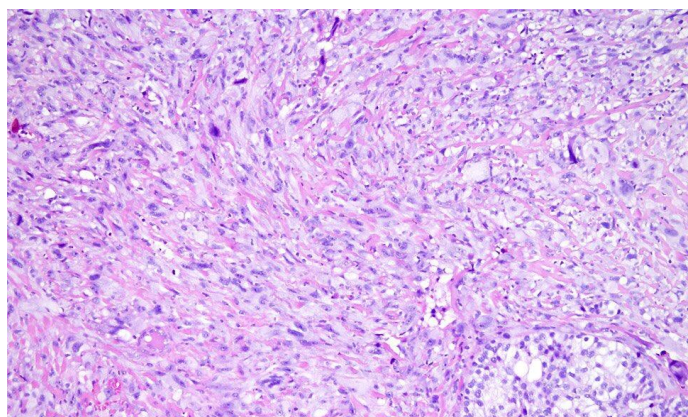
Hypernephroid variant (vanishing variant)
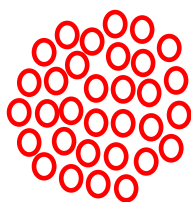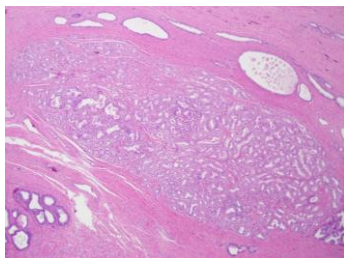Sheets of cells with abundant clear cytoplasm.
Gleason pattern 4
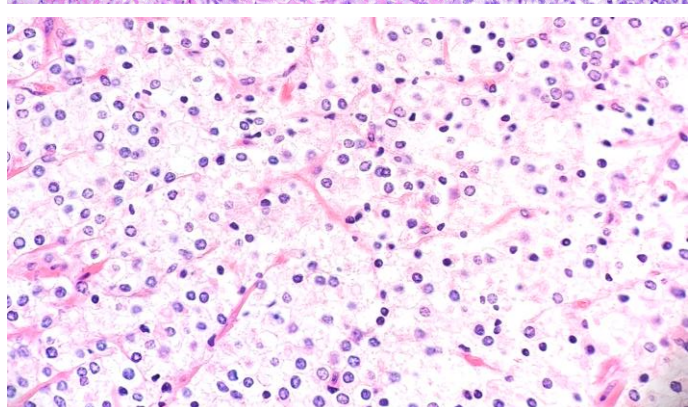
Pleomorphic giant cell variant (not pictured)
Giant bizarre anaplastic cells with pleomorphic nuclei and with<u>out</u> a spindle cell component.
Poor prognosis.

Gleason Grading
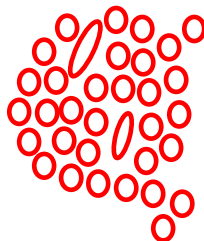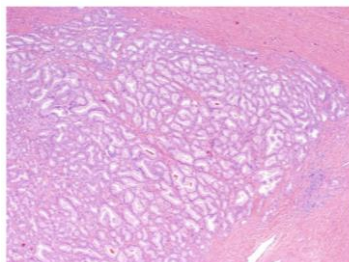*Based on architecture at <u>low power</u> (using 4x or 10x objective).*

1

Circumscribed nodule of closely packed but separate, uniform, rounded to oval, medium-sized acini

Should **not** be diagnosed regardless of the type of specimen, with extremely rare exceptions
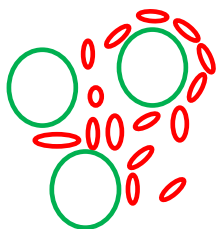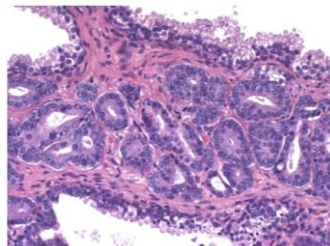
2

Fairly circumscribed, yet at the edge of the tumor nodule there may be minimal infiltration

Do not diagnose on biopsy, rarely diagnosed regardless of specimen.

Glands are more loosely arranged and not quite as uniform as Gleason pattern 1

3

Well-formed glands *(with lumina)*
Separate, discrete, Non-fused

Infiltration

4
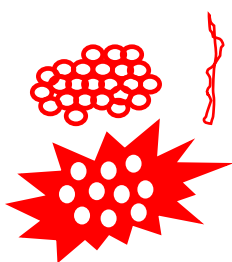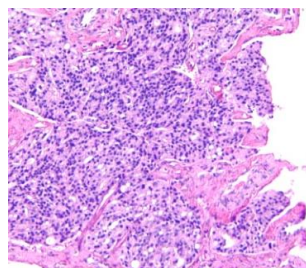
Ill-defined, poorly formed glands
Gland fusion
Cribriform glands
Hypernephromatoid
Glomerulations

Ductal Adenocarcinoma (without necrosis)

==**Often Disqualifies from Active Surveillance**==

5
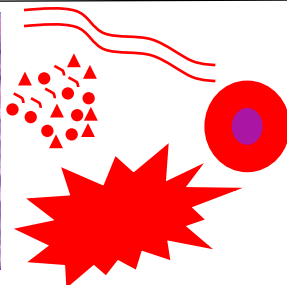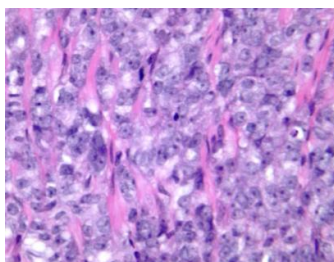
Essentially **no glandular differentiation:**
- Single cells
- Cords
- Solid sheets
- Linear arrays

Comedocarcinoma with central necrosis

Notes: Given the importance of distinguishing between patterns 3 and 4 for active surveillance, getting levels can be helpful to differentiate tangential sectioning of small well-formed glands (pattern 3) from poorly-formed glands (pattern 4) and also for pattern 4 vs 5.

Only very occasional poorly-formed glands is insufficient to diagnosis pattern 4. In cases with borderline morphology and/or artifacts, the lower grade should be favored. Have a low threshold for showing it to a colleague!

Gleason Scoring

Biopsies:

Most common pattern + Second most common pattern = Score

- If the tumor has only one pattern, then add the same pattern twice.
- No tertiary pattern assigned.
- In the setting of high-grade cancer one should ignore lower-grade patterns if they occupy less than 5% of the area of the tumor. (e.g., 98% pattern 4 and 2% pattern 3 → 4+4=8)
- High-grade tumor of any quantity, as long as it was identified at low to medium magnification should be included. (e.g., 98% pattern 3 and 2% pattern 4 → 3+4=7)
- On needle biopsies with patterns 3, 4, and 5, both the primary pattern and the highest grade should be recorded. Consequently, tumors with Gleason score 3 + 4 and a tertiary pattern 5 would be recorded as Gleason score 3 + 5 = 8.

Prostatectomies:

Most common + Second most common = Score, with tertiary pattern if present

- In the setting of high-grade cancer one should ignore lower-grade patterns if they occupy less than 5% of the area of the tumor.

Grade Groups

Grade Group	Gleason Score	
1	≤6	Only individual discrete well-formed glands
2	3+4=7	Predominantly well-formed glands with a lesser component of poorly formed/fused/cribriform glands
3	4+3=7	Predominantly poorly formed/fused/cribriform glands with a lesser component of well-formed glands
4	8	- Only poorly formed/fused/cribriform glands - Predominantly well-formed gland and lesser component lacking glands - Predominantly lacking glands and lesser component of well-formed glands
5	9-10	Lack gland formation (or with necrosis) with or without poorly formed/fused/cribriform glands

For cases with >95% poorly formed/fused/cribriform glands or lack of glands on a core or at radical prostatectomy, the component of <5% well-formed glands is not factored into the grade.

Immunohistochemical Stains

Markers of Prostatic Origin

Prostate Specific Antigen (**PSA**), Prostatic Acid Phosphatase (**PSAP**), **NKX3.1**, Prostein

Each marker ~95% sensitive. NKX3.1 is the most specific.
PSA & PSAP can decrease after androgen deprivation therapy and are less specific (e.g., also get some salivary gland tumors).

Markers of limited utility due to poor sensitivity or specificity: ERG, AR, AMACR.

Cancer vs Benign Glands
Most useful for the _confirmation_ of a small quantity of tumor.

Basal cells are _absent_ in invasive prostatic adenocarcinoma (usually).

Stains for basal cells
Cytoplasm: High-molecular weight cytokeratins (HMWCK) (e.g., 34βE12, CK5/6)
Nuclear: p63, p40

AMACR (aka P504S or Racemase): frequently overexpressed in glandular neoplasia of the prostate (~90%) with granular cytoplasmic staining. Needs to be done in combination with basal markers as HGPIN is often positive.

ERG: expression is highly specific for neoplastic prostate glands, but has a low sensitivity (~50%), so doesn't have much value over AMACR.

Notable Pitfalls:
Loss of basal cells is not specific for cancer and may be observed in benign mimics like atrophy, partial atrophy, and adenosis.
Rare cases of adenocarcinoma can stain for basal markers (even though they don't have basal cells) in a non-basal distribution.
AMACR expression can be seen in benign mimics such as atrophy, adenosis, and nephrogenic adenoma.
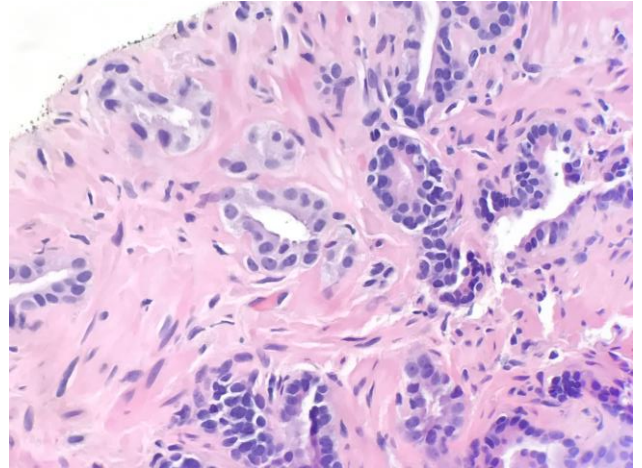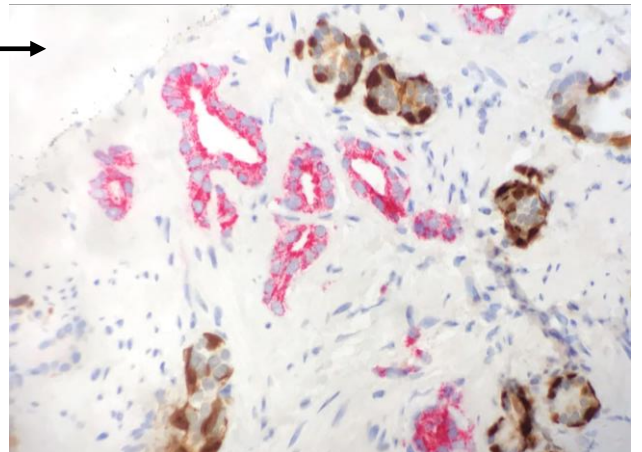

Common triple stain:
HMWCK + p63 → **Brown cytoplasmic and nuclear, respectively, staining of basal cells in benign glands**

AMACR → **Red cytoplasmic staining in neoplastic glands (that in this case are also lacking basal cells) supports the diagnosis of cancer.**

Note: faint pink blush may be seen in benign glands

Diagnosing Limited Cancer

Major Criteria for diagnosing prostate cancer (no single criteria is diagnostic):
1) **Infiltrative growth**
2) **Absence of basal cells**
3) **Nuclear atypia (nuclear enlargement with prominent nucleoli)**

How many glands do you need?
There is no absolute number, but many urologic pathologists like to see **at least 3 glands** with cytologic/architectural features of cancer.

**Atypical Small Acinar Proliferation ("ASAP") suspicious for cancer**
Or
Atypical glands suspicious for cancer ("ATYP")

A descriptive term (not an entity) designed to be used when you have a collection of small glands suspicious for cancer but lack definitive diagnostic features or they are too small to be certain that they do not represent the edge of a benign lesion.

IHC in ASAP: Basal cells may be missing in benign small glands, so, immunohistochemistry is primarily useful to disprove cancer, not to prove cancer. Detection of even rare basal cells in any of the glands of the suspicious population essentially excludes carcinoma for the entire population.

Clinical follow-up for ASAP: Repeat biopsy
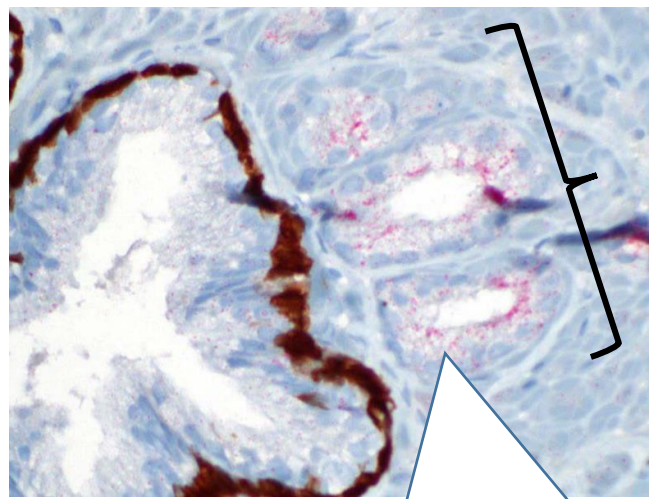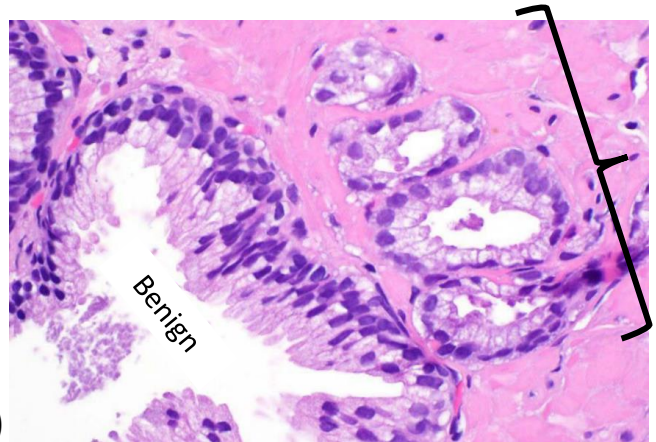
Benign

What to do with these 4 glands?
This is potentially a borderline case. If this is all you had, it'd probably safest to go "ASAP" given how limited they are and the absence of prominent nucleoli, but some might call it 3+3

Benign Glands	Prostatic Adenocarcinoma
Big, regularly spaced glands	Small, infiltrative angulated glands with haphazard spacing
Papillary infoldings	Sharp luminal contours
Small nuclei without nucleoli	Large nuclei with prominent nucleoli and frequent hyperchromasia
Abundant pale, clear apical cytoplasm	Amphophilic cytoplasm
Corpora amylacea	Eosinophilic or blue mucin secretions

Biopsy Reporting

For each biopsy specimen/location report:
- Gleason Score and Grade Group
- Fraction of cores with cancer (or for TURPs the number of positive chips and total number of chips)
- Linear extent of cancer in each core (percentage and/or length)
- Perineural invasion or extraprostatic extension (if present)
- Percentage of pattern 4 should be recorded in cases with a Gleason score 7 (with very limited pattern 4, the patient may still be eligible for active surveillance)

> **PROSTATE, LEFT MEDIAL TRANSITION ZONE, BIOPSY:**
> **- Prostatic adenocarcinoma, Gleason Score 3+4=7 (Grade Group 2), 10% Pattern 4, Involving 1 of 1 cores, 25% of tissue. Tumor is/ is not cribriform.**

Discontinuous Cancer

Controversial! Several studies have shown that the linear total ("end to end") method correlates better with prostatectomy findings as they often represent portions of the same tumor. However, there is no consensus so consider reporting *both* for now.

5%   **Additive Total = 10%**   5%

Linear Total = 95%
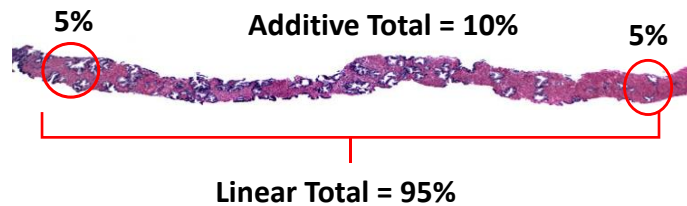
Extraprostatic Extension   "EPE"

Presence of tumor beyond the confines of the prostate gland. EPE *Includes*:
- **Invading fat**
- Involving loose connective tissue beyond the plane of the prostate (does not need to be directly touching adipocytes)
- Involving perineural spaces in the neurovascular bundles
- In the apex and base, EPE is determined when the tumor extends beyond the confines of the normal glandular prostate (can be hard to clearly define)
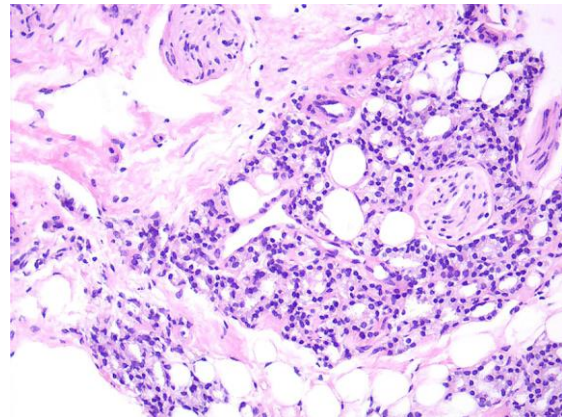
Invasion of the urinary bladder neck: neoplastic glands involve the thick intersecting smooth muscle bundles characteristic of the bladder neck region in the absence of associated benign prostate tissue.

Seminal vesicle involvement: invasion of the muscular wall of seminal vesicle (must be *Extra*prostatic)

Warning: Invasion of skeletal muscle does not count as skeletal muscle is present in the anterior and apical parts of the prostate

Genetics

Recurrent mutations in the ETS family of transcription factors: most commonly **TMPRSS2-ERG fusion**
Other frequent mutations: TP53, PTEN

Prostate cancer is one of the most heritable cancer types, driven by numerous common mutations (and some rare germline mutations). This risk is mostly associated with many SNPs with each having relatively low risk/penetrance (but the effect can be multiplicative).

BRACA2→ significantly increased risk of prostate cancer

Treatment effect

Can show minimal or extensive changes in both benign and malignant glands. Use stains liberally.
Do not grade if significant treatment effect (behave better than grade would suggest).

Radiation therapy:
Benign glands: atrophic, basal cell immunophenotype, may show marked radiation atypia.
Adenocarcinoma: often inconspicuous with vacuolated cytoplasm and smudged/ inconspicuous nuclei/nucleoli

Hormonal therapy:
Benign glands: diffuse atrophy with prominent basal cells
Adenocarcinoma: "Clear cell, nucleolus-poor": atrophic with vacuolated cytoplasm and inconspicuous nucleoli

Benign Gland with Radiation atypia

Tumor with Treatment effect
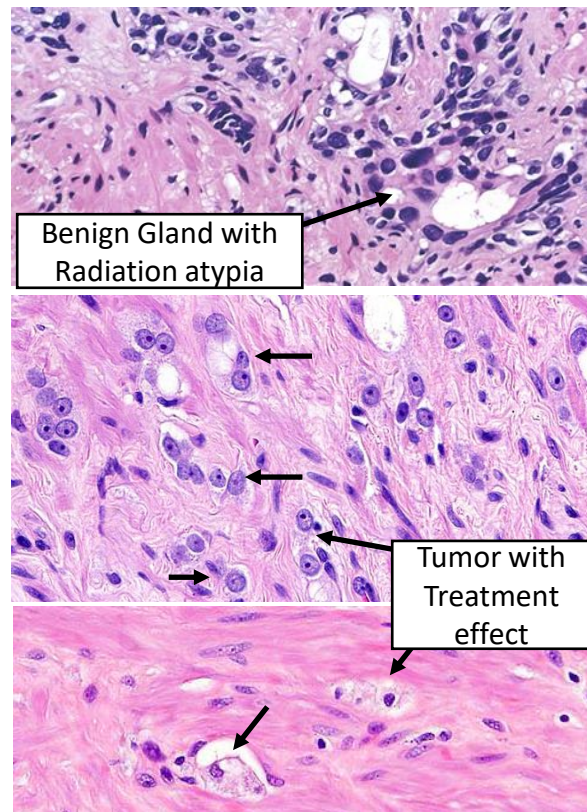
Active Surveillance

Management strategy where patients diagnosed with prostate cancer undergo **regular follow-up** with serum PSA tests and repeat biopsies (looking for progression), rather than receiving immediate definitive treatment with curative intent. Focus on low and very low risk patients

NCCN Inclusion Criteria:
Absolute (Low risk):
- Gleason Score ≤6
- PSA <10 ng/mL
- Clinical stage <T2a (Tumor involves one-half of one lobe or less)

Especially if (*Very* low risk):
- Fewer than 3 prostate biopsy cores positive, all ≤50%
- PSA density <0.15 ng/mL/g

PNI allowed

NCCN Progression Criteria: *(initiates transition to curative therapy)*
- Gleason grade 4 or 5 on repeat biopsy
- Prostate cancer found in a greater number of biopsies or greater extent of biopsies

Excluded if: any variant other than acinar adenocarcinoma (e.g., ductal, sarcomatoid, small cell), intraductal carcinoma

Active Surveillance Protocol: Serum PSA monitoring, Digital rectal exam, repeat prostate biopsies (6-12 months after initial) yearly for up to 10 years.

Intraductal Tumors
Non-invasive tumors growing within ducts

High-grade Prostatic Intraepithelial Neoplasia ("HGPIN")

Pre-invasive neoplastic proliferation. Often multifocal.

Cytologic changes resembling cancer:
- **Nuclear enlargement**
- **Prominent nucleoli**
- **Hyperchromasia**
- **Clumped chromatin**

Although non-invasive, <u>basal cells may be patchy</u> (so be careful interpreting IHC!)

Four main architectures: tufting, micropapillary, cribriform, and flat

Often cytoplasmic AMACR staining

Clinical importance: associated with subsequent detection of cancer (more HGHPIN→ higher risk)
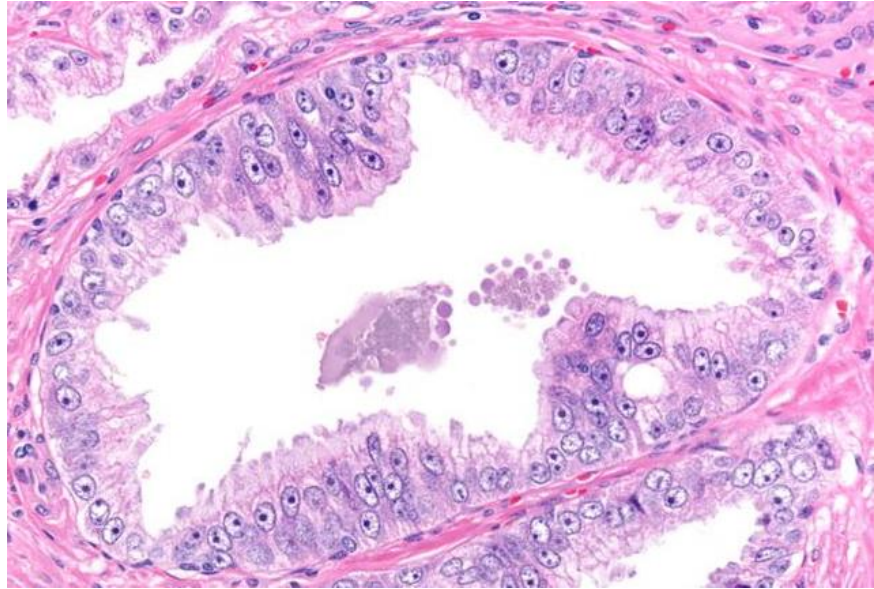
## Intraductal Carcinoma

Diagnostic requirement:
Malignant epithelial cells filling large acini and prostatic ducts, with <u>preservation of basal cells</u> with either:
- <u>Solid or dense cribriform pattern</u> (more glands than lumina), or
- A loose cribriform or micropapillary pattern with either:
    - <u>Marked nuclear atypia</u> (nuclei 6x normal or larger)
    - <u>Comedonecrosis</u>

Can be seen in two scenarios:
1) Intraductal spread of a high-grade invasive cancer (majority of cases)
2) Distinct precursor lesion (separate from HGPIN) with high risk of progression to cancer

IHC often required for diagnosis to demonstrate basal cells. Can show loss of PTEN (rarely seen in HGPIN)

Comedonecrosis
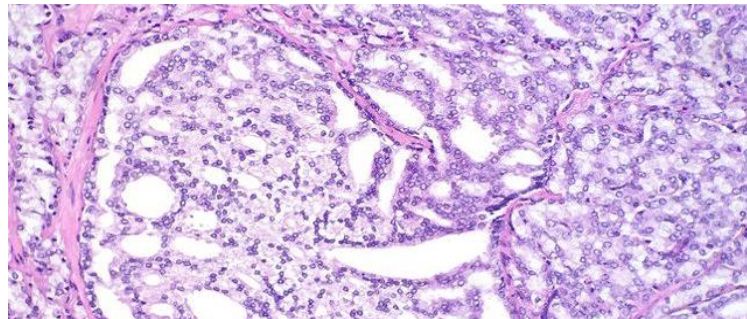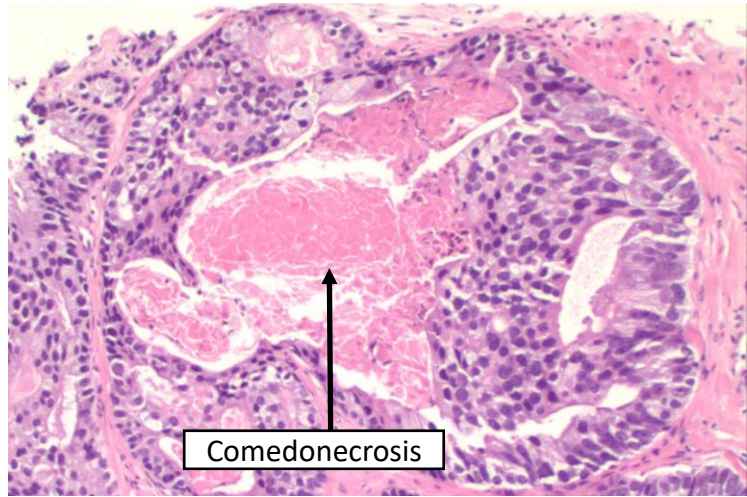
If seen on biopsy→ often treat with radical prostatectomy as highly associated with cancer and multiple adverse factors (high Gleason grade, high tumor volume, etc..). Sometimes repeat biopsy immediately. Controversial as to whether to incorporate into Gleason grading (Contradictory society guidelines).

If a lumen-spanning atypical lesion morphologically falls short of Intraductal Carcinoma, best to call "***Atypical Intraductal Proliferation***" and recommend immediate repeat biopsy.

Other Tumors

Ductal Adenocarcinoma

Subtype of prostatic adenocarcinoma with **tall, columnar, pseudostratified epithelium**

Cytoplasm is usually <u>amphophilic</u>.
Often **elongate nuclei** with more cytologic atypia that acinar type.
Prominent nucleoli, coarse chromatin, and lots of mitotic figures.
Frequent <u>necrosis</u>.

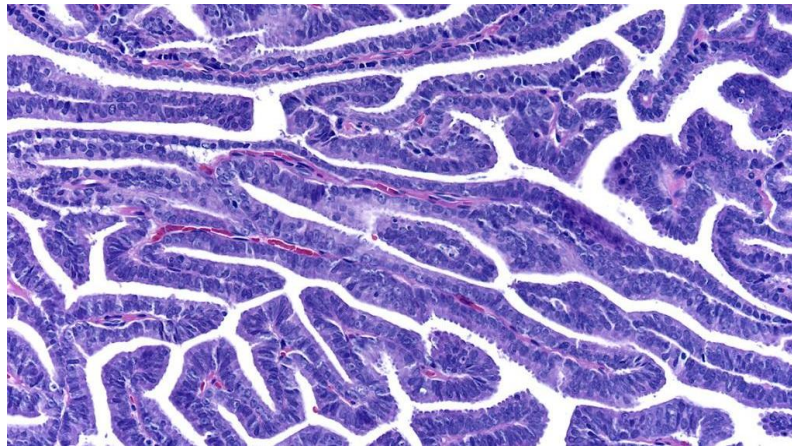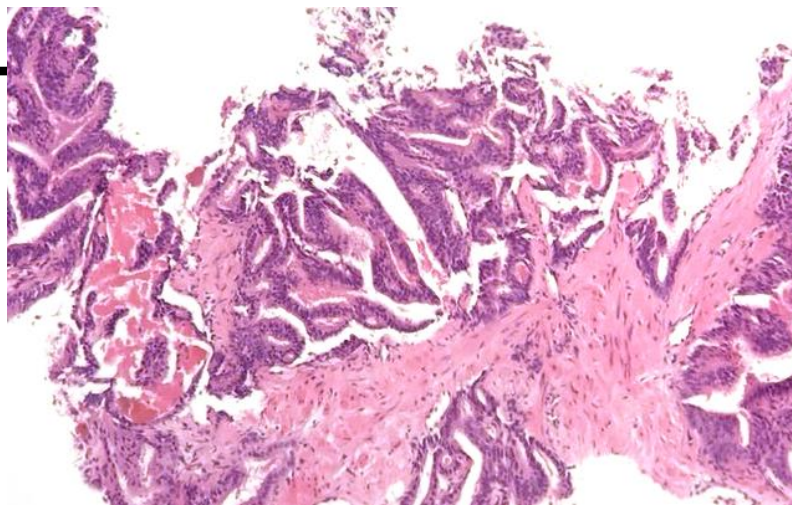Combination of **papillary and cribriform architecture** in dilated glands

Old name: "endometrioid" (looks like endometrioid adenocarcinoma of uterus)

Typically **periurethral location**

Similar IHC to acinar type: no basal cells, AMACR positive.

More aggressive than average acinar adenocarcinoma.
Grade as **pattern 4**, but if necrosis as 5

Basal Cell Carcinoma

Malignant neoplasm **composed of basal cells**

Most cases show various proportions of:
- **adenoid cystic/cribriform pattern** with inspissated secretions, and a
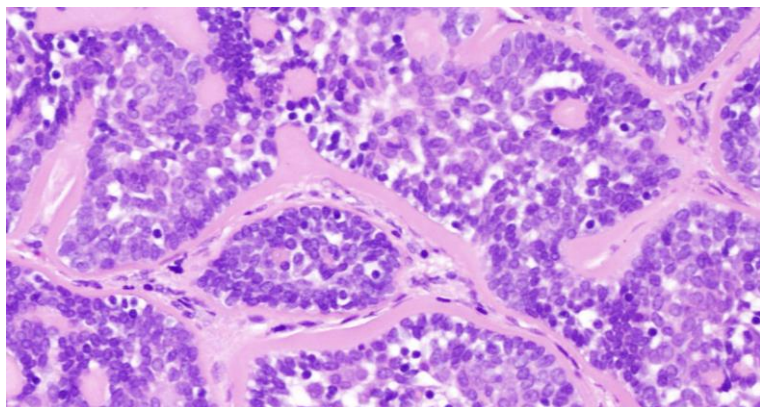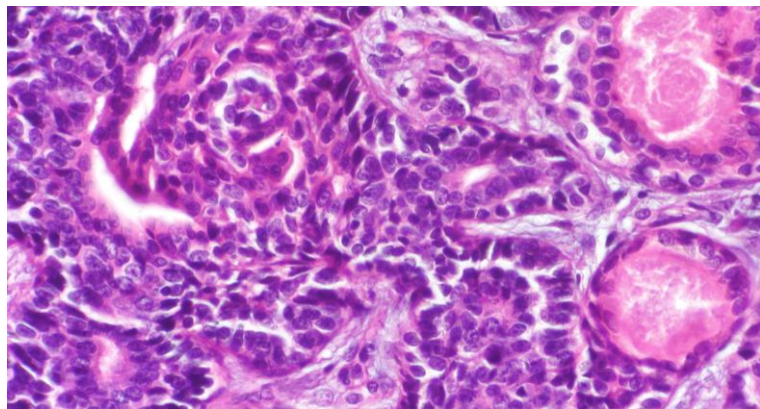- **basaloid pattern** with small solid nests of basal cells

Desmoplastic stroma. Can have hyaline rim.

IHC: basal cell markers usually label outermost layers (sparing luminal cells), while luminal cells stain with CK7.
HER2/neu overexpressed.

Some cases with Adenoid cystic morphology have MYB-rearrangements (like elsewhere)

Normal PSA

Can be aggressive.

Urothelial Carcinoma

Most often ***secondarily* involving the prostate** from the bladder and/or prostatic urethra.

Note: Determining which site the urothelial carcinoma is coming from is very important for staging!! Bladder → Prostate stroma =T4, while Prostatic urethra → Prostate stroma = T2

Morphology similar to urothelial carcinoma of bladder (often pleomorphic epithelioid cells with frequent squamous differentiation).

Frequent spread of CIS or pagetoid spread into ducts. Invasion elicits desmoplastic stroma.

IHC: p63, HMWCK, **GATA-3 (+),** NKX3.1 & PSA (-)

Pagetoid Spread of CIS
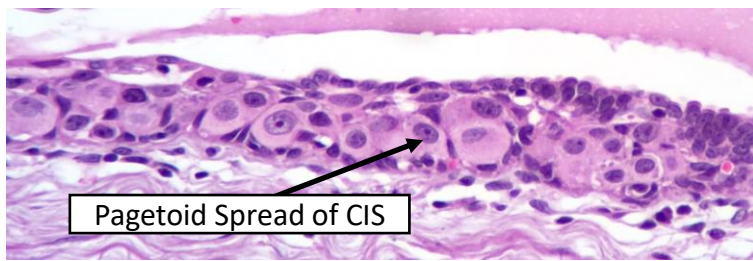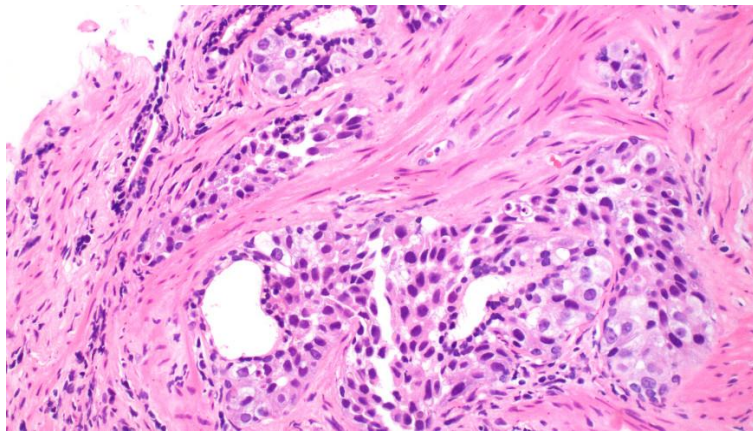
Squamous Neoplasms

Very Rare. Arise through either divergent differentiation of basal cells or transdifferentiation of usual adenocarcinoma following hormone therapy.

Squamous Cell Carcinoma: Pure squamous morphology. Similar morphology/IHC to SCC elsewhere. Must be distinguished from secondary involvement of a bladder/urethral SCC or TCC.

Adenosquamous Carcinoma: Both glandular (acinar) and squamous morphology.

Neuroendocrine Tumors

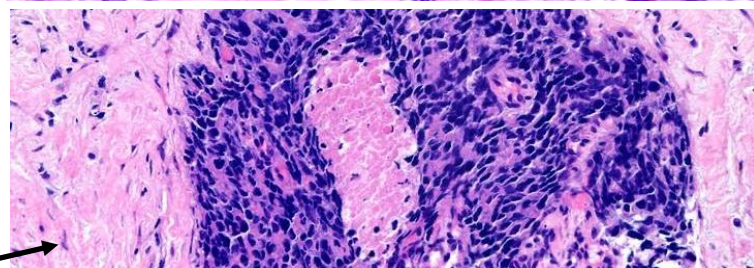**Adenocarcinoma with neuroendocrine cells**
Neuroendocrine cells can be seen on IHC in many usual prostate cancers, does not seem to be clinically significant, so no need to stain routinely

Some cases show "***Paneth cell-like neuroendocrine differentiation***" with eosinophilic granules. Can see similar changes in benign glands.
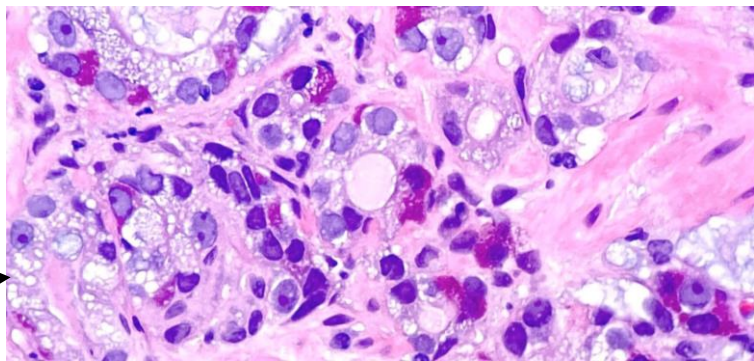
Well-differentiated Neuroendocrine Tumor
Very rare. Must exclude adenocarcinoma with neuroendocrine differentiation (with more typical areas).

Small Cell Neuroendocrine Carcinoma. Morphologically identical to in the lung (small cells with scant cytoplasm and stippled, hyperchromatic nuclei). May be admixed with acinar adenocarcinoma or pure. Do not Gleason grade. Stains with at least 1 neuroendocrine marker usually. May be TTF-1 positive. Ki67 near 100%. Very aggressive.

Mesenchymal Tumors

## Stromal Tumor of Uncertain Malignant Potential (*"STUMP"*)

Tumor of **specialized prostatic stroma**.
Often present with urinary symptoms.

Several growth patterns:
- **Hypercellular stroma with scattered degenerative-appearing cells admixed with benign glands**.
- **Phyllodes subtype** with leaf-like branching
- Also: myxoid, epithelioid, hypercellular bland stroma

IHC: **Express CD34 and PR**

Usually good prognosis. My recur or progress
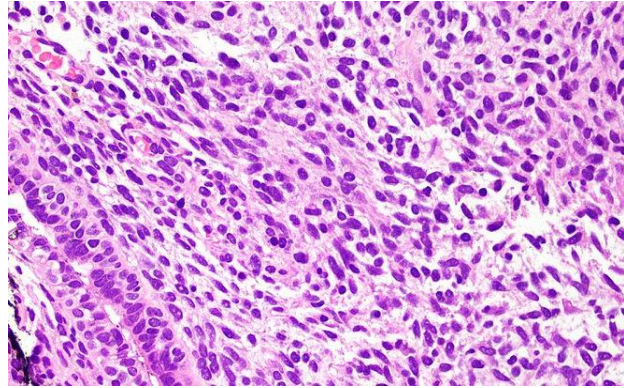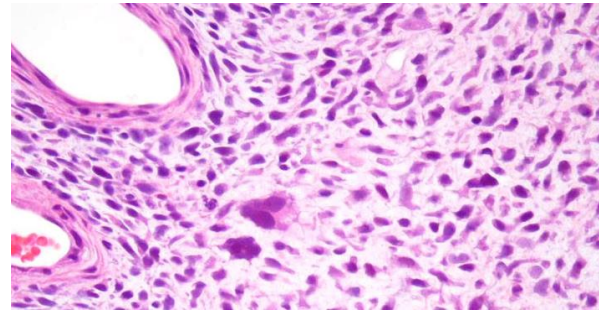

Stromal Sarcoma

Malignant tumor of specialized prostatic stroma.

Phyllodes-like growth pattern with malignant, pleomorphic stroma or **fascicular growth** similar to a leiomyosarcoma

IHC: Express CD34 and PR

Can behave aggressively.

Other Tumors

Leiomyoma
Leiomyosarcoma
Rhabdomyosarcoma
Angiosarcoma

Synovial Sarcoma
Inflammatory Myofibroblastic Tumor (IMT)
Solitary Fibrous tumor (SFT)
Hemangioma
Granular cell tumor

Immunohistochemistry of Mesenchymal Lesions:

	STUMP	Stromal Sarcoma	Leiomyosarcoma	Rhabdomyosarcoma	IMT	SFT	GIST
CD34	+	+	-	-	-	+	+
SMA	+/-	-	+	+	+	-	-
Desmin	+/-	-	+	+	-/+	-	-
Myogenin	-	-	-	+	-	-	-
CD117	-	-	-	-	-/+	-	+
ALK1	-	-	-	-	+/-	-	-
PR	+	+	+/-	-	-	+/-	-

*Modified from: Epstein and Netto. Biopsy Interpretation of the Prostate. 5th Edition*

Seminal Vesicle

Normal Anatomy

Complex papillary folds lined with pseudostratified tall columnar epithelium with microvesicular lipid-filled cytoplasm and **prominent lipofuscin pigment** (golden-brown and refractile granules, which <u>help distinguish it from prostate</u>).

Moderate to severe cytologic atypia with large irregular hyperchromatic nuclei with coarse chromatin and prominent nucleoli. Likely degenerative.
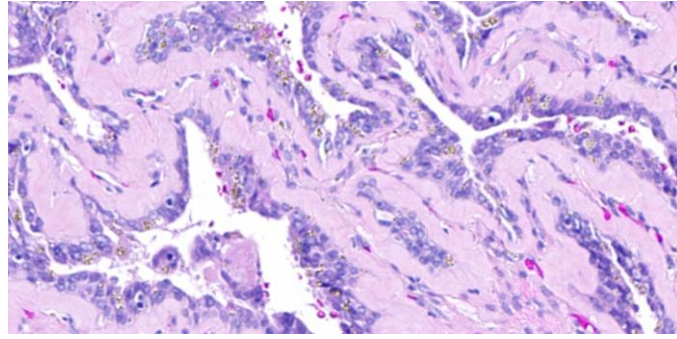
Stains with GATA-3
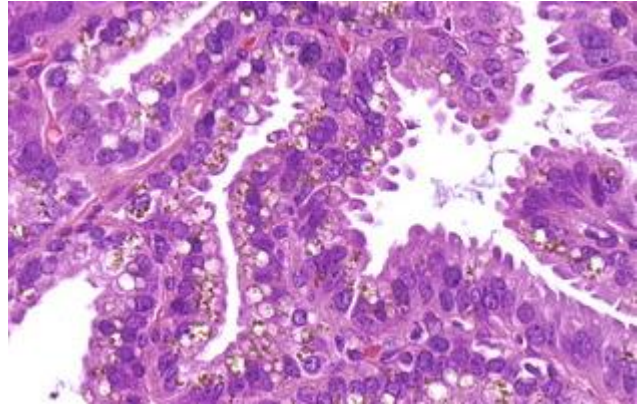
Amyloidosis

Linear or massive nodular subepithelial deposits of **amorphous eosinophilic fibrillar material**.

Relatively **common benign incidental finding**. Not associated with systemic amyloidosis.

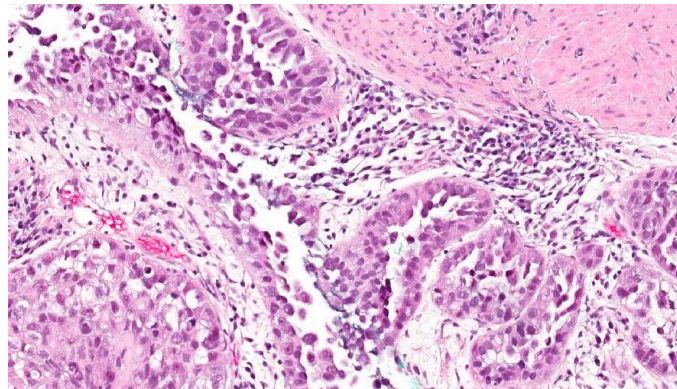Highlighted with Congo Red with "Apple-green" birefringence

Adenocarcinoma

<u>**Always first consider secondary involvement**</u>, most commonly by <u>prostatic acinar adenocarcinoma.</u>

Primary adenocarcinoma is **RARE**. It has a variety of patterns. Most often a <u>papillary clear cell tumor</u>, but can be hobnail, etc..

IHC: CK7(+), CK20(+/-), Prostate maker (-).
Often poor prognosis.

Mixed Epithelial and Stromal Tumors ("MEST")

Biphasic tumors with stromal and benign epithelial components. Cystic to solid masses.

Cystadenoma→ Lobular pattern. Branching lumens and cysts of various sizes.

Fibroadenoma→ Spindle cell component is more pronounced.

Adenosarcoma→ Stroma is densely cellular and condenses around distorted gland spaces (like Phyllodes tumors or adenosarcoma of uterus)
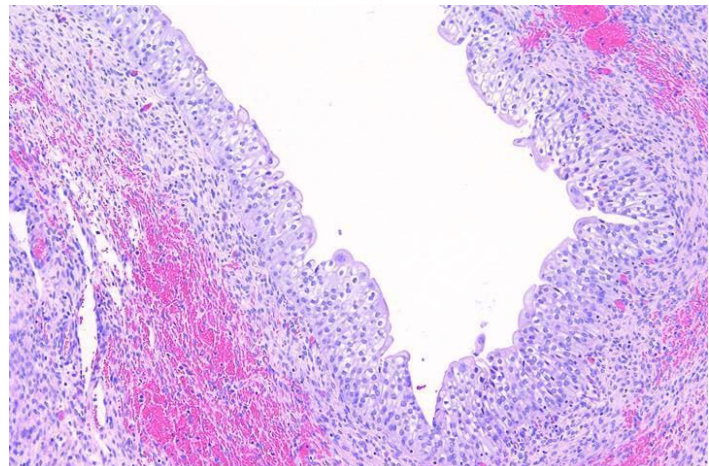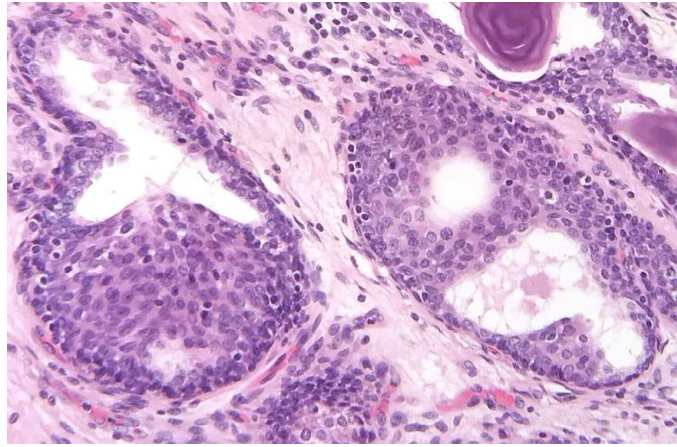
Mimics of Cancer

Basal Cell Hyperplasia

Proliferation of basal cells piling up and filling tubules/glands→ may form solid nests
Appear very blue due to crowded nuclei with scant cytoplasm.

Retains lobular architecture and smooth borders.
Nuclei are very bland with very small nucleoli
Basal cell markers very strongly positive.

Central Zone Sampling

Anatomic zone with characteristic complex architecture. Stratified eosinophilic cytoplasm and prominent basal cell layer. Low-grade cytology.
Intra-luminal bridges ("Roman arches")
Can mimic HG-PIN, so in biopsies from the mid-base, have higher threshold for HG-PIN & r/o normal anatomy!

Verumontanum mucosal gland hyperplasia
Crowded glands near verumontanum. Often nearby urothelium. Corpora amylacea often present
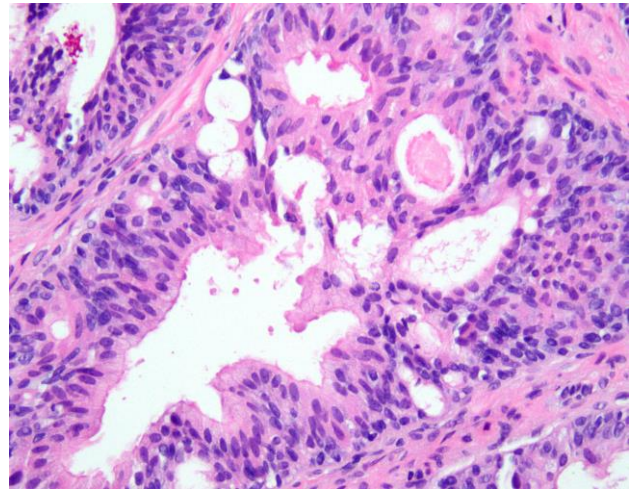
## Adenosis

(aka Atypical Adenomatous Hyperplasia)

Well-circumscribed tightly packed, largely uniform glands. Lobular architecture. Pale to clear cytoplasm. Admixture of small and larger glands.

Occurs in the **transition zone** (mostly seen in TURPs and Prostatectomies)

Some features suggestive of carcinoma may be seen such as prominent nucleoli and crystalloids/mucin, but often merge with benign glands.

Principal differential diagnosis is Gleason grade 2 carcinoma. This distinction requires IHC for basal cells:
- Basal cells may be decreased in Adenosis
- Demonstration of any basal cells indicates adenosis in this context
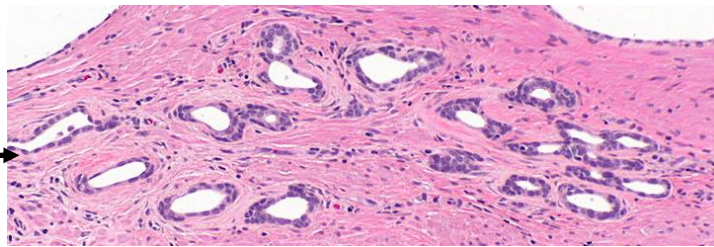- Carcinoma must lack basal cells completely
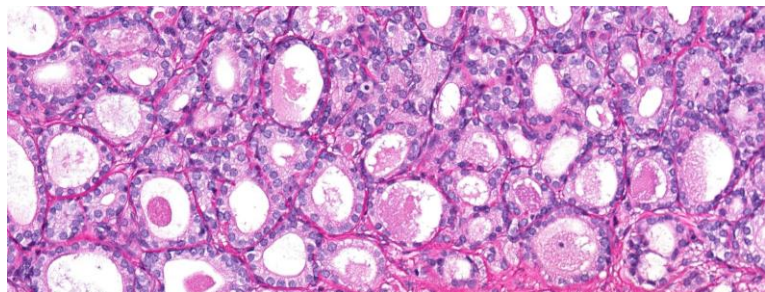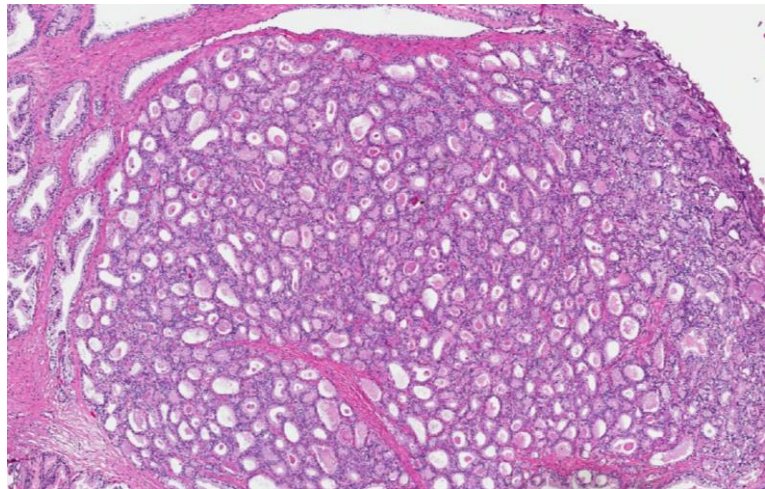
Atrophy

"Simple" Atrophy
Basophilic glands with scant cytoplasm (both apically and laterally).
Normal caliber glands with normal spacing.

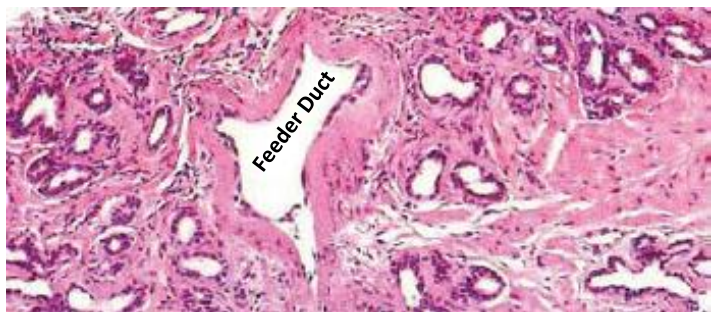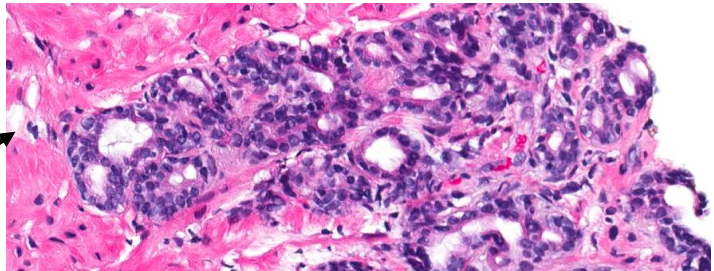### *Postatrophic Hyperplasia ("PAH")*
Tightly packed very small cytologically bland glands. Very blue at low-power.
Usually clustered around a larger dilated "feeder" duct *(Think: TDLU of breast)*
Bland nuclei without prominent nucleoli
Basal cells present
Stroma often sclerotic

Feeder Duct

Partial Atrophy
Retain moderately abundant pale/clear cytoplasm *lateral* to the nuclei (with reduced apical cytoplasm), which may produce pale glands that lack the blue appearance of atrophy.
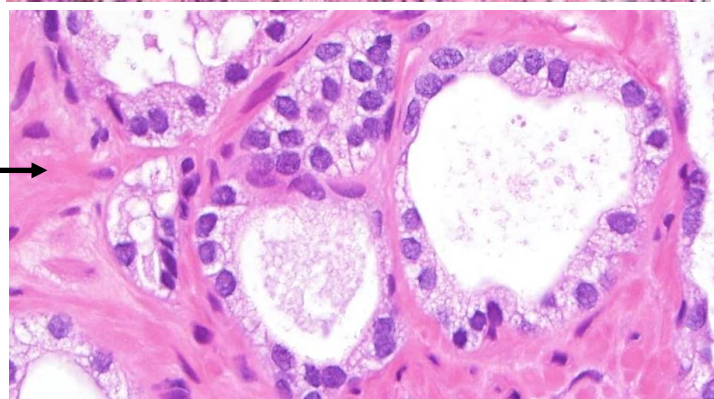Frequently merges with nearby atrophy.
Bland nucleoli without prominent nucleoli.
No infiltrative growth.
Undulating luminal surfaces.
Retained (but possibly decreased) basal cell markers.
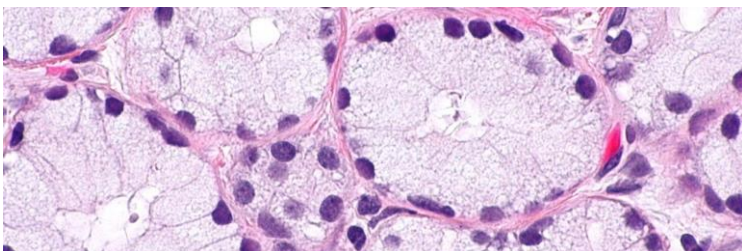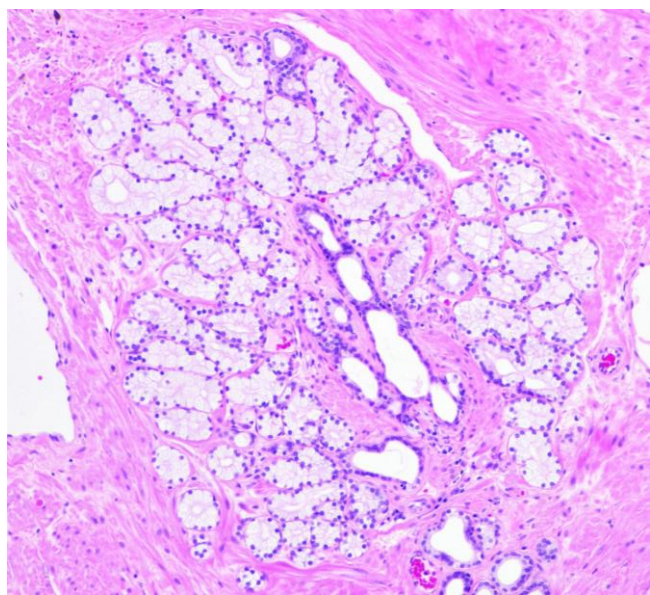
Cowper's Glands

Periurethral, near apex
Lobular architecture with central duct
Abundant mucin-filled cytoplasm (PASd+)
No nuclear atypia or prominent nucleoli.
Basal cells markers positive, frequently muscle-specific actin positive (unlike in prostate)
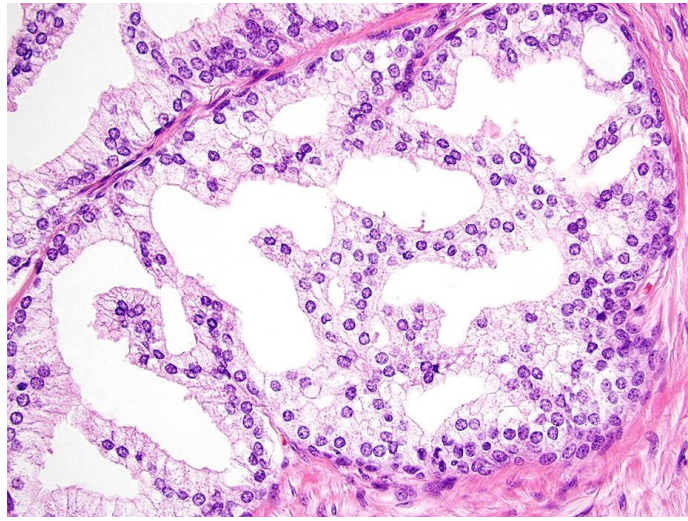IHC: PSAP negative (PSA may be positive)

Clear Cell Hyperplasia

Big nodules of clear cells with cribriform pattern. Smooth gland borders and lobular pattern.

Uniform bland nuclei without prominent nucleoli
Intact basal cell markers.

Most often seen in central zone on TURP in setting of BPH.

Sclerosing Adenosis

Dense spindled stroma with compressed and distorted epithelial elements

Entrapped epithelium ranges from small acini to cords and single cells. **No cytologic atypia.**
Can have surrounding hyaline sheath

Basal cells present with unique immunologic profile
Usual markers positive (p63, HMWCK)
Also express myoepithelial markers (smooth muscle actin, S100)
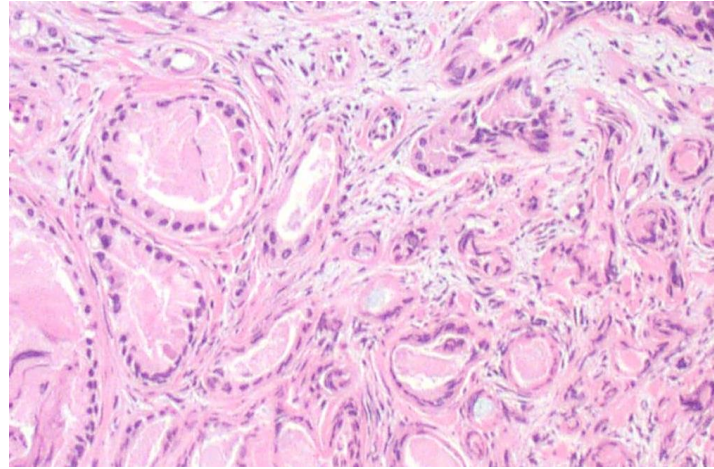
Other Mimics

Nephrogenic adenoma
Malakoplakia
Seminal Vesicle
Mesonephric hyperplasia
Colonic mucosa
Urothelial metaplasia
Granulomatous prostatitis
Signet-ring lymphocytes
Paraganglia (because of nucleoli)