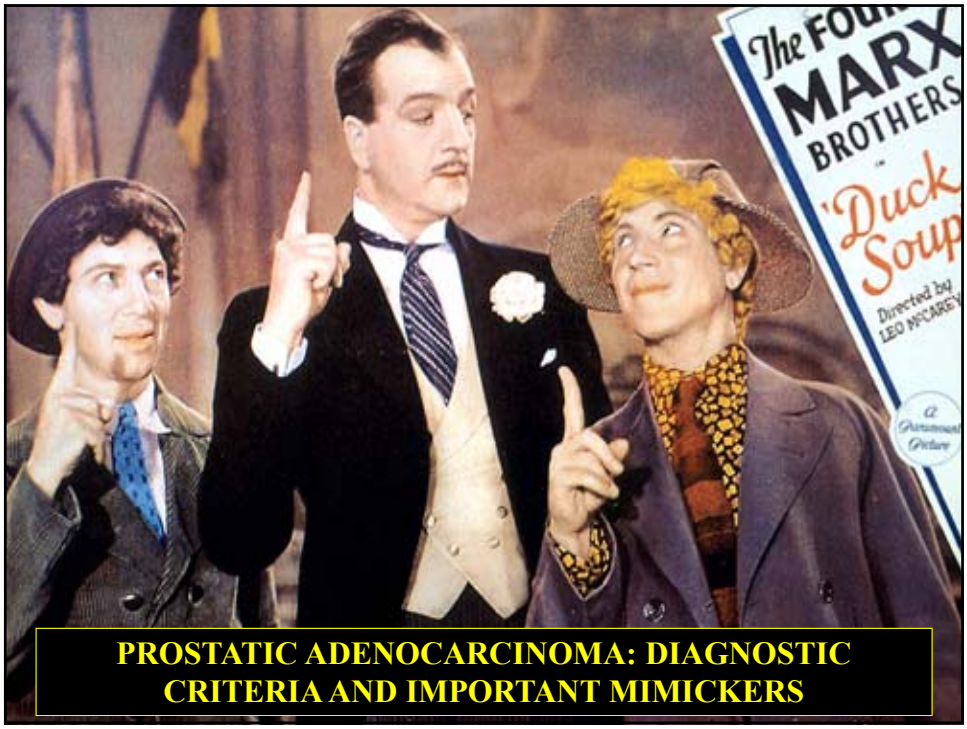
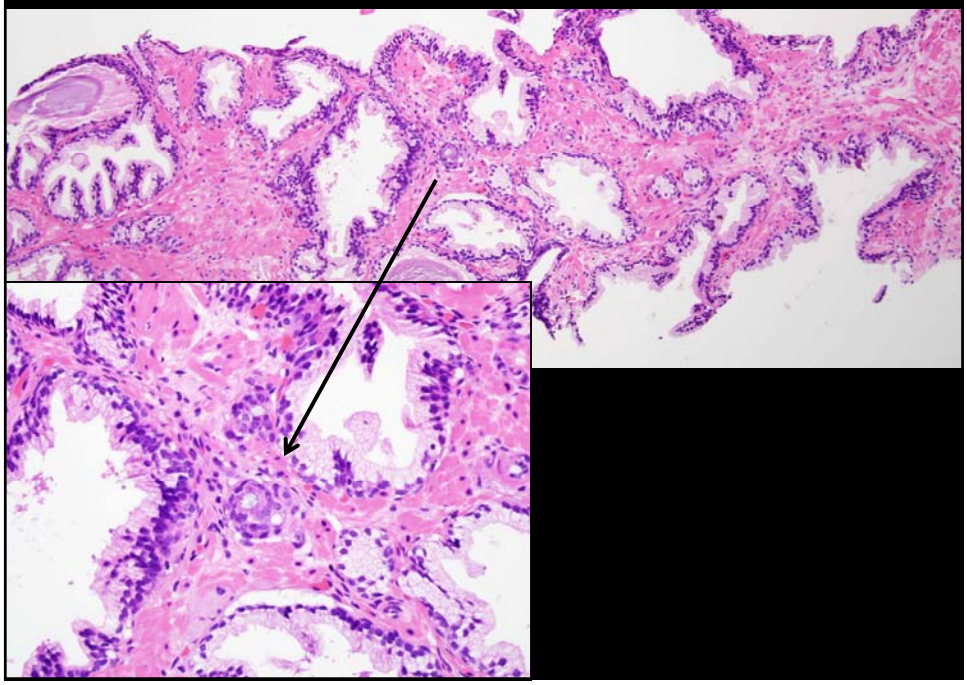
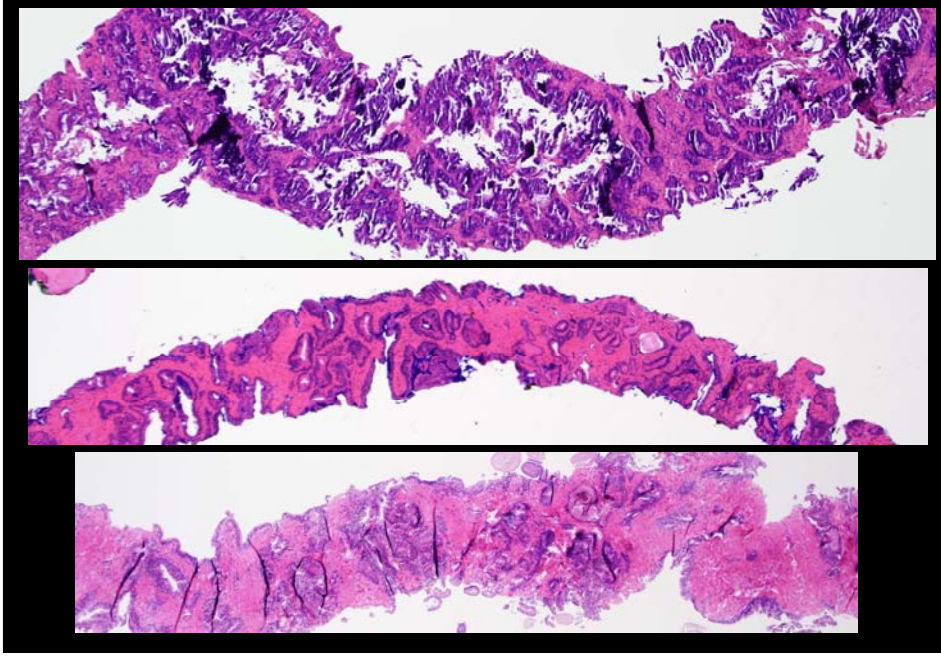


PROSTATIC ADENOCARCINOMA: DIAGNOSTIC CRITERIA AND IMPORTANT MIMICKERS

PROSTATIC ADENOCARCINOMA: DIAGNOSTIC CRITERIA



A good H & E helps!



ADENOCARCINOMA DIAGNOSTIC CRITERIA

Relatively uniform proliferation

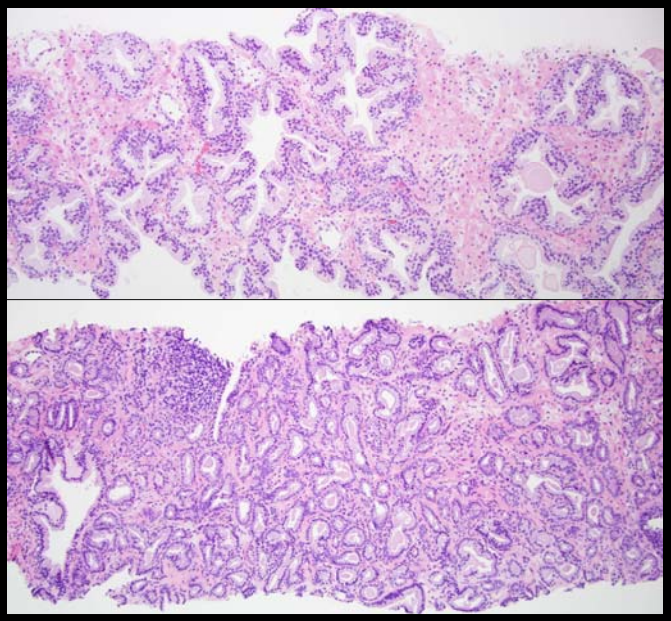
Small round glands

Single cell layer

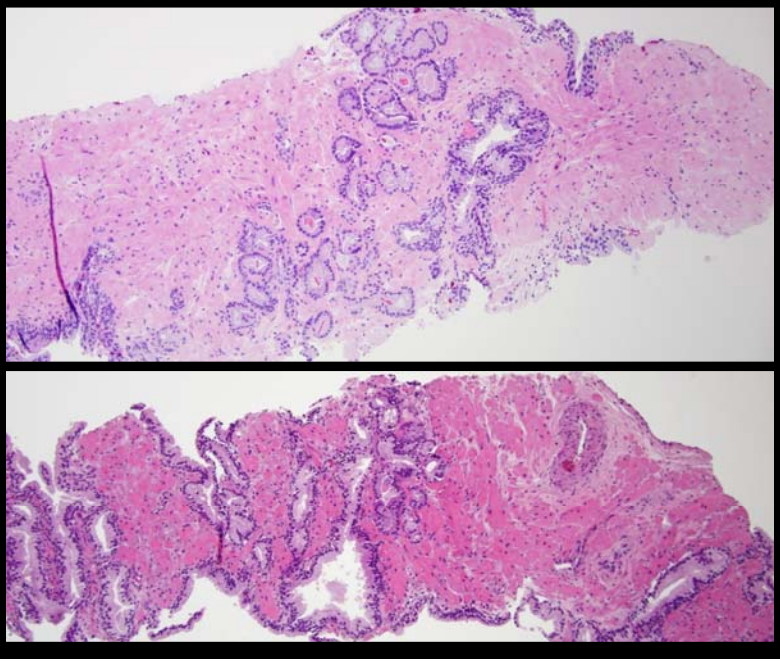
Some prominent nucleoli

Gleason DF. Am J Surg Pathol 9:53, 1985

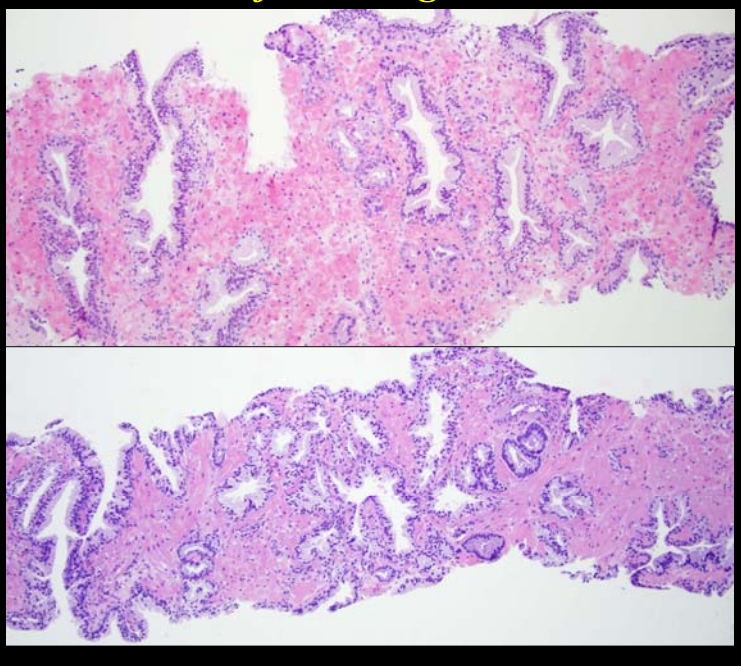
Relatively Uniform Proliferation of Small Round Glands



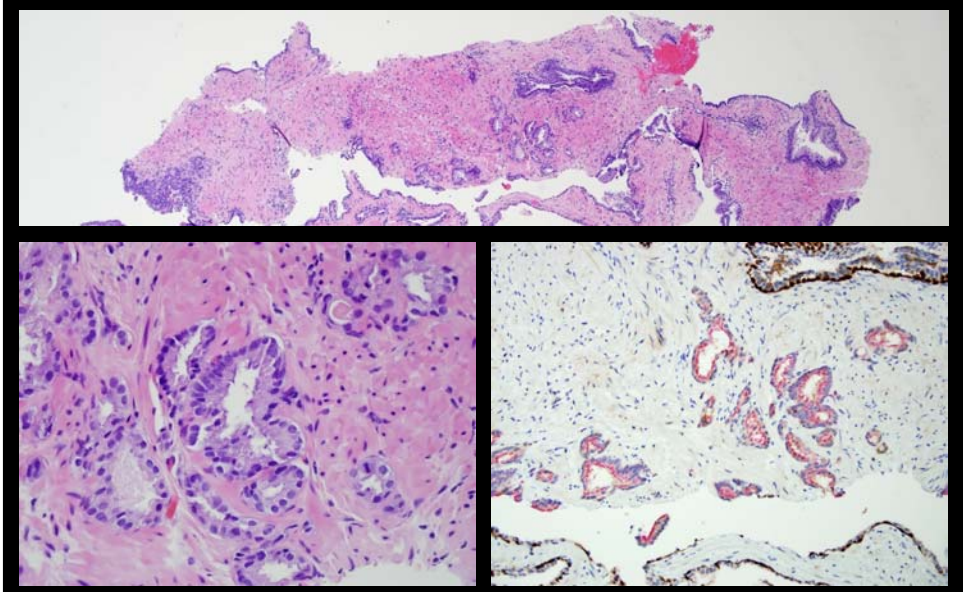
Relatively Uniform Proliferation of Small Round Glands



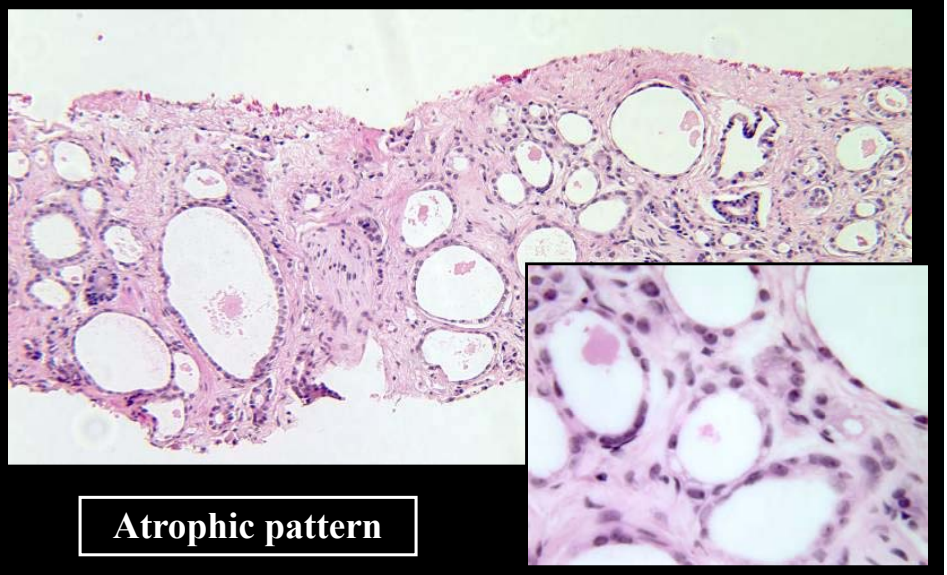
Infiltrative growth



Relatively Uniform Proliferation of Small Round Glands

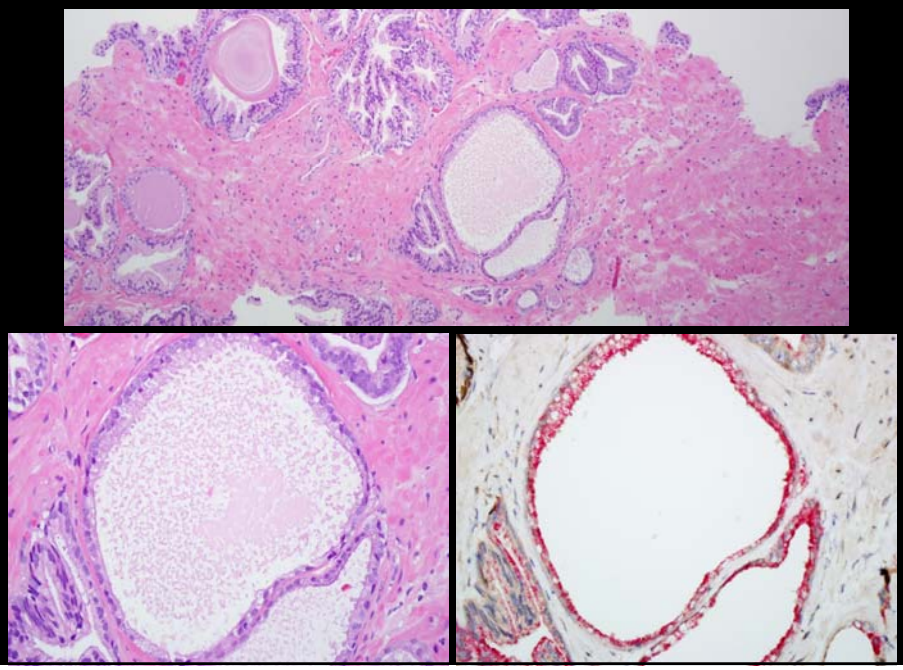


Relatively Uniform Proliferation of Small Round Glands

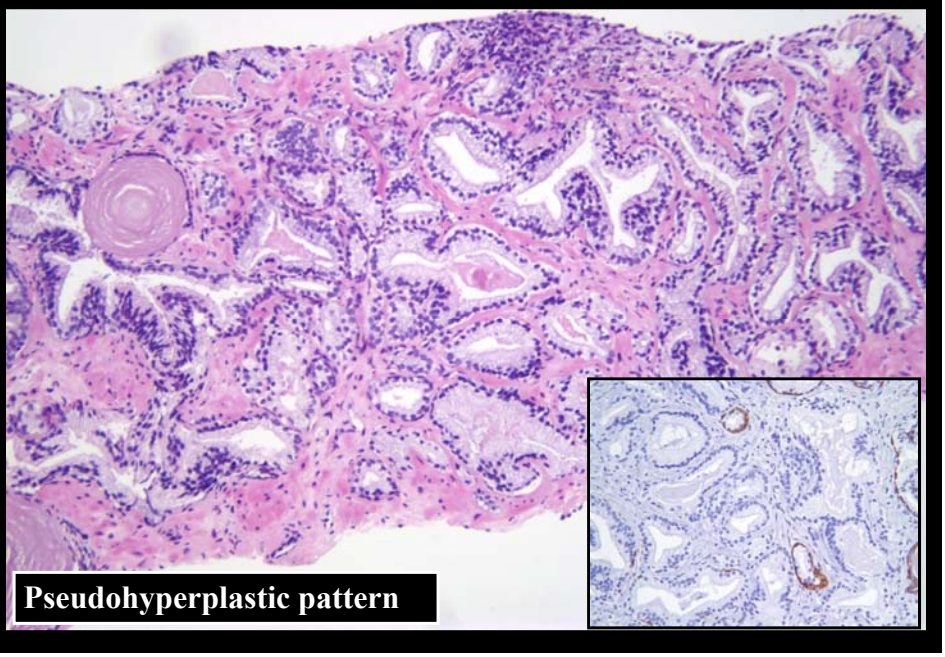


Atrophic pattern

Relatively Uniform Proliferation – Atrophic pattern

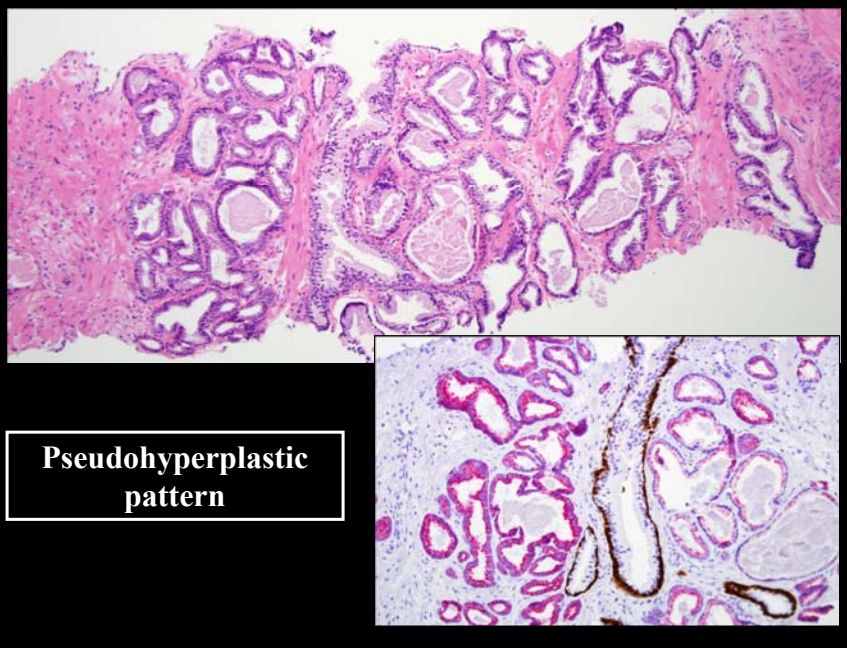


Relatively Uniform Proliferation of Small Round Glands



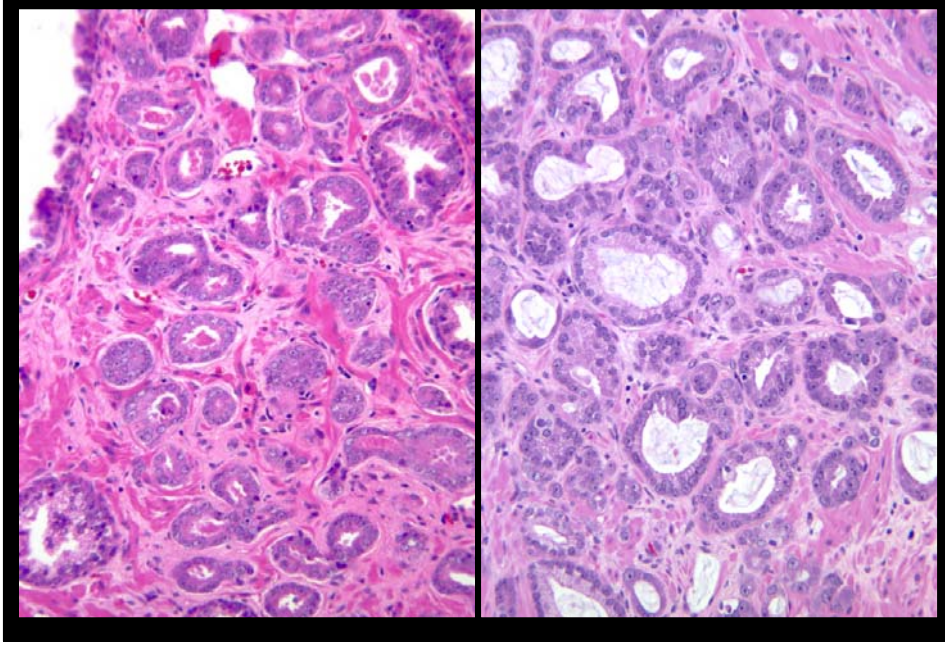
Pseudohyperplastic pattern

Relatively Uniform Proliferation of Small Round Glands

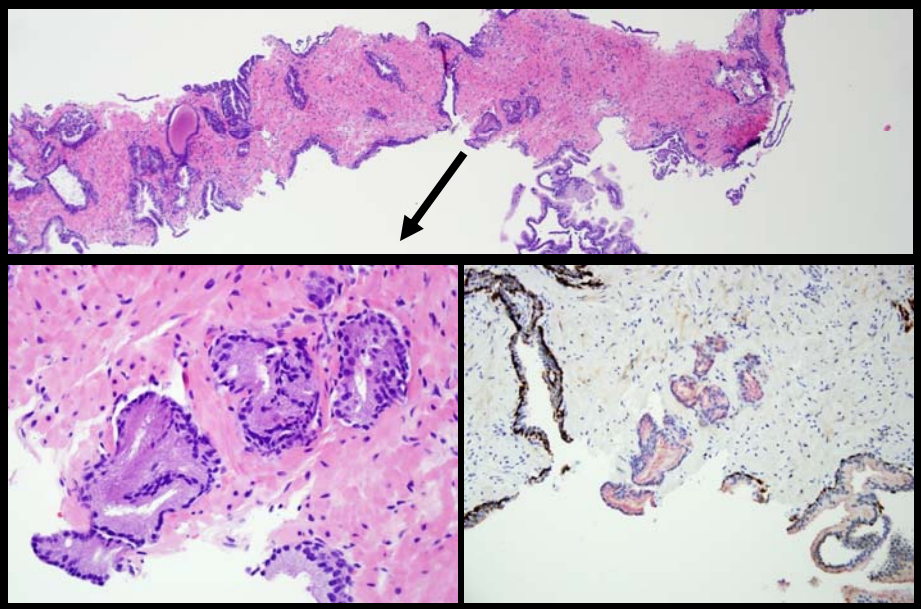


Pseudohyperplastic pattern

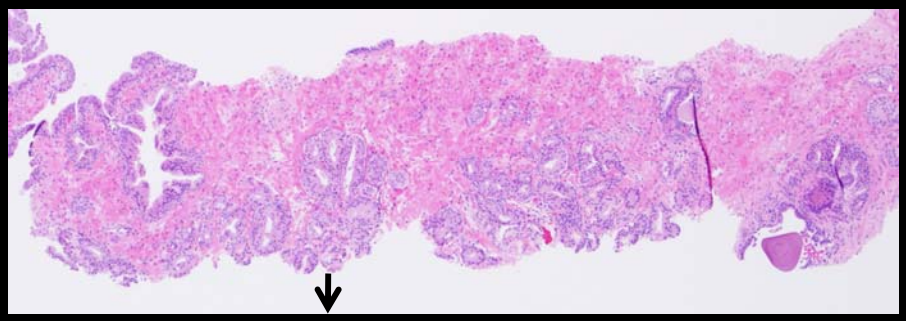
Single cell layer and at least some prominent nucleoli

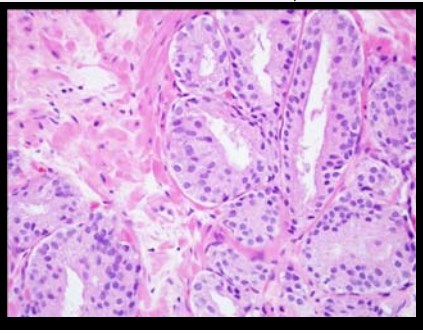


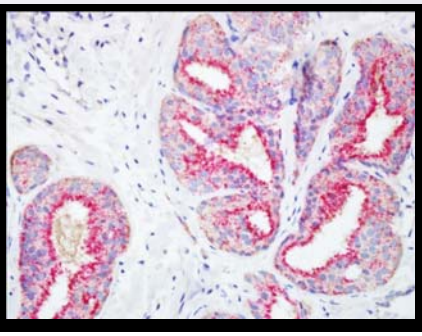
Single cell layer (loss of basal cells)



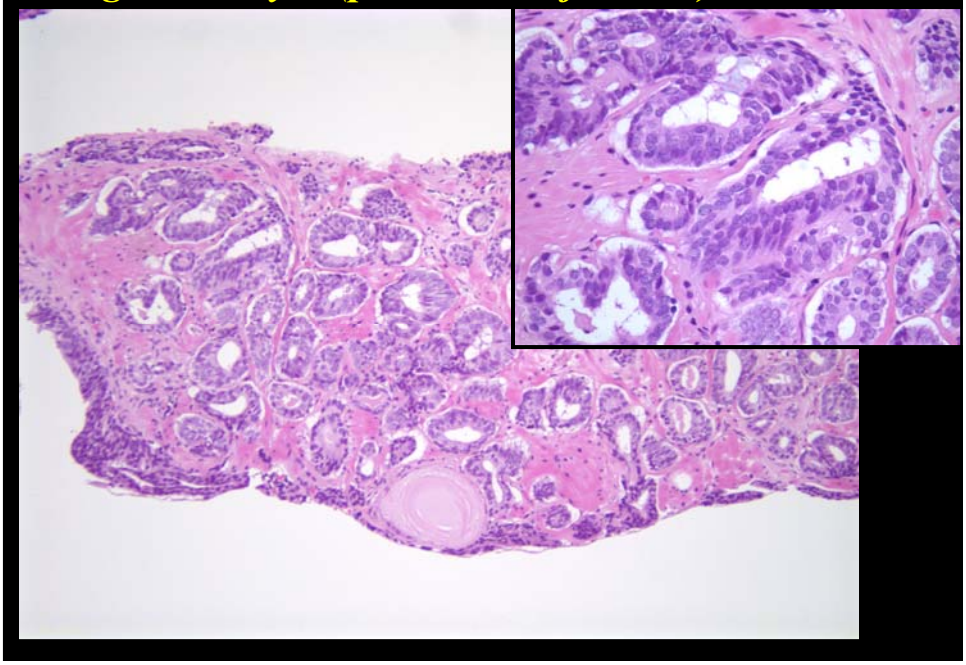
Single cell layer (loss of basal cells)



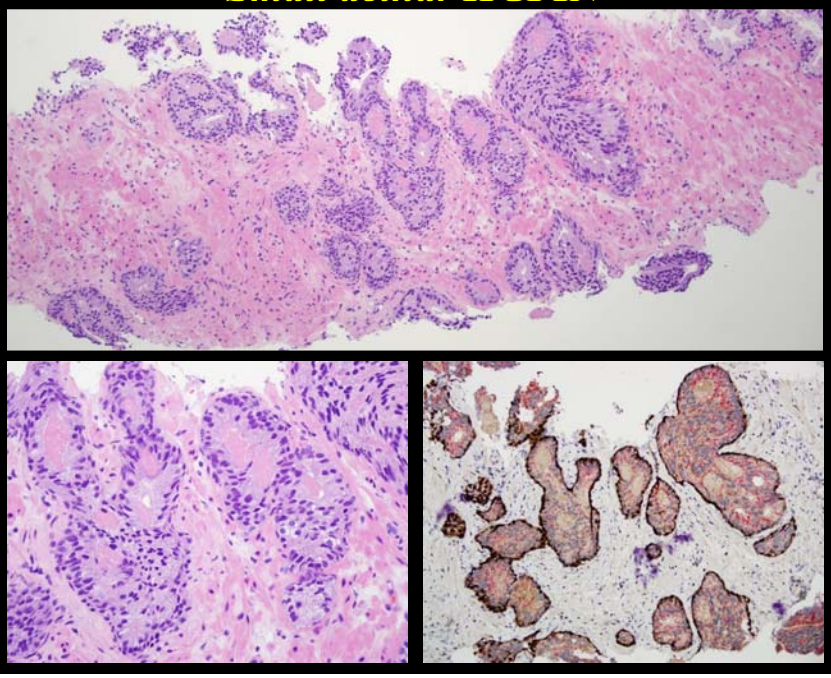




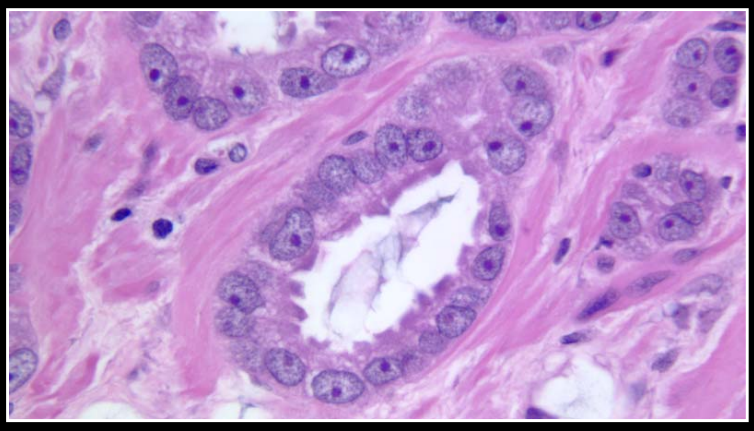
Single cell layer (pseudostratification) "PIN-like"



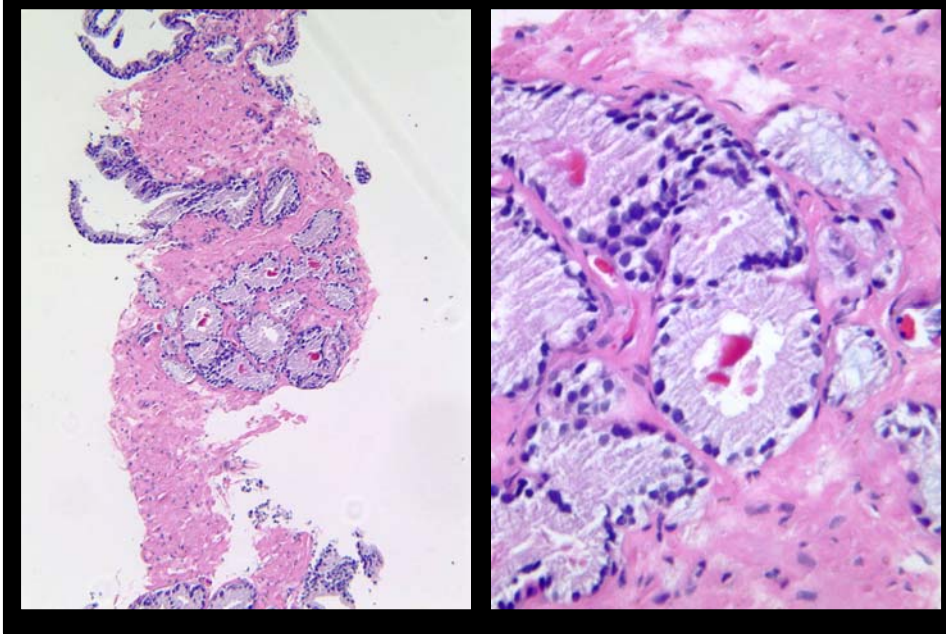
Small acinar HGPIN



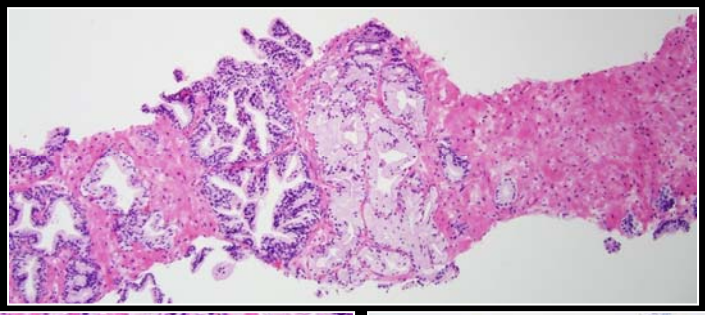
PCa DIAGNOSTIC CRITERIA
THE NUCLEOLUS

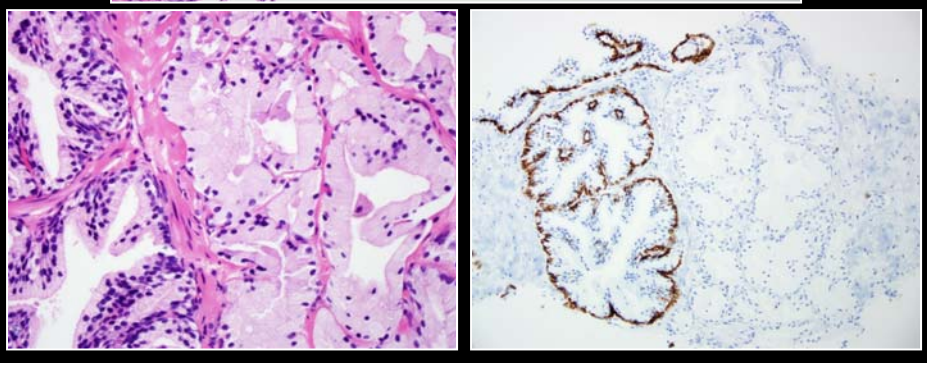


THE NUCLEOLUS

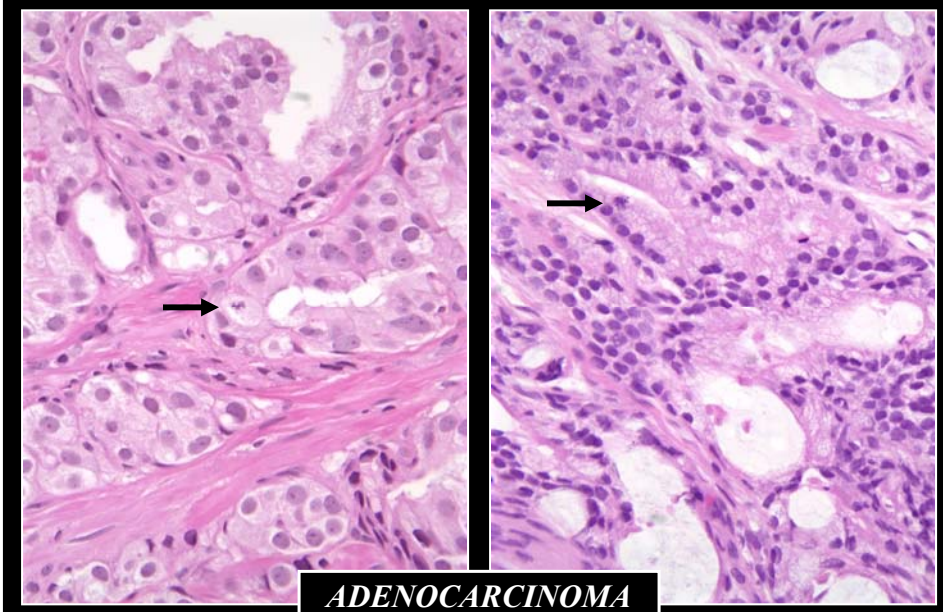


THE NUCLEOLUS



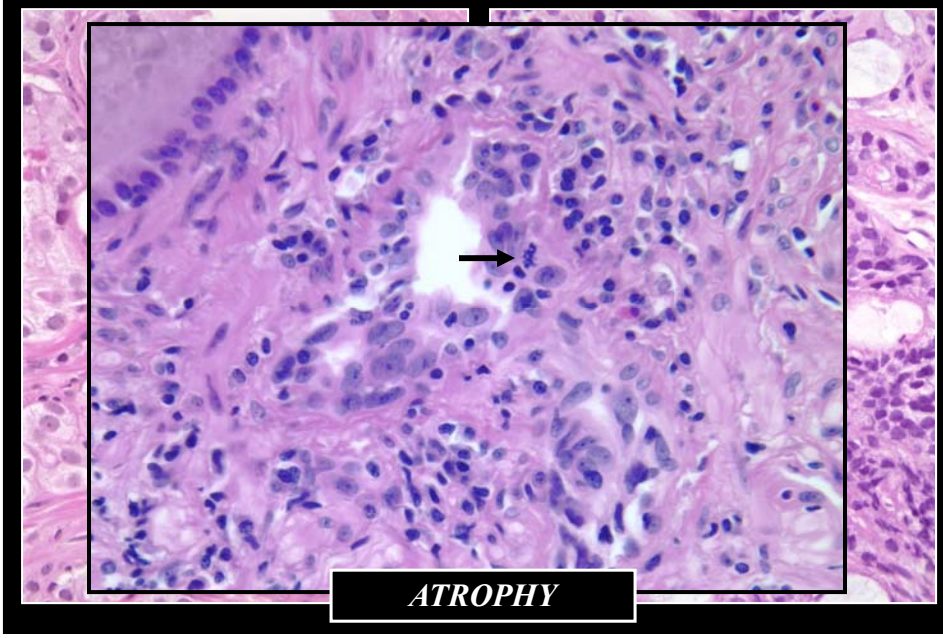


MITOTIC FIGURES



ADENOCARCINOMA

MITOTIC FIGURES

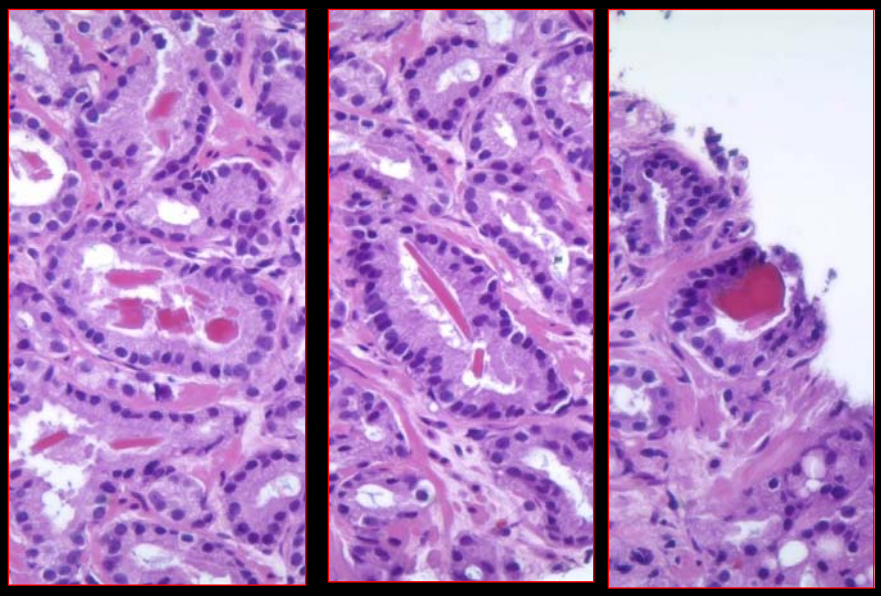


ATROPHY

ADENOCARCINOMA
ANCILLARY DIAGNOSTIC CLUES

Crystalloids
Basophilic (acid) mucin
Eosinophilic secretions
Collagenous micronodules
Cytoplasmic amphophilia
Glomerulations
Perineural invasion
IHC markers

PROSTATIC CRYSTALLOIDS



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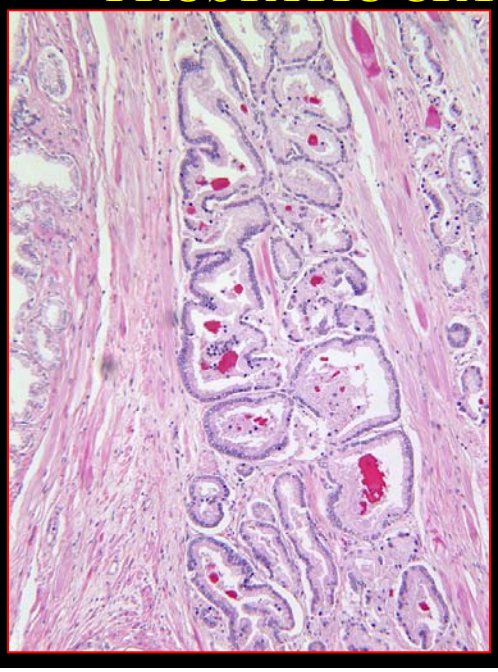
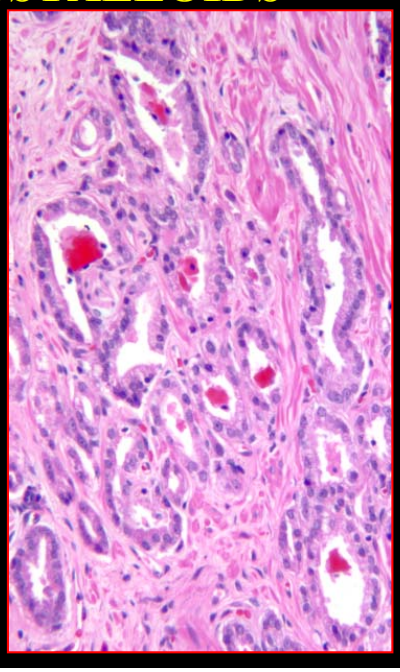
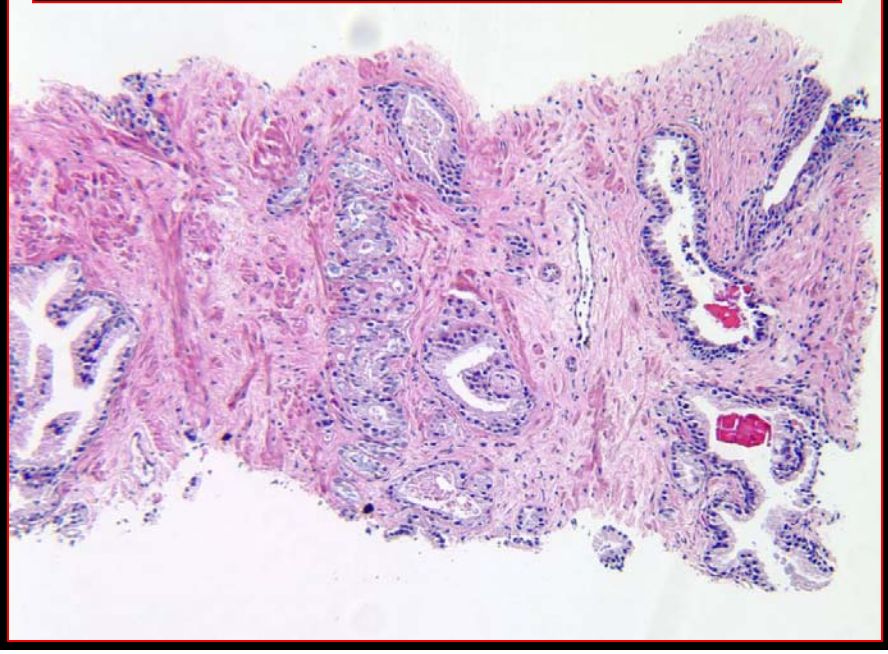
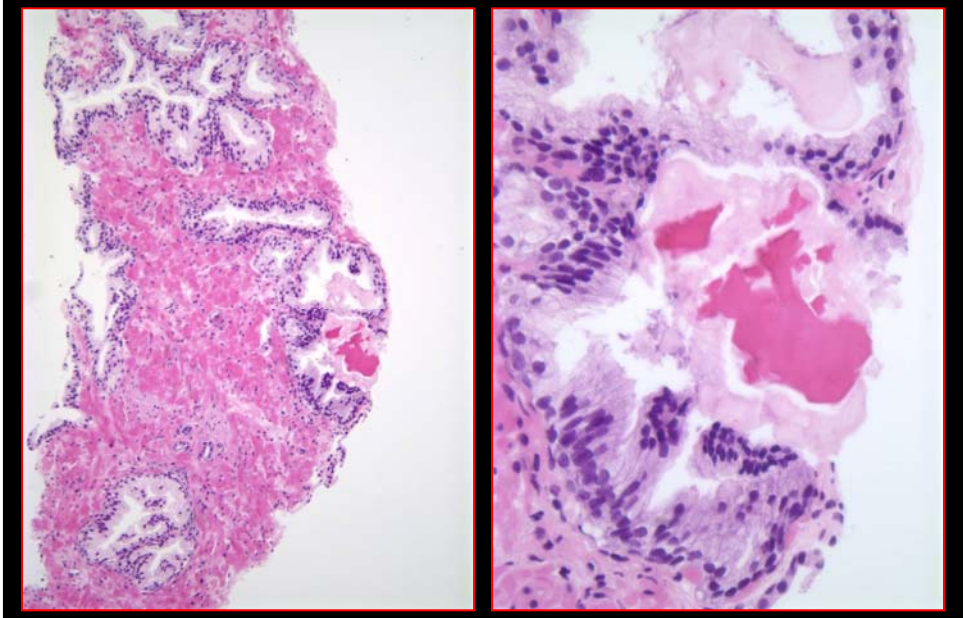




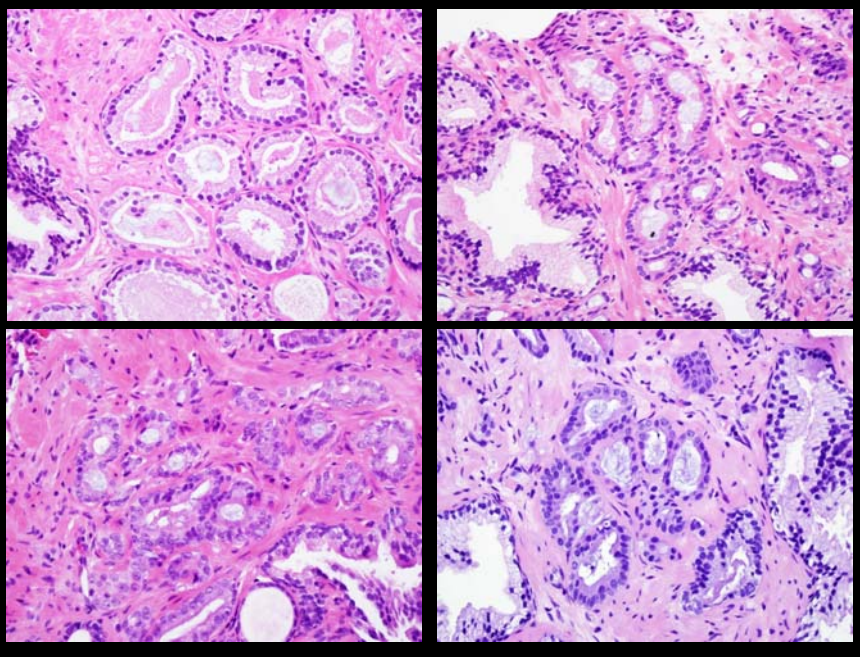
PROSTATIC CRYSTALLOIDS



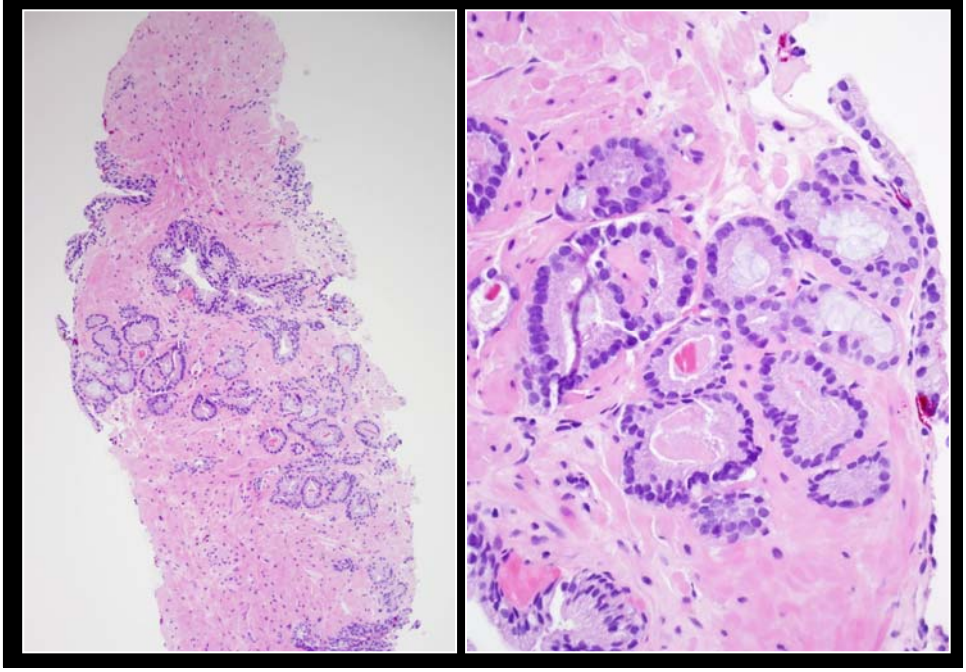
PROSTATIC CRYSTALLOIDS



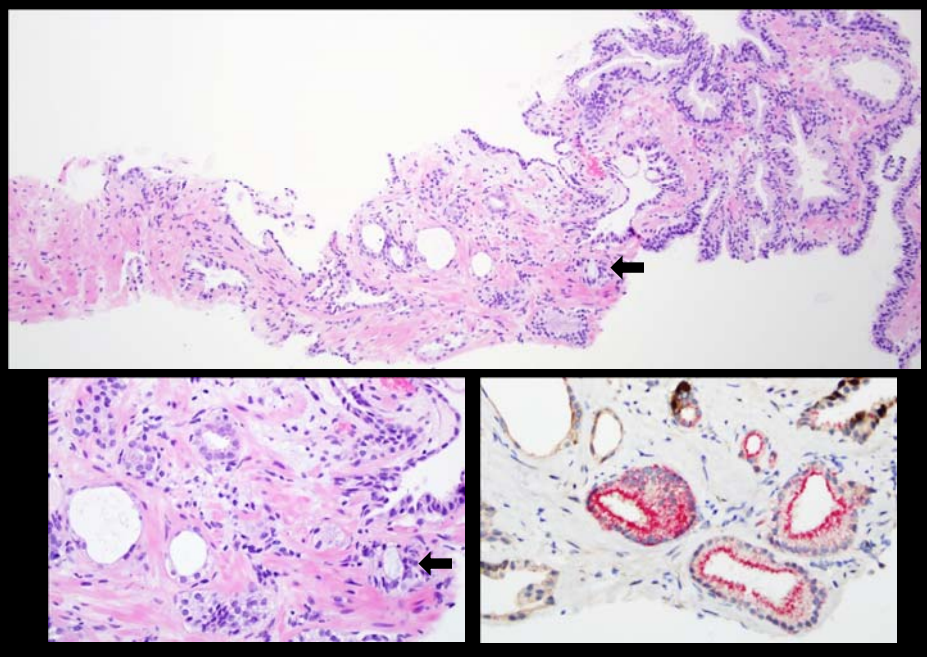
BASOPHILIC MUCIN



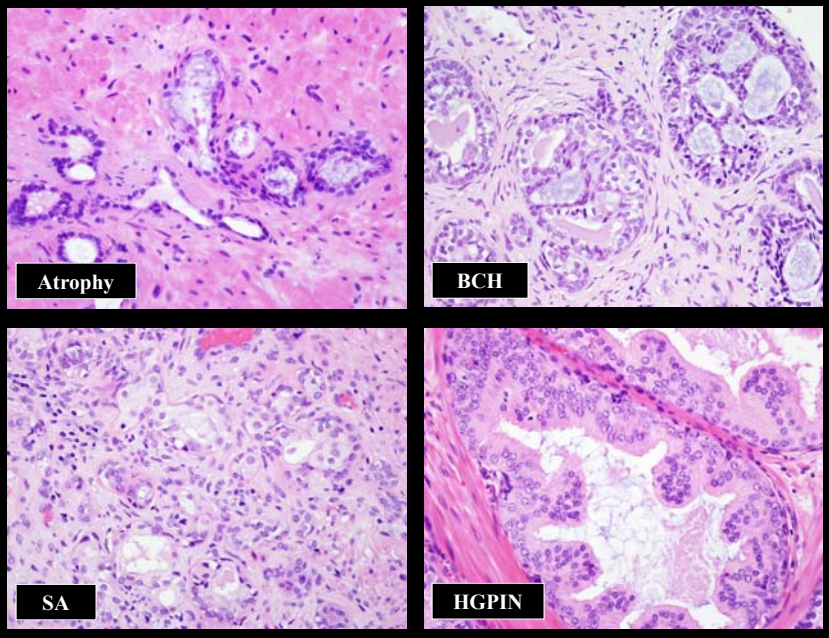
BASOPHILIC MUCIN/CRYSTALLOIDS



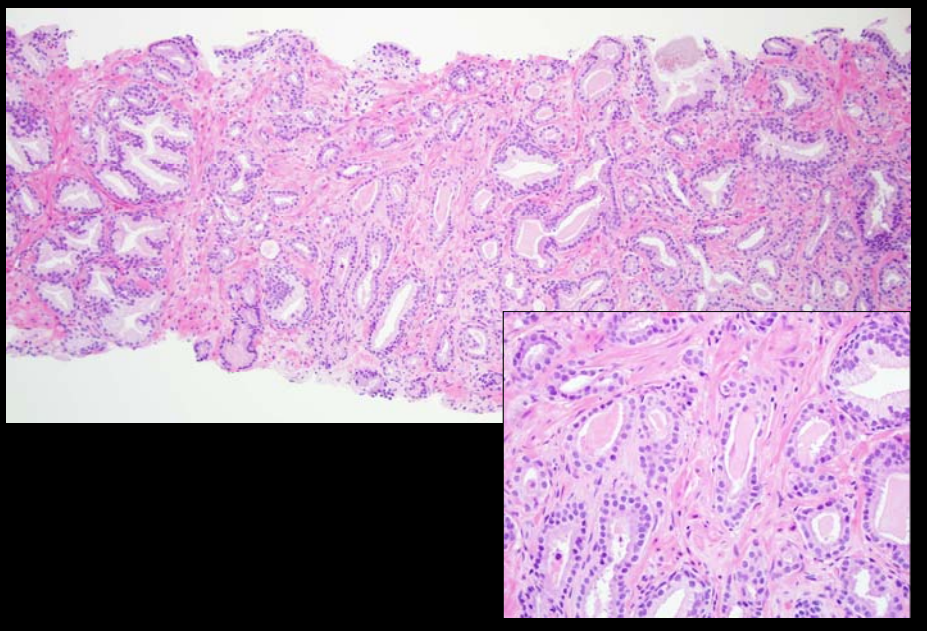
BASOPHILIC MUCIN



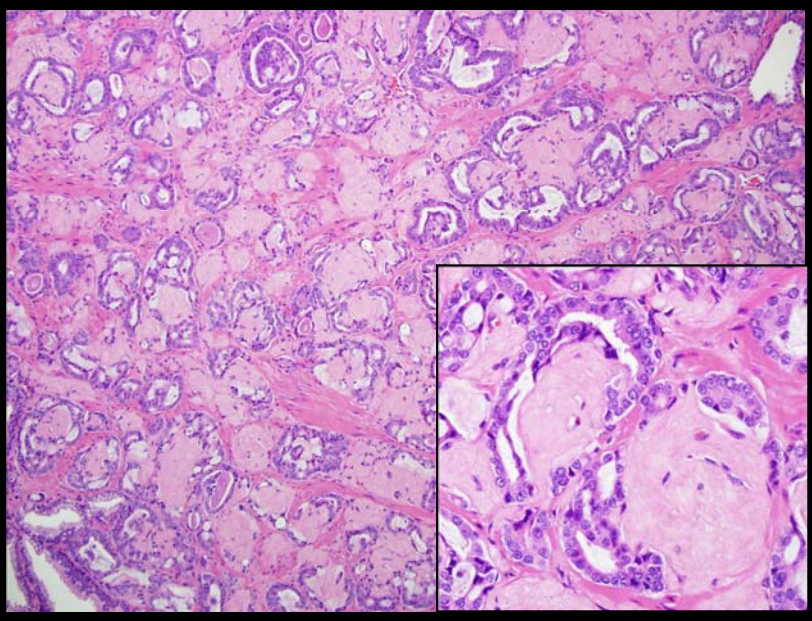
BASOPHILIC MUCIN



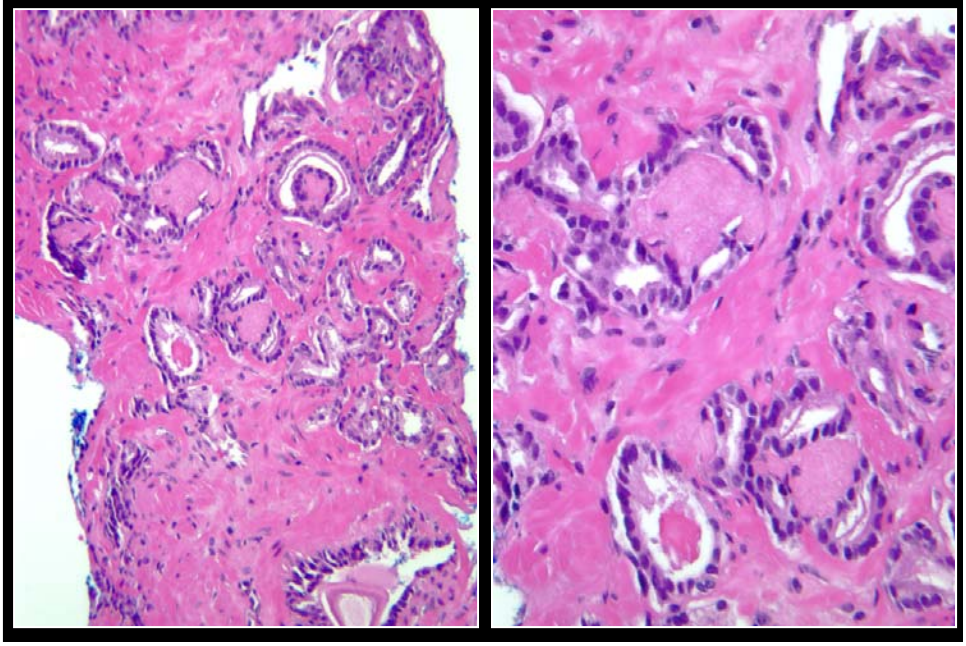
LUMINAL SECRETIONS



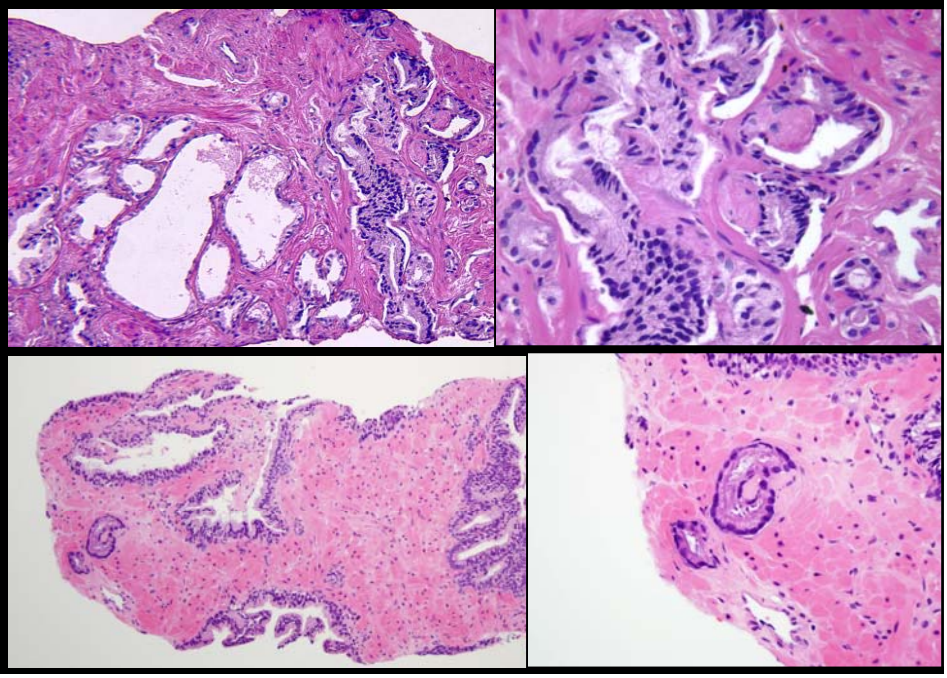
COLLAGENOUS MICRONODULES



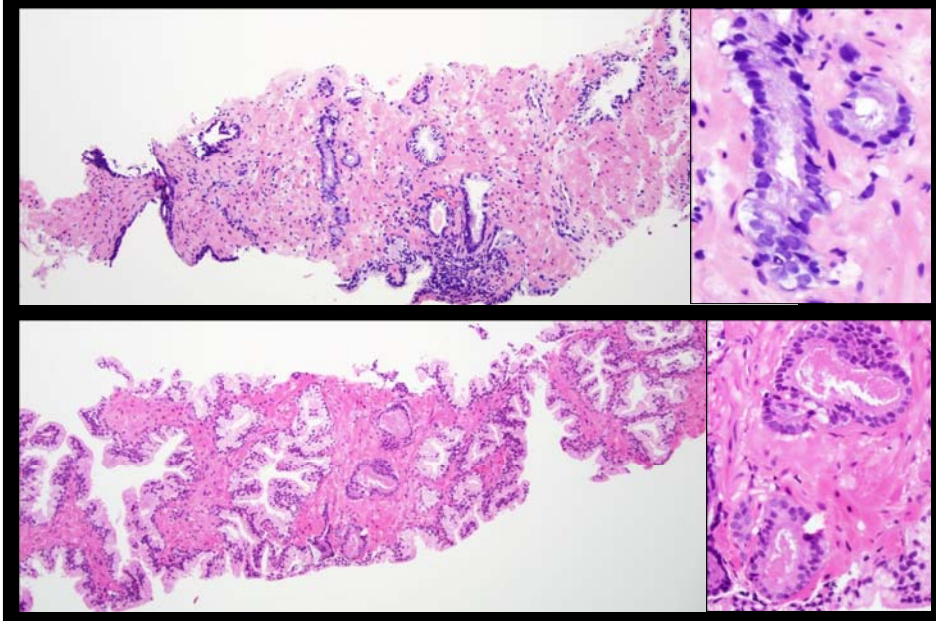
COLLAGENOUS MICRONODULES



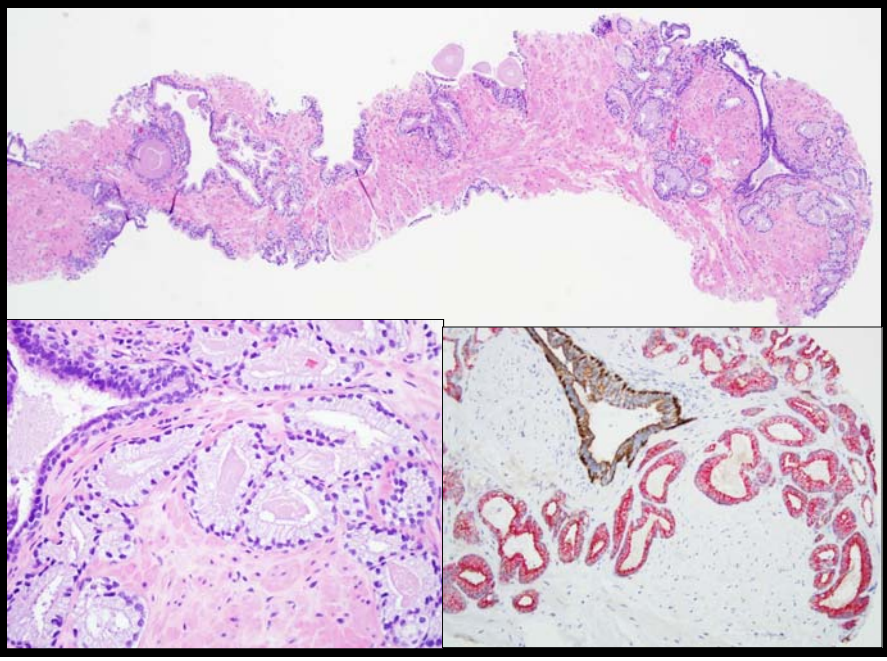
COLLAGENOUS MICRONODULES



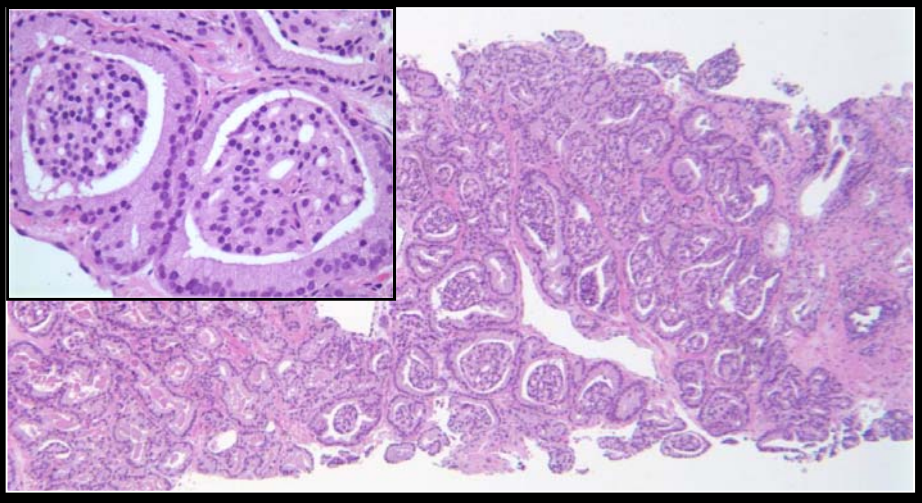
CYTOPLASMIC FEATURES



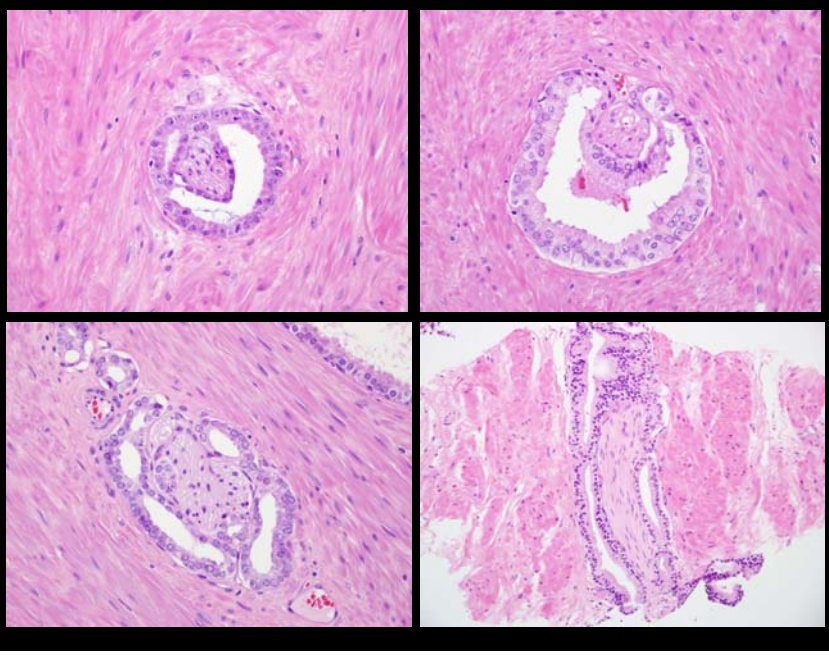
CYTOPLASMIC FEATURES



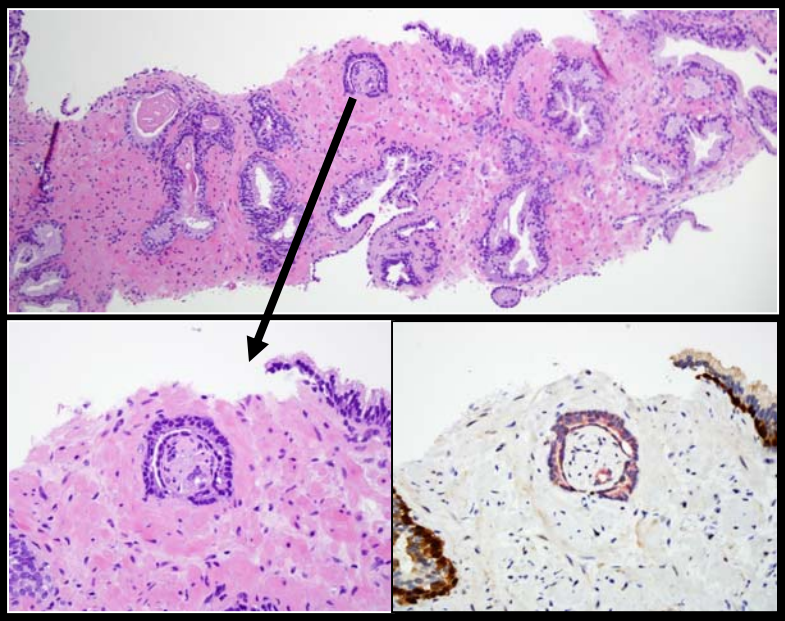
GLOMERULATIONS



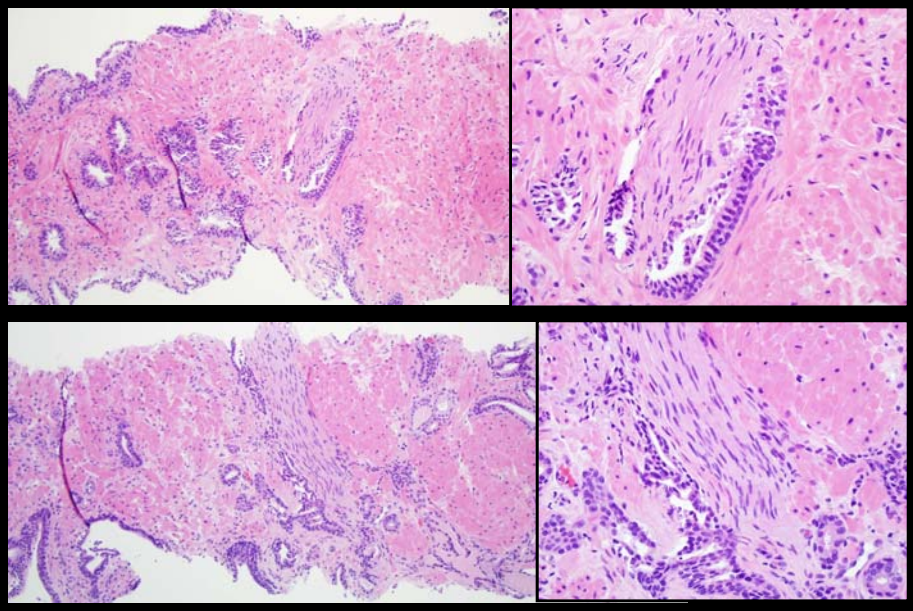
PERINEURAL INVASION



PERINEURAL INVASION

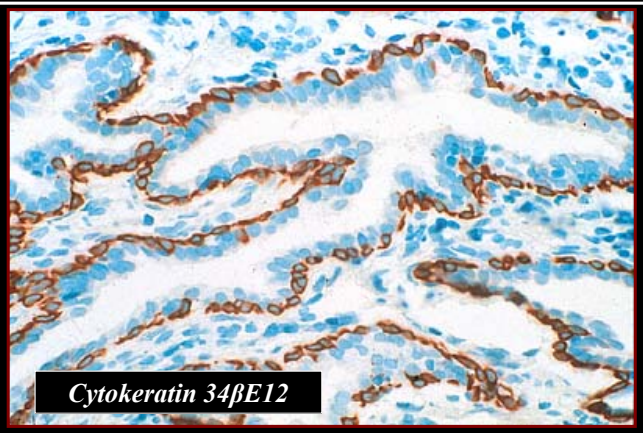


PERINEURAL INVASION - BENIGN

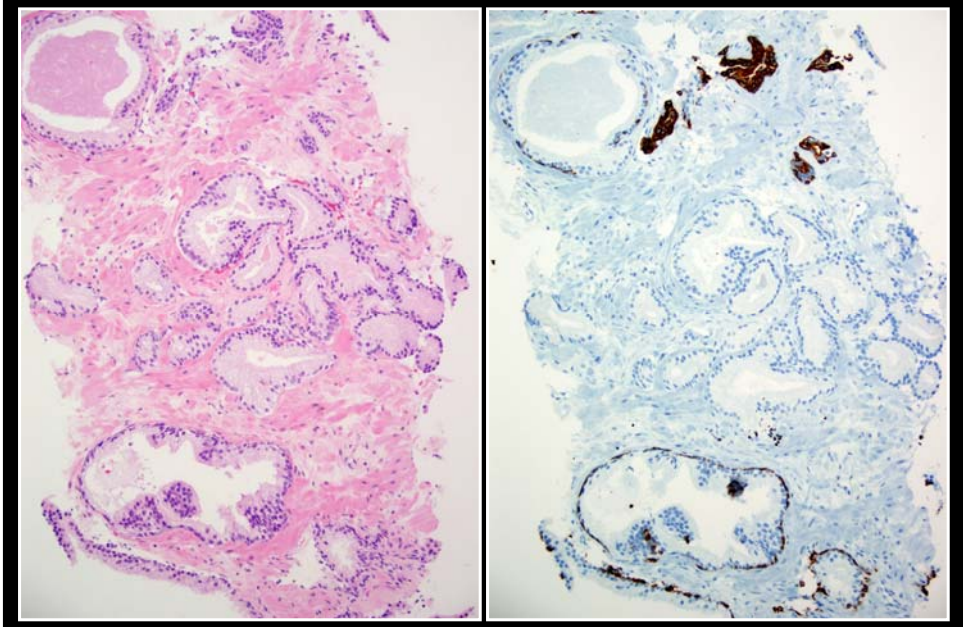


PCa DIAGNOSTIC CRITERIA IMMUNOHISTOCHEMISTRY

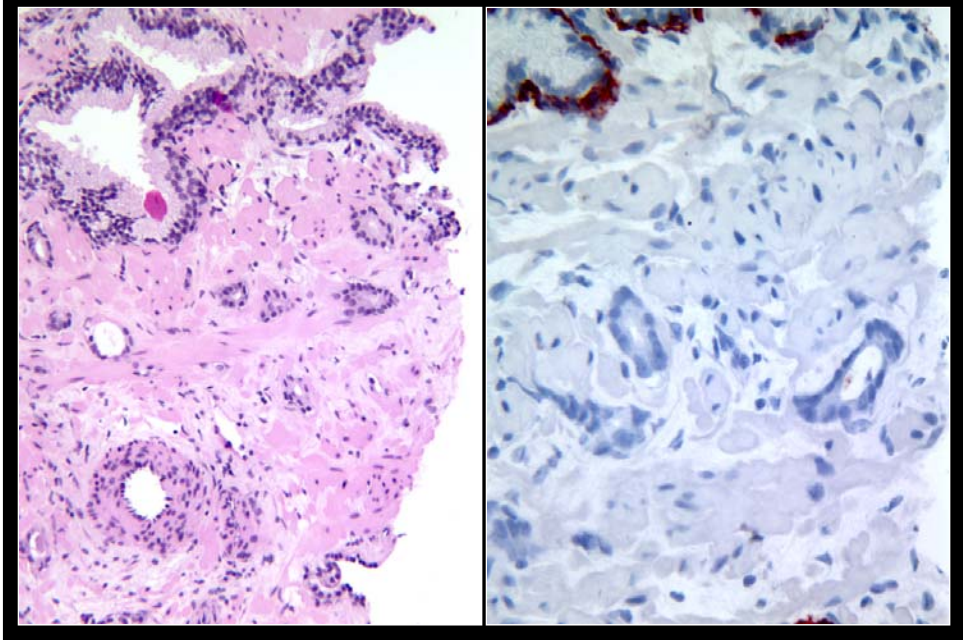
- **Basal cell markers: HMW cytokeratins + p63**
- **Cancer markers: AMACR (racemase, p504s) + ERG**



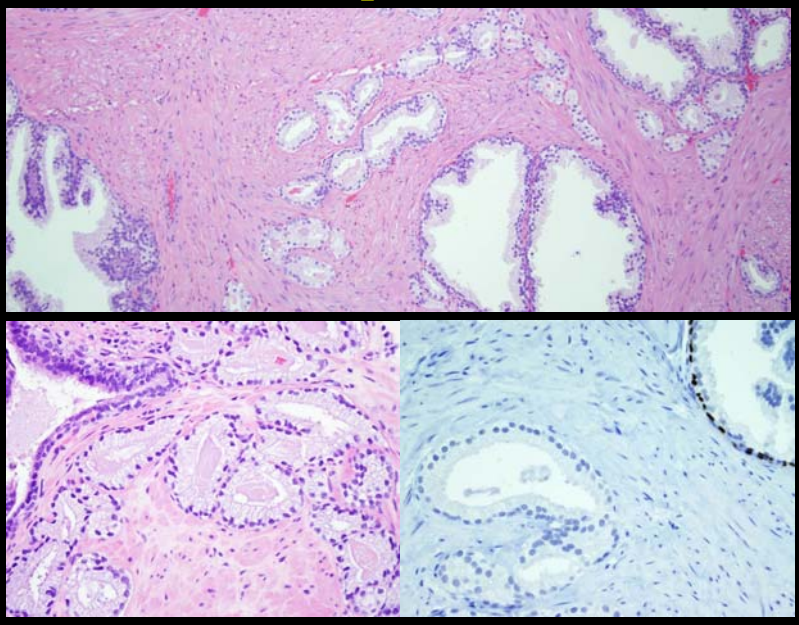
HIGH MOLECULAR WEIGHT CK



HIGH MOLECULAR WEIGHT CK



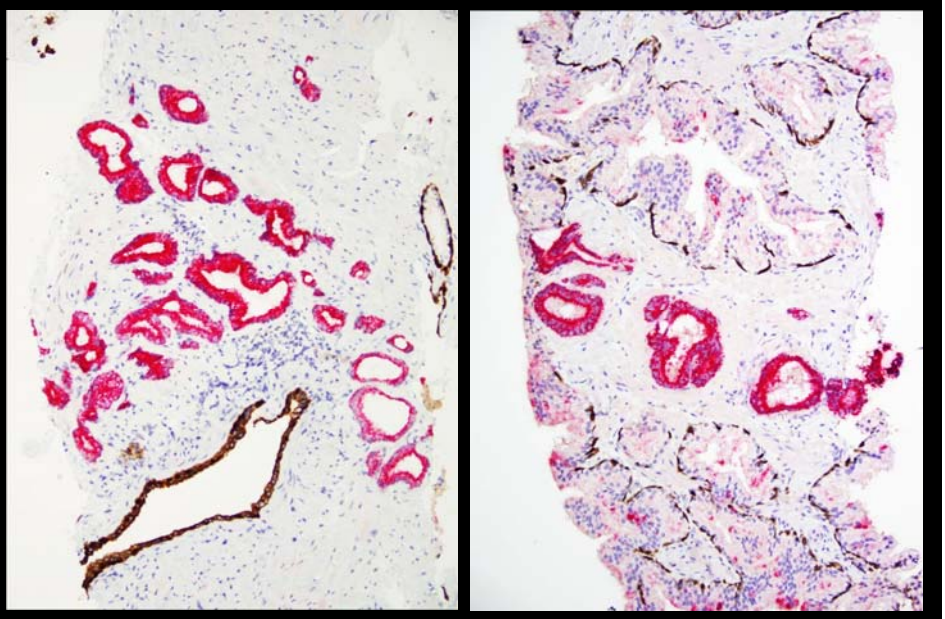
p63



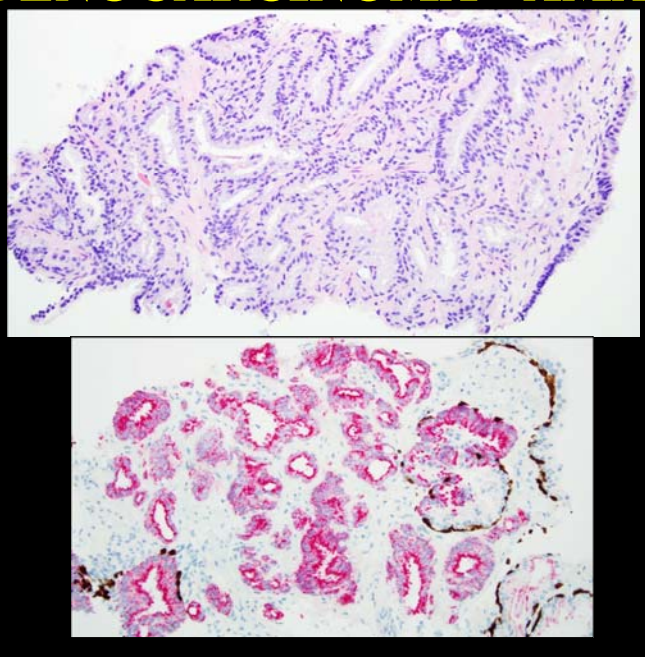
Alpha-methylacyl-CoA racemase (AMACR, p504s)

- Enzyme involved in ß-oxidation of branched chain fatty acids
- Identified as up regulated in prostate cancer through DNA microarray studies of prostate cancer
- Over-expression of protein in ~80% of cancers
- Not specific for cancer: overexpression also seen in:
  - Normal, hyperplasia, AAH (adenosis) and atrophy
  - Usually patchy and weaker but can be strong

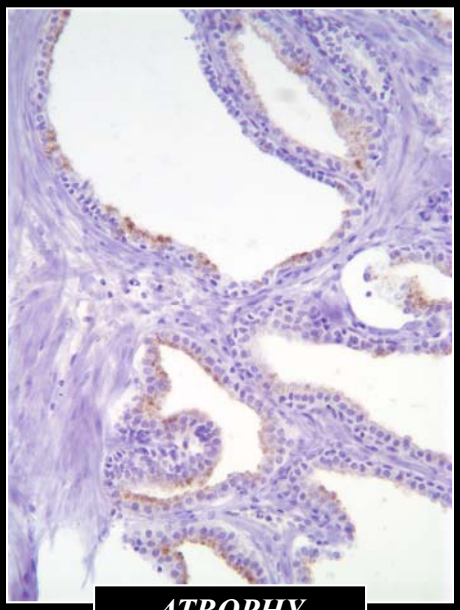
Alpha-methylacyl-CoA racemase



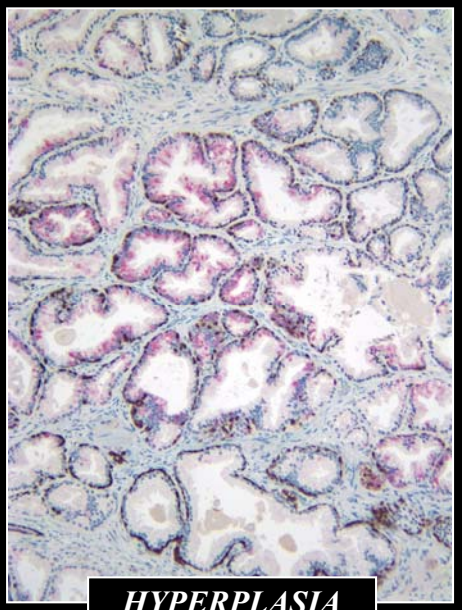
ADENOCARCINOMA - AMACR



Alpha-methylacyl-CoA racemase

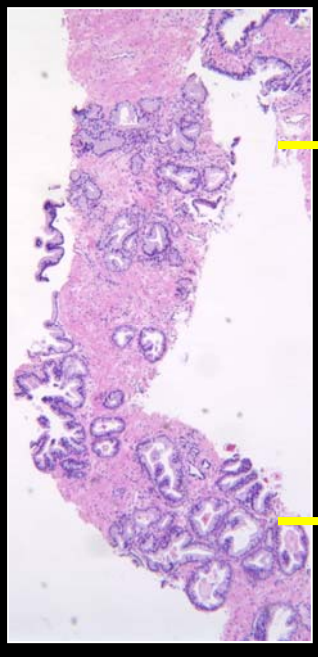


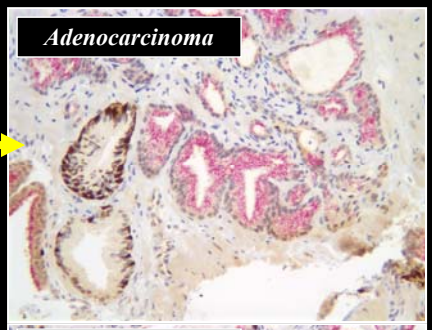
ATROPHY



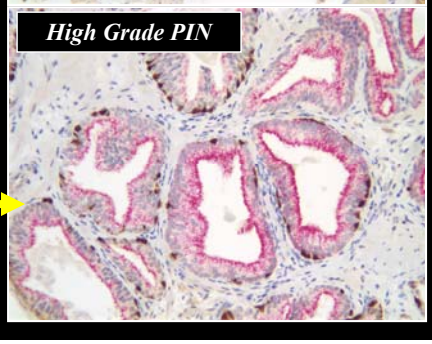
HYPERPLASIA

IHC – p504s + p63 + hmwck



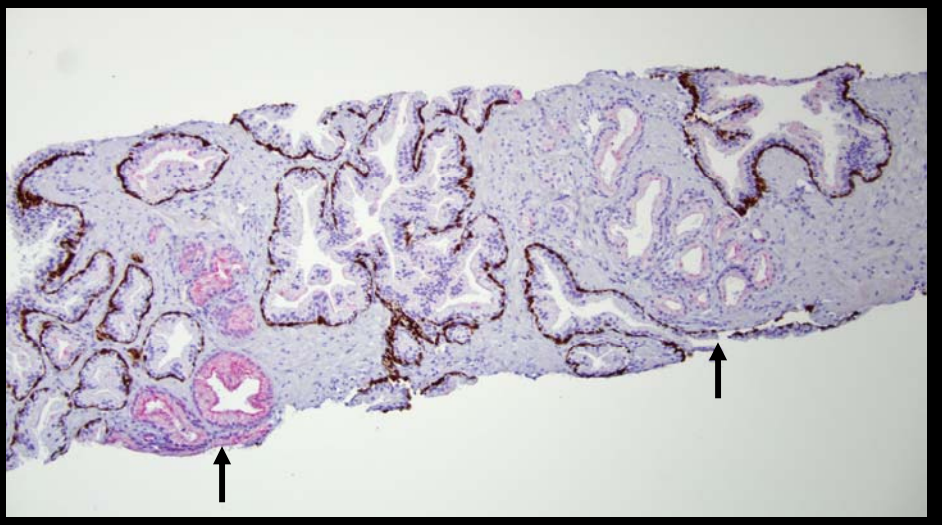


Adenocarcinoma



High Grade PIN

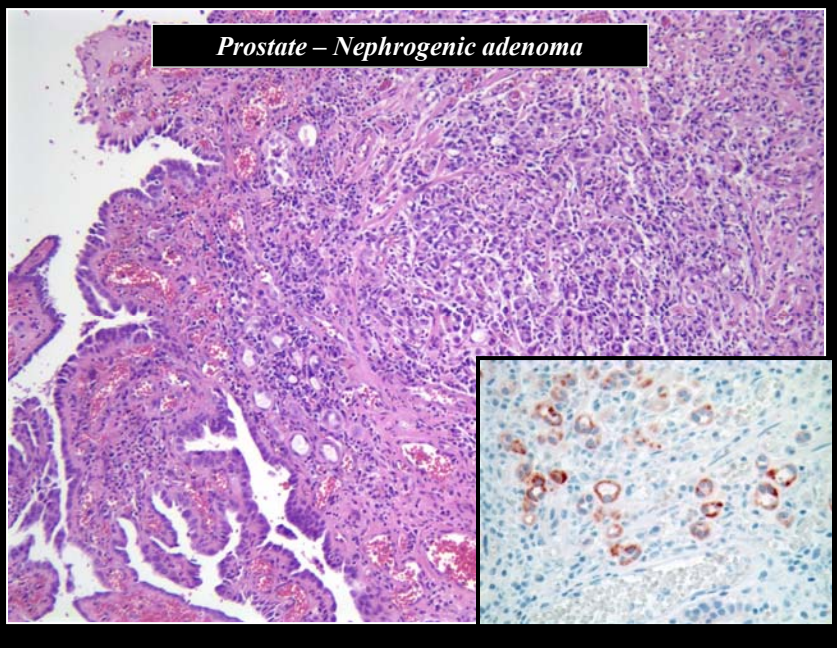
Alpha-methylacyl-CoA racemase



Positive adenocarcinoma

Negative adenocarcinoma

Alpha-methylacyl-CoA racemase

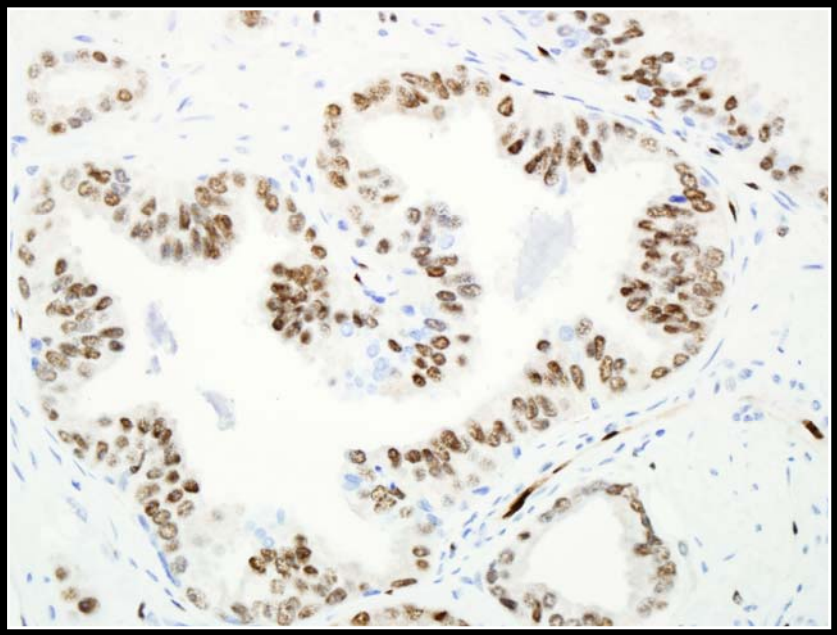


PROSTATE CANCER
TMPRSS2:ERG FUSION

- 15% - 78% of prostate cancer may have a chromosomal rearrangement at 21q22.3
- Are multiple different breakpoints
- This involves several genes
  - *TMPRSS-2* (transmembrane protease serine 2)
  - ETS family transcription factors
    - *ERG* (21q22.2) or *ETV1* (7p21.2) or *ETV4* (17q21)
- *TMPRSS-2* is highly expressed in normal and neoplastic prostate under androgen regulation
- Appears to be an early event (present in HGPIN)

ERG - IMMUNOHISTOCHEMISTRY

ERG - IMMUNOHISTOCHEMISTRY

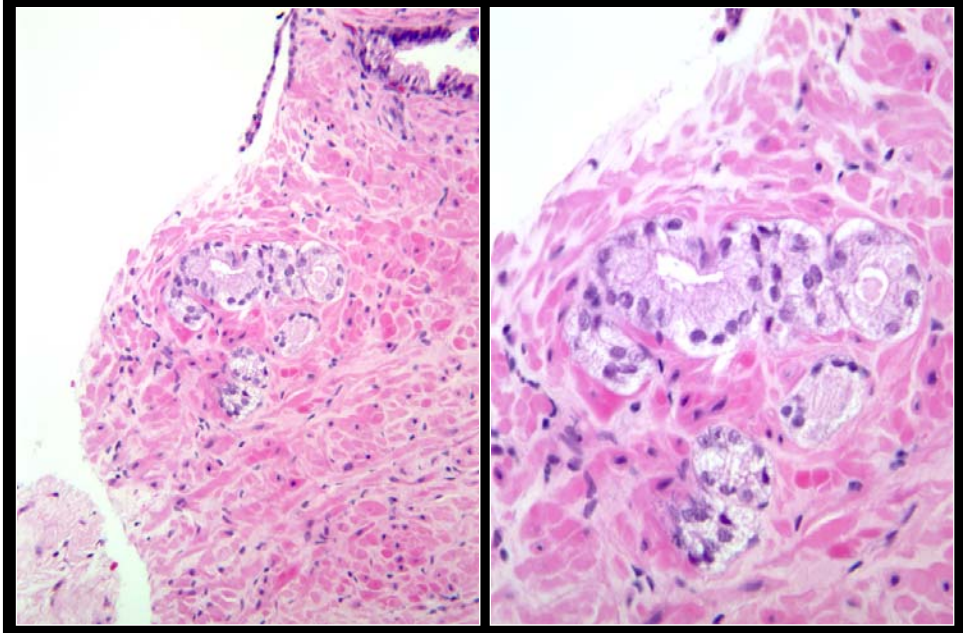


PROSTATIC ADENOCARCINOMA
MOST USEFUL DIAGNOSTIC CRITERIA

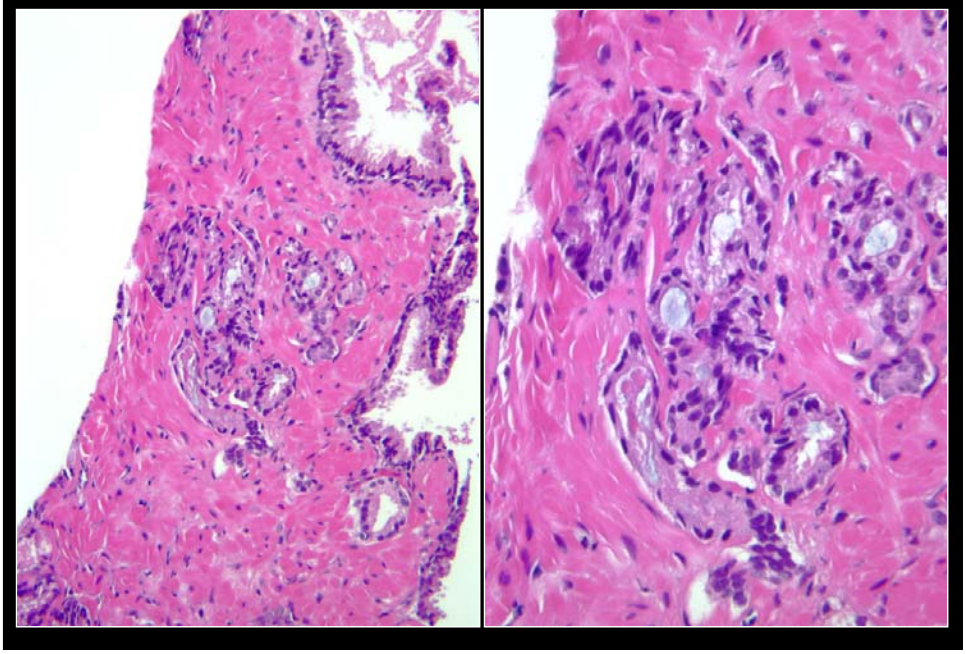
- **Prominent nucleoli**
  - **largest nucleolar diameter**
  - **mean nucleolar diameter**
  - **nucleolar diameter > 1µm**
- **Infiltrative borders**
- **Crystalloids**
- **Basophilic mucin**

Bostwick et al Hum Pathol 24:19 1993

ADENOCARCINOMA



ADENOCARCINOMA



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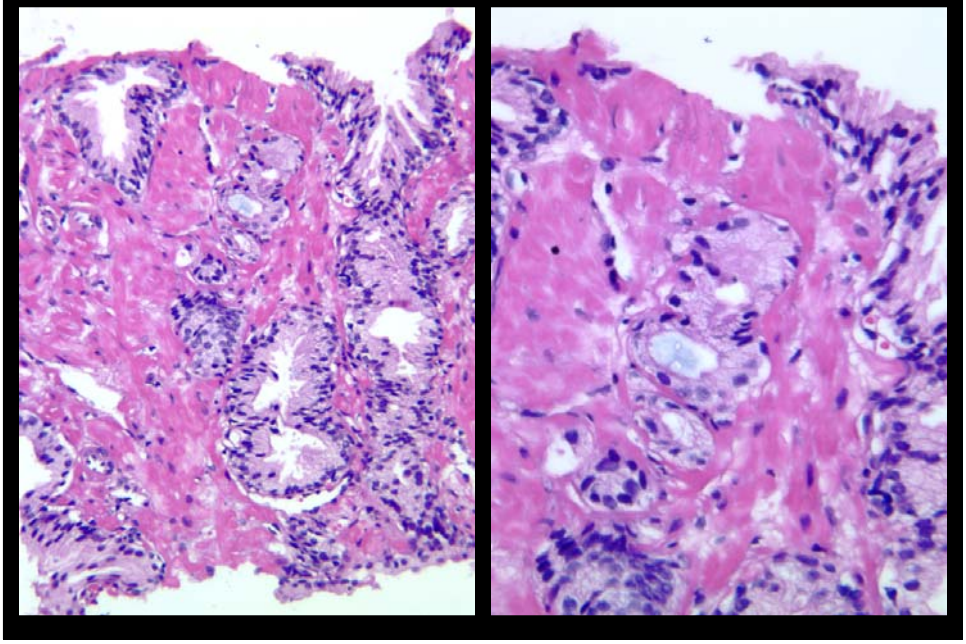
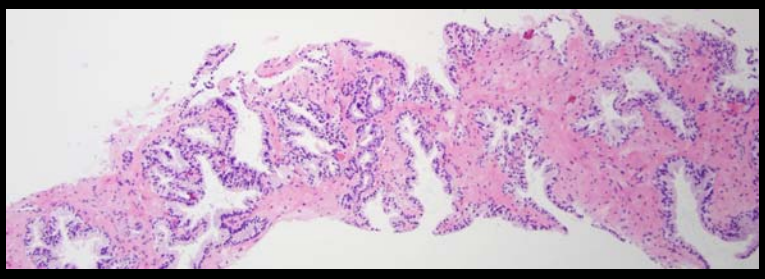
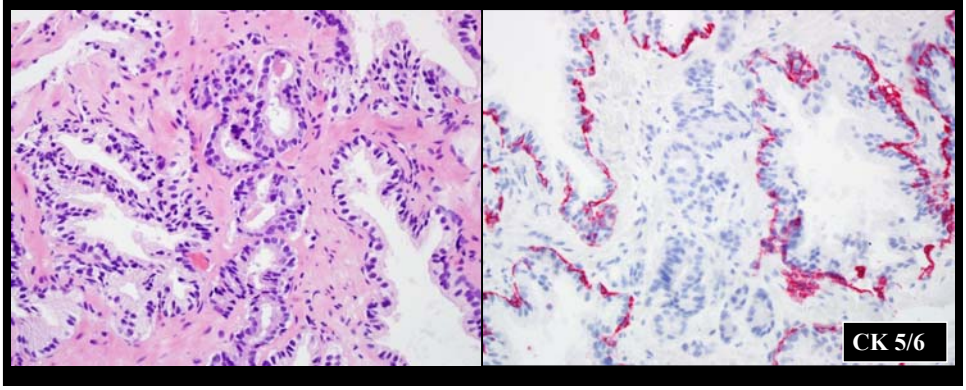


ADENOCARCINOMA





SMALL ACINAR PROLIFERATIONS DIFFERENTIAL DIAGNOSIS

Normal tissues
- Cowper's glands
- Seminal vesicle
- Paraganglionic tissue

Inflammatory
- Granulomatous prostatitis
- Xanthoma

Atrophy

PIN (outpouching)

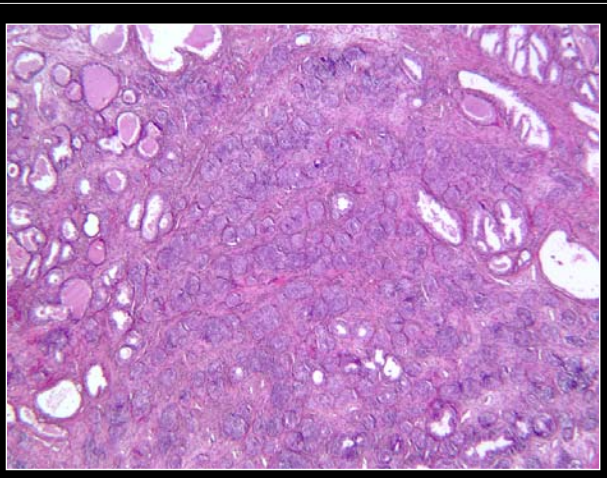
Proliferative lesions
- Basal cell hyperplasia
- Clear cell cribriform hyperplasia
- Sclerosing adenosis
- VMGH
- Mesonephric hyperplasia
- AAH (adenosis)

Other
- Nephrogenic adenoma

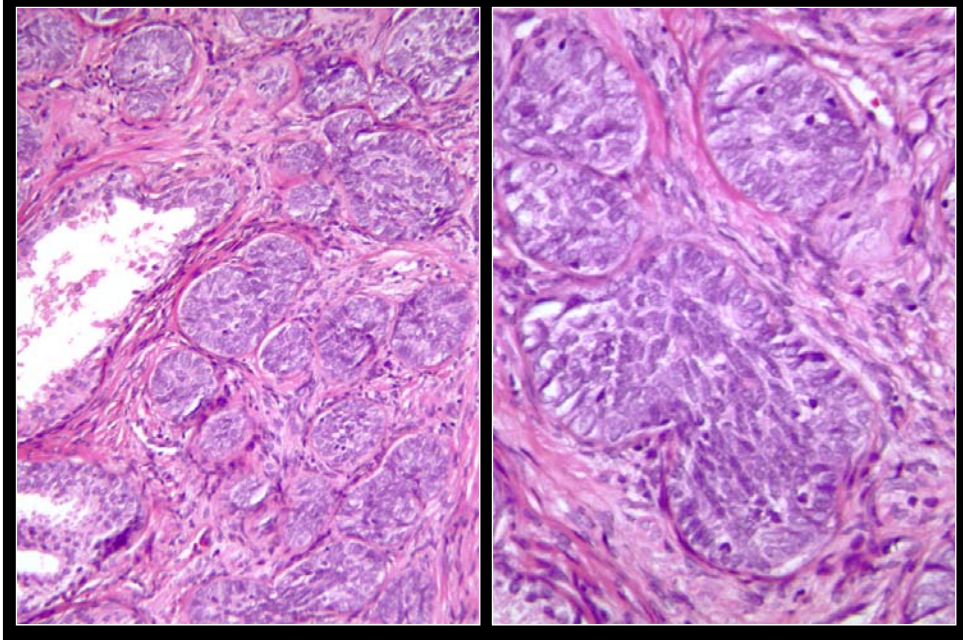
PROLIFERATIVE LESIONS

BASAL CELL HYPERPLASIA

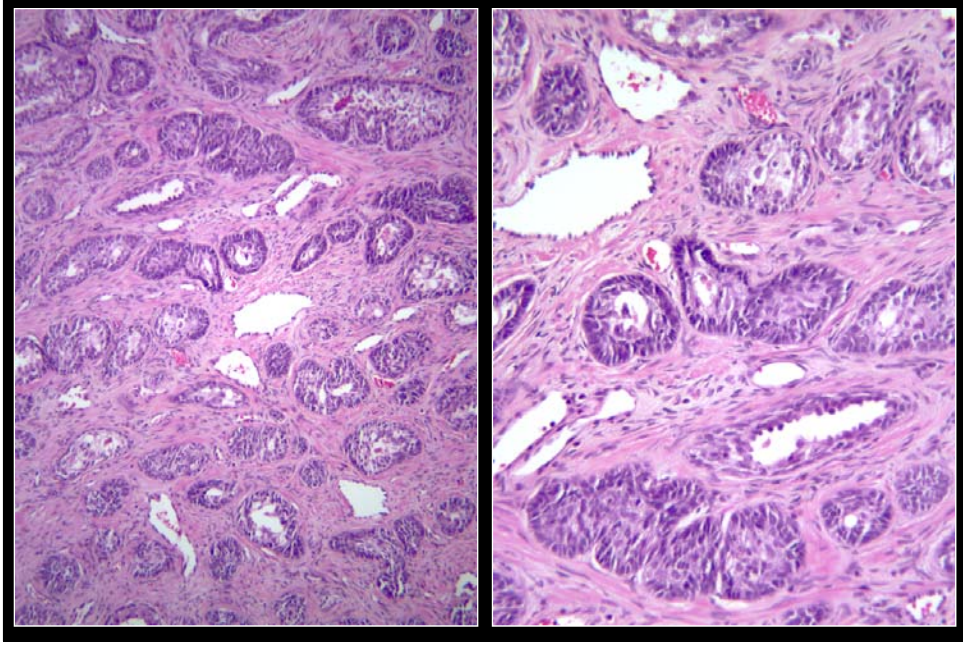
- TZ lesion – variation on usual hyperplasia
- Round or slightly irregular glands completely or partially filled with basal cells



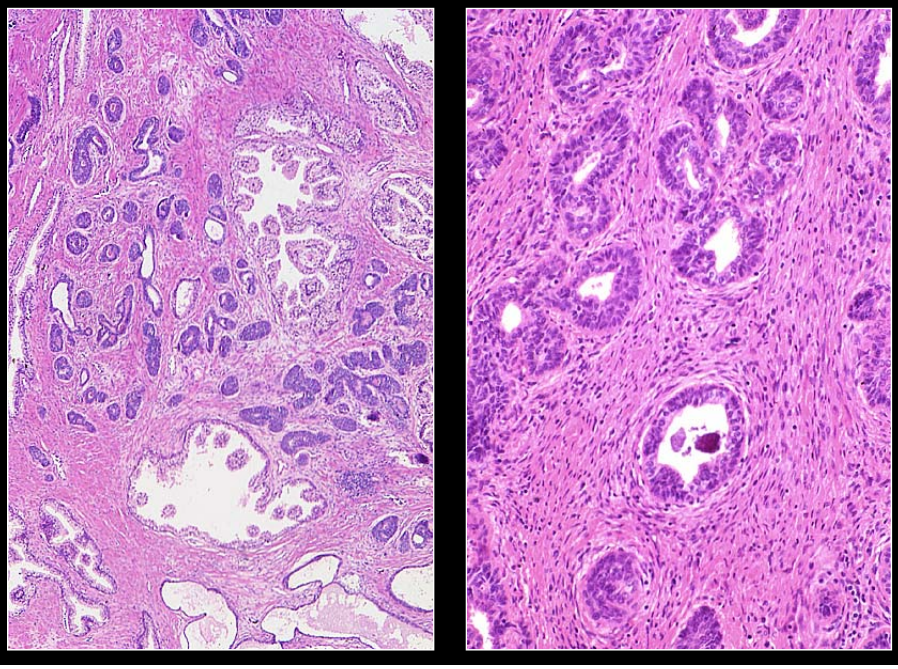
BASAL CELL HYPERPLASIA



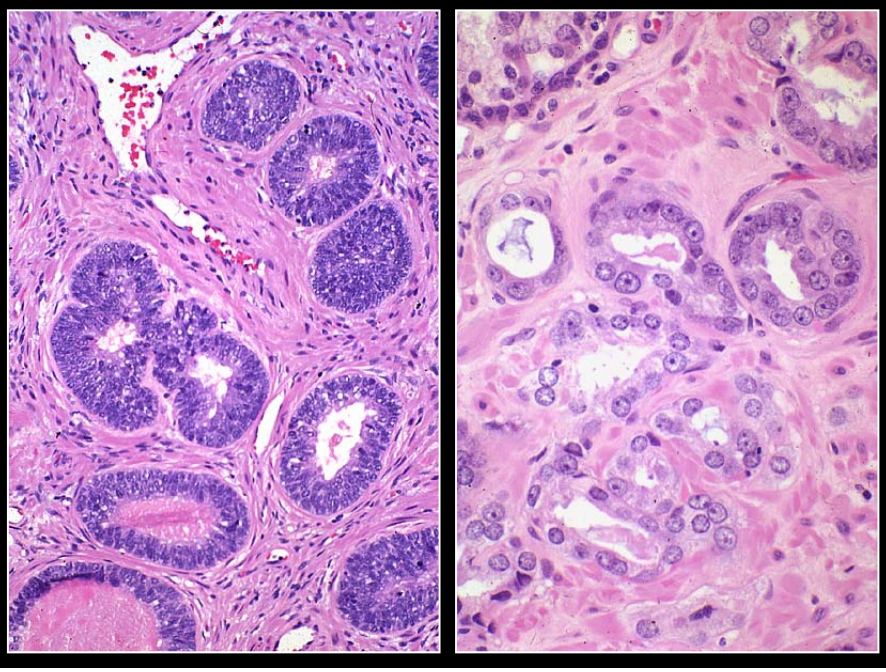
BASAL CELL HYPERPLASIA



BASAL CELL HYPERPLASIA

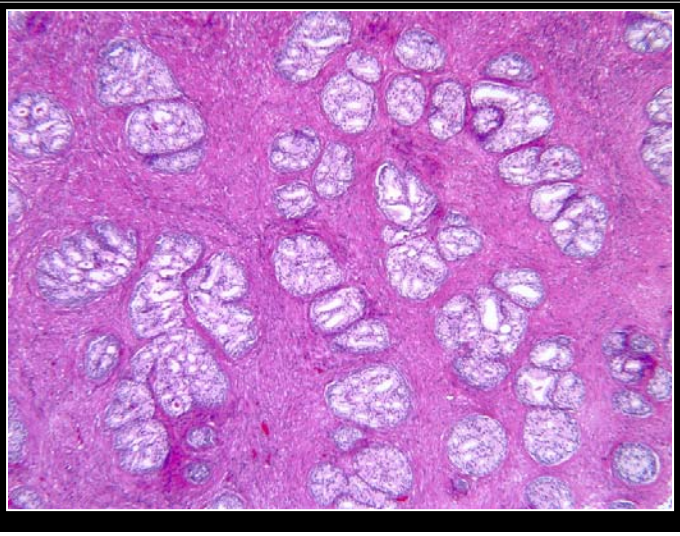


BCH *vs* CARCINOMA

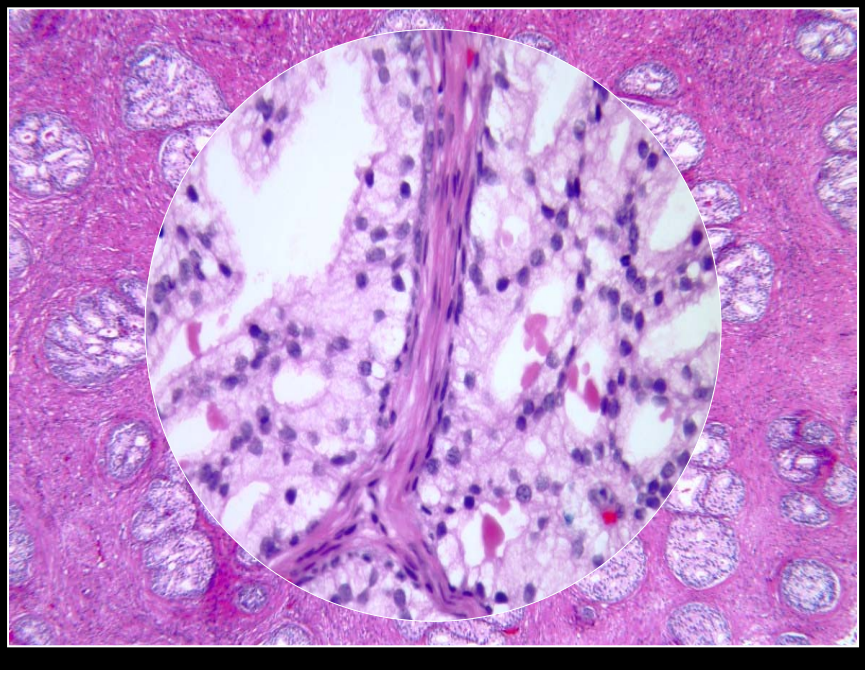


CLEAR CELL CRIBRIFORM HYPERPLASIA

- **TZ lesion – variant of usual hyperplasia**
- **Cribriform glands with cells having pale cytoplasm and no nuclear atypia**

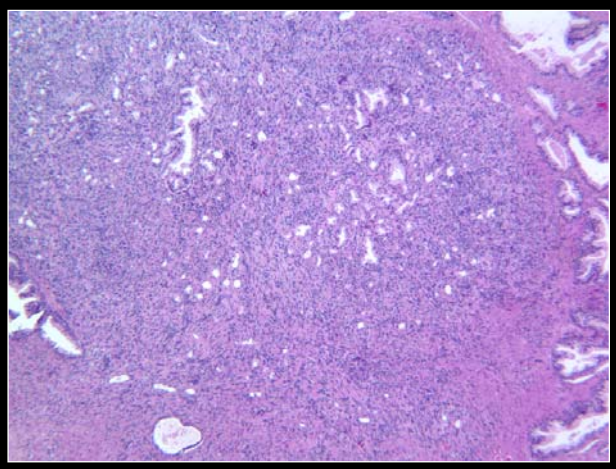


CLEAR CELL CRIBRIFORM HYPERPLASIA

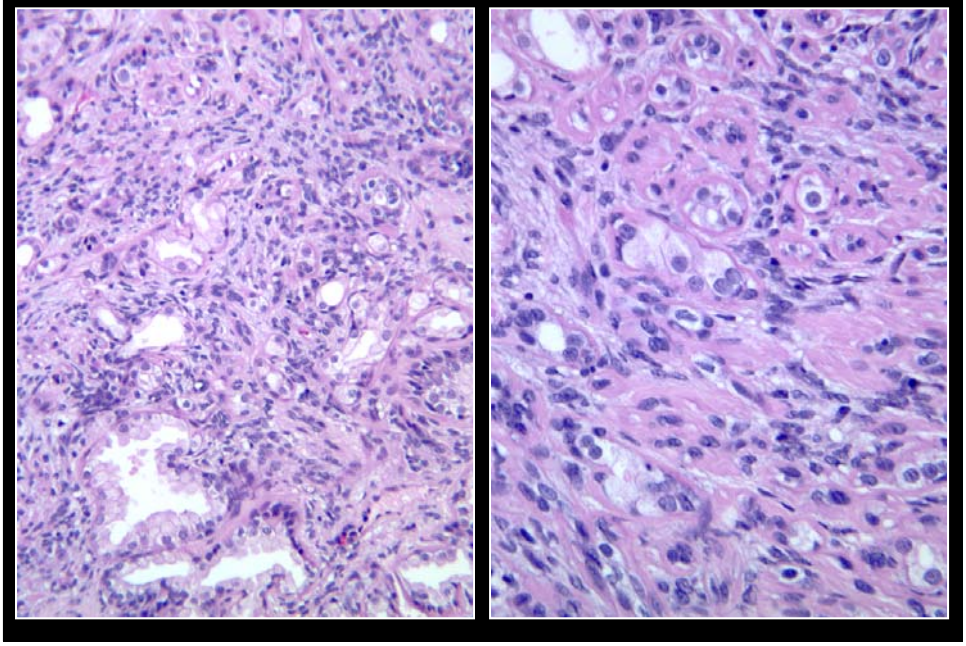


SCLEROSING ADENOSIS

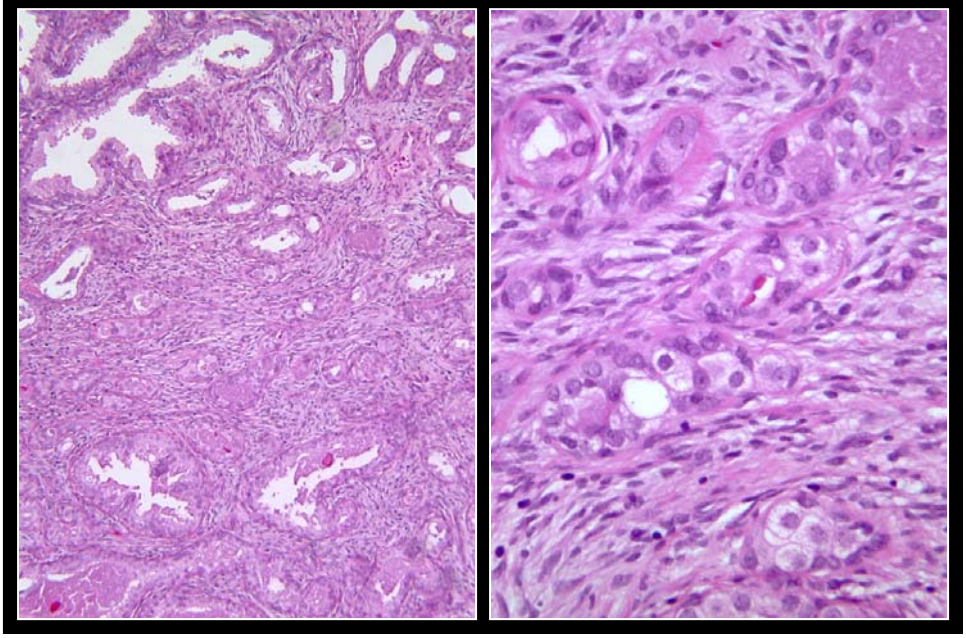
- Rare TZ lesion – incidental finding in TURP or RP
- Busy lesion with small to irregular glands
- Basal cells undergo myoepithelial metaplasia



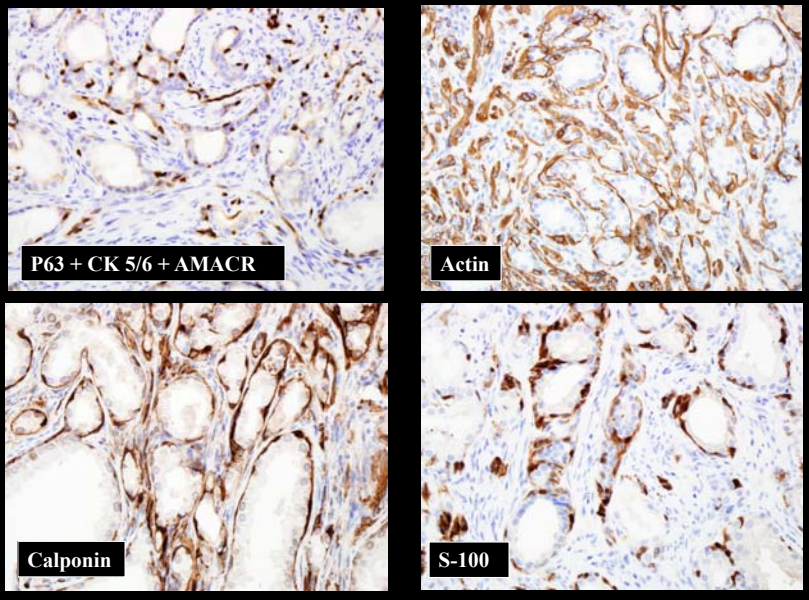
SCLEROSING ADENOSIS



SCLEROSING ADENOSIS

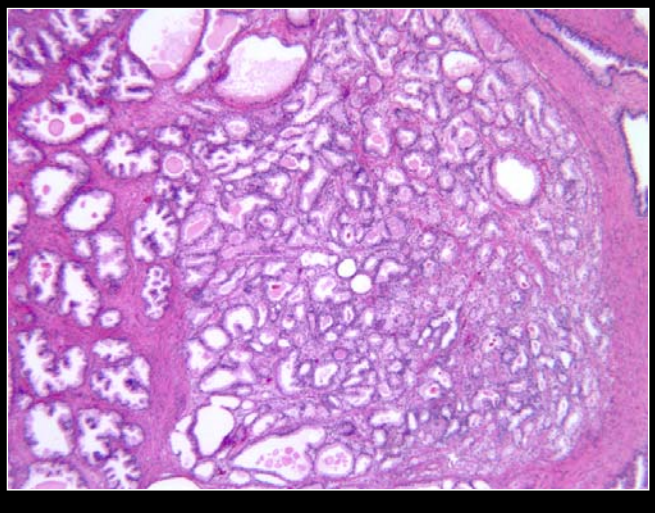


SCLEROSING ADENOSIS

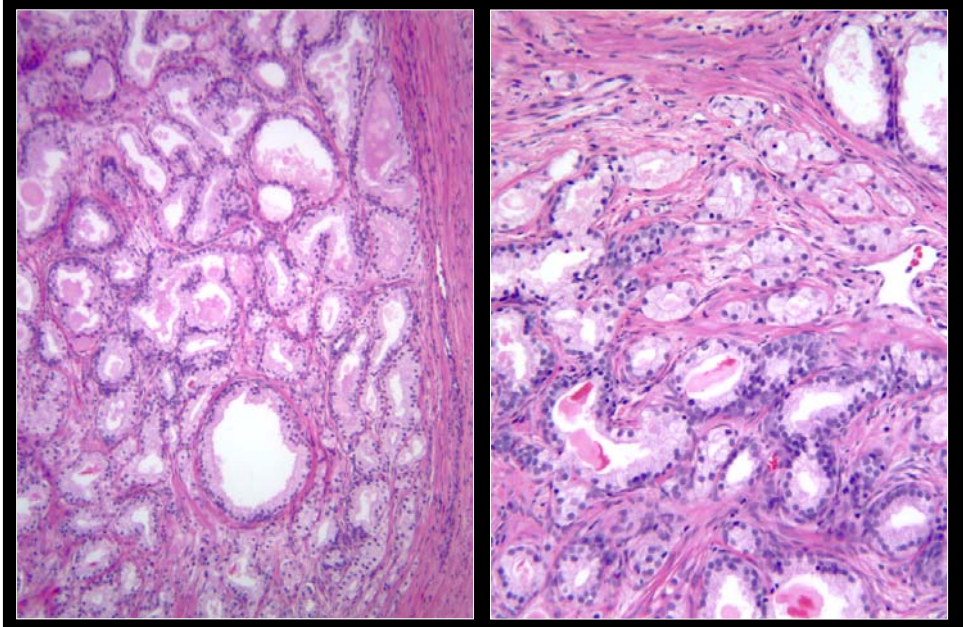


ATYPICAL ADENOMATOUS HYPERPLASIA (ADENOSIS)

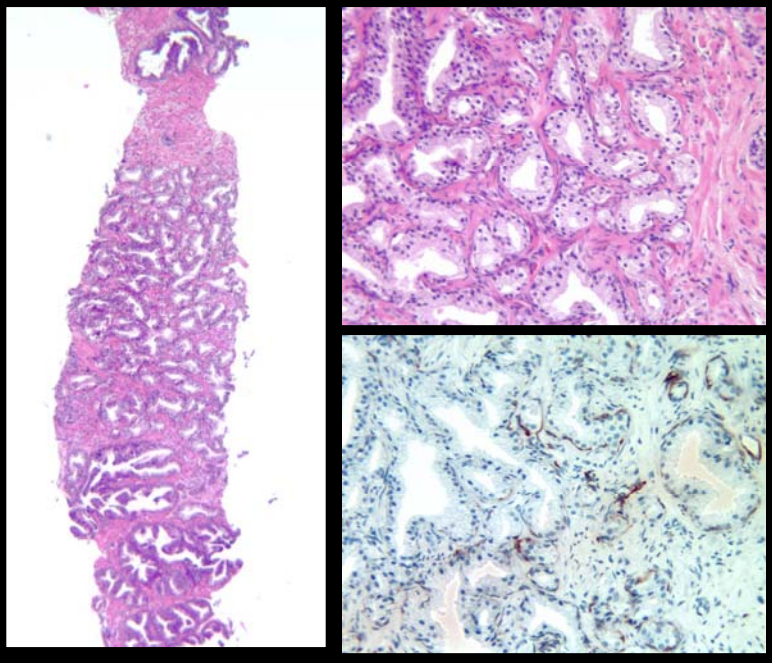
- Predominantly TZ lesion – part of usual hyperplasia
- Transition of obvious benign to worrisome small glands
- Patchy loss of basal cells and overexpression of racemase



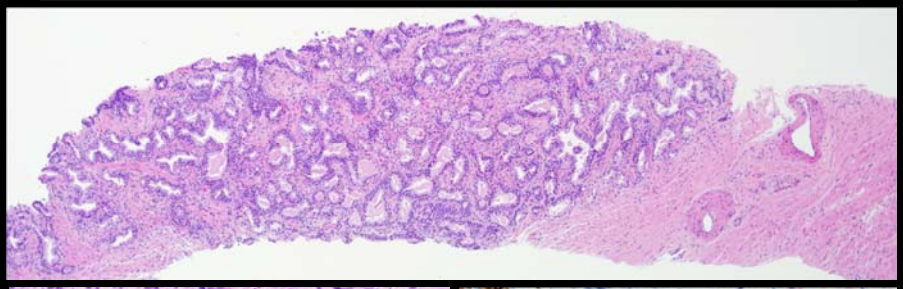
ATYPICAL ADENOMATOUS HYPERPLASIA (ADENOSIS)

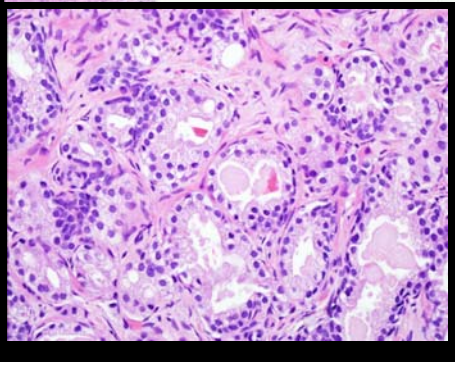


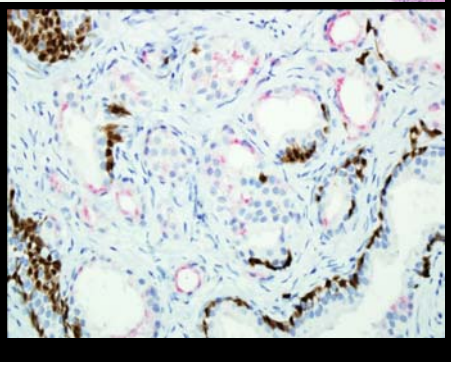
ATYPICAL ADENOMATOUS HYPERPLASIA (ADENOSIS)



Atypical Adenomatous Hyperplasia

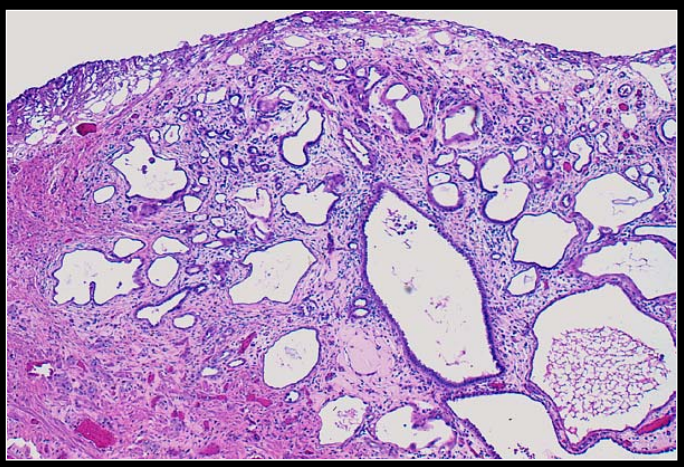




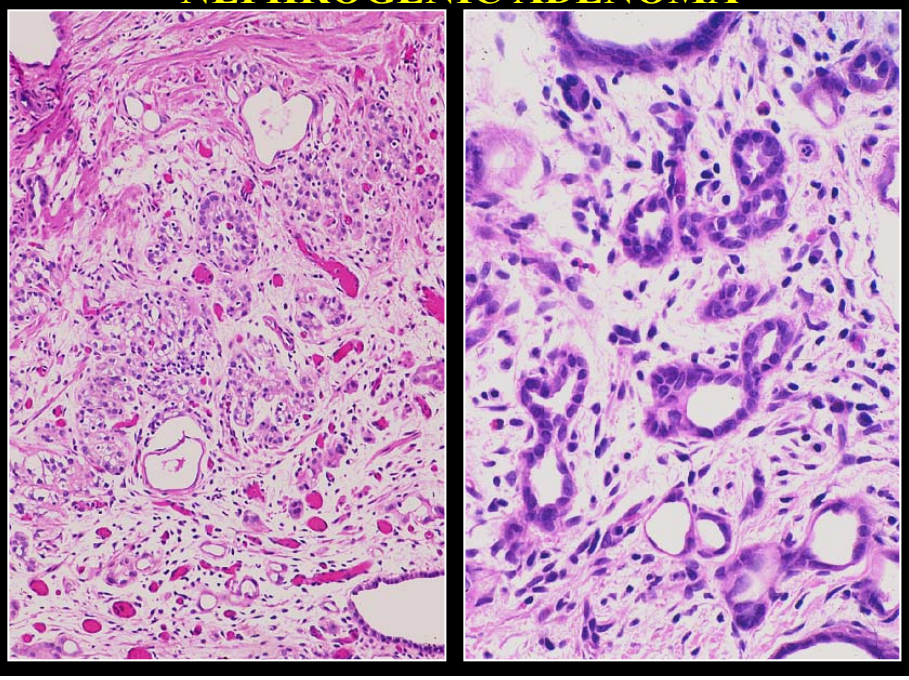


NEPHROGENIC ADENOMA

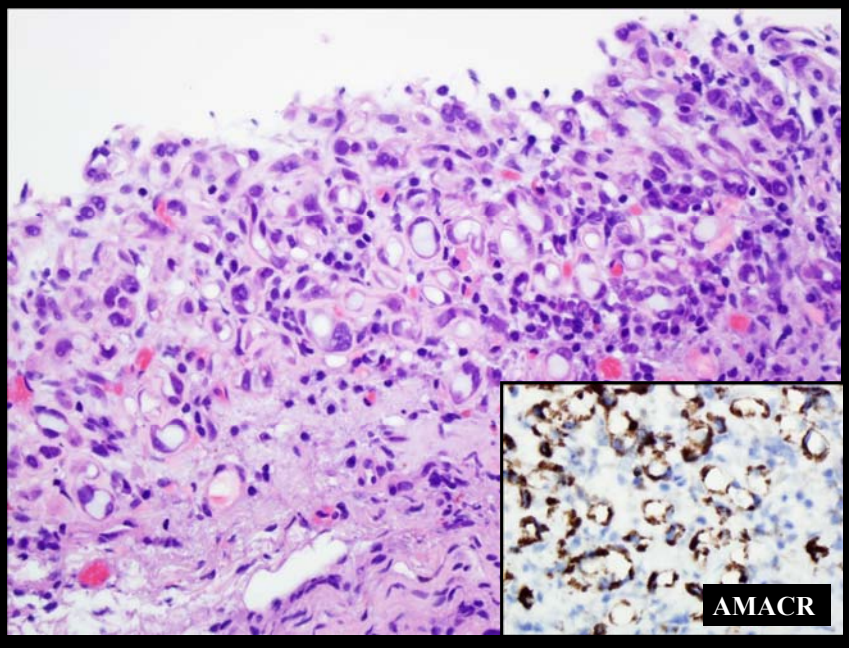
- Infrequently involves the prostatic urethra
- Tubules (with thick BM) and papillary structures
- Positive for AMACR and PAX8



NEPHROGENIC ADENOMA

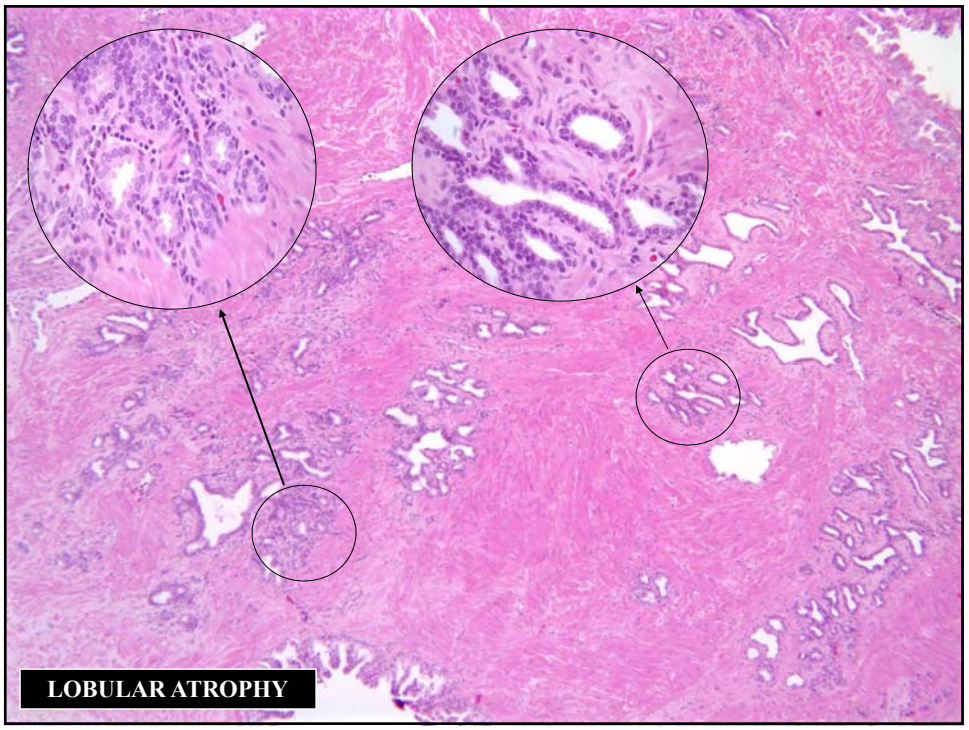


NEPHROGENIC ADENOMA

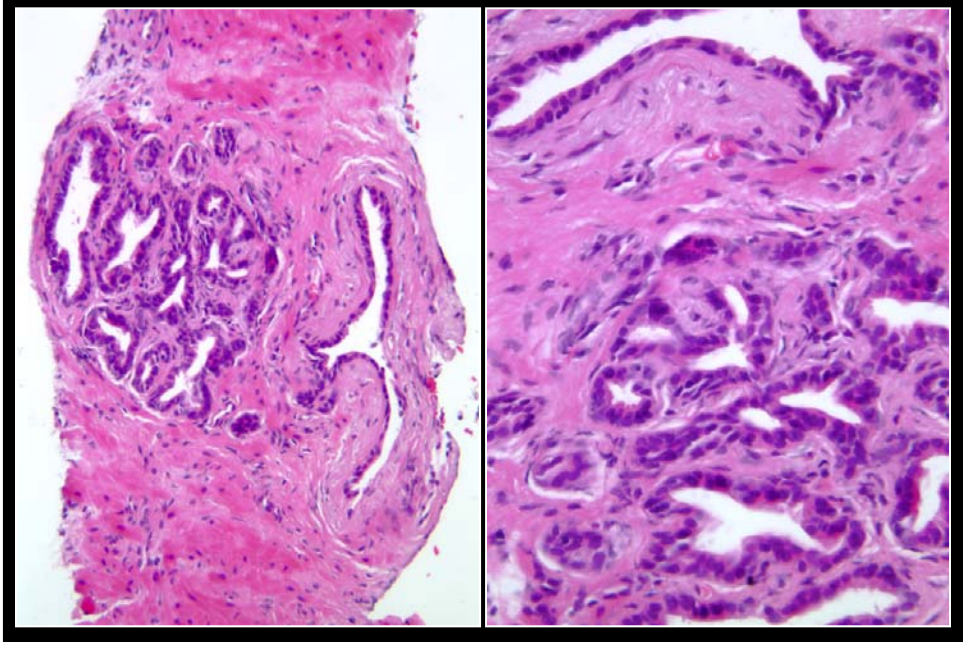


PROSTATIC ATROPHY

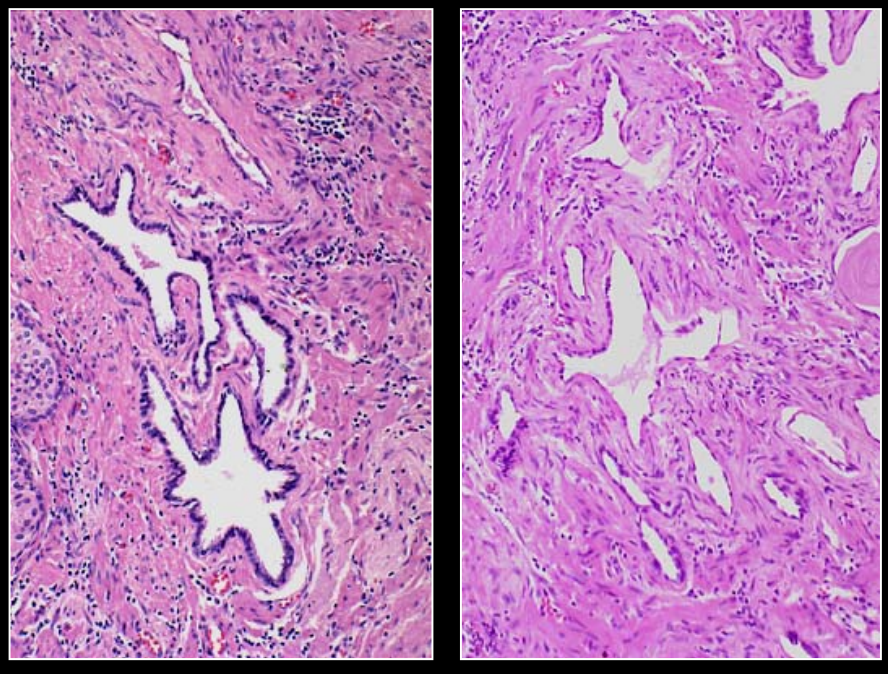
- Foci appear as early as 3rd decade
- Associated with prior inflammation
- May be side by side with BPH
- Clinical significance:
  - Can mimic CA on US (hypoechoic)
  - Can mimic CA on histology
  - Can cause elevated PSA (?)



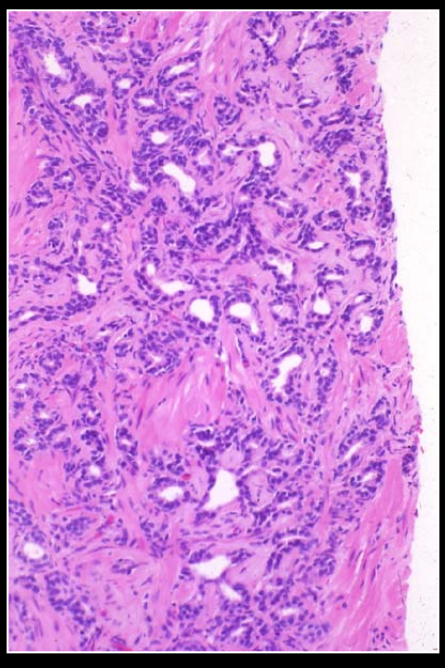
SIMPLE LOBULAR ATROPHY

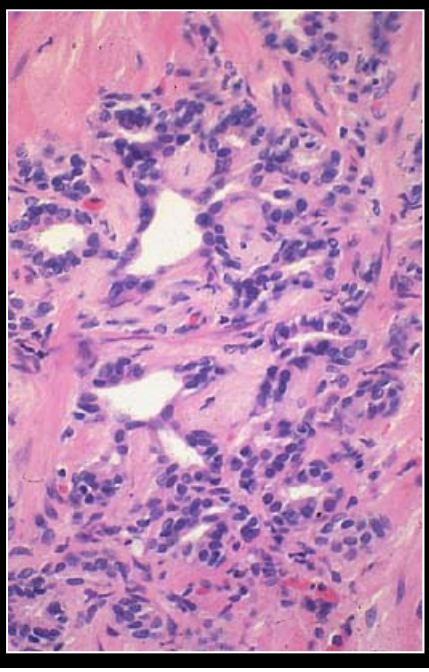


SCLEROTIC ATROPHY

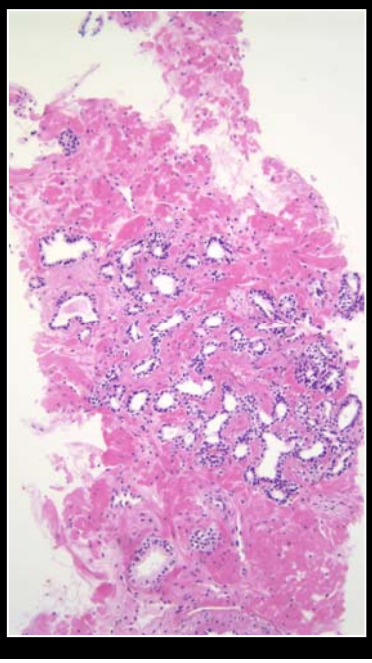


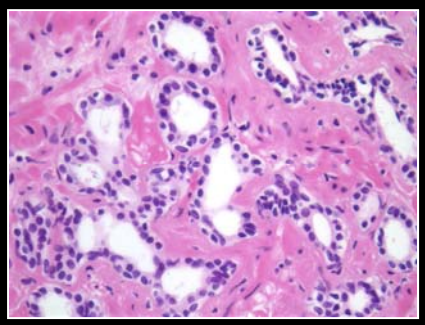
POSTATROPHIC HYPERPLASIA

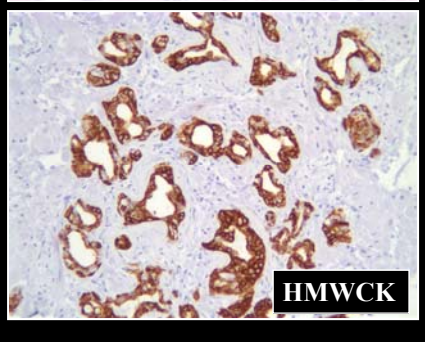




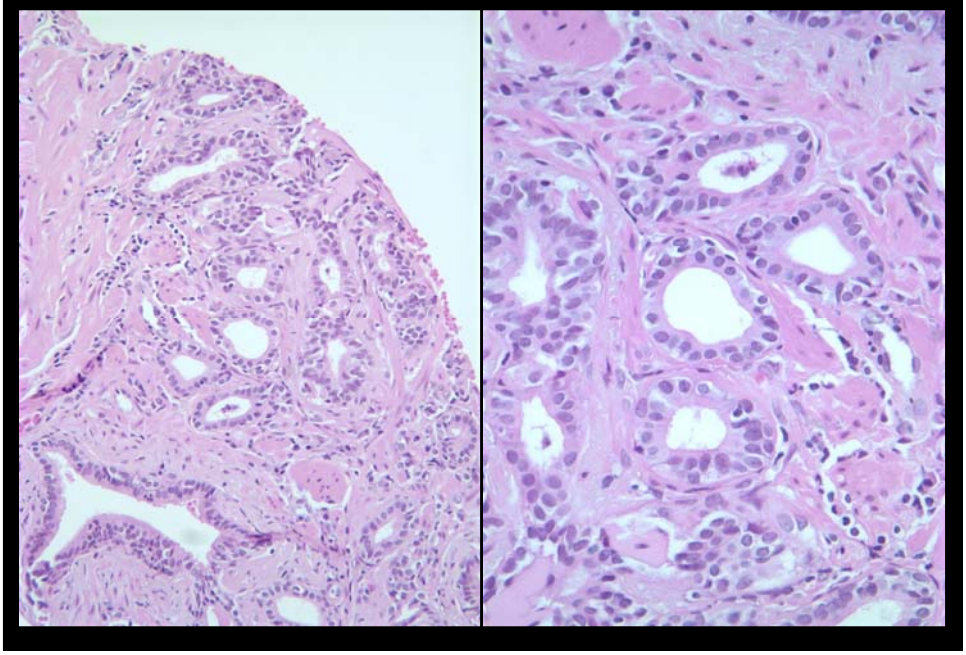
POSTATROPHIC HYPERPLASIA



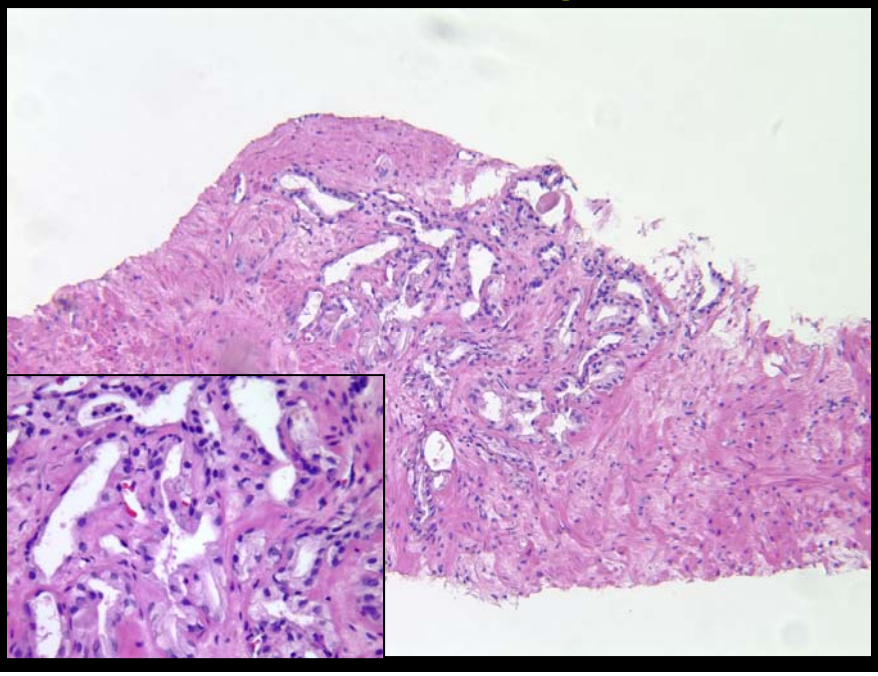


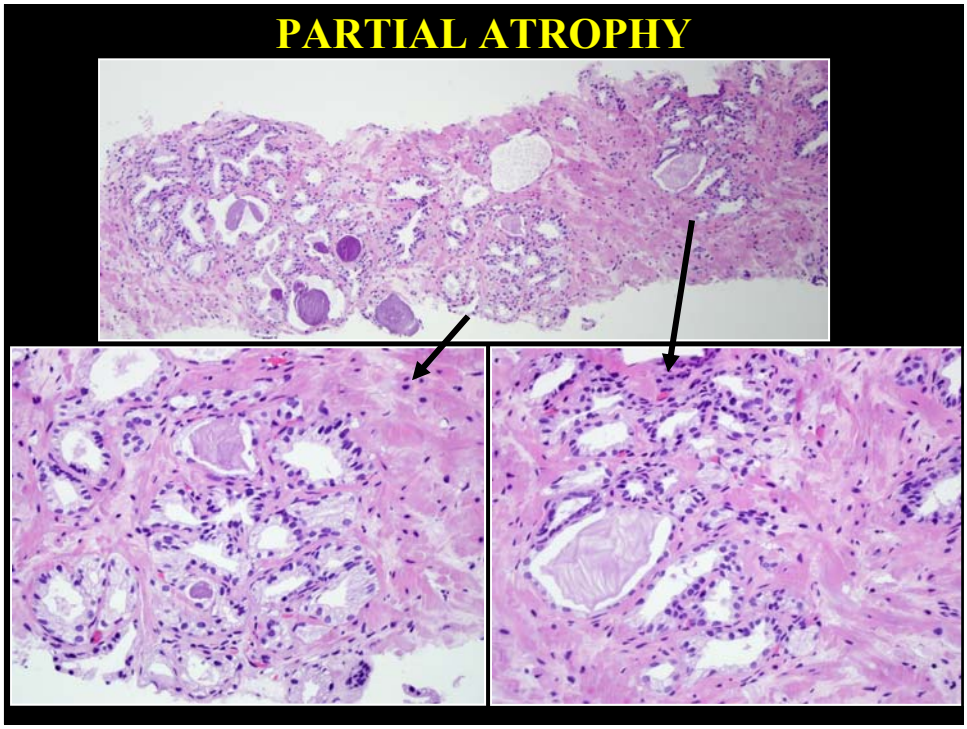


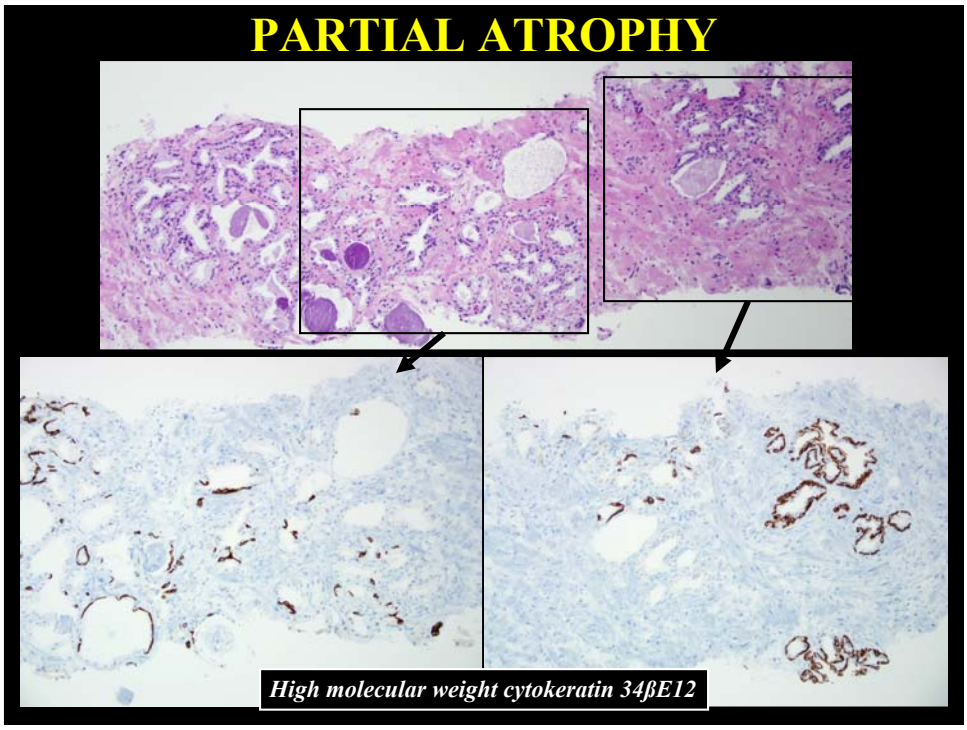
POSTATROPHIC HYPERPLASIA



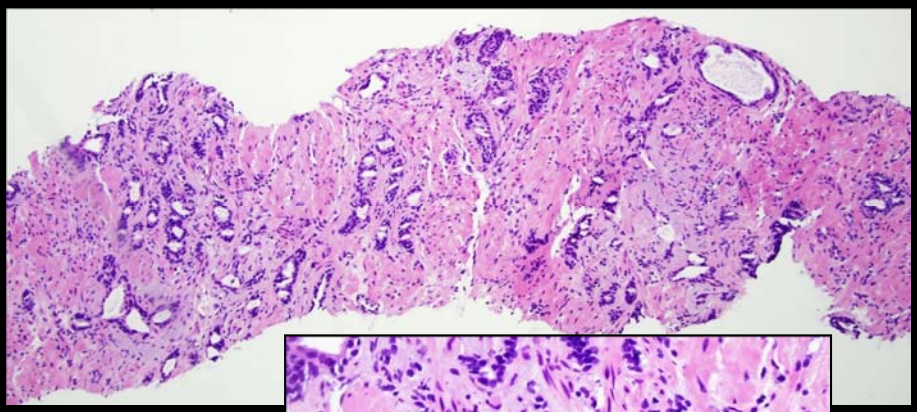
PARTIAL ATROPHY



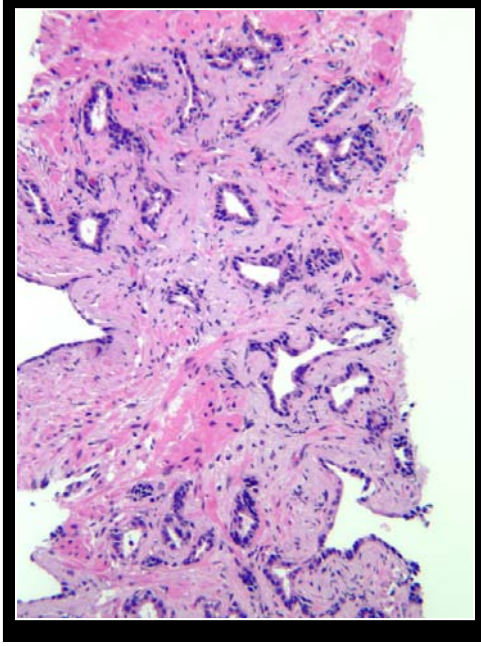

PARTIAL ATROPHY

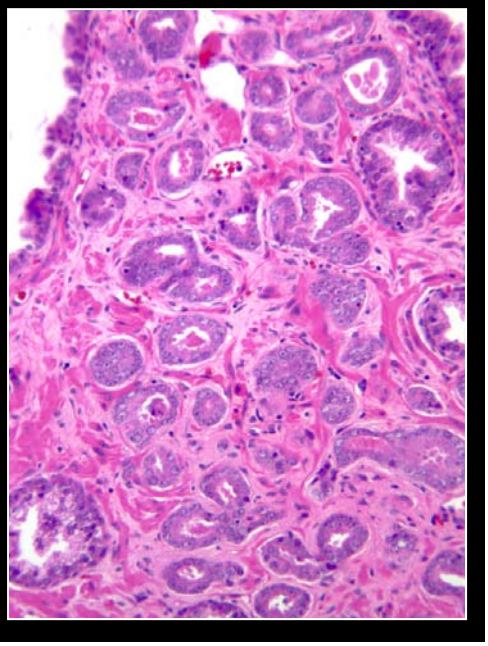

PARTIAL ATROPHY
High molecular weight cytokeratin 34ßE12

ATROPHY – "Infiltrative growth"



ATROPHY *vs* CARCINOMA

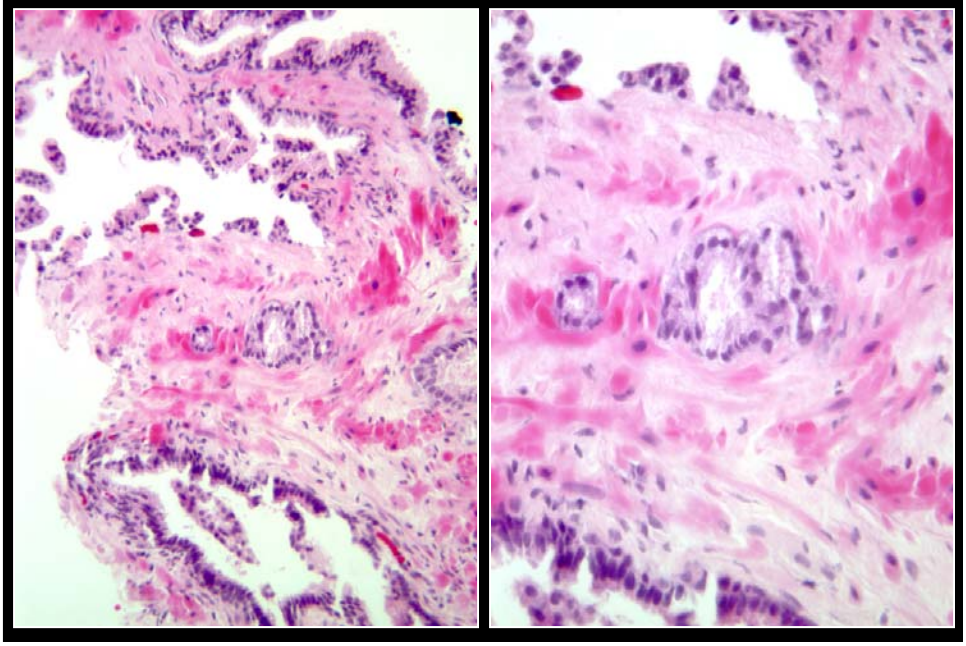




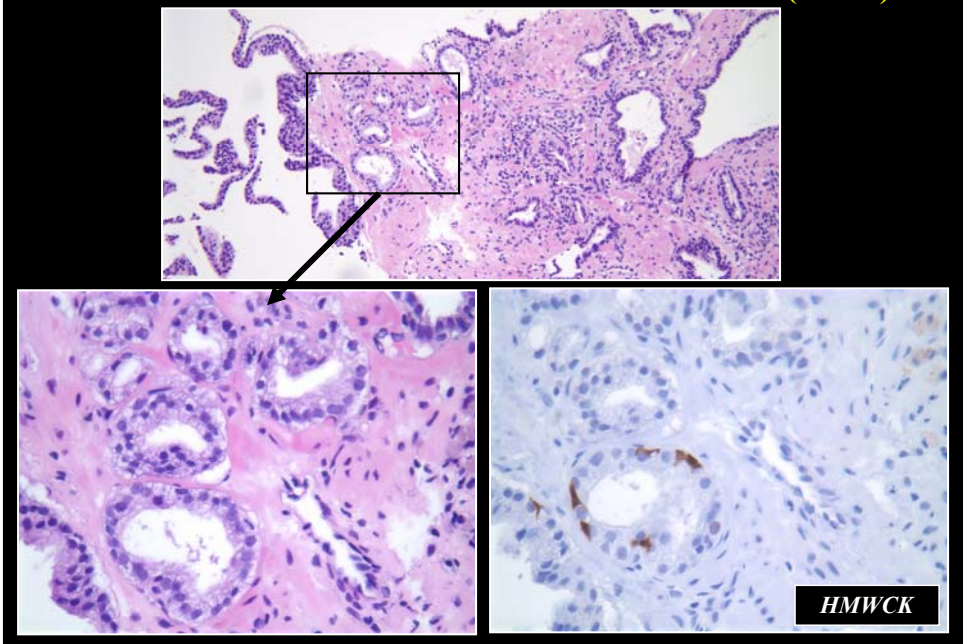
ATYPICAL SMALL ACINAR PROLIFERATION (ASAP)

- Term used for cases where a definitive benign or malignant diagnosis cannot be rendered
- Is not a specific pathologic entity
- In many cases represents small foci of carcinoma that do not fulfill diagnostic criteria
- Others represent benign processes such as atrophy where cancer cannot be excluded
- Re-biopsy yields cancer in about 50% of cases

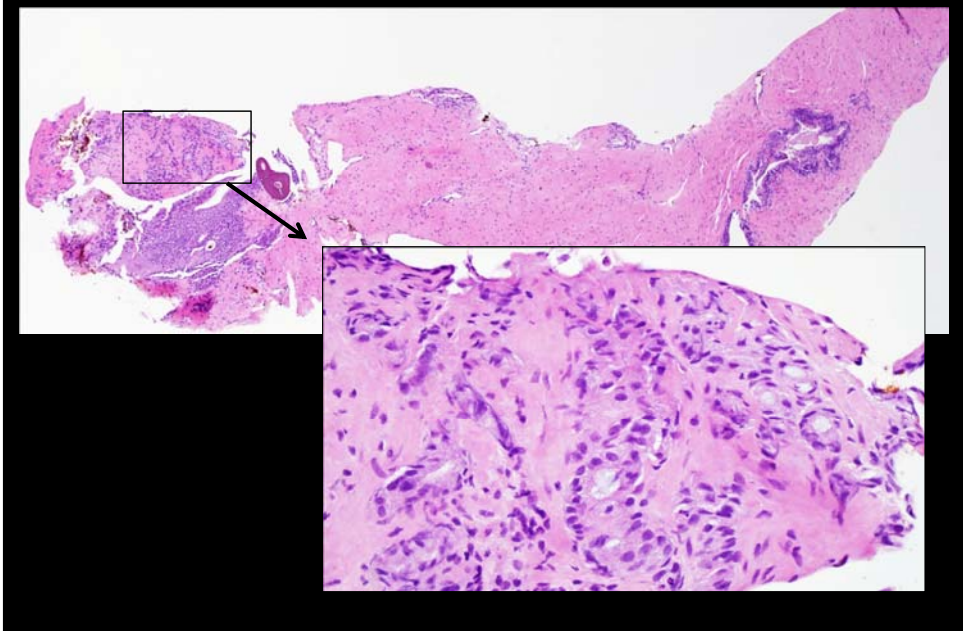
ATYPICAL SMALL ACINAR PROLIFERATION (ASAP)

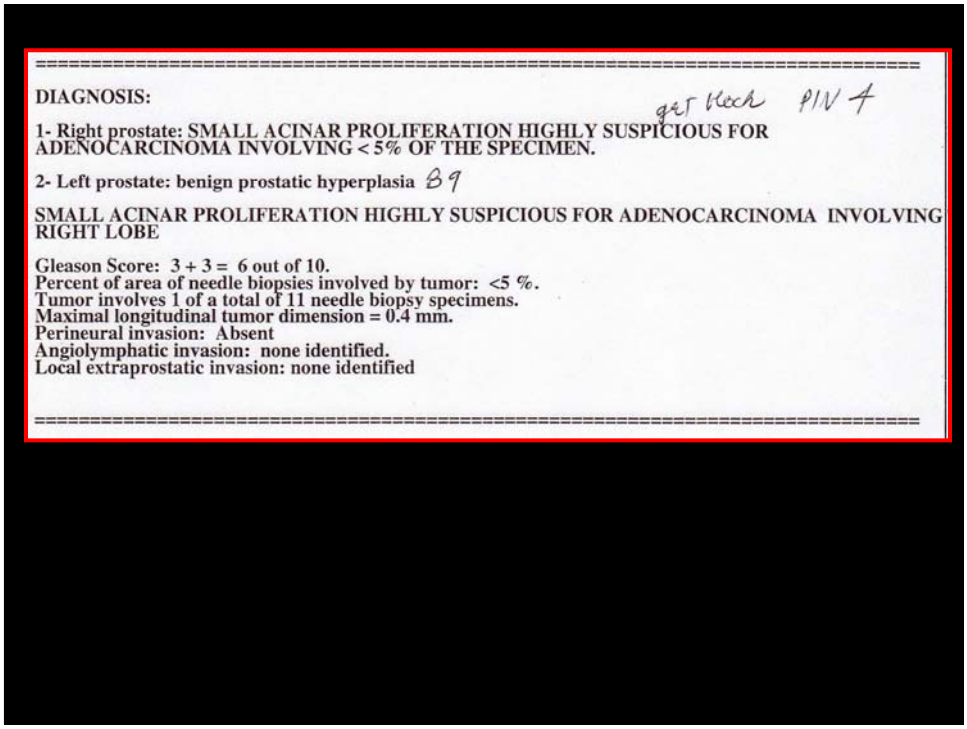


ATYPICAL SMALL ACINAR PROLIFERATION (ASAP)



ATYPICAL SMALL ACINAR PROLIFERATION (ASAP)





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DIAGNOSIS:

1- Right prostate: SMALL ACINAR PROLIFERATION HIGHLY SUSPICIOUS FOR ADENOCARCINOMA INVOLVING < 5% OF THE SPECIMEN.

2- Left prostate: benign prostatic hyperplasia

SMALL ACINAR PROLIFERATION HIGHLY SUSPICIOUS FOR ADENOCARCINOMA INVOLVING RIGHT LOBE

Gleason Score: 3 + 3 = 6 out of 10.
Percent of area of needle biopsies involved by tumor: <5 %.
Tumor involves 1 of a total of 11 needle biopsy specimens.
Maximal longitudinal tumor dimension = 0.4 mm.
Perineural invasion: Absent
Angiolymphatic invasion: none identified.
Local extraprostatic invasion: none identified

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