Prostate cancer

Mohan Arianayagam
Urologic Oncologist
Nepean Hospital

What is PSA

- 34kDa
- Serine protease
- Liquefies coagulum to liberate sperm
- High concentration in seminal fluid
- Action inhibited in prostate by zinc
- Serum half life about 3 days

Factors lowering PSA

- Obese men
- Statins
- 5 alpha reductase inhibitors
- TURP, prostatectomy, radiotherapy
- LHRH agonist, androgen inhibitors

5 alpha reductase inhibitors

- finasteride, dutasteride
- PSA reduced by 50% at about 12 months
- Even low dose (propecia) will reduce PSA
- Require PSA levels to be done prior to starting

5 alpha reductase and Ca P

- Finsteride vs placebo (PCPT)
  - Reduced overall risk of prostate cancer
  - Increased risk of higher grade cancers
- Dutasteride vs placebo (REDUCE)
  - 23% reduction in prostate cancers
  - No increase in higher grade cancers

Factors that may raise PSA

- Prostate cancer
- Benign prostate enlargement
- Prostatitis/UTI
- Stimulation/ejaculation
- Prostate massage
- TURP/cystoscopy

PSA and cancer risk

PSA	DRE	Cancer risk
0-2	-	12%
2-4	-	15-25%
4-10	-	50%
>10	-	40-60%
>10	+	70-90%

PSA derivatives

- Density
- Velocity
- Isoforms
  - Free PSA >25% - low risk
  - (validated for PSA 4 – 10)

Practical approach

- Counsel before ordering PSA
- If PSA is within normal range, check annually (&DRE)
- Refer if elevated or rising
- If significantly elevated/associated LUTS try antibiotics first

What is screening?

- Test for disease in healthy asymptomatic populations

What is goal of screening

- Improve overall health by identifying and treating disease at early stage
- But the treatment may also lead to harm

Prostate cancer screening trials

- ERPSC trial
  - Reduced advanced/metastatic disease and reduced mortality
  - To save one life screen 1400 men and treat 48
- PLCO
  - No difference

What is the difference

- Localised
- Locally advanced
- metastatic

Symptoms of prostate cancer

- Early/localised
  - none
- Locally advanced
  - Urinary symptoms
  - Ureteric obstruction
  - Haematospermia
  - ED
  - Reduced ejaculate volume

Symptoms of prostate cancer

- Metastatic
  - Bone pain
  - Fractures
  - Anaemia
  - Lower extremity oedema
  - Malignant retroperitoneal fibrosis

staging

- Determine extent of disease
- Helps with prognostication
- Requires
  - PSA
  - DRE
  - Gleason sum
  - Number of cores positive
  - CT and/or bone scan

TNM staging

- TX Primary tumour cannot be assessed

- T0 No evidence of primary tumour

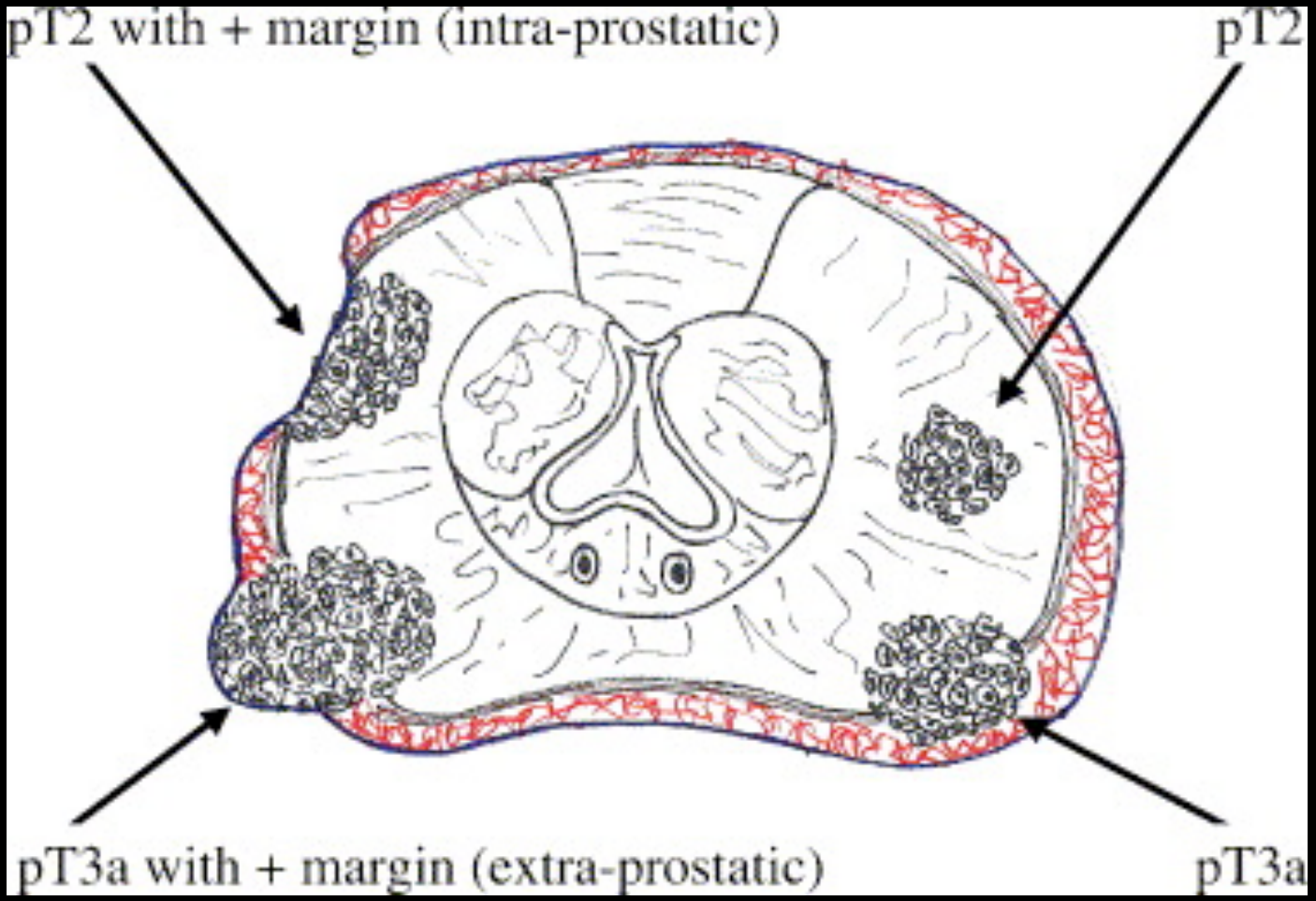
- T1 Clinically inapparent tumour not palpable or visible by imaging
- T1a Tumour incidental histological finding in 5% or less of tissue resected
- T1b Tumour incidental histological finding in more than 5% of tissue resected
- T1c Tumour identified by needle biopsy (e.g. because of elevated prostate-specific antigen [PSA]
- level)

- T2 Tumour confined within the prostate
- T2a Tumour involves one half of one lobe or less
- T2b Tumour involves more than half of one lobe, but not both lobes
- T2c Tumour involves both lobes

- T3 Tumour extends through the prostatic capsule2
- T3a Extracapsular extension (unilateral or bilateral) including microscopic bladder neck
- involvement
- T3b Tumour invades seminal vesicle(s)

- T4 Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall

staging


pT2 with + margin (intra-prostatic)
pT2
pT3a with + margin (extra-prostatic)
pT3a

staging

- **N - Regional lymph nodes**
- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis

- **M - Distant metastasis**
- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis
  - M1a Non-regional lymph node(s)
  - M1b Bone(s)
  - M1c Other site(s)

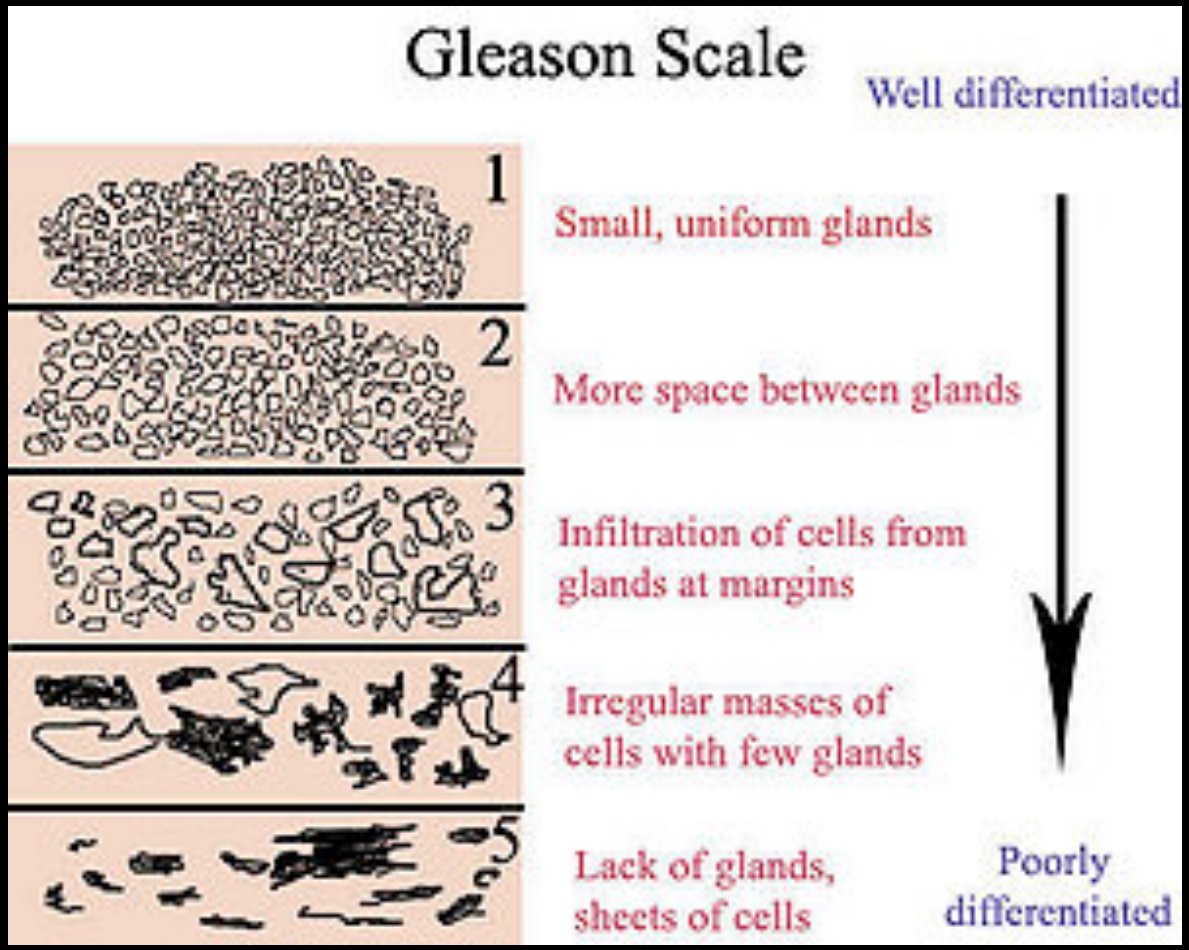
staging

- Clinical staging vs pathological staging

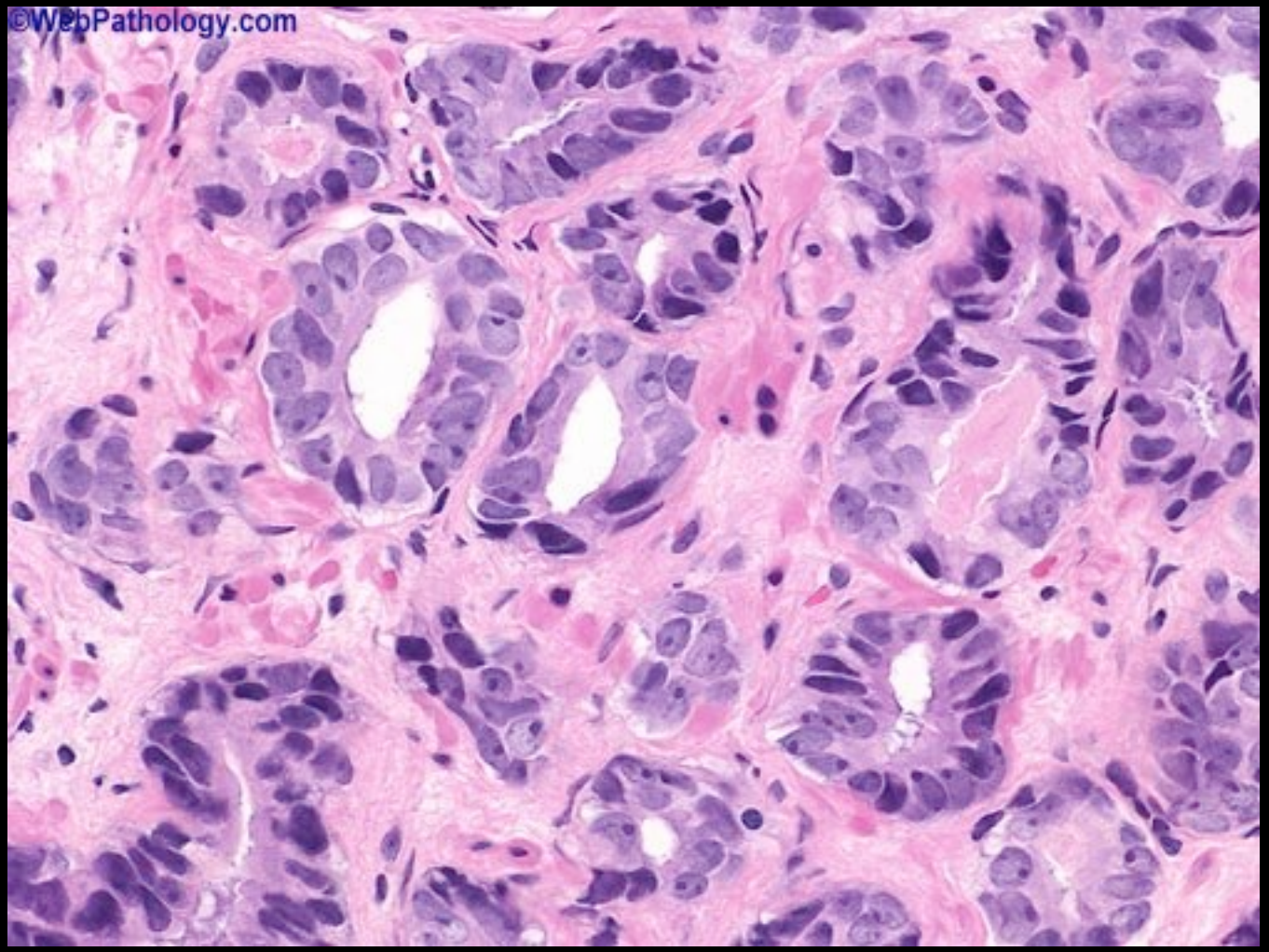
Grade

- Gleason score
  - Sum of two most common patterns (grades 1 – 5)
  - Score is 2 - 10

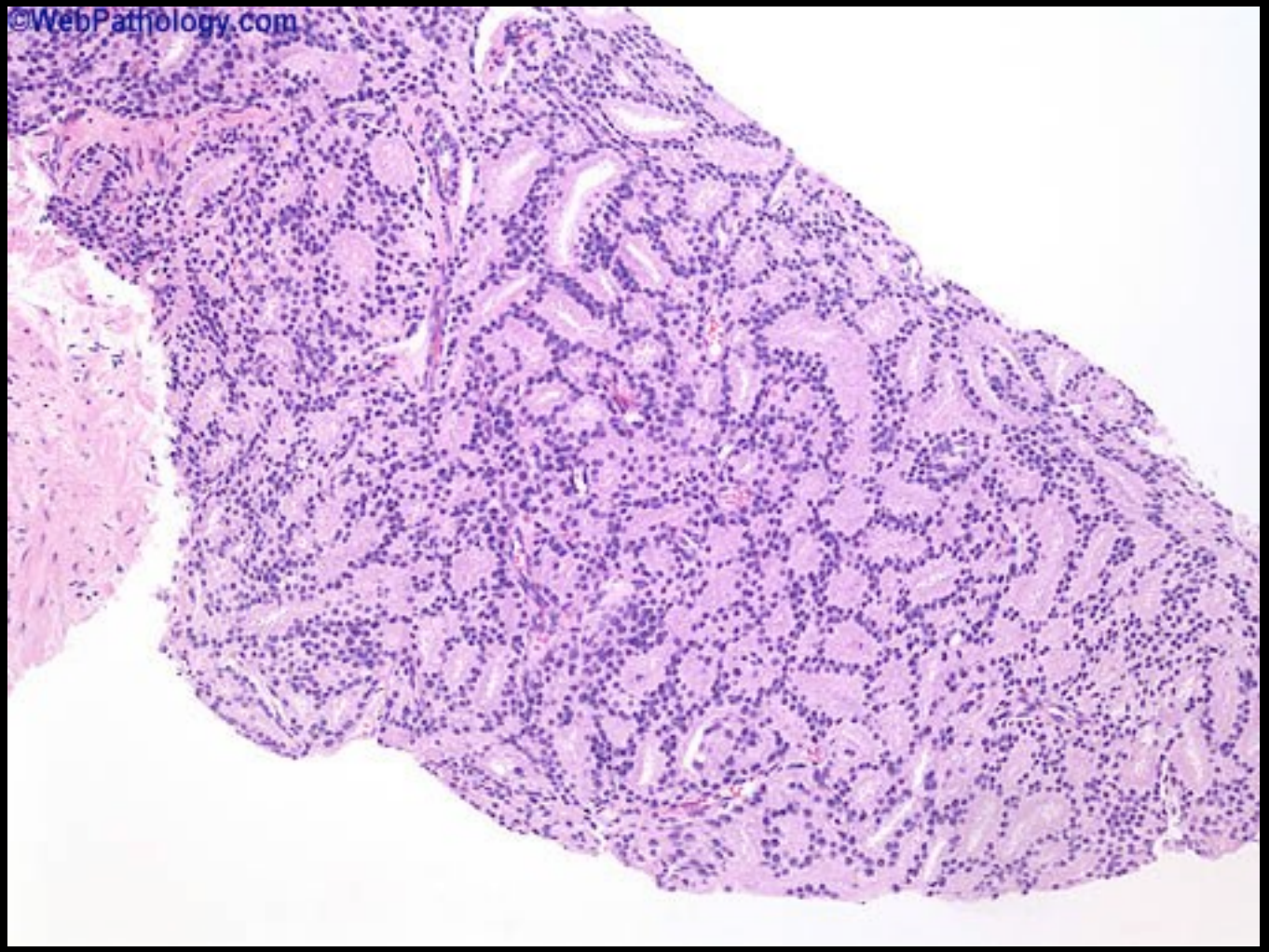
Gleason scale



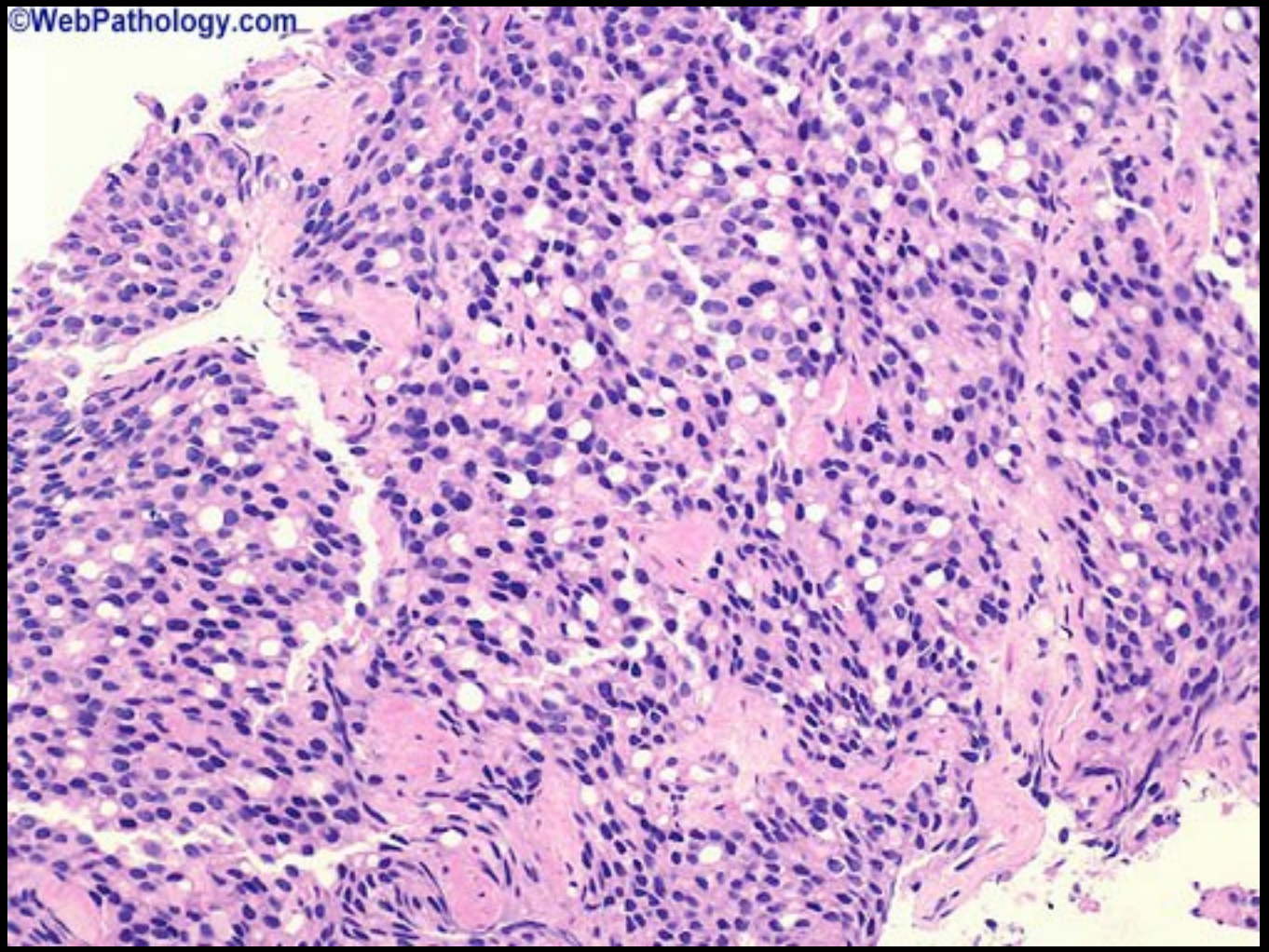
Gleason 3



Gleason 4



Gleason 5



Risk factors

- Age
- Genetics
  - One 1st deg relative 2X risk
  - Two or more 10X risk
- Hereditary prostate cancer
  - 3 or more relatives diagnosed before age 53

When should screening start

- Without risk factors age 50 – annual DRE and PSA
- With risk factors – start at 40
- PSA <1.0 at age 40 can quantitate risk of CaP in later years

Diagnosis

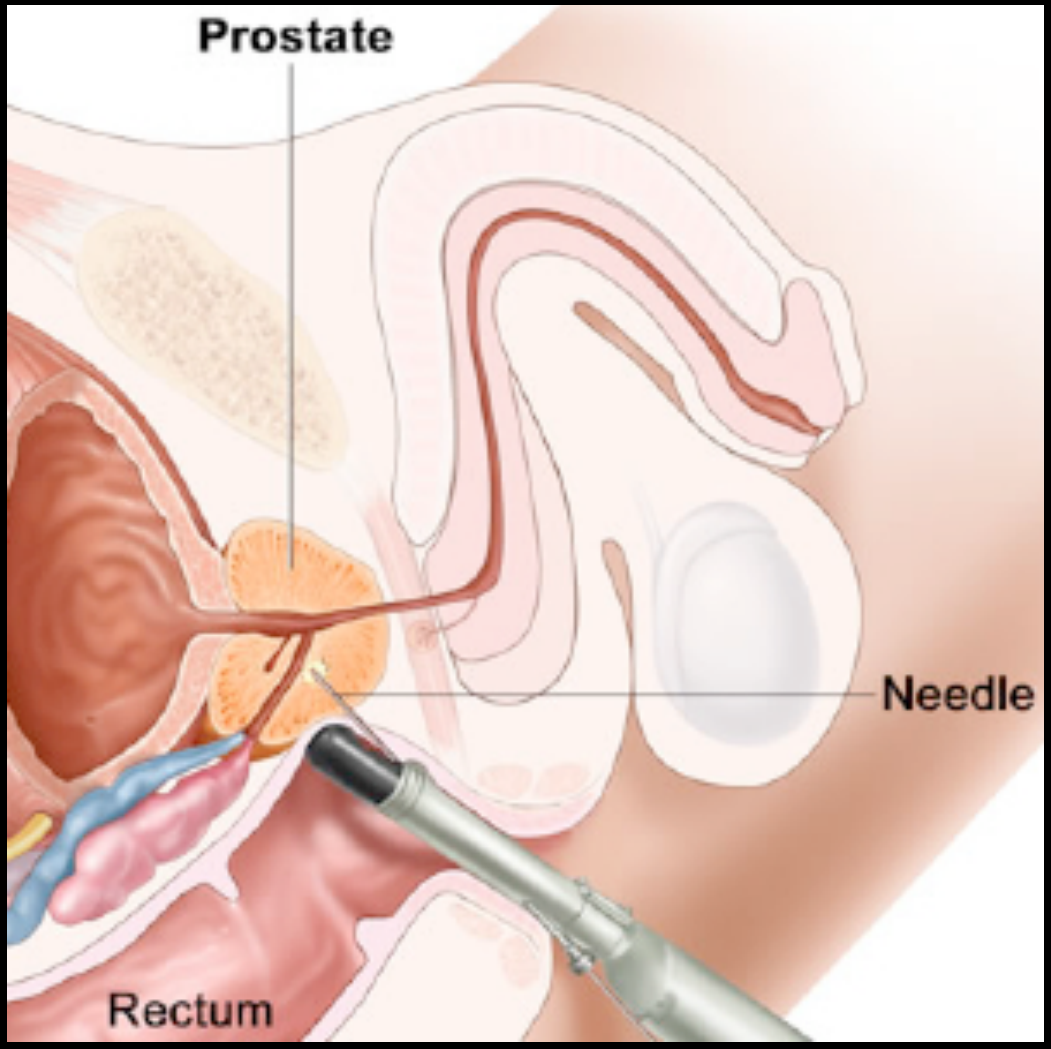
- So you've decided to have a biopsy…..
- Abnormal DRE and/or elevated PSA
- School fees

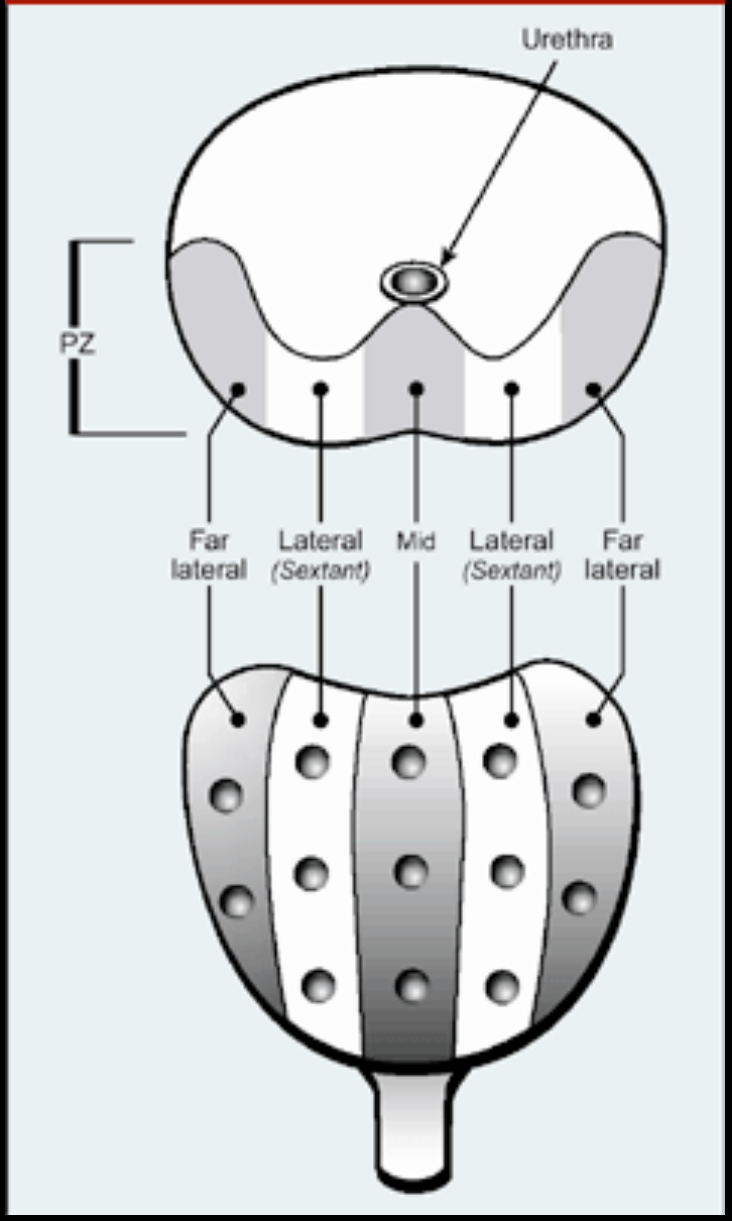
Before the biopsy

- Ensure PSA is truly elevated
- Ie no ejaculation, manipulation, etc

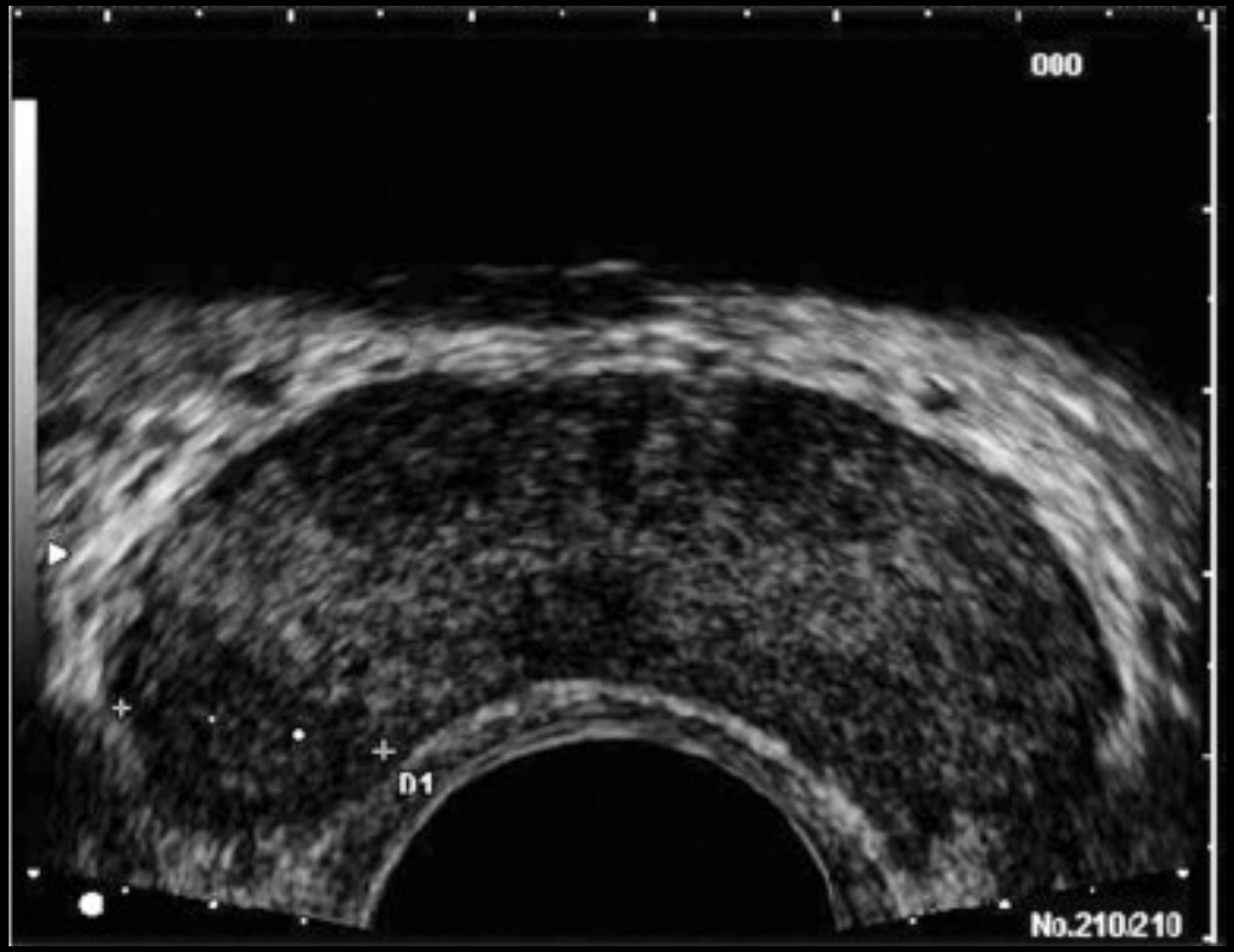
Repeat biopsy

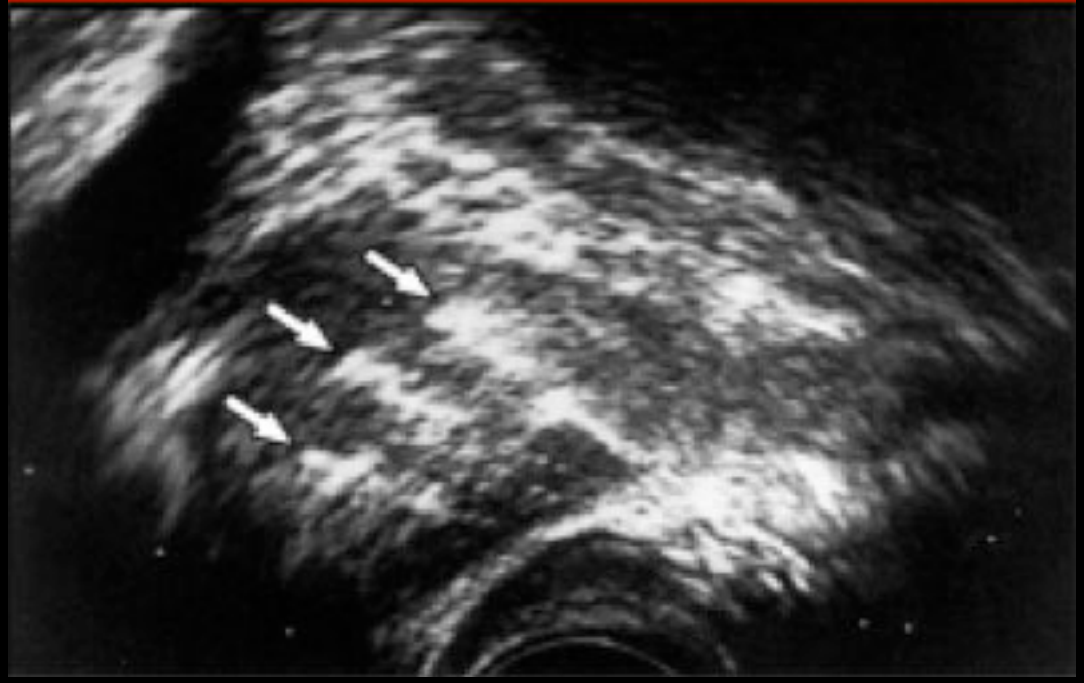
- Rising and/or persistently elevated PSA
- ASAP with high index of suspicion
  - Rising PSA
  - Family history
  - Abnormal DRE
- Saturation biopsy or transperineal


Prostate
Needle
Rectum


Urethra
PZ
Far lateral
Lateral (Sextant)
Mid
Lateral (Sextant)
Far lateral

Transverse view





Risks of biopsy

- Sepsis
- Haematuria
- Haematospermia
- PR bleeding
- pain

Risk stratification

- low-risk (clinical stage T1 to 2a, PSA 10 ng/mL or less and Gleason score 6 or less),
- intermediate-risk (stage T2b, PSA greater than 10 but less than 20 ng/mL or Gleason score 7),
- high-risk disease (stage T2c, PSA greater than 20 ng/mL or Gleason score 8 to 10)

What is the difference?

- Prostatectomy for BPH
- Radical prostatectomy
- TURP

Treatment options

- Radical prostatectomy (the best)
- Seed brachytherapy (+/- external boost)
- External beam radiotherapy with hormones
- Hormones/orchiectomy
- High dose rate brachytherapy
- HIFU
- Active surveillance

Life expectancy over 15 years

- RP
- Radiotherapy

- Low risk disease – brachy, AS

Life expectancy <15 years

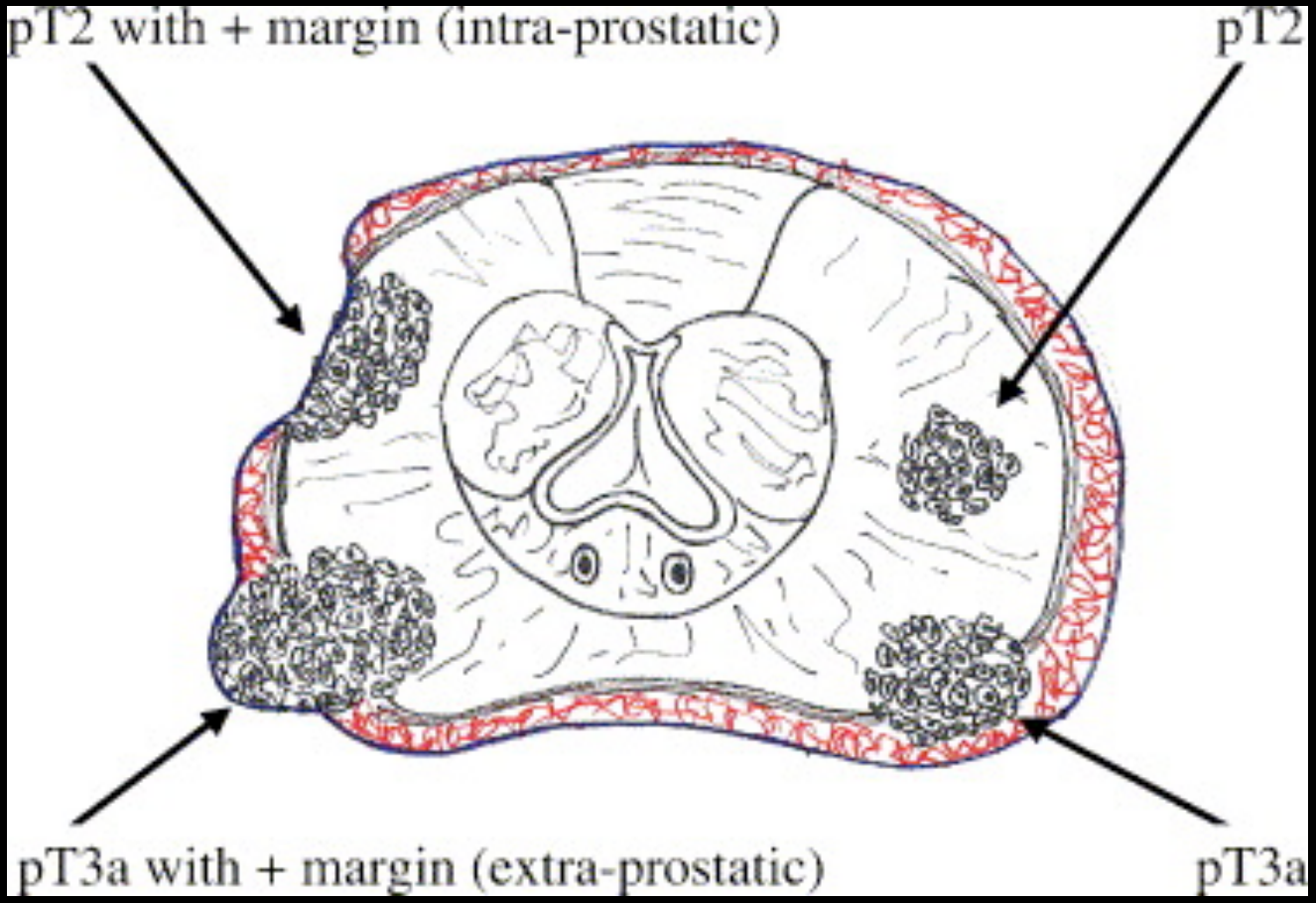
- Radiation based treatments

metastatic

- Initially hormonal manipulation
- If hormone refractory – taxotere & other poisons
- Bony lesions are osteoblastic – may need radiotherapy

Post surgery

- If positive margin – consider adjuvant radiotherapy or just monitoring
- Positive lymph nodes – start hormones


pT2 with + margin (intra-prostatic)
pT2
pT3a with + margin (extra-prostatic)
pT3a

Risks of surgery

- Incontinence
- ED
- Rectal injury
- PSA recurrence
  - Local – radiotherapy
  - Distant - hormones

The trifecta

- Potent
- Continent
- Undetectable PSA

- Torrential haemorrhage
- Rectal injury
- Ureteric injury