Raised PSA, BPH and UTIs.

Mr Saheel Mukhtar, Consultant Urological Surgeon

Mr Saheel Mukhtar

Consultant Urological Surgeon
MBBS BSc (Hons) MRCS, MSc (Urol), FRCS (Urol)

Mr Saheel Mukhtar is a highly skilled Consultant Urological Surgeon, working at Bishops Wood Hospital. He specialises in the diagnosis and management of general urological conditions, with a particular focus on urinary infections, prostate cancer and urinary tract stones.

Mr Mukhtar has a strong focus upon delivering excellent patient focussed care. He is passionate about managing patients' urinary symptoms (male and female), blood in the urine, urine infections, benign prostate enlargement, incontinence, and conditions affecting the bladder, testicles, and penis.

He has a holistic patient-centred approach, concentrating on delivering the right management plan for each individual - whether that be through simple advice or the prescription of treatments. Where necessary, he performs a range of surgical procedures, and is one of the few urologists to perform laser treatments (HoLEP and greenlight laser) for prostate problems, Rezum, Urolift, as well as more traditional procedures such as TURP.

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RAISED PSA

Criteria for referral

- **Suspect prostate cancer in men who have:**
  - Lower back or bone pain.
  - Anorexia/weight loss.
  - Lethargy.
  - Erectile dysfunction.
  - Lower urinary tract symptoms (LUTS).

- **PSA testing should be:**
  - Considered in men with suspected prostate cancer.
  - Offered to men > 50 years who request a PSA test.
  - Offered to men > 45 years with a positive family history
  - Offered to Black Men > 45 years

Avoiding PSA testing

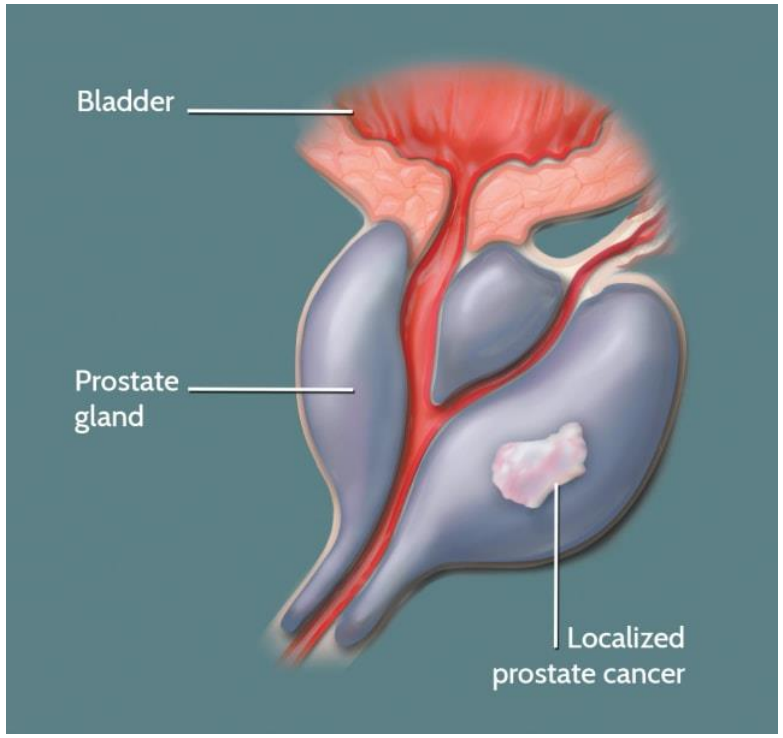
- **Before a PSA test, people should not have:**
  - An active urinary infection or within previous 6 weeks.
  - Ejaculated in previous 48 hours.
  - Exercised vigorously, e.g. cycling, in the previous 48 hours.
  - Had a urological intervention e.g. prostate biopsy, in the previous 6 weeks.

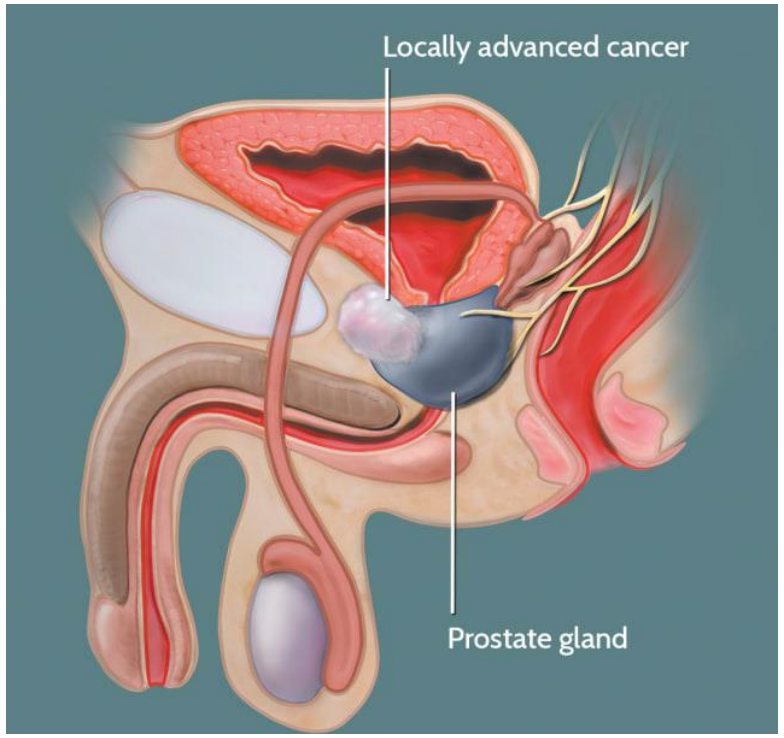
- Not typically recommended for asymptomatic men with <10 years' life expectancy.

Criteria for referral

Age (years)	PSA threshold (micrograms/L)
Below 40	Use clinical judgement
40–49	More than 2.5
50–59	More than 3.5
60–69	More than 4.5
70–79	More than 6.5
Above 79	Use clinical judgement

Prostate Cancer





PIRADS Scoring system

PI-RADS 1	Very low (clinically significant cancer is highly unlikely to be present)
PI-RADS 2	Low (clinically significant cancer is unlikely to be present)
PI-RADS 3	Intermediate (the presence of clinically significant cancer is equivocal)
PI-RADS 4	High (clinically significant cancer is likely to be present)
PI-RADS 5	Very high (clinically significant cancer is highly likely to be present)

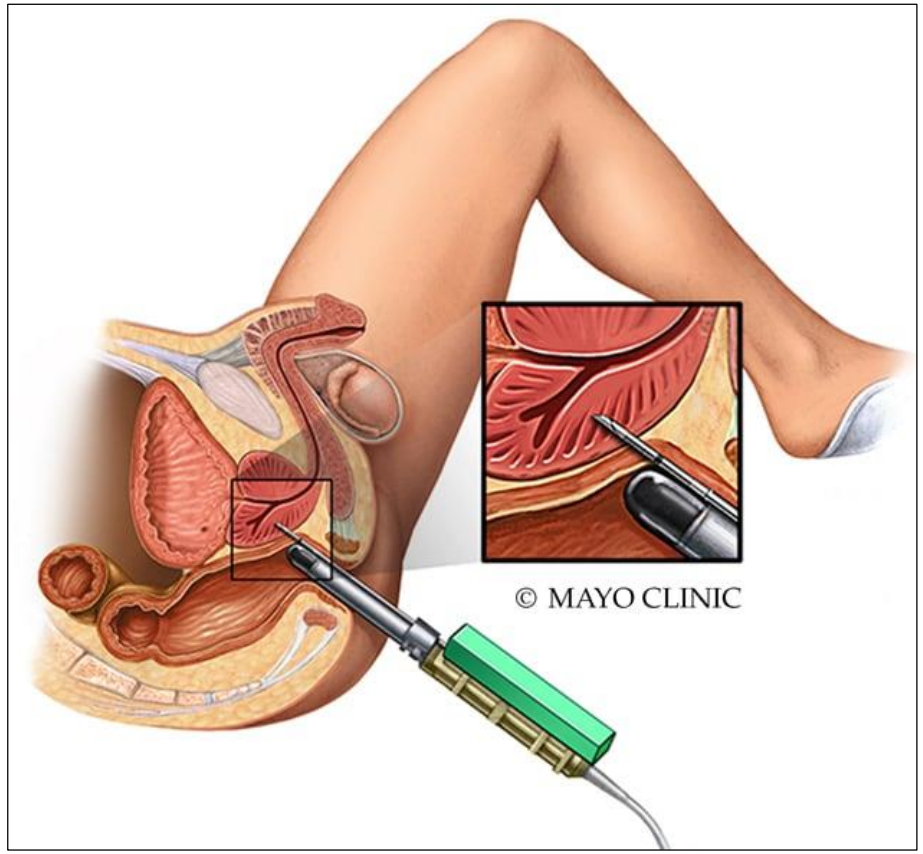
Prostate Volume and PSA Density

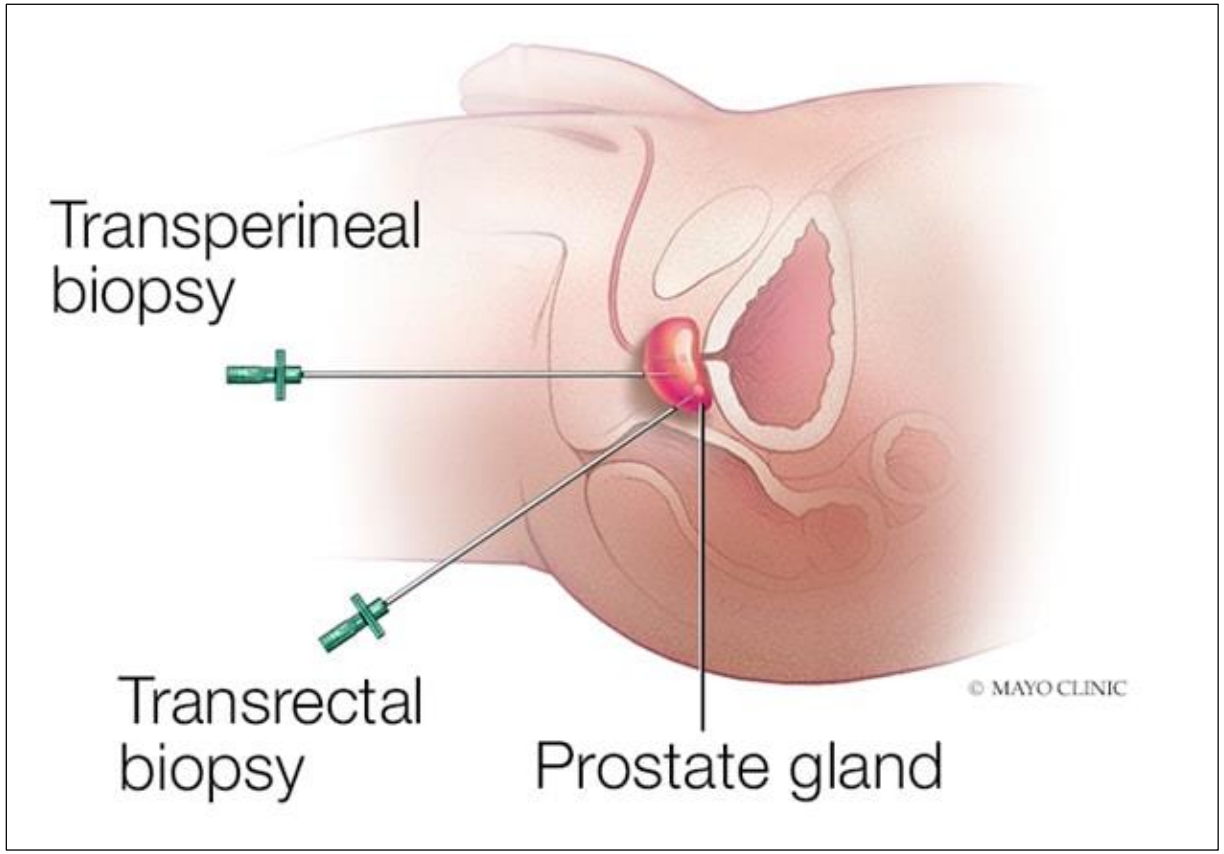
- Calculate Prostate density

- PSA density (ng/ml/ml) = $\frac{\text{Prostate Volume (mls)}}{\text{PSA (ng/ml)}}$

- Cut offs of <0.10ng/ml/ml & 0.15ng/ml/ml

Transperineal vs Transrectal biopsy





Complications

Complication	Transrectal prostate biopsy	Transperineal prostate biopsy
Fever	4%	0%
Retention	1%	3%
Rectal Bleeding	1%	0%
Haematuria	0%	0%

Does a PR examination increase PSA?

Prospective, randomised, placebo-controlled trial

n=143

Two cohorts (n=72, n=71) 2 serum PSAs

Prostate Cancer (33%)

BPH (60%)

Chronic Prostatitis (7%)

Minimal change in PSA
Greatest change in PSA is 0.4ng/ml
Median increaseis inconsequential

Chybowski *et al*.
J Urol. 1992 Jul;148(1):83-6.


DON'T FEAR THE FINGER.
PAPROSTATECANCER.ORG
PENNSYLVANIA
PROSTATE

Does Vasectomy increase PSA?

- Lassen PM, Thompson IM Jr, Helfick B
- n=25
- Patients undergoing vasectomy were studied with serial PSA determinations prior to and following vasectomy.
- PSA is not affected by previous vasectomy.

The PSA test is a prostate cancer test

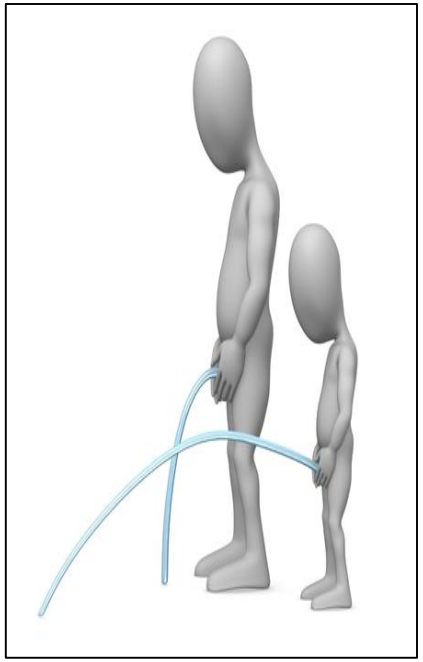
- PSA tests measures levels of prostate-specific antigen in the prostate, *not* cancer.
- No absolute cut-off for a diagnosis of prostate cancer
- High levels may not be associated with prostate cancer and vice versa
- Can be elevated due to
  - prostatitis,
  - benign prostatic hyperplasia
  - infection, or,…
  - cancer.

Treatment for prostate cancer always causes incontinence or impotence

- While erectile dysfunction (ED) and urinary incontinence are possibilities can occur, not true that all men experience complications.
- Dependent on multiple factors.
- Numerous therapies and aids can improve erectile function and limit incontinence following treatment
- Nerve sparing surgical procedures have improved outcomes for patients as well.

Benign Prostatic Hyperplasia

Lower urinary tract symptoms - LUTS



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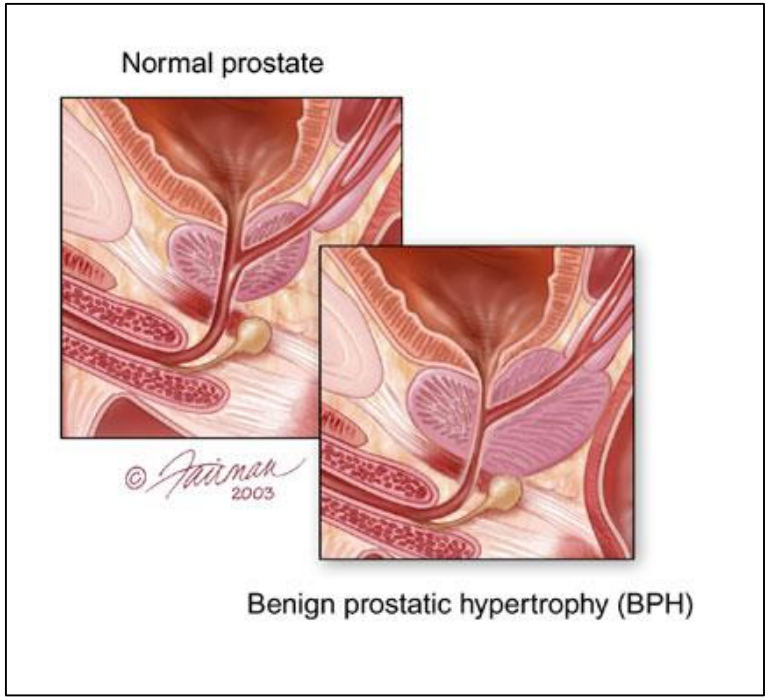
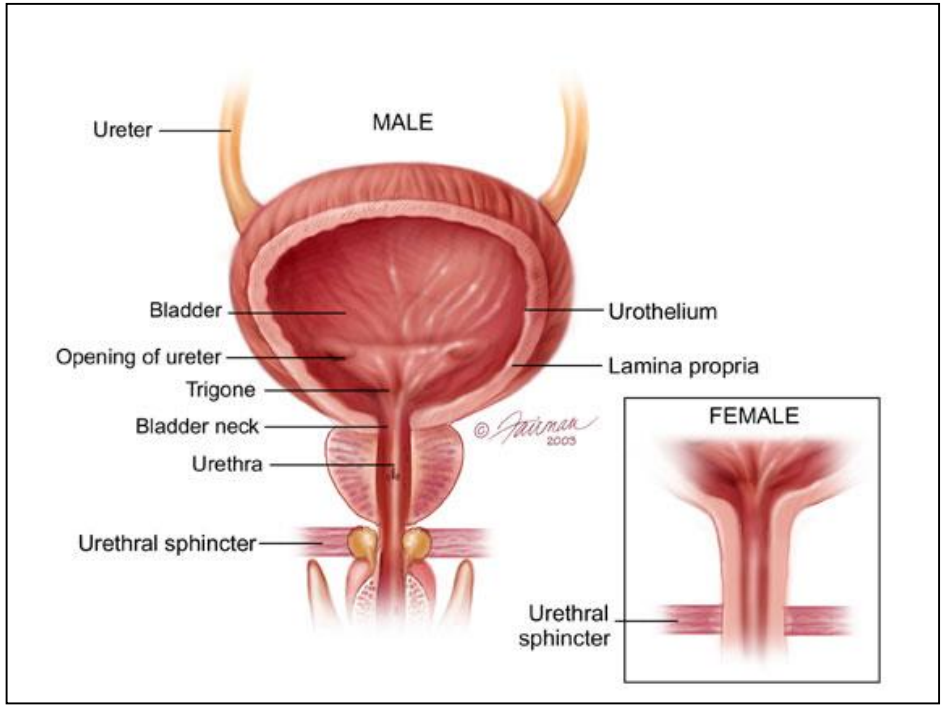
Anatomy





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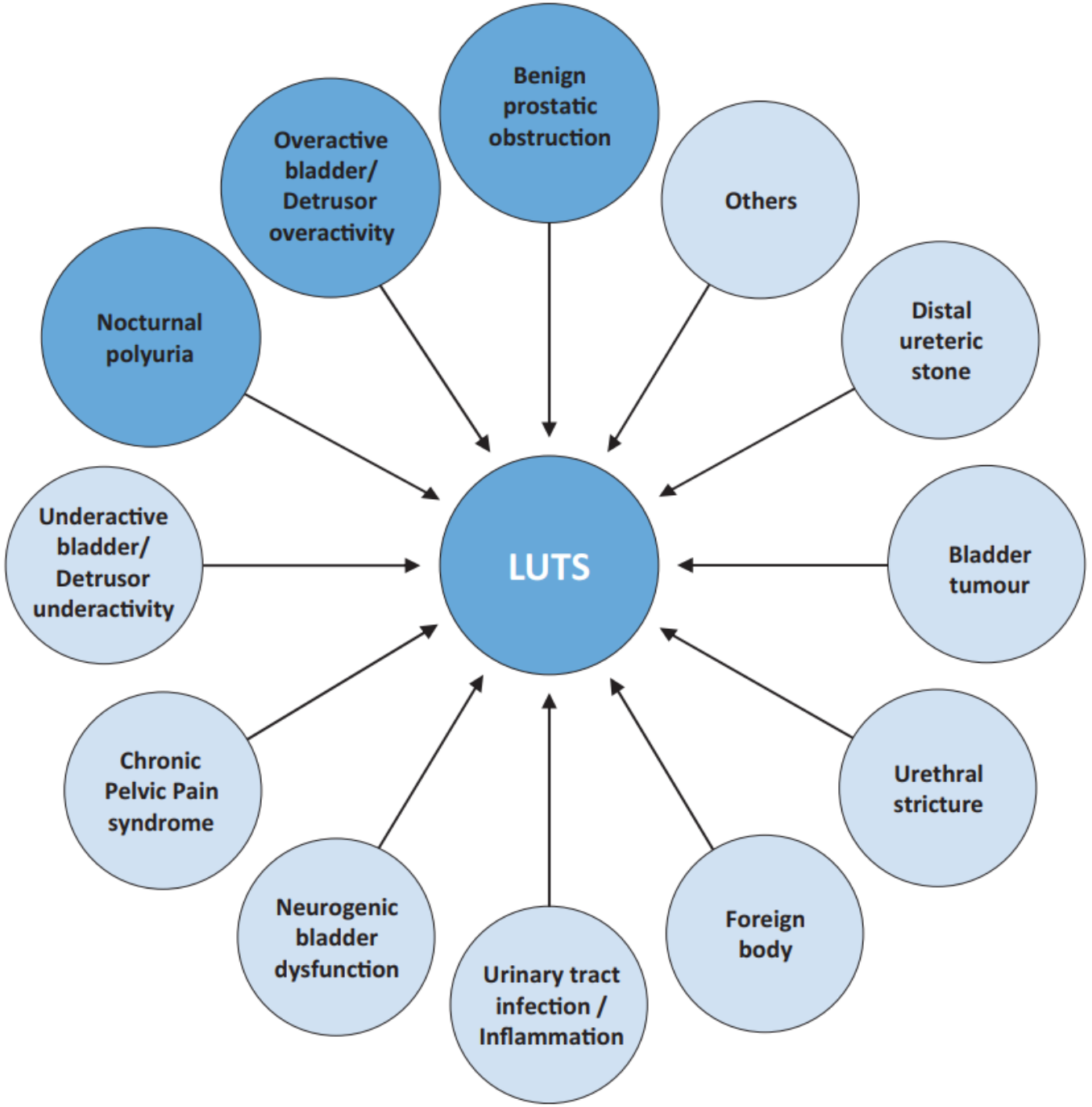
Aetiology



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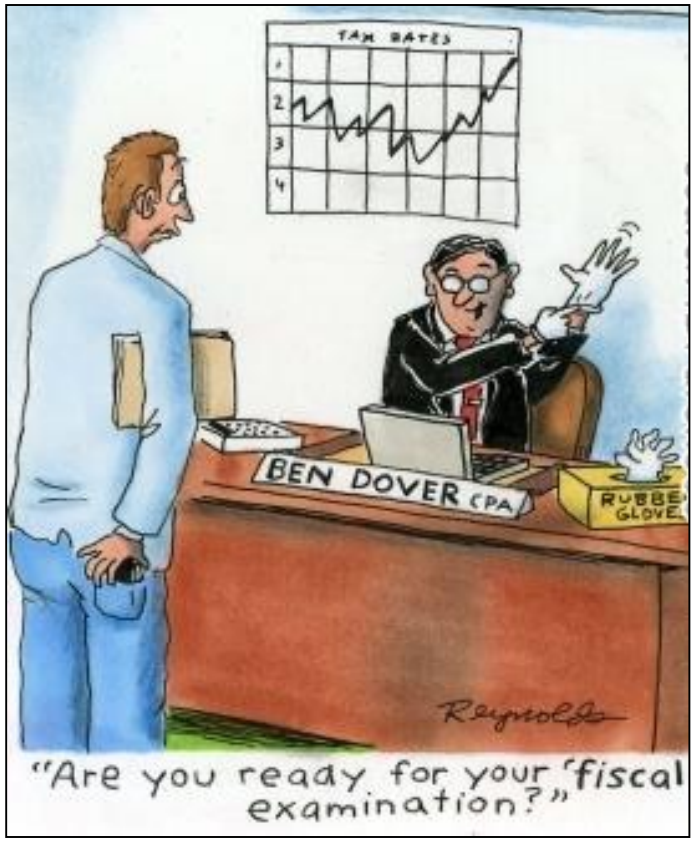
Assessment

History

- Take a complete medical history.
- Use a validated symptom score questionnaire including bother and quality of life assessment during the initial assessment and for re-evaluation during and/or after treatment.
- Use a bladder diary where there is a prominent storage component or nocturia.
- Tell the patient to complete a 3 day bladder diary.

Examination

- Abdominal examination
- External Genitalia examination
- Digital rectal examination.



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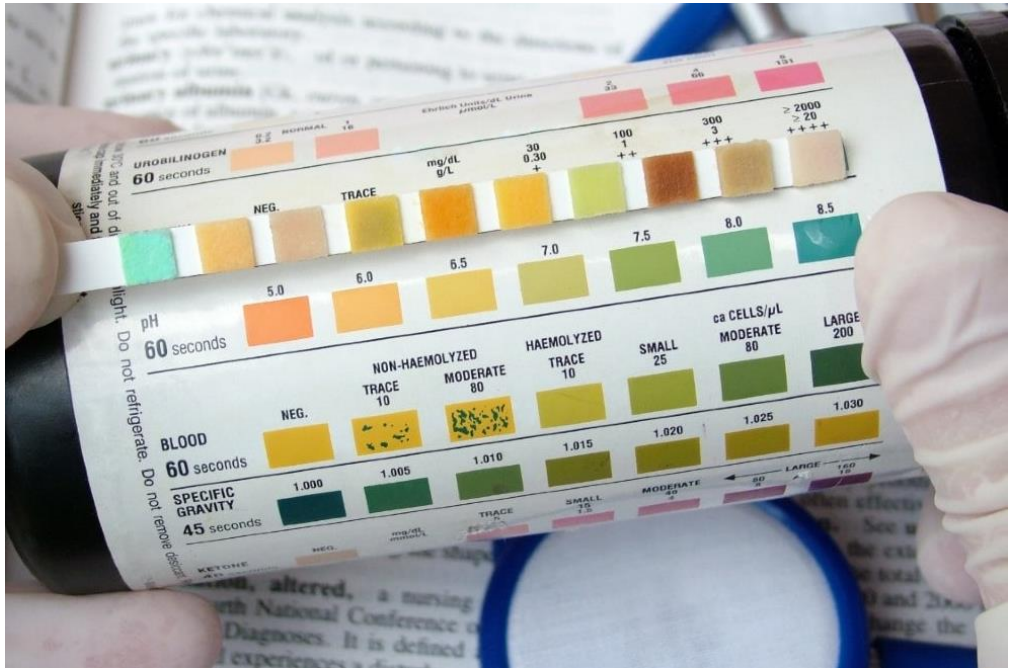
Investigations

Urinalysis
- Bedside urinalysis.

Blood tests
- Assess renal function.
- Assess PSA after appropriate counselling.

Uroflowmetry
- Measure post-void residual.
- Perform uroflowmetry where appropriate.



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Questionnaires

INTERNATIONAL PROSTATE SYMPTOM SCORE (I-PSS)

Patient Name: Date:	Not At All	Less Than 1 Time In 5	Less Than Half The Time	About Half The Time	More Than Half The Time	Almost Always	YOUR SCORE
1. Incomplete Emptying Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
2. Frequency Over the past month, how often have you had to urinate again less than two hours after you have finished urinating?	0	1	2	3	4	5	
3. Intermittency Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream Over the last month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	None	Once	Twice	3 times	4 times	5 or more	YOUR SCORE
7. Nocturia Over the past month how many times did you most typically get up each night to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5	
Total I-PSS Score							

Scores:

- 0-7 = mildly symptomatic;
- 8-19 = moderately symptomatic;
- 20-35 = severely symptomatic.

Quality of life score

- 0-6

Quality of Life due to Urinary Symptoms	Delighted	Pleased	Mostly satisfied	Mixed	Mostly unhappy	Unhappy	Terrible
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?	0	1	2	3	4	5	6

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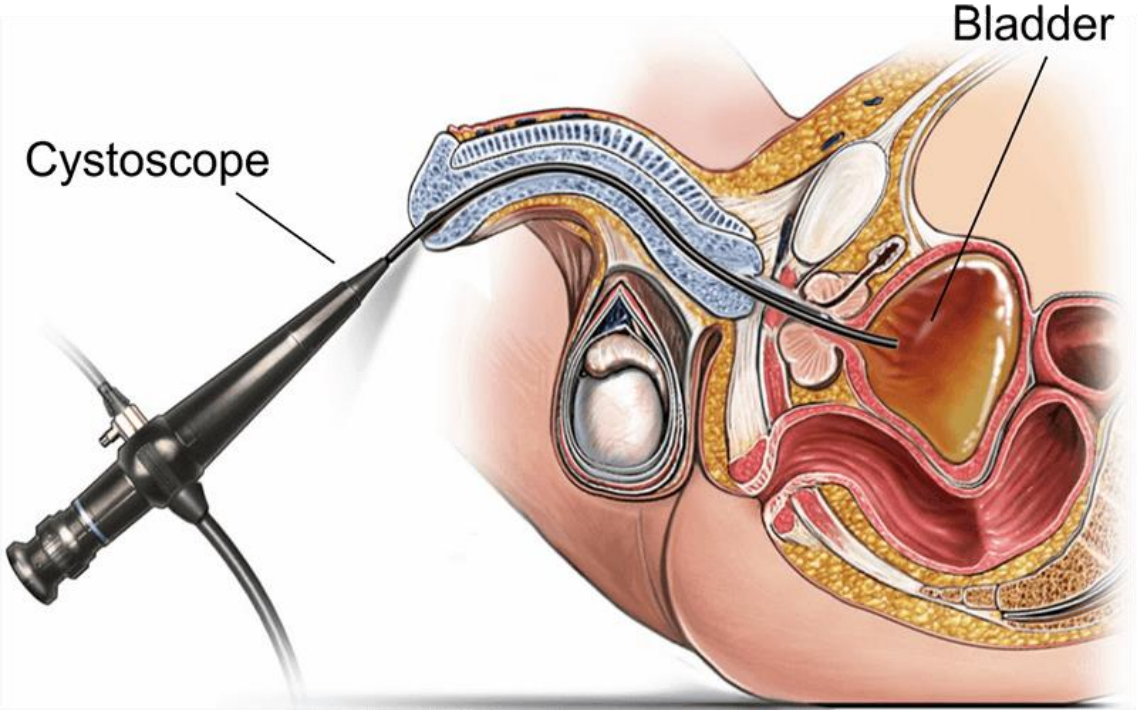
Flexible Cystoscopy

- Short procedure
- Under local anaesthetic
- Good tolerability
- Low risk of infection
- Exclude stricture
- Assess prostate size and degree of occlusion
- Exclude urothelial abnormality, bladder cancer



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Management

	No treatment	Medical	Surgery
MILD	63%	27%	10%
MODERATE	45%	31%	24%
SEVERE	33%	28%	39%

Scores:
0-7 = mildly symptomatic;
8-19 = moderately symptomatic;
20-35 = severely symptomatic.

Five Centres Study *J Urol* (1997)

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Conservative management

	N	Qmax	Change in symptoms
Placebo	185	+ 0.6	-21.6
Tamsulosin MR	364	+ 1.6	-36.6

- α1a : prostate stroma
- α1b : prostate epithelium

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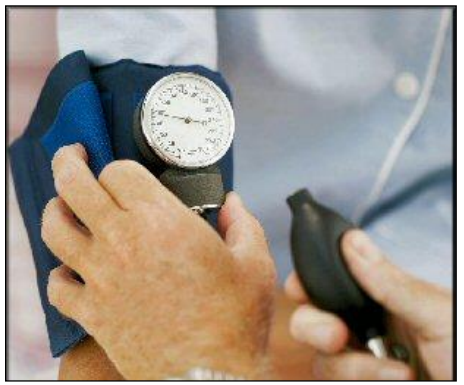
Alpha Blockers

- α1-blockers reduce IPSS by ~30% and increase Qmax by ~20-25%. (Substantial improvements occurred in corresponding placebo arms).

- Prostate size does not affect α1-blocker efficacy (FU <1 year),
- α1-blockers more efficacious in patients with smaller prostates (<40cc) in longer-term studies.

- α1-blockers neither reduce prostate size nor prevent AUR in long-term studies



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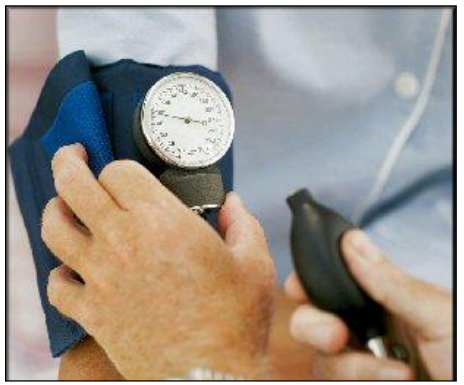
Alpha Blockers

- Side effects: commonest in those with cardiovascular co-morbidity and/or vaso-active medication.

- Asthenia, dizziness and hypotension.

- Vasodilating effects most pronounced with doxazosin and terazosin.
- Intra-operative floppy iris syndrome (IFIS) affects cataract surgery.
- Ejaculatory dysfunction seen (young age is a risk factor)

- α1-blockers do not affect libido or cause erectile dysfunction (ED).



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5-alpha reductase inhibitors

	FINASTERIDE	DUTASTERIDE
	TYPE 2 ENZYME INHIBITION	TYPE 1& 2 ENZYME INHIBITION
PROSTATE SIZE REDUCTION	18-28%	18-28%
SERUM DHT REDUCTION	70%	95%
PROSTATE DHT REDUCTION	85-90%	85-90%
PSA	50% reduction after 6 months	
Time to max plasma conc	2hrs	1-3 hours
Half life	6-8 hrs	3-5 weeks

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5-alpha reductase inhibitors

- Minimum treatment duration: at least 6 to 12 months.
- 2-4 years of treatment

• 5ARIs	Reduce LUTS (IPSS) by ~15-30%, Decrease prostate volume by ~18-28% Increase Qmax by ~1.5-2.0 mL/s.
• Prostate Size	>40cc
• Dutasteride	Reduce IPSS, Prostate volume Risk of acute urinary retention

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5-alpha reductase inhibitors

Side Effects	Incidence
Impotence	4.7%
Decreased libido	3%
Ejaculatory disorders	1.4%
Gynaecomastia / Breast Pain	0.5%

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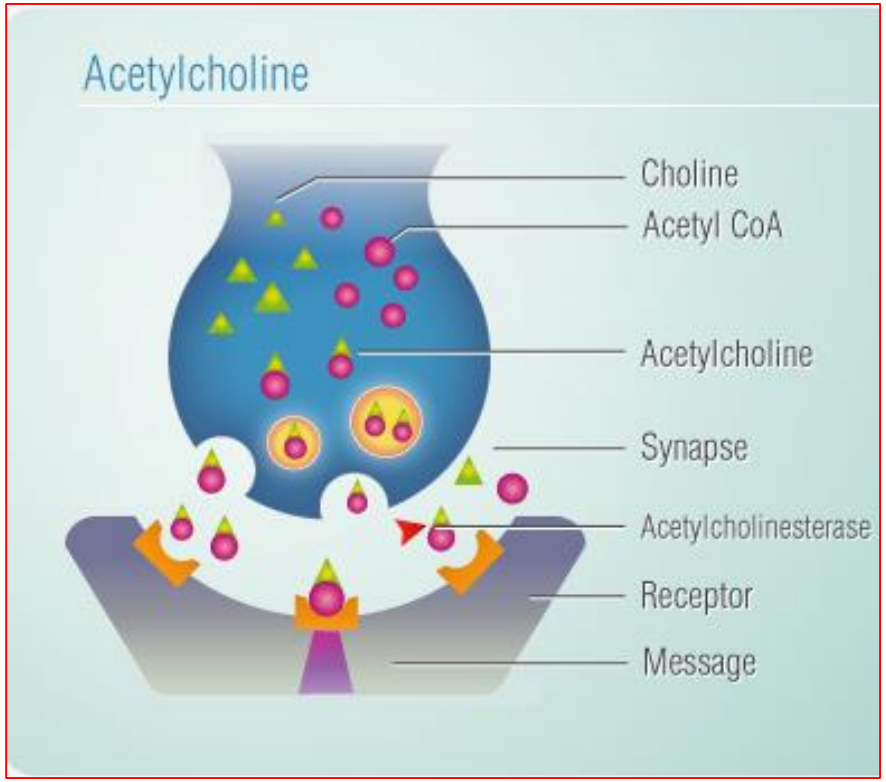
Anti-muscarinics

- ACh stimulates muscarinic receptors on detrusor muscle.
- Five muscarinic receptor subtypes (M1-M5)

- M2 (80%) & M3 subtypes (20%) are expressed in the detrusor.
- Only M3 seems to be involved in bladder contractions.

- Acetylcholine stimulates postsynaptic muscarinic receptors
- Calcium release in the sarcoplasma reticulum
- Calcium channels of the cell membrane
- Smooth muscle contraction.

- Muscarinic receptors blockade results in smooth muscle cell relaxation.



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Anti-muscarinics – side effects

- Muscarinic receptors - salivary glands, nerve cells of the PNS or CNS

- Antimuscarinic drug trials show ~3-10% withdrawal, (similar to placebo).

- Drug-related adverse events
- Dry mouth (up to 16%),
- Constipation (up to 4%),
- Micturition difficulties (up to 2%),
- Nasopharyngitis (up to 3%),
- Dizziness (up to 5%).

- Fesoterodine 8 mg showed higher PVRs (+20.2 mL) than placebo (-0.6 mL).
- Symptoms appeared during the first two weeks of treatment and mainly affected men aged 66 years or older.

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Phytotherapy

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Beta-3 agonists

- Beta-3 adrenoceptors - predominant beta receptors in the detrusor smooth muscle cells.
- Stimulation induces detrusor relaxation.

- Reduced frequency, urgency and UUI rates, as well as an improved voided volume with a statistically significant improvement of nocturia vs placebo and tolterodine.

- Combination therapy of mirabegron & solifenacin

- Mirabegron significantly improved patient reported perception of their condition and QoL whether or not patients were incontinent.

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Beta-3 agonists

- Side events: hypertension, UTI, headache and nasopharyngitis.
- **Contraindicated in severe uncontrolled hypertension (systolic BP≥180 mmHg or diastolic BP≥110 mmHg, or both).**
- Blood pressure measured before starting treatment and monitored regularly during treatment.
- 13 studies (396 patients) showed that OAB treatments (anticholinergics or mirabegron) were **not associated with an increased risk of hypertension or cardiovascular events** compared to placebo
- Dry mouth & constipation **was notably lower** than other OAB agents

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Procedures

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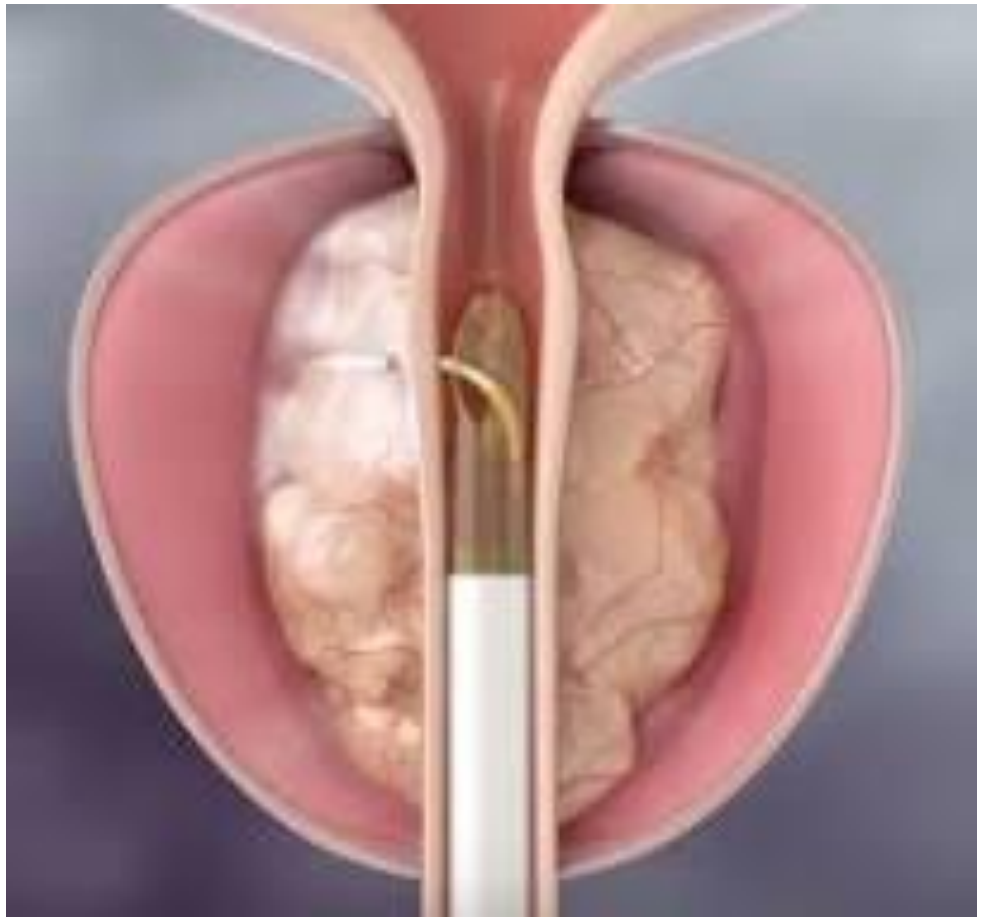
Rezum

- The Rezūm procedure involves injecting steam into the obstructing prostate
- Prostate tissue shrinks over the following 3-6 months
- Improves urinary symptoms without the need for burning or removing any prostate tissue
- Day-case procedure
- Catheter for a few days after the procedure
- Sexual side-effects such as erectile dysfunction (impotence) are very rare
- Retrograde (dry) ejaculation is also very uncommon
- Small number of men further treatment may be needed at a later stage



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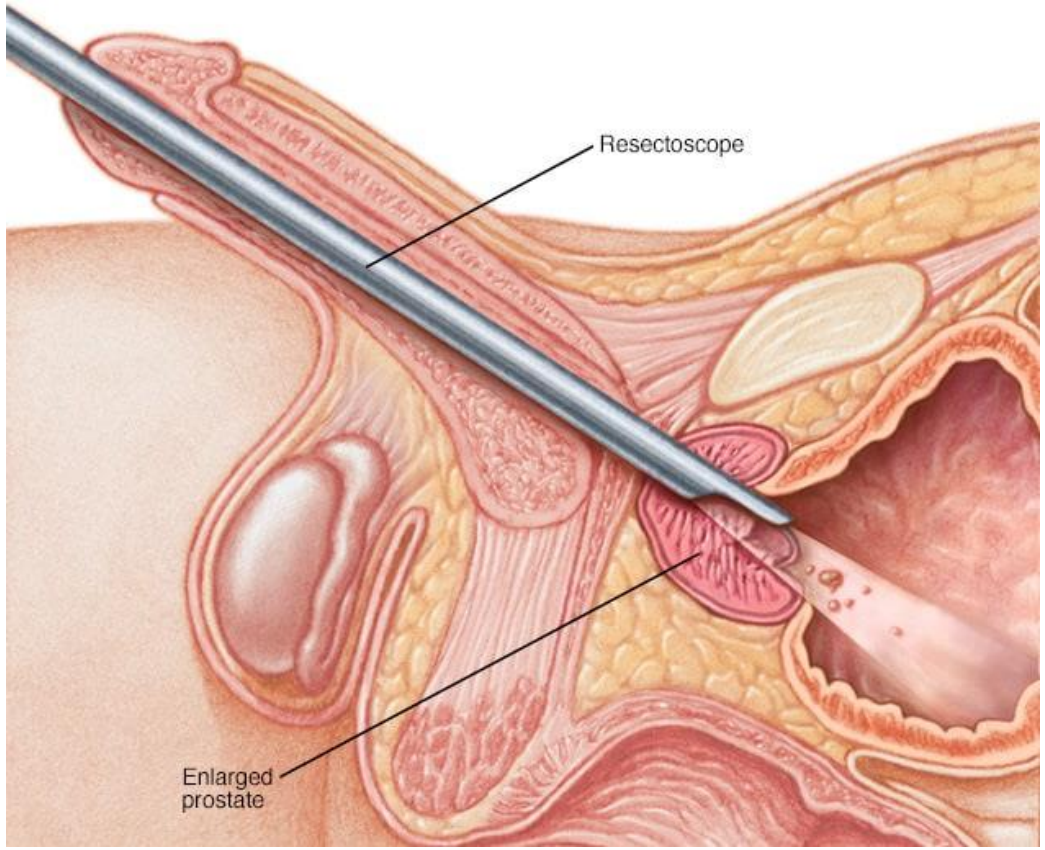
TURP & Bipolar TURP

- Wasson *et al.* (1995) demonstrated a mean improvement in LUTS in >70% of individuals.
- Further meta-analysis of 29 trials demonstrated improvements of 71% in TURP arms (range 66-76%).
- Improvements in Qmax (10.5 mL/s) with IPSS (-15.2).
- Follow-up > 3 years, the initially observed significant improvements remained durable for the bipolar and monopolar arm
- Qmax (20.5 vs. 21.5 mL/s).



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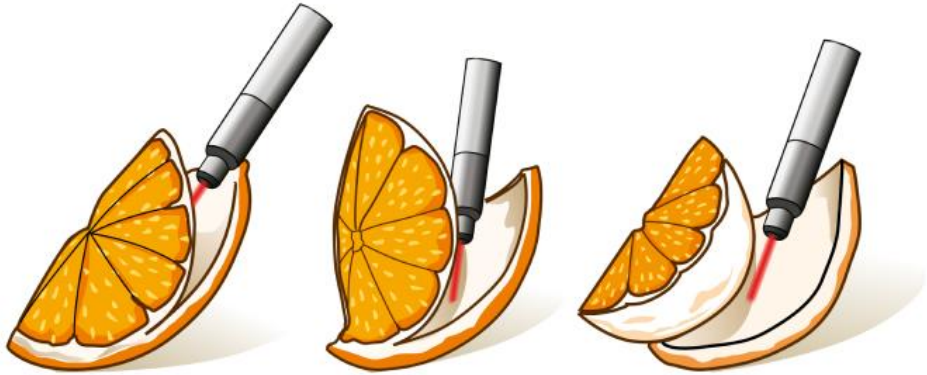
Holmium laser enucleation of prostate

- End firing laser fibre enucleates the prostate adenoma. The lobes are pushed into the bladder where they are morcellated and aspirated.



- Very effective treatment option
- Large prostate volumes
- Less Bleeding
- Shorter hospital stay
- Acute and Chronic retention
- Immediate improvements in symptom
- Quality of life scores, flow rates (4.5-9.0 ml/sec).

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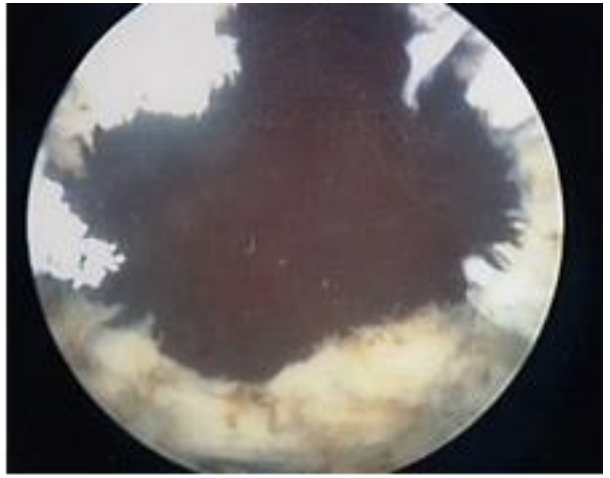
Green Light Laser PVP

- Green light laser prostatectomy (photoselective vaporisation of the prostate (PVP)) involves vaporizing obstructing prostate tissue using a laser fibre
- Less bleeding and earlier discharge vs TURP
- Day cases procedure
- Remove your catheter within 72 hrs
- Just as effective as TURP but has fewer side-effects
- Dry ejaculation,
- Can be associated with dysuria, urgency and frequency

Before



After

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Q&A's

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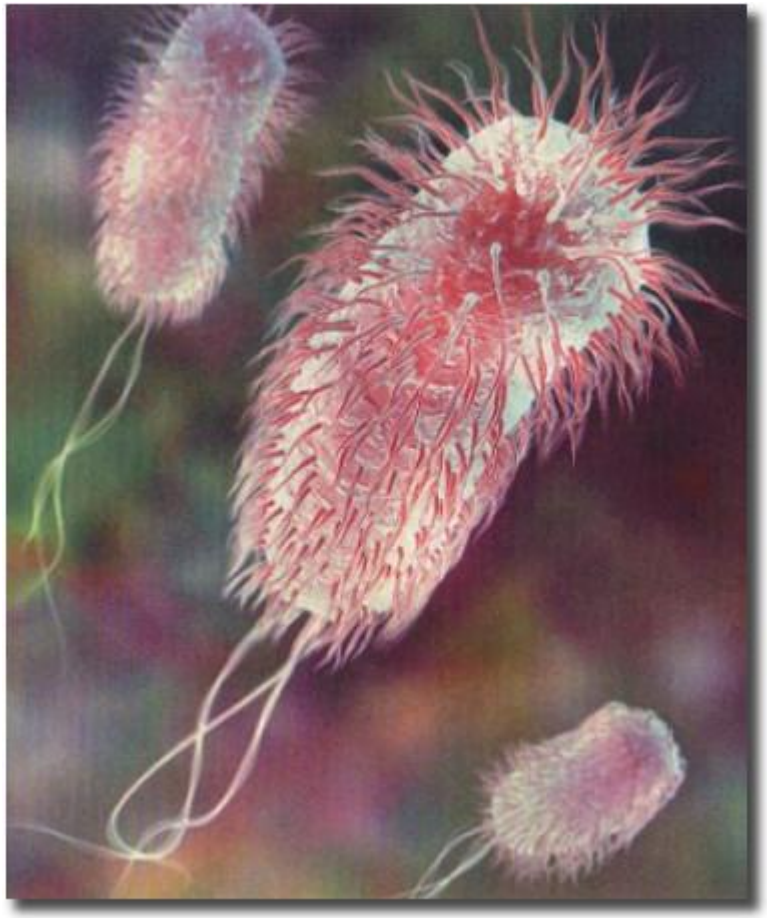
Objectives

- Simple Urinary Tract infections (UTIs)
- Complicated UTIs
- Recurrent UTIs

- Differences in treatment in different scenarios

- Alternatives to antibiotics



E.Coli

Important Definitions

A urinary tract infection is a combination of

- bacteria in MSU
- symptoms of UTI

Definitions

- 10^3 uropathogens/mL in acute uncomplicated cystitis (females).
- $>10^4$ uropathogens/mL in acute uncomplicated pyelonephritis (females)
- $> 10^5$ uropathogens/mL (women) or 10^4 uropathogens/mL (men)
- Suprapubic puncture specimen, any count of bacteria is relevant.

Important Definitions

Simple UTI

A simple, or uncomplicated, urinary tract infection (UTI) is a bacterial infection of the bladder (also known as cystitis) occurring in an otherwise healthy individual with a normally functioning urinary tract, typically in non-pregnant women, and is generally straightforward to treat with standard antibiotics

Complicated UTI

A complicated urinary tract infection (UTI) is a UTI that occurs in individuals with structural or functional abnormalities of the urinary tract, or in those with certain medical conditions or risk factors, increasing the likelihood of treatment failure, complications, or recurrence.

Recurrent UTI

Recurrent urinary tract infections (UTIs) are 2 or more episodes of acute bacterial cystitis, associated symptoms within the last 6 months, or at least 3 episodes within the previous year.

Resistant UTI

A resistant urinary tract infection (UTI) occurs when bacteria causing the infection become resistant to commonly used antibiotics, making it difficult to treat and potentially leading to complications

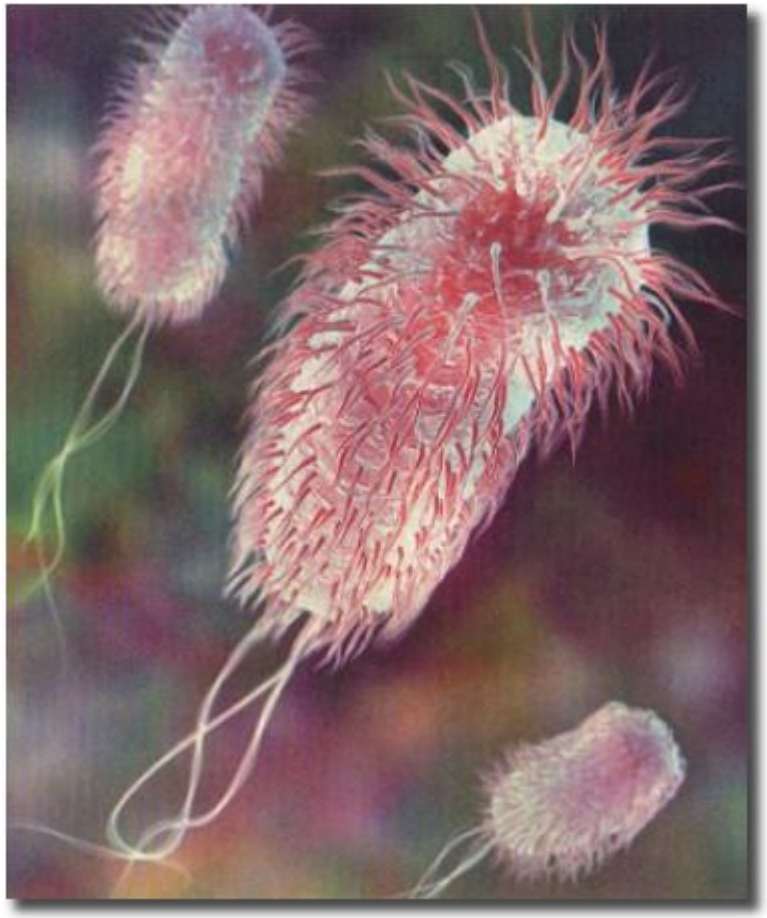
Urinary tract infections

What is a urinary tract infection?

- Bacteriuria can be identified in the urine on 3-8% of occasions at any given time.
- Kass criteria > 10^5 cfu per ml in MSU

- Affects a significant proportion of the population

- Both Males and Females



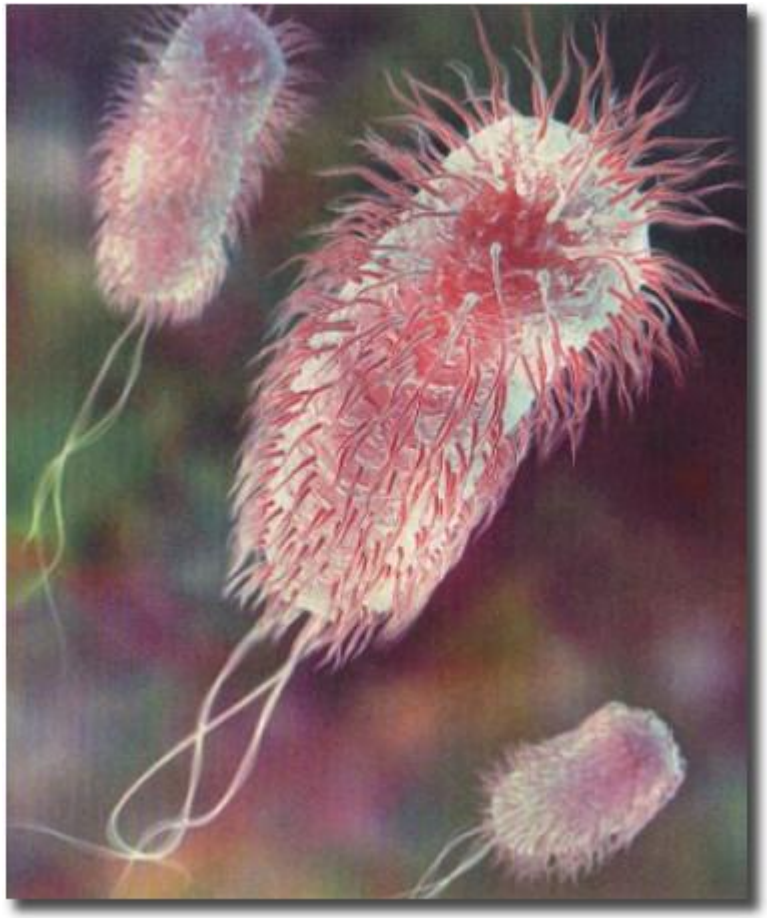
E.Coli

Urinary tract infections

Lower urinary tract infection vs Upper urinary tract infection?

Lower urinary tract UTI:
Bacteria around the anus can contaminate tissue around the urethra and migrate upwards causing an bladder infection (cystitis).

Upper urinary tract UTI:
Bacteria travel up into kidney via the ureter to cause a pyelonephritis.



E.Coli

Case presentation 1

25 year old female patient attends on recent dysuria and a possible UTI?

History

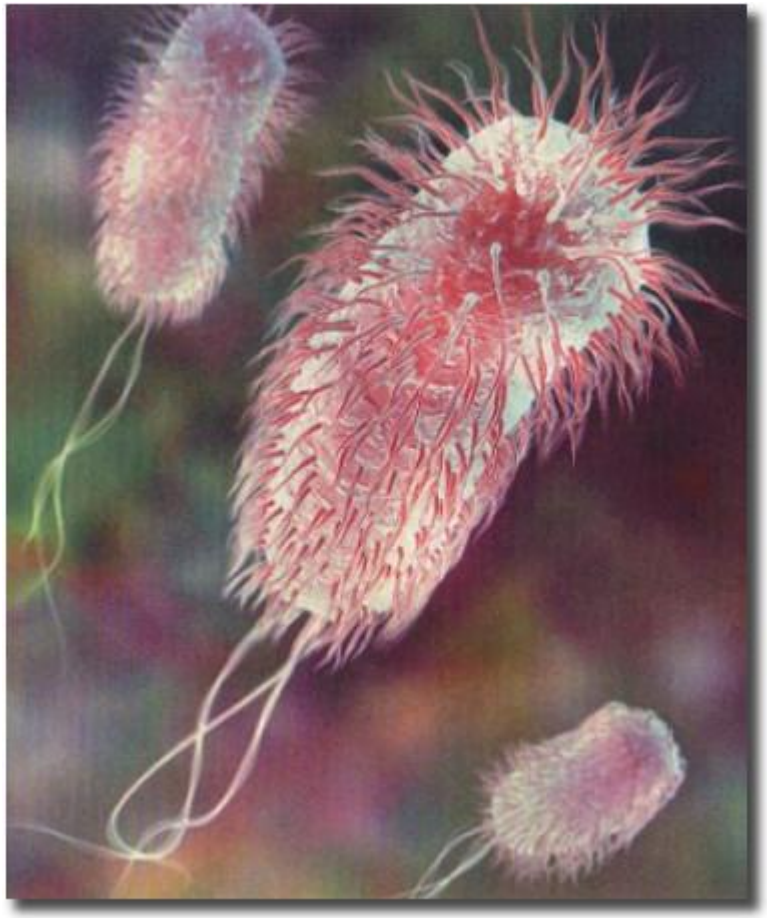
- Nature of symptoms
- Vaginal itch
- Vaginal / Urethral discharge
- Loin pain
- Partner's symptoms
- Post intercourse
- Contraception

Urinary tract infections

What can predispose your patient to a urinary tract infection?

Host factors:
Female gender
Sexual activity
Hygiene practices
Immune defence
Anatomical structure
Menopause
Catheterisation / instrumentation

Bacterial factors:
Type of pathogen – *E.Coli*
Biofilm formation
Virulence: adhesion, colonisation, toxin release



E.Coli

Case Presentation 1 - Management

25 year old female patient attends on background of simple UTI?

- MSU
- Bacterial virulence / resistance patterns
- Guide further management

Treatment

- Female UTI – 3 days of antibiotic treatment
- Male UTI – 7 days of antibiotic treatment

Antibiotic treatment for simple UTIs

Trimethoprim

- Blocking the reduction of dihydrofolate to tetrahydrofolate by susceptible organisms.
- Inhibitory activity for most gram-positive aerobic cocci and some gram-negative aerobic bacilli
- Peak serum concentrations within 1-4 hours of antibiotic dose
- Trimethoprim half-life ranges from 8-10 hours, but may be prolonged in patients with renal dysfunction
- Passes into a variety of different secretions

Nitrofurantoin

- Nitrofurantoin is converted by bacterial nitroreductases to electrophilic intermediates.
- These inhibit the citric acid cycle as well as synthesis of DNA, RNA, and protein.
- More resistant to the development of bacterial resistance because it has multiple targets
- Taking nitrofurantoin with food increases the absorption and duration of therapeutic concentrations in the urine
- 27-50% of an oral dose is excreted in the urine as unchanged nitrofurantoin.[3] 90% of the total dose is eliminated in the urine
- Rate of absorption of NFN may be decreased whilst taking Citric acid as it may decrease GI absorption.

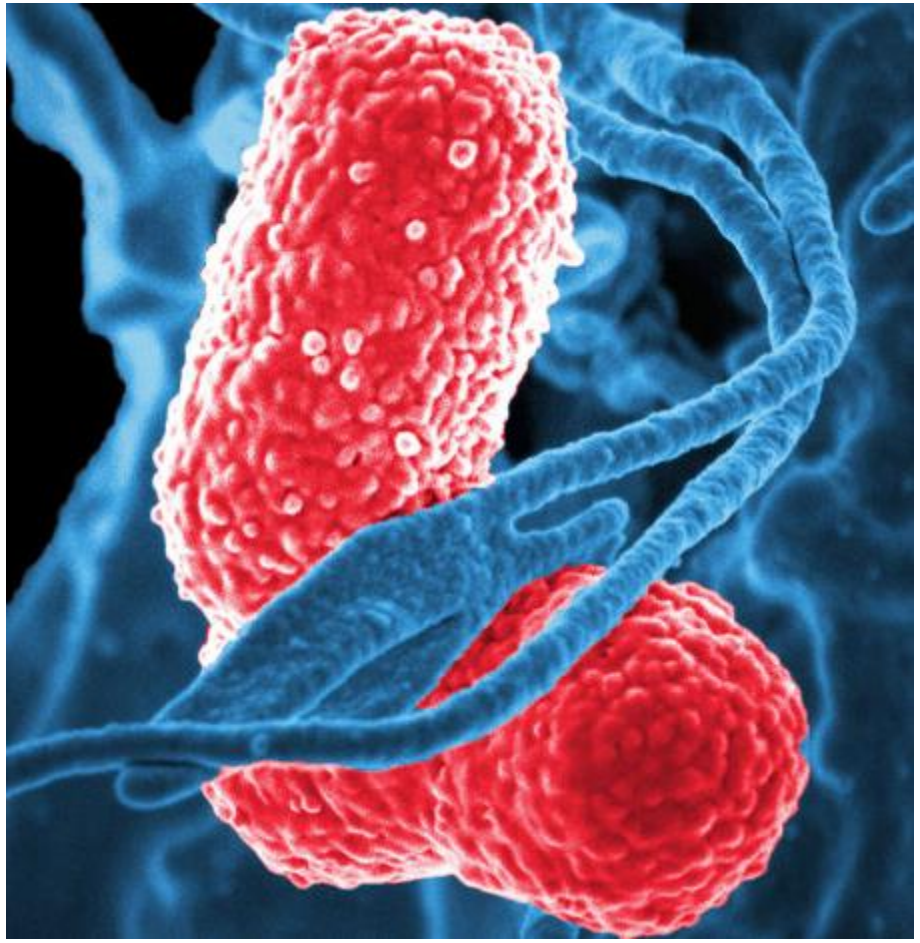
1.McOsker CC, Fitzpatrick PM. J Antimicrob Chemother. 1994 May;33 Suppl A:23-30
2.Novelli A, Rosi E. J Chemother. 2017 Dec;29

Complicated urinary tract infection

What is a complicated urinary tract infection?

A complicated urinary tract infection is the term used to indicate the presence of a structurally or functionally abnormal urinary tract, or UTI in the presence of underlying disease which is known to increase the risk of acquiring infection or failing therapy.

- Male
- Elderly
- Pregnancy
- Indwelling catheter
- Recent instrumentation



Kliebsiella spp.

Recurrent urinary tract infections

What is a recurrent urinary tract infection?

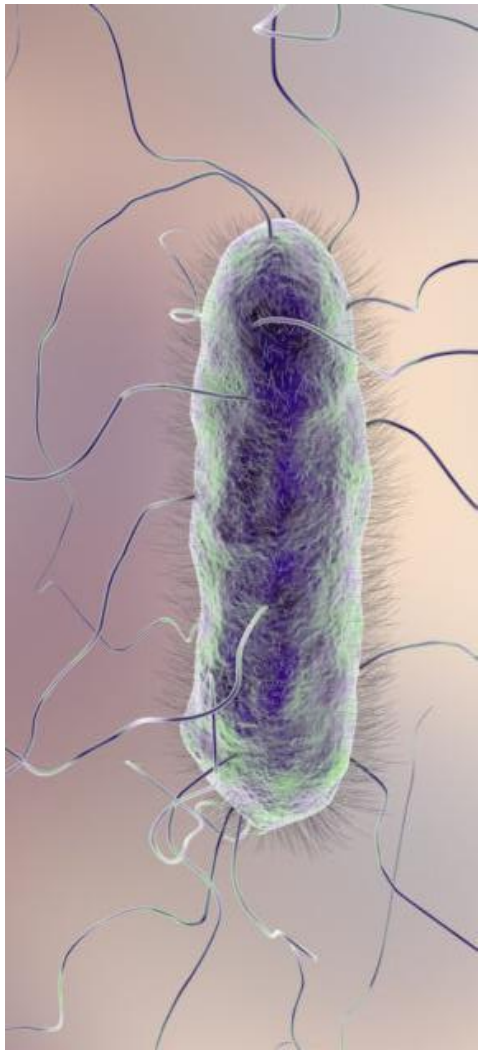
Recurrent UTI is an episode of urinary tract infection after the successful resolution of an earlier episode.

- Presence of 3 or more infections in 12 months or
- Presence of 2 or more infections in 6 months.

Can either be:

- Persistent UTI is persistent positive culture with same organism.
- Reinfection UTI refers to recurrent episodes of UTI caused by different organisms.

- More than 95% of all recurrent UTIs in female patients are due to reinfection.



Proteus spp

Case presentation 2

53 year old female patient attends on the background of recurrent UTIs?

History

- Frequency of infections
- Nature of symptoms
- Vaginal / Urethral discharge
- Loin pain

Case presentation 2

53 year old female patient attends on the background of recurrent UTIs?

History

- Childhood history of recurrent infections
- Previous diagnosis (First UTI<15 years)
- Oral contraceptive agents (possible interactions with antibiotics)
- Family history of recurrent infections
- Smoker (?)
- Maternal history of UTI
- Diabetes mellitus
- Pregnancy
- Elderly
- Immunosuppressant treatment or disease
- New partner
- Multi-orifice SI
- Constipation

Case presentation 2

53 year old female patient attends on the background of recurrent UTIs?

Examination

- Chaperone & Consent
- Focussed abdominal examination
- Any loin tenderness, palpable bladder
- Vaginal examination: assess
  - degree of oestrogenisation
  - prolapse
  - urethral caruncle

Case presentation 2

53 year old female patient attends on the background of recurrent UTIs?

Investigation

- Urinalysis
- MSU (multiple over time)
- Cytology if smoker over the age of 45
- USS KUB with Flow rate and post void residual
- Flexible cystoscopy

Case presentation 2

53 year old female patient attends on the background of recurrent UTIs?

What upper tract abnormalities might be detected?

- Urinary obstruction (hydronephrosis, hydroureter)
- Vesico-ureteric reflux
- (Upper) urinary tract calculi
- Renal scarring
- Interstitial nephritis
- Papillary necrosis
- Medullary sponge kidney
- Congenital calyceal obstruction

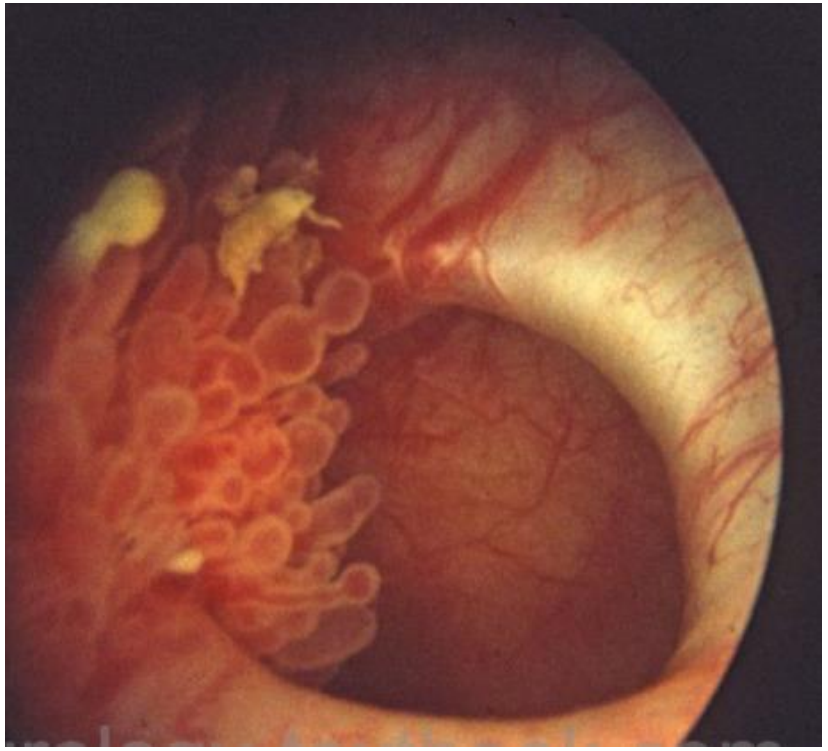
Left sided hydronephrosis

Case presentation 2

53 year old female patient attends on the background of recurrent UTIs?

Why do a flexible cystoscopy?

- 8% yield
- macroscopic haematuria
- microscopic haematuria between UTIs
- persistent UTI
- >45 years old



Diagnoses

- Bladder cancer
- Cystocoele
- Inflammatory conditions of the bladder
- Bladder stones
- Bladder diverticulum

Case presentation 2 - treatment

53 year old female patient attends on the background of recurrent UTIs?

General advice

- Hygiene
  - Generally overclean
  - Women do know how to wipe their bottoms!!!
- Increase fluid intake (1.5+L/day)
- Avoid bubble baths
- Avoid spermicidal contraceptives, lubricants
- Double voiding
- Void after sexual intercourse

- Low dose oestrogen for atrophic vaginitis

Case presentation 2 - antibiotic treatment

- Peri-intercourse therapy
- Self-start antibiotics

- NICE advice for recurrent UTIs – unclear duration mentioned
- Long-term low dose prophylaxis (3/6/12 months)

Circle Health Group

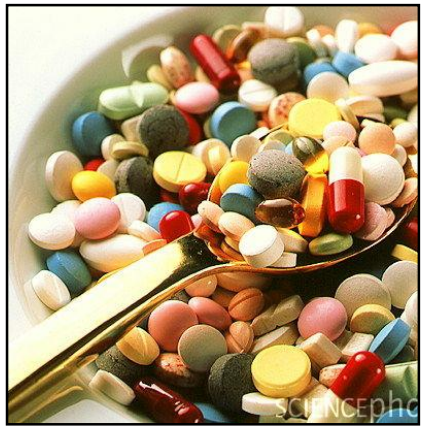
Case presentation 2 – alternatives to antibiotics

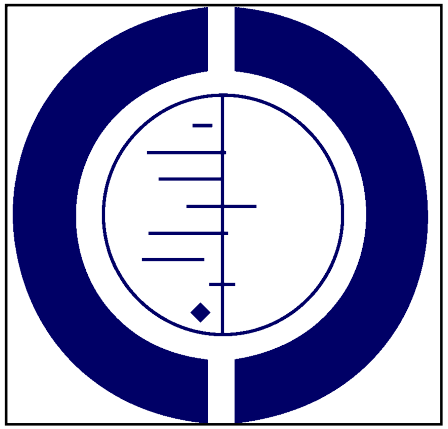
53 year old female patient attends on the background of recurrent UTIs

General advice

- Sodium Citrate
  - alkalinising agent – makes the urine less acidic
  - reduces symptoms
- Cranberry juice
  - Proanthocyanidins
  - Block bacterial adherence to urothelium
- Live yoghurt (+/-)
  - Restore lactobacillus to vaginal introitus

Does cranberry work doctor?





50 trials

8857 pts

- Cranberries (juice, tablets or capsules) reduced the number of UTIs in women with recurrent UTIs, in children with UTIs and in people susceptible to UTIs following an intervention e.g. bladder radiotherapy.
- UTIs did not appear to be reduced in elderly institutionalised men and women, in adults with neuromuscular bladder dysfunction and incomplete bladder emptying, or in pregnant women.

Q&A’s