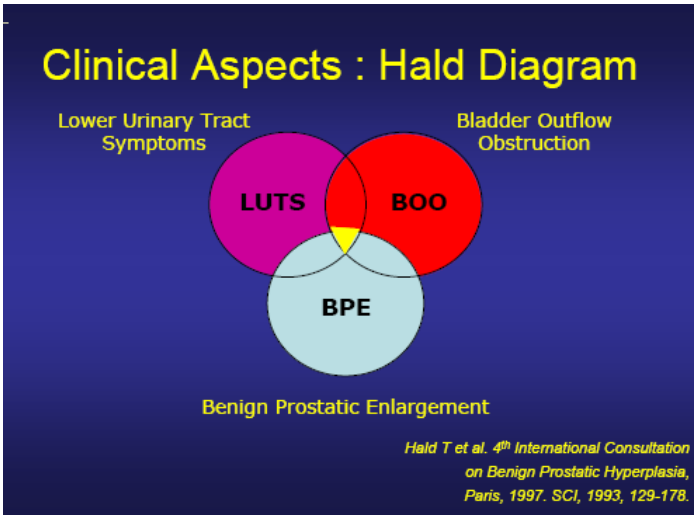
Benign prostate hyperplasia and bladder outflow obstruction

Benign prostate hyperplasia (BPH)	histological diagnosis
Benign prostate enlargement (BPE)	clinical diagnosis based on DRE
Bladder outflow obstruction	clinical diagnosis
Lower urinary tract symptoms (LUTS)	constellation of symptoms which neither gender or organ specific

Interplay of relationships between BPH, BPE and LUTS represented by Hald diagram (shaded yellow portion represents patients with symptomatic BPH



Demographics

Extremely common

Difficult to ascertain prevalence as no epidemiological definition of BPH (see above)

Histologically (post-mortem; Berry 1984)

- 23% of men aged 41 to 50 yrs
- 42% of men aged 51 to 60 yrs
- 71% of men aged 61 to 70 yrs
- 82% of men aged 71 to 80 yrs

Clinically (IPSS moderate/severe; multiple studies: figures below from Olmstead County)

- ~ 1 in 8 men in 40s
- ~ 1 in 3 men > 65yrs

More common in westernised countries but ? due to reporting

Probably more common in blacks cf. asians

Risk factors

- **Ageing**
  - ? epithelial cell maturation and apoptosis
- Hormonal status
  - Increased oestrogen-androgen ratio
  - Increased oestrogens
    - Obesity
    - Hypercholesterolaemia
  - Reduced androgens
    - Age related (andropause)

Hypogonadism
Alcohol (reduced circulating androgens)

Genetic factors
Increased risk on MZ twins
One first degree relative affected = RR x4

Diabetes
Obesity and increased insulin (IGFs)

NB. No convincing evidence for vasectomy, diet, smoking status, sexual activity

Pathology

Hyperplasia due to reduced apoptosis vs. increased proliferation
Dysregulated stromal-epithelial interaction - normal stromal-epithelial ratio increases from 2:1 to 3:1/4:1 in BPH
Major increase in connective tissue
Initially micronodule formation in TZ and PUZ
Periurethral zone stroma
Transition zone stroma and glands
Later enlargement of micronodules into - lateral (TZ) and median (PUZ) 'lobes' of BPH

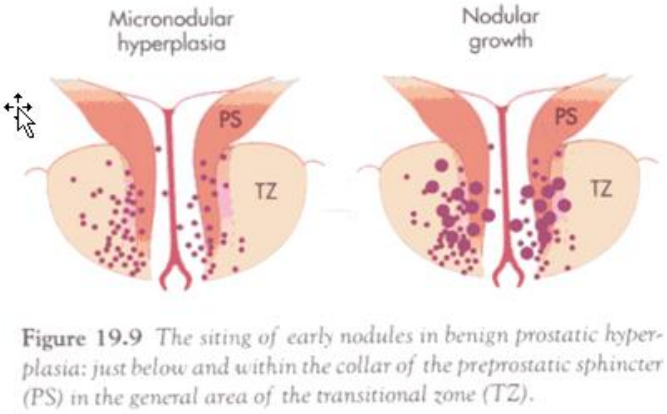
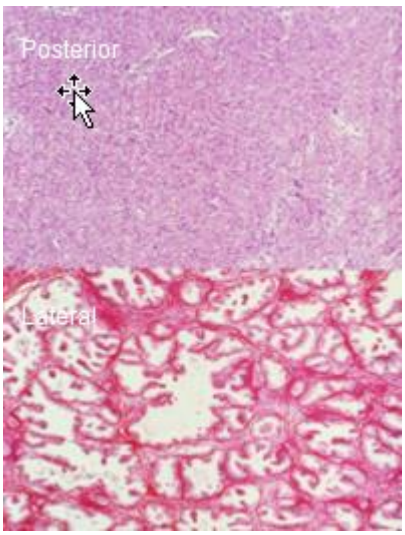


Figure 19.9 *The siting of early nodules in benign prostatic hyperplasia: just below and within the collar of the preprostatic sphincter (PS) in the general area of the transitional zone (TZ).*



Increased fibromuscular stroma – increased sympathetic tone (alpha 1a adrenoceptors predominate)
Contributes to pressure-flow dynamics – antagonism with alpha blockers (non-selective, selective, super selective)
Additional ?constricting effect of prostate capsule (humans vs. dogs)
Pathogenesis

(i) Androgens
Impair cell death, stimulate proliferation, and withdrawal associated with involution
No evidence androgens mitogens – believed to be permissive
No increased growth in cell-culture or animal models after permissive threshold reached
Serum androgens decline with age (intraprostatic DHT and AR levels preserved but not elevated in BPH)

May exert effects indirectly – ?reciprocal relationship with TGFα

(ii) Oestrogens

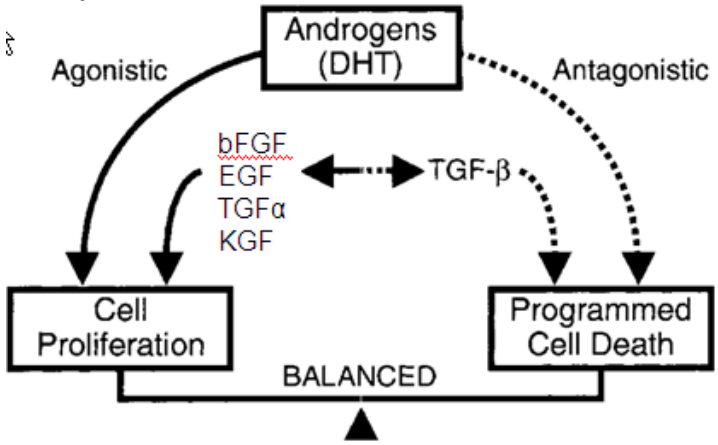
Animal evidence suggests oestrogens contribute to BPH
Total and relative serum oestrogen levels increase with age
Serum oestrogen levels higher in BPH cf. controls (increased with size)
? Induction and stabilisation of AR

(iii) Growth factors

Prostate cell growth in culture reliant on non-plasma constituents
Under influence of unknown stimulus* normal stromal epithelial interaction becomes disordered

bFGF drives proliferation in stromal cells
KGF drives proliferation in epithelial cells
TGF beta stimulates apoptosis in both

* Causes of dysregulation unclear - ?andropause vs. u-bend theory



Evaluation

<u>Recommended</u>

History

Symptom score

I-PSS score

International prostate symptom score
Also known as AUA symptom index
7 symptom question and one QOL question
Symptom questions = frequency, nocturia, urgency, hesitancy, poor stream, intermittency and incomplete emptying
Each scored 0-5; maximum score 35 (QOL score not included)

Mild	0-7
Moderate	8-19
Severe	20-35

IPSS predicts both progression and outcome

Bother score

Either question 8 on IPSS or Medical Outcomes Study Short-Form (SF-36)

Voiding diary

Polyuria > 3L/day
Nocturnal polyuria > third of daily output during 8 hours of sleep

Examination
- Abdominal exam
- DRE
  - Assesses anal tone
  - May identify prostate cancer
  - Not accurate for predicting prostate volume – usually underestimates when volume >30ml. TRUS better.
  - Knee-elbow equivalent to left lateral cf. adequacy of exam
- Focused neurological examination

Urinalysis

Serum creatinine
- Controversial
- Rates of *progressive* renal deterioration in MTOPS minimal - not recommended by AUA. However:
  - Cheap to perform
  - Incidence of renal insufficiency at presentation ~10% (Gerber 1997)
  - If normal no requirement for renal tract USS (Koch 1995)
  - Identification of at-risk patients for surgery - renal insufficiency increases risk of complications and death after TURP

<u>Optional</u>

Cytology
- Only recommended for smoker with irritable symptoms

PSA
- Predicts prostate volume
- May identify cancer
- Predicts progression of BPH

Flow rate
- Inaccurate if the voided volume < 125mL
- Insufficient evidence to recommend a cutoff value
- Qmax more specific than Qave
- Normal values
  - Men < 40 >= 21 ml/s
  - Men 40-60 >= 18 ml/s
  - Men > 60 >= 13 ml/s
  - Women < 50 >= 25 ml/s
  - Women > 50 >= 18 ml/s
- Poorer outcomes after prostatectomy if Qmax >15ml/s
- Qmax < 15 mL/s does not differentiate between obstruction and bladder decompensation.

Post-void residual
- Length x width x height x 0.7 (x 0.52 or pi/6 for prostate volume)
- Significant intra-individual variability – at least 2 measurements
- Poor correlation with other parameters
- *May* predict a slightly higher failure rate with a strategy of watchful waiting, but threshold volume uncertain.
  - 78% normal men have PVR > 5ml
  - 100% normal men have PVR < 12 ml

?predicts renal insufficiency – Bates 2003 (2/93 patients with PVR > 250ml developed hydronephrosis and elevated creatinine – average PVR was 425 with an associated FR of <5ml/s)
No evidence that raised PVR a/w increased risk of UTI

Flexible cystoscopy
Risk of UTI ~2.5%
Features a/w obstruction
Occlusive prostate
High bladder neck
Trabeculation
Sacculation and diverticula
Bladder stones
Relationships generally not firm enough for prognostication, with the exception of bladder stones, which are clearly associated with BOO.
Trabeculation a/w BOO, but false negative in 15% and false positive in 8% (El Din 1996)
Not recommended unless haematuria, suspicion of calculi

Urodynamics
Reserved for:
Younger men (<50 yrs)
Equivocal urolowmetry
Elderly patients
Flow rates > 15ml/s
Very low flow and suspected bladder failure
Patients with neurological symptoms or after radical pelvic surgery
Previous unsuccesful invasive treatment
Severe irritative symptoms
High pressure low flow predicts outcome after TURP
No value for UDS in predicting response to medical Rx
25% of patients with BOO and OAB have unstable bladder contractions after surgery

Natural history

Best evidence from PLESS and Olmstead County. Overall <u>BPH considered a progressive disease</u>. Symptom severity and frequency, bother, interference, disease-specific HRQOL, maximum flow rate, and prostate volume (TRUS) all tend to worsen with advancing age. Correlations generally weak except:

Symptoms with prostate volume √
Symptoms with Qmax √
IPSS and Qmax √
IPSS and residual volume √

Natural history has been assessed in 3 ways:
(i) Longitudinal cohorts of men with LUTS (watchful waiting)
(ii) Longitudinal cohorts of undiagnosed men (e.g. Olmstead County)
(iii) Non-intervention arms of controlled trials (e.g Wasson 1995, PLESS, MTOPS)

(i) Watchful waiting
Few studies; problems with recruitment compliance and self-reporting

(ii) Olmstead County

Minnesota. Data reported by Mayo clinic group (Rochester, Minnesota) including Oesterling and Jacobsen.
Long term has shown:
Increased symptoms score with age 0.3-0.6/yr
Increased volume 0.6ml/yr
Reduced flow rate -2% per year
Greatest degree of change older patients (>60) and those with initial poor baseline levels

(iii) Non-intervention arms

a) Wasson et al 1995 NEJM (updated by Flanigan 1998)
556 men with moderate symptoms/bother
Random assignment to WW vs. TUR
Initially 40% of patients in WW arm improved, 33% stayed the same and 27% crossed over to TURP, 21% for treatment failure (death, UTI, RV >350, stone , IPSS >= 24, doubled creatinine)
At five years 36% had surgery and 64% stayed same/improved
Interestingly patients initially randomised to WW did worse after TURP than those undergoing immediate TURP

b) PLESS (McConnell 1998)
Placebo arm (n=1504)
Stratified according to prostate sized estimated on PSA
Significant placebo effect impairing true natural history
Reduced symptom score (-1) and peak flow rate, decreased flow rate over 4 years
7% AUR and 8% TURP

c) MTOPS
Placebo arm (n=737)
Clinical progression in only 17 % of patients in placebo arm at end of study; however lesser degrees of deterioration not discussed
Results for placebo group below:

Event	Rate / per 100 person yrs	Cumulative incidence (%)
Clinical progression	4.5	17
>= 4 points IPSS increase	3.6	14
AUR	0.6	2
Incontinence	0.3	<1
UTI	0.1	<1
Renal insufficiency	0.0	0
Invasive therapy	1.3	5

Predictors of progression (6)
Baseline (6)
Age > 60
Prostate volume > 30 ml
PSA > 1.4
Symptom score > 7 (IPSS)
Qmax < 12 ml/s
PVR > 50 ml
Dynamic (5)

Increasing IPSS
Increasing bother
Previous AUR
Increasing PVR
Failure to respond to medical therapy

Complications of BPH

Symptom progression	17-40%
AUR	1-2% per year
UTI	0.1% -12%
Bladder calculi	0.3-3.4%
Renal insufficiency	<2.5%
Incontinence	>1%
Haematuria	

AUR due to BPH

In at-risk populations:

0.68 per 100 person years	Olmstead County
0.6 per 100 person years	MTOPs
1.8 per 100 person years	PLESS

May be spontaneous or precipitated
Cause of spontaneous retention unclear (?infection, overdistension, sexual activity). Role of infarction controversial
Increased risk with:
Increased age (4th to 7th decade = 8 fold)
Increased symptoms (IPSS > 7 = 3 fold)
Poor flow rate (< 12mls/sec = 4 fold)
Larger prostates (> 30mls = 3 fold)
Larger PVR (> 50mls = 3 fold)

Management

Watch and wait
Medical therapy
Alpha blockade
5 alpha-reductase inhibitors
Phytotherapy
Surgical intervention
Other
Prostate luminal stents

<u>Conservative therapy</u>

Suitable for mild/moderate symptoms with minimal bother
Approximately 2/3 stay the same or improve at 5 years without Rx
Remember to counsel re. prostate cancer – multiple studies have shown that men with LUTS have no increased risk of prostate cancer cf. asymptomatic men of same age
Lifestyle changes important [reduced caffeine and fluid, treat constipation, bladder retraining etc.]

Medical therapy

a) 5 alpha reductase inhibitors (Type II 5-ARI dominant isoform)

- Finasteride
  - **Type 2** 5ARI
  - Reduces prostate volume ~20-30%
  - Improves symptom scores ~15%
  - Improves urinary flow ~ 1.5%
  - Maximal effect only after 6 months
  - Durable effect lasting at least 10 years
  - More effective in larger prostates > 40ml
  - Efficacious in reducing haematuria due to BPH*
  - Reduces total PSA by ~50%. Conflicting evidence of effects on free PSA
  - No evidence that impairs the detection of prostate cancer on Bx
  - Side effects
    - Reduced libido
    - Erectile dysfunction (5%)
    - Reduced ejaculate volume
    - Rarely rash and breast symptoms (~1%)
  - * 75% experienced no further bleeding at mean follow-up 3 yrs (Kearney 2002; n= 57)
- Dutasteride
  - **Type 1 and Type 2** (dual) 5ARI
  - Very little evidence to suggest superiority of dutasteride over finasteride despite improved supression of DHT
  - EPICS study (Enlarged Prostate International Comparator Study) showed exactly the same reduction in volume (27.4%) and similar improvements in IPSS (~ 6 points) at 12 months

b) Alpha adrenoceptor blockers

- First introduced in late 1970s
- Phenoxybenzamine used but high side-effect profile
- Selective alpha-1 adrenoceptor blockers better tolerated
- Similar efficacy and side-effect profile
- Thought to reduce dynamic element of obstruction by reducing smooth muscle tone – however no improvement in UDS features of obstruction with alpha blockers ? central mechanism
- Djavan and Marberger meta-analysis 1999 (cf. placebo)
  - **30-40% improved symptoms**
  - **16-25% improved flow rate, average 3ml/s**
- Side effects
  - Dizziness
  - Postural hypotension
  - Asthenia
  - Nasal congestion
  - Retrograde ejaculation (lowest rates with alfuzosin)
  - Erectile dysfunction (~5%)

Floppy iris syndrome reported with tamsulosin but believed to be a class effect – makes cataract surgery difficult by causing relaxation of iris dilator muscle

c) Combination therapy

Rationale for combination 5ARI and alpha blockers well established
Combination therapy more effective than either drug alone in reducing clinical progression (IPSS score, AUR, surgery; see MTOPS/COMBAT in appendix)
RCT comparing combination therapy for 9 months with cessation of alpha blocker at 6 months (SMART-1) showed worsening of symptoms in 16% and 42% of men with moderate and severe symptoms respectively (Barkin 2003).

d) Phytotherapy

Saw Palmetto

Bent 2006 NEJM – very tightly controlled RCT using taste/smell matched placebo in 225 men with moderate/severe LUTS. No difference in either symptom score or flow rate after 12 months.
Recently corroborated by Cochrane database (Tacklind 2009), in contrast to previous findings (Wilt 2002)
NB. Saw Palmetto does not influence PSA levels, PC-SPES does however

e) PDE5 inhibitors

PDE5 isoenzymes isolated from prostate
Severe LUTS a/w increased risk of ED
Recent studies suggest improvement in LUTS with PDE5i over placebo.
Possible additive effect of combination therapy with alpha-blockers
Mechanism unknown

<u>Surgical management</u>

Indications for surgery (RUSHES)

R - Recurrent or refractory urinary retention
U - Recurrent UTIs
S - Bladder stone
H - Haematuria refractory to 5ARI therapy
E - Elevated creatinine due to BOO
S - Symptom deterioration despite maximal medical Rx

Endoscopic

TUIP
Electrosurgical TURP
Laser TURP

Green Light
HOLEP
Thulium

Open

Millen's retropubic prostatectomy
Transvesical prostatectomy

Choice of procedure depends on prostate size:

<30ml TUIP equivalent to TURP in patients with no middle lobe
TUIP a/w reduced complications vs. TURP

30-80ml TURP Rx of choice
A/w improvement in 70%
Only beneficial in men with moderate/severe IPSS
Flow rate and RV improved in majority
Nocturia can remain problematic
Risks of TURP*

Infection	4%
Bleeding	2% transfusion rate
DVT/PE	
Asymptomatic DVT	10%
Symptomatic VTE	0.6%
BN contracture	4%
Urethral stricture	4%
Impotence	6.5%
Retrograde ejaculation	68%
Incontinence**	2%
TUR syndrome	0.5%
Death	0.2%
Re-operation	1% per year

* Increased with large glands, resection time >90mins, AUR, renal insufficiency, age >80 yrs, blacks
** Up to one third of patients experience transient incontinence after TURP which typically settles
Data from National Prostatectomy Audit 1997 (DE Neal)

Alternatives

- Bipolar TURP
  - 16 RCTs (Mamoulakis C)
  - Minimal long term data
  - Reduced TUR syndrome, clot retention, irrigation and catheterisation
  - Equivalent short-term efficacy
- HOLEP
  - 4 RCT vs. TURP
  - Longer resection time (morcellation), but:
  - Reduced bleeding, catheterisation, stay and more tissue resected
  - Equivalent efficacy and sexual function
- Green light laser
  - Nd-YAG (1064nm) laser with frequency-doubling crystal to produce green light. Originally potassium titanyl phosphate crystal (KTP-80W), now lithium borate crystal (LBO-120W).
  - 4 RCTs vs. TURP (best Costello 2010)
  - Reduced catheterisation/stay
  - Similar efficacy and sexual function

BUT higher re-operation rate and inferior outcome in glands >70cc

>80ml Open prostatectomy

Millen's retropubic prostatectomy procedure of choice

- Direct visualisation of adenoma
- Accurate determination of distal extent of enucleation (preserves sphincter)
- Clearly identifiable bleeding points
- No bladder trauma
- Complications

Retrograde ejaculation	80-90%
Erectile dysfunction	5%
Bladder neck contracture	5%
Haemorrhage	<5%
Stress incontinence	<1%
DVT/PE	<1%

Transvesical prostatectomy (aka suprapubic prostatectomy) a/w higher complication rate. Rarely performed except with:

- Large bladder calculi
- Diverticulectomy
- Very large median lobe

Alternatives

- HOLEP
  - 3 RCTs
  - Longer duration
  - Reduced bleeding, catheterisation, stay and more tissue resected
  - Equivalent efficacy and sexual function
  - Results out to 5 yrs (Kuntz 2008)

<u>Other alternatives</u>

(i) TUNA

- Radiofrequency ablation at 490kHz
- Fibreoptic visualisation of needle insertion
- Can be performed under LA/sedation
- 40% initial retention
- 40-60% patients improved
- Limited long-term data
- 20% other Rx at 5 years

(ii) TUMT

- Prostatron (Technomed), Prostcare (Brucker), Prostalund (Lund) and Targis (Urologix)
- Microwave generator and cooling mechanism to prevent urethral injury
- Poor results with low-energy protocols
- Improved outcomes with high energy protocols but still inferior to TURP
- Side-effects perineal pain and need for prolonged catheter drainage

(iii) HIFU

- General anaesthesia/heavy sedation required
- Improvement in 40-50%
- Long-term data unavailable
- No RCTs

(iii) Prostatic stents

- Two types; permanent and temporary
- Permanent first described – most widely known UroLume (AMS)
- Initial reports suggested high voiding rates in men with previous urinary retention and relatively low complication rates (Chapple 1990)
- Larger studies with longer follow-up identified diffiicult deployment and significant long-term complications
    - Painful ejaculation
    - Stent migration
    - Epithelial hyperplasia
    - De-novo bladder irritation
- Removal rate almost 50% on long-term follow-up – most within 2 years

Appendix

IPSS score

Symptoms / Score	Not at all	Less than 1 time in 5	Less than half the times	Around half the times	More than half the times	Almost always
Do you have a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5
Do you have to urinate again less than 2 hours after you finish urinating?	0	1	2	3	4	5
Do you stop and start several times when you urinate?	0	1	2	3	4	5
How often is it difficult to postpone urination?	0	1	2	3	4	5
Do you have a weak urinary stream?	0	1	2	3	4	5
Do you often have to push or strain to begin urination?	0	1	2	3	4	5
	Never	1 Time	2 Times	3 Times	4 Times	5 Times
How many times do you get up to urinate from the time you go to bed at night until you get up in the morning?	0	1	2	3	4	5

Not a perfect questionnaire. Does not diagnose bladder ouflow obstruction. 3 of 7 questions related to storage.

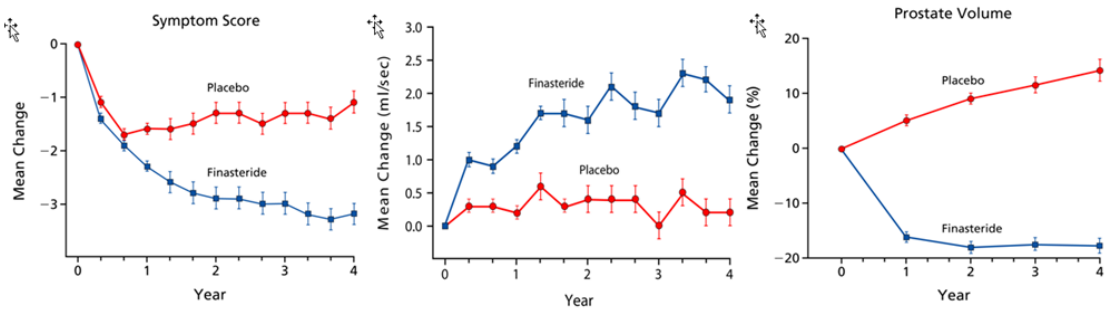
Polyuria
- > 3L per day
- Perform urine osmolality
  - If > 250 mosm/kg solute diuresis (DM, post-obstructive, post-op)
  - If < 250 mosm/kg water diuresis (DI, polydipsia)

Nocturnal polyuria
- > one third of daily output over 8 hours of sleep
- Solute diuresis due to nocturnal natriuresis (?ANP production due to recumbency), therefore **not** secondary to impaired ADH secretion at night
- Unknown cause
  - Fluid restriction
  - Diuretics
  - DDAVP
    - No real rational but can help
    - Hyponatraemia in 5% - check U+E for first 3 days after commencing
    - Avoid in elderly and cardiac failure

Important medical trials in BPH

i) PLESS (McConnell 1998; n=3040; 4 year follow-up)

Proscar long-term efficacy and safety study
Moderate/severe symptoms; reduced flow and PSA <10
Finasteride 5mg vs placebo; randomised 1:1
Primary endpoint I-PSS score



Reduced volume by 18%, improved symptoms score by 1.6 points and improved flow by ~2ml/s
Reduced risk of surgery and acute retention of ~55%
Side effects

Reduced libido	6.4%
Impotence	8.1%
Reduced ejaculate volume	3.7%
Rash	<1%
Breast enlargement/tenderness	<1%

(ii) MTOPS (McConnell 2003; n= 3047; 4.5 yr follow-up)

Medical therapy of prostatic symptoms
Men >50 yrs, IPSS >7, flow <16ml/s
Finasteride 5mg, doxazosin 4mg and doxazosin 8mg
Doxazosin commenced at 1mg and doubled weekly to 8mg. Those unable to tolerate 8mg given 4mg. Numbers of patients receiving reduced dose not mentioned in text
Primary endpoint – time to clinical progression
Clinical progression defined as:

- IPSS >= 4 point increase (on 2 occasions within 4 weeks)
- AUR
- Recurrent UTI
- Renal insufficiency (≥50% rise in baseline serum creatinine and ≥1.5 mg/dl (creatinine 133ug/l))
- Incontinence

Outcomes (see below)
Essentially

- Only 17% of patients in placebo group progressed
- Vast majority due to raised IPSS score (~80%)
- No patient developed acute renal insufficiency (however mean PVR was only 40ml)
- Combination therapy reduced risk of clinical progression by ~ two thirds when compared with placebo.

5 α reductase Inhibitors

- MTOPS : Primary end point events

	Placebo (%)	Doxazosin (%)	Finasteride (%)	Combination (%)
Progression	17	10	10	5
IPSS	14	7	9	5
AUR	2	1	<1	<1
Incontinence	<1	<1	<1	<1
UTI	<1	<1	0	<1
Intervention	5	3	2	1

McConnell et al NEJM 2003

MTOPS Results Summary At 4 Years

- Reduction in risk of BPH 'Clinical' Progression* (primary endpoint)
  - Combination 66% (p<0.001)
  - Finasteride 34% (p=0.002)
  - Doxazosin 39% (p<0.0010
- Reduction in risk of other endpoints:

	AUR	Invasive Therapy
Combination	81% (p<0.001)	67% (p<0.001)
Finasteride	68% (p=0.009)	64% (p<0.001)
Doxazosin	35% (p=0.23)	3%

- Improvement in:

	Symptoms	Qmax
Combination	7 points (p<0.001)	3.7ml/s (p<0.001)
Doxazosin	6 points (p<0.001)	2.5ml/s (p<0.001)
Finasteride	5 points (p<0.047)	2.2ml/s (p<0.047)
Placebo	4 points	1.4ml/s

(iii) COMBAT (Roehborn 2009; n=4844; 4yr follow-up)

Analysed combination of dutasteride and tamsulosin vs. either drug alone in men > 50 yrs with IPSS>=12, vol>=30 and flow between 5 and 15 ml/s

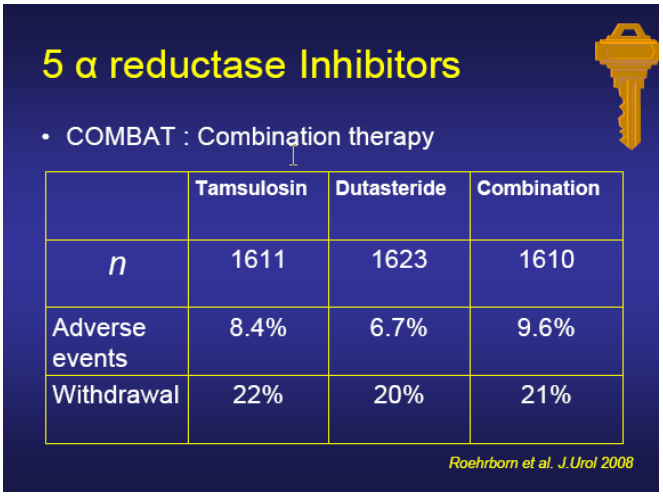
No placebo arm – considered unethical. Therefore can only compare combination with single drug therapy. No assessment of placebo effect, whcih is substantial in trials of this type.

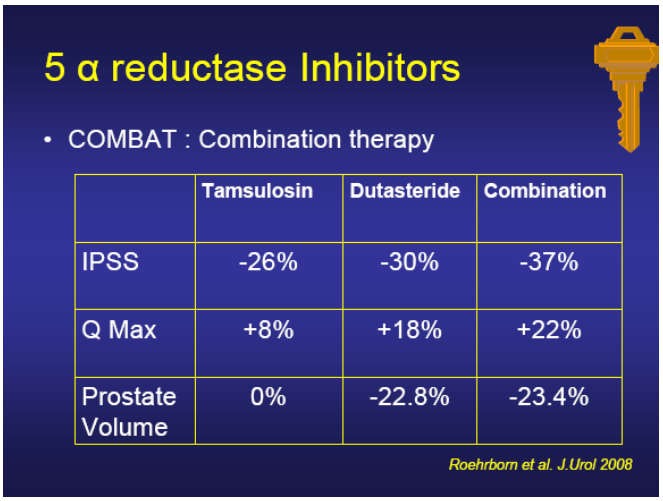
Primary endpoint different to MTOPS: AUR or surgical intervention

Combination therapy superior to tamsulosin but not dutasteride for preventing AUR or surgery. Better symptom control than either drug.

Better flow rates and prostate volumes with dutasteride, but no additional effect with combination therapy.

Dropout rate slightly higher side-effect profile cf. either drug alone but similar dropout rate (see below).





(iii) Alf-AUR (McNeill 2005)

ALFAUR trial - Alfuzosin 10mg od two doses a/w increased likelihood of sucessful TWOC cf. placebo (62% vs. 48%; relative risk of failure reduced by 27%). Risk reduction maintained in groups at high risk of failure (age > 65; residual > 1L).
Of those with sucessful TOV, alfuzosin reduced need for surgery over the next six months by 29%.

NICE guidelines for male LUTS (published May 2010)

Coalescence of evidence from ICUD, Cochrane database, meta-analyses

Essentially:

- History and examination
- Frequency voiding chart mandatory to exclude nocturnal polyuria syndrome
- Urinalysis
- Flow rate and residual
- U+E only if renal impairment suspected

- Reassurance only for mild LUTS
- Medical therapy for moderate/severe LUTS
  - Initially alpha-blocker
  - 5-ARI for LUTS and large prostates
  - Consider adding in anticholinergics
- Surgery
  - Not recommended
    - Vaporisation techniques
    - Botox injections
    - Green light laser (RCTs not considered good enough)

TUR syndrome

Triad of **fluid overload, dilutional hyponatraemia and neurotoxicity**

Relatively uncommon

Complicates ~ 0.5% monopolar TURPs

Due to absorption of hypotonic irrigant. Average fluid absorption 20ml/min (1200ml/hour). Glycine particularly problematic as metabolised to ammonia which causes encephalopathy. Glycine itself is a neurotransmitter for the eye, which may explain visual disturbances.

Risk factors

- Duration > 90 mins
- Large gland > 45cc
- Early capsular perforation
- Smoking
- Inappropriate irrigant height

Symptoms

- Confusion
- Agitation
- Nausea and vomiting — [Glycine] > 10mmol/l
- Headache
- Visual disturbance — [Gycine] > 5mmol/l
- Seizures
- Coma

Signs

- Hypertension
- Bradycardia
- Hyperkaelaemia
- Hyponatraemia

Diagnosis

- Serum [Na] < 125 mmol/l

Avoid it

- Continuous irrigating resectoscope (of Iglesias)
- Limit resection time
- Avoid capsular perforation
- Height of irrigant no more than 60cm above pubic symphysis (doubles if raised from 60-70cm)
- Bipolar TURP

Recognise it

- Input/output
- Table weight
- Alcohol in irrigant and breathalyser
- Spinal anaesthesia
- Bradycardia/hypertension

Treat it

- Terminate procedure as quickly as possible, but ensuring adequate haemostasis (prolonged irrigation undesirable)
- IV diuretics
  - 1g/kg IV mannitol 20% solution over 30 mins (for 70kg man = 350mls)
  - 40 mg IV frusemide

Theoretically mannitol makes more sense than frusemide and conserves Na, but as more free water is lost than Na, probably makes little clinical difference

Transfer to critical care

Consider Na replacement using hypertonic saline. Campbells suggest 200ml 3% saline, very slowly over a period of time! NB. care needed as may precipitate central pontine demylelination