Approximately 1/3 of men over 50 have moderate to severe lower urinary tract symptoms

3.2 million men in UK

"As man draws near the common goal
   Can anything be sadder
   Than he who, master of his soul
   Is servant to his bladder"

Lower Urinary Tract Symptoms

- Why LUTS and not 'prostatism' or BPH?

Why LUTS & not ‘prostatism’ or BPH?

- Urgency
- +/- Urgency Incontinence
- Frequency
- Nocturia

Storage symptoms
**Voiding symptoms**

- Poor flow
- Intermittency
- Hesitancy
- Straining
- Terminal dribble

**Post-Micturition symptoms**

- Post micturition dribble
- Incomplete emptying

**Assessment of LUTS**

- History - general
- Storage & Voiding LUTS
- Frequency Volume Chart (voiding diary)
- Consider use of IPSS
- Ask about bother

**Correlation between severity of LUTS & ED**

- MSAM: Multinational survey of the ageing male
- N = 12,815 men aged 50-80 years

**MSAM – Age / LUTS / ED**

Incidence erectile problems (%)

- Mild
- Moderate
- Severe

Lifestyle Intervention – LUTS/BPH

- "In older men, central obesity and higher physical activity associated with increased & decreased risks of incident LUTS, respectively ...." ^1
- "Prevention of chronic urinary symptoms represents another potential health benefit of exercise in elderly men ...." ^1
- "Statin use associated with 6.5 to 7 year delay in the onset of moderate / severe LUTS ...." ^2

Conclusion – LUTS / ED / Met Syndrome

- Strong link between BPH & ED
- Increasing evidence linking BPH & ED with metabolic syndrome & cardiovascular risk factors
- Primary Care ideal setting for holistic management of male LUTS – but who can deliver this?
- The prostate as the ‘gateway to men’s health’

IPSS

- Assess changes in severity - with time - after intervention
  - Mild ≤ 7; Mod 8 – 19; Severe ≥ 20
- QoL question: If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?
  - Will not determine the consequences of other facets of BPH and its treatments:
    - worry about cancer
    - sexual dysfunction
    - effects upon relationships

Assessment of LUTS

- Mandatory for ALL new patients:
  - General ‘focused’ physical examination
  - Abdominal examination
  - External genitalia
  - DRE
- Investigations:
  - Urine dipstick
  - If serum creatinine – only if clinical indication of renal impairment
  - PSA
Assessment of LUTS – PSA testing

Offer men information, advice and time to decide if they wish to have a PSA test if:

- Their LUTS are suggestive of bladder outflow obstruction due to BPE
- Their prostate feels abnormal on DRE
- They are concerned about prostate cancer

Uncomplicated vs Complicated

Uncomplicated LUTS
- Gradual onset
- Impalpable bladder
- Normal external genitalia
- Benign feeling prostate
- Normal PSA
- No infection / haematuria

Complicated LUTS
- Raised PSA / Abnormal DRE
- Pelvic / Urogenital pain
- UTI / Dysuria
- Palpable bladder
- Incontinence
- Haematuria
- Severe symptoms

Management strategies

- Exclude contributing causes (e.g. heart failure).
- Self-management:
  - Caffeine avoidance
  - Evening fluid restriction
  - Timing of diuretic
  - Bladder training
- Reassurance
- Containment devices?

Medical therapy for BPH

Alpha Blockers

- E.g. Tamsulosin, Alfuzosin, Doxazosin
- Reduce tone of bladder neck / prostate
- Ideal first line drug in primary care for ‘mixed LUTS’
- Rapid onset 4-6 weeks
- Symptom control quickly achieved
- No effect on PSA level or prostate size
- BUT do not prevent progression of BPH (AUR / surgery)

5-alpha reductase inhibitors

- E.g. Finasteride or Dutasteride [Avodart/Combodart]
- Inhibit conversion of testosterone to DHT
- Reduce prostate volume
- Most effective in prostates >40g
- Improves symptoms and decreased rate of AUR / surgery
- S/E: Fatigue, ED, loss of libido, gynaecomastia
- Full effects take ≥ 6 months to develop
**5ARIs reduce PSA level**

![Graph showing the mean change in PSA level with treatment months.](image)

1. Adapted from Roehrborn CG et al. Urology 2002; 60: 434-441.

**Risk Factors for Progression**

- Progression:
  - Deterioration in symptoms
  - Acute retention
  - BPH related surgery
  - Age over 70 with LUTS
  - Moderate to severe symptoms i.e. IPSS > 7
  - PSA > 1.4 ng/ml
  - Prostate volume over 30ccs (i.e. feels enlarged on DRE)
  - Flow rate <12 ml/sec

**Risk of AUR by Baseline Serum PSA in Untreated Men (Placebo Group)**

![Graph showing the risk of AUR by baseline serum PSA level.](image)


**NICE 2010**

![Image of NICE guidelines.](image)

**Combination therapy**

**What combinations?**
- Alpha blocker + 5-alpha reductase inhibitor
- Alpha blocker + PDE5 inhibitor
- PDE5 inhibitor + 5-alpha reductase inhibitor
- Alpha blocker + antimuscarinic
- Other?

**Why combination therapy?**
- Inadequate symptom control on monotherapy
- Prevention of disease progression
- Worsening symptoms
- Acute urinary Retention
- BPH-related surgery

**Combination Therapy**

- **MTOPS & CombAT**
  - Most effective for controlling symptoms
  - Most effective for reducing progression to AUR or surgery
  - At 4 years in CombAT combination reduced relative risk AUR / surgery by 70% vs tamsulosin
  - 7.7% actual risk reduction (NNT=13)
Minimal important difference

- MID: "the smallest change which can be recognised by a patient as being clinically significant".
- NICE LUTS GUIDELINE 2010: The MID used for IPSS / AUA7 was 3 points, based on a study which found a change of:
  - 3 points was correlated with "slight" improvement.
  - 5 points corresponded to "moderate" improvement.
  - 8 points related to "marked" improvement.

Symptom control – is combination therapy better than 5ARI Monotherapy in terms of MID?

<table>
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<tr>
<th>Trial</th>
<th>Alpha Blocker</th>
<th>5ARI</th>
<th>Placebo</th>
<th>Combination</th>
<th>Combination vs 5ARI</th>
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<td>-6.3</td>
<td>-1.0</td>
</tr>
</tbody>
</table>

Alpha blocker withdrawal

- Symptom Management after Reducing Treatment (5ARI) trial
  - 397 BPH patients randomised:
    - 0.5mg dutasteride & 0.4mg tamsulosin for 36 weeks (D136)
    - 0.5mg dutasteride & 0.4mg tamsulosin for 24 weeks followed by dutasteride & tamsulosin placebo for the remaining 12 weeks (D24H-012).
  - In the men with an IPSS ≥20 who changed to dutasteride monotherapy at week 24, 84% switched without a noticeable deterioration in their symptoms.
  - In the 27% of men with severe baseline symptoms (IPSS ≥30) who had withdrawal of tamsulosin therapy at week 24, 42.5% reported a worsening of their symptoms compared with 14% in the D136 group.

Sexual side effects of combination therapy

- Erectile Dysfunction
  - COMBAT: ED 9% combination vs 7% dutasteride vs 5% tamsulosin
  - MTOPS: ED 5.1% combination vs 4.2% dutasteride vs 3.5% doxazosin vs 3.3% placebo

- Ejaculatory Dysfunction
  - Meta-analysis of 4 RCT's, 4800 patients
  - ED Combination vs Alpha blocker monotherapy:
    - 9.2% vs 2.7%, OR 3.75, p<0.001
  - ED Combination vs 5ARI monotherapy:
    - 9.2% vs 3.5%, OR 2.7, p<0.02
Don’t Forget Overactive Bladder

- Absence of or minimal VOIDING symptoms
- Syndrome of:
  - Urgency (+/- urgency incontinence)
  - Frequency
  - Nocturia
- Treat with anti-cholinergic NOT alpha blocker
- Bladder training (supervised)

Medical treatment of storage symptoms

Anti-muscarincs

- E.g. Oxybutynin, Tolterodine, Solifenacin
- No compelling evidence of difference in efficacy within class
- Side effect profiles may differ
- Caution in initiating in elderly with significant voiding symptoms – assess PVR first (OK if <250mls)
- Use alongside alpha blocker in BPH if storage symptoms not controlled
- Use high doses alone in elderly – effect on cognitive function

- β-3 Adrenoceptor Agonists
  - E.g. Mirabegron (Betmiga)
  - Studies suggest similar efficacy to anti-cholinergics, although no published head to head comparisons
  - Side effect profile may be better (e.g. dry mouth in <3%)
  - NICE 2013 recommend only use when anti-cholinergics: Contraindicated
  - Not tolerated
  - Ineffective

Serenoa repens = SAW PALMETTO

- 17 RCT’s of Saw palmetto monotherapy versus placebo
- All generally mild and comparable to placebo
- ‘does not improve LUTS or Qmax compared with placebo even at double or triple the usual dose’

PDE Inhibitors for LUTS / BPH

- PDE inhibitors improve both ED and LUTS in comorbid men
- Significant improvement in IPSS scores
- No change seen in urodynamic variables
- May be more effective when combined with alpha blocker

Surgery for BPH

- TURP remains gold standard
- Promising laser interventions:
  - Holmium laser enucleation
  - Green light laser
- Minimally invasive treatments
  - TUNA, TUMT, TEAP, HIFU
‘Urolift’ – the Prostatic Urethral Lift

- Procedure to secure the prostatic lobes in retracted positions & increase the lumen of the urethra
- LA or GA procedure
- NICE Jan 14: current evidence adequate to support the use of this procedure
- RCT: 206 pts – 140 Urolift vs 66 sham procedure
- At 3 months IPSS decreased by 11 pts vs 6 pts. p<0.002
- Qmax increased by 4ml/sec vs 2ml/sec. p<0.005
- 5% required retreatment within 1 year

Other Tips

- Add anti-cholinergic to control bothersome STORAGE symptoms in men with BPH
- Consider afternoon diuretic (furosemide 20-40mg @ 4pm) for nocturia
- Desmopressin second line for nocturia
- Refer to secondary care if treatment unsuccessful

Summary

- LUTS common, under-reported & bothersome
- Strong link with ED / Metabolic Syndrome
- Holistic assessment – symptoms, fluid intake etc
- Lifestyle intervention especially fluid intake
- Medical therapy according to symptoms
- BPH is progressive condition
- Refer if not responding or atypical

WANTED: GPs, Nurses with interest in Urology
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Contact: drjonrees@gmail.com