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Western Health

Benign prostate hyperplasia

Its association with metabolic syndrome and Medical management of LUTS

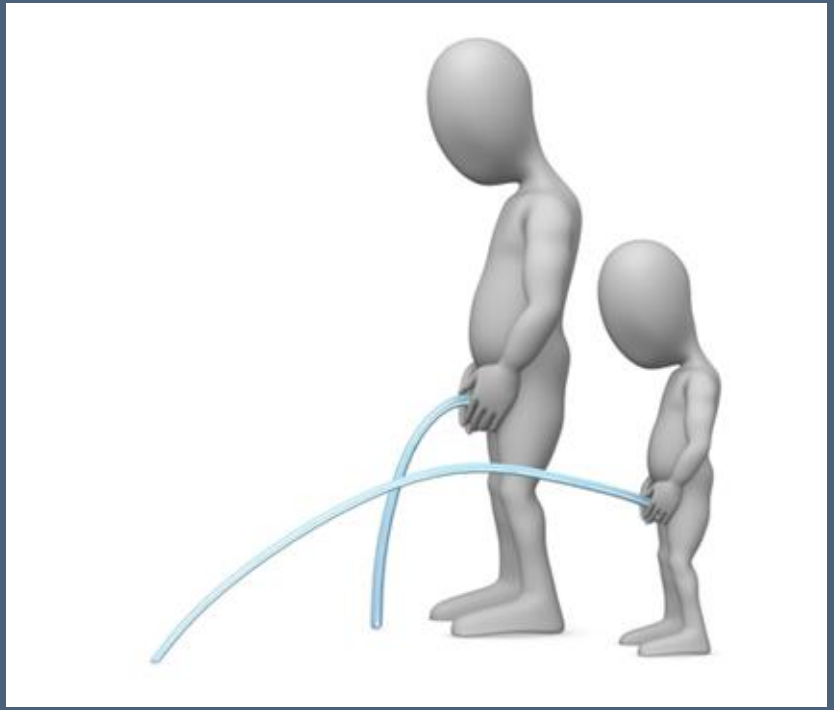
Dr Jason Ooi. FRACS (Urology)

Western Health

- No disclosures

BPH - Prevalence

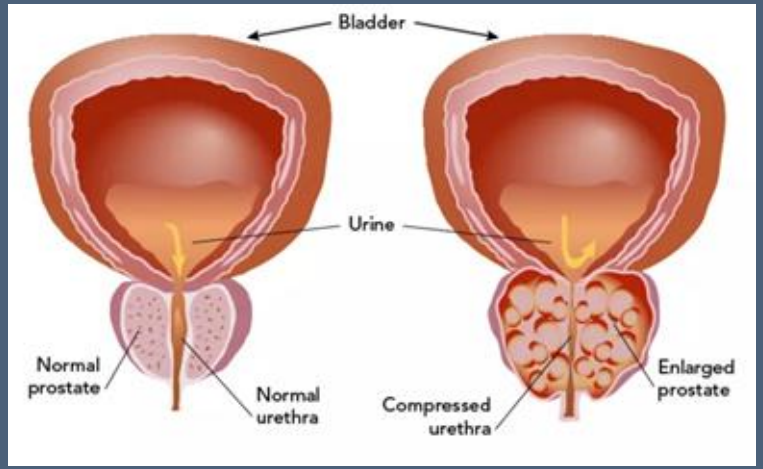
- Increases with advancing age
  - Men 60-69 years old - 50-60%
  - Men > 70 years old - 80-90%
- Common cause of lower urinary tract symptoms (LUTS) - obstructive (voiding), storage (irritative) or mixed



B. Chughtai, J.C. Forde, D.D. Thomas, L. Laor, T. Hossack, H.H. Woo, et al.
Benign prostatic hyperplasia
Nat. Rev. Dis. Primers. (2016). 10.1038/nrdp.2016.31

BPH - Pathogenesis

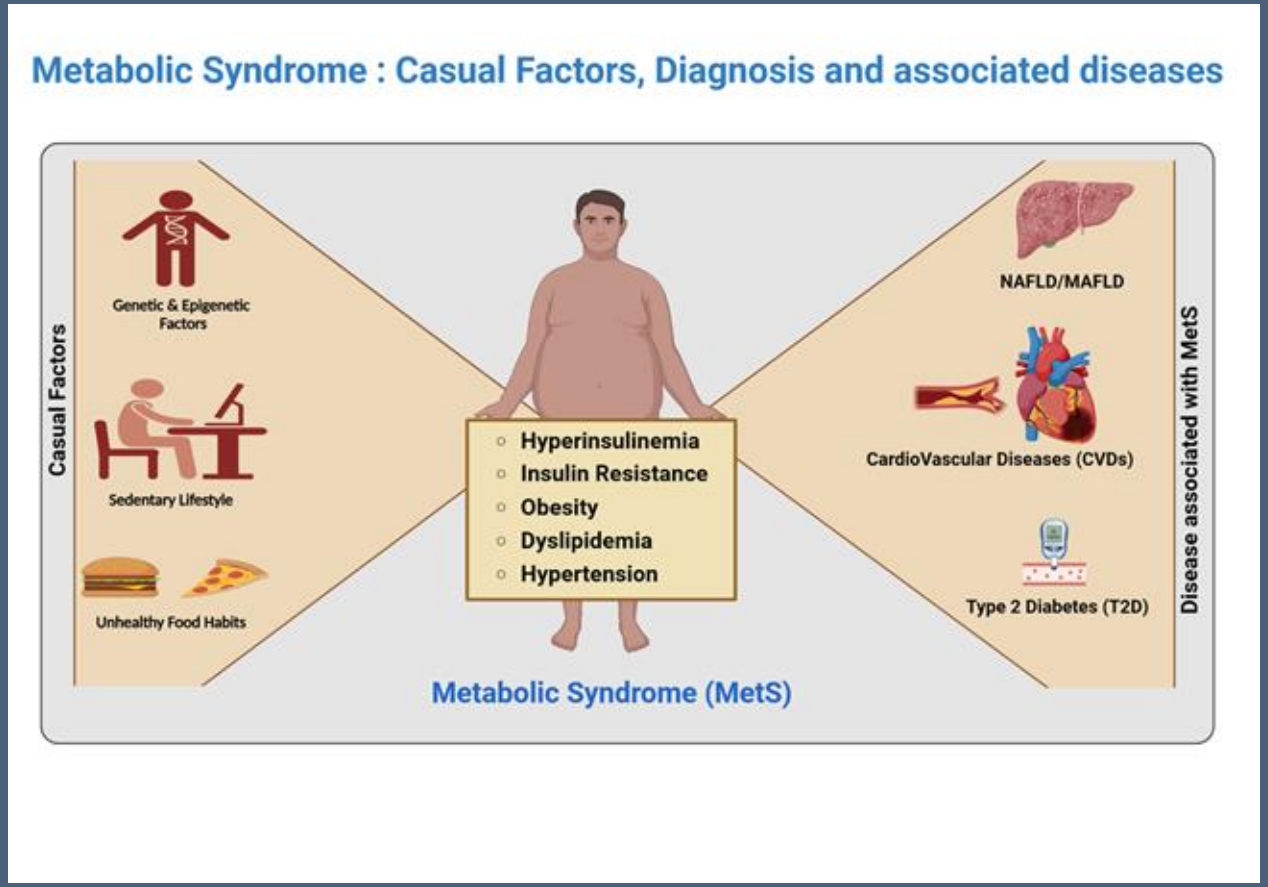
- Histological proliferation of smooth muscle, epithelium and stromal cells within transition zone of prostate with occludes the proximal urethra
- Symptoms arise from 2 mechanisms:
- 1. Static - Hyperplastic tissue compresses urethra
- 2. Dynamic- increased adrenergic nervous system and smooth muscle tone
- Overtime bladder may develop reduced compliance from detrusor muscle hypertrophy, fibrosis, develop detrusor overactivity, or decompensated with end stage detrusor failure



BPH

- Risk factors
  - *Age, genetics, geography*
  - *Metabolic syndrome (MetS)*
    - BPH is increasingly recognised as a metabolic disease; a manifestation of metabolic syndrome (MetS)
    - Up to 40% of aging men (>40 years old) have MetS
    - MetS affects 33 to 51 % of men presenting with LUTS*
    - MetS accelerates the progression of BPH because of systemic inflammation and oxidative stress

* Xiong Y, Zhang F, Wu C, Zhang Y, Huang X, Qin F, Yuan J. The Circadian Syndrome Predicts Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia Better Than Metabolic Syndrome in Aging Males: A 4-Year Follow-Up Study. Front Med (Lausanne). 2021 Sep 21;8:715830. doi: 10.3389/fmed.2021.715830. PMID: 34621761; PMCID: PMC8490706.



BPH

CVA

Alzheimers disease

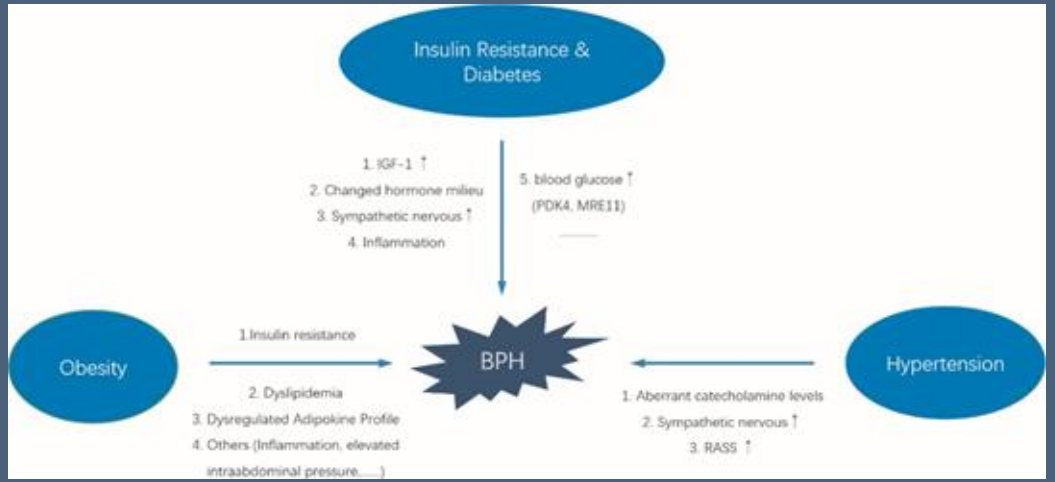
Cancers

- Pancreatic
- Renal
- Colorectal
- Leukemia

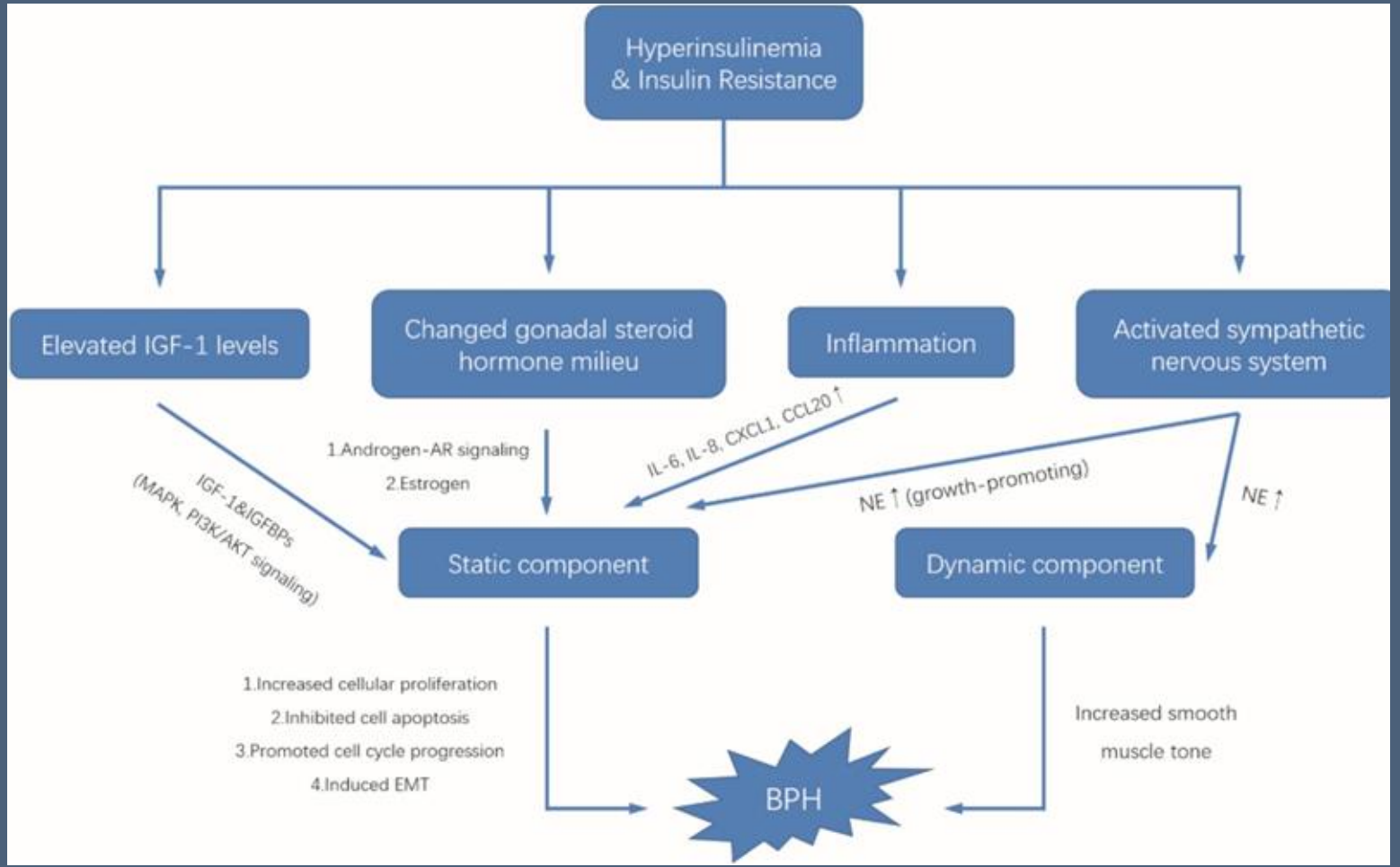
Pothiwala P, Jain SK, Yaturu S. Metabolic syndrome and cancer. Metab Syndr Relat Disord. 2009 Aug;7(4):279-88. doi: 10.1089/met.2008.0065. PMID: 19284314; PMCID: PMC3191378.

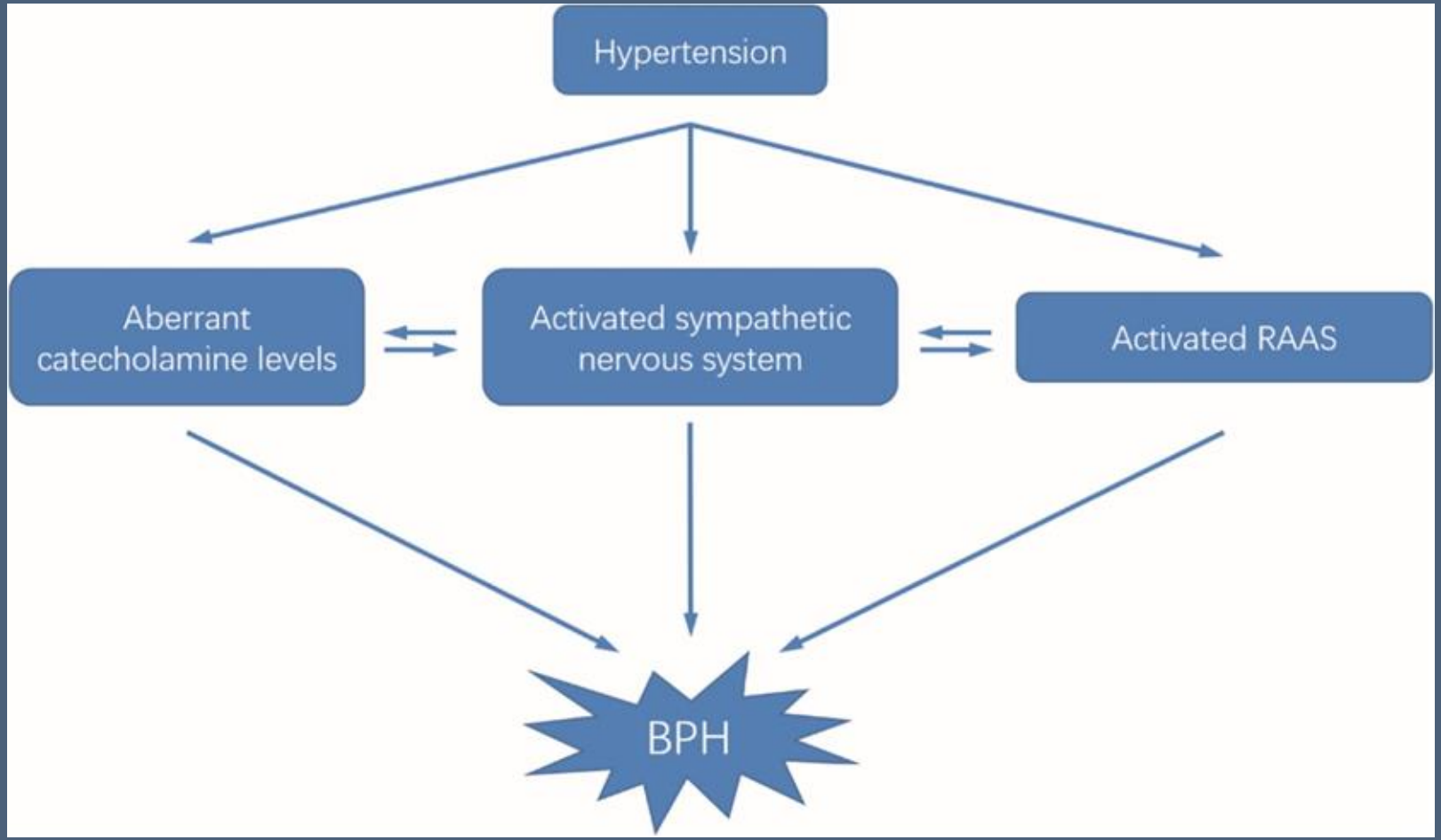
BPH and MetS

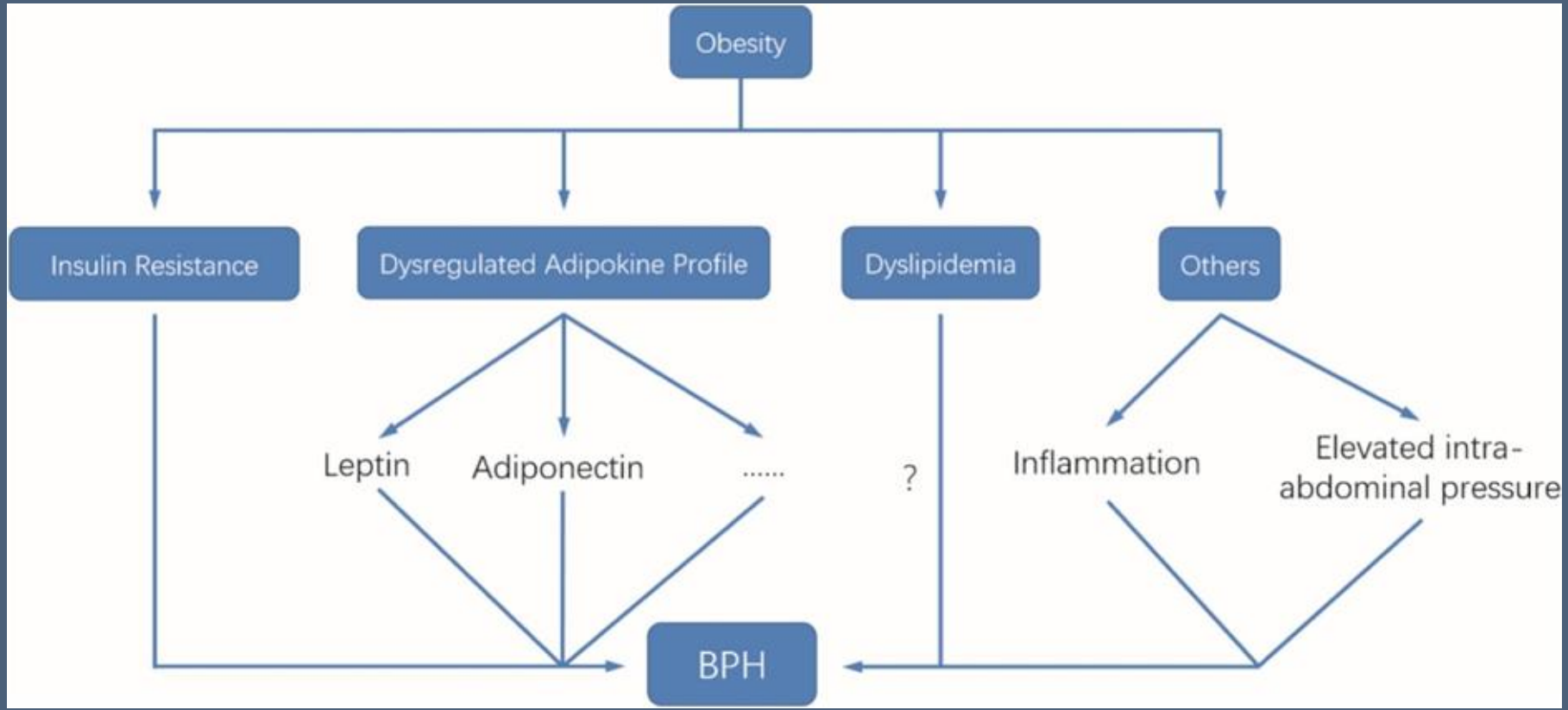
- MetS play important roles in pathogenesis of BPH
  - Hormones such as Insulin, Insulin like growth factor 1 (IGF-1), Androgen & Oestrogen imbalance , Adipokines, Cytokines



Xun Fu, Yutao Wang, Yi Lu, Jiang Liu, Hongjun Li,
Association between metabolic syndrome and benign prostatic hyperplasia: The underlying molecular connection,
Life Sciences, Volume 358, 2024,


Hyperinsulinemia & Insulin Resistance
Elevated IGF-1 levels
Changed gonadal steroid hormone milieu
Inflammation
Activated sympathetic nervous system
IGF-1&IGFBPs (MAPK, PI3K/AKT signaling)
1.Androgen-AR signaling
2.Estrogen
IL-6, IL-8, CXCL1, CCL20 ↑
NE ↑ (growth-promoting)
NE ↑
Static component
Dynamic component
1.Increased cellular proliferation
2.Inhibited cell apoptosis
3.Promoted cell cycle progression
4.Induced EMT
Increased smooth muscle tone
BPH


Hypertension
Aberrant catecholamine levels
Activated sympathetic nervous system
Activated RAAS
BPH

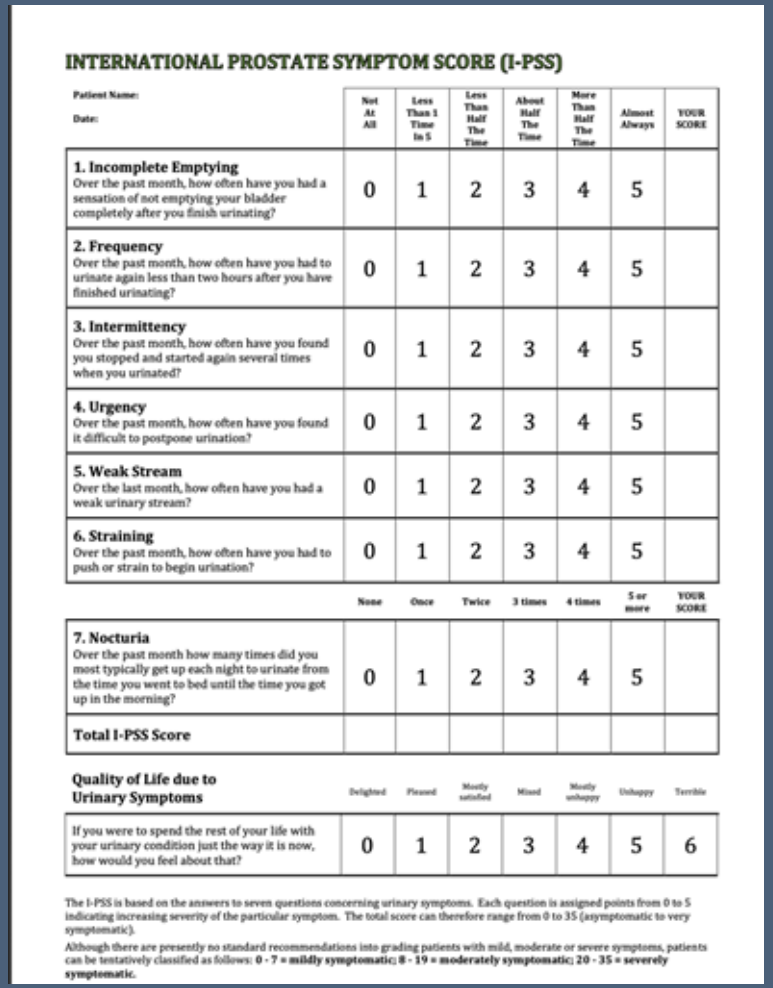

Obesity
Insulin Resistance
Dysregulated Adipokine Profile
Dyslipidemia
Others
Leptin
Adiponectin
.....
?
Inflammation
Elevated intra-abdominal pressure
BPH

BPH

Management

- History
  - Poor urine flow, Storage symptoms, Nocturia, Dysuria, UTIs, Haematuria
  - Fluid intake - water, coffee, tea, soda, ETOH
  - Snoring - undiagnosed obstructive apnea
  - Neurological deficits
  - Risk factors for urethral stricture - penile/pelvic trauma, Indwelling catheters, STI
  - Family history of prostate cancer, BPH
  - MetS - NIDDM, HL, HT, Obesity
  - Medications- Diuretics
  - IPSS score

International Prostate Symptom Score



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							

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

The I-PSS is based on the answers to seven questions concerning urinary symptoms. Each question is assigned points from 0 to 5 indicating increasing severity of the particular symptom. The total score can therefore range from 0 to 35 (asymptomatic to very symptomatic).

Although there are presently no standard recommendations into grading patients with mild, moderate or severe symptoms, patients can be tentatively classified as follows: **0 - 7 = mildly symptomatic; 8 - 19 = moderately symptomatic; 20 - 35 = severely symptomatic.**

BPH

Management

- Examination
  - DRE
  - Presence of phimosis, meatal stenosis
  - Signs of CCF
  - HT
- Investigations
  - MSU, CUE, PSA (>50 year old)
  - Renal tract ultrasound
  - Fasting Glucose, HBA1C, Cholesterol studies
  - Urine flow test
  - Urodynamics for selected cases - eg Neuropathic bladder

BPH

Management Principles

- Mild symptoms IPSS < 7 - Watchful waiting, lifestyle and dietary modifications
- Moderate to severe symptoms IPSS >8 - Medical, Surgical management
- Manage concurrent MetS
  - MetS is associated with higher prevalence and severity of BPH. Thus possible to postpone BPH progression by lowering blood glucose , improving insulin resistance and reducing inflammation through healthy lifestyle and clinical treatment

BPH

Medical Management

- Lifestyle modifications
  - Modify fluid intake (Stop eating 3 hours and drinking 2 hours before sleeping)
  - Reduce consumption of caffeine, soft drinks and alcohol
  - Reduce intake of sugar, carbohydrate, ultra processed foods, practice intermittent fasting to address hyperinsulinemia
  - Dietary advice, Referral to a dietician
  - Regular exercise
  - Quit smoking
  - Address stress and poor sleep
- Manage NIDDM, HL, HT, Obesity

Haile ES, Sotimehin AE, Gill BC. Medical management of benign prostatic hyperplasia. Cleve Clin J Med. 2024 Mar 1;91(3):163-170. doi: 10.3949/ccjm.91a.23027. PMID: 38429006.

BPH

Medical Management

Alpha 1-Blockers Tamsulosin, Silodosin, Alfuzosin	IPSS: - 4-6 pts Flow: + 1 to 2 ml/s Qmax	Rapid onset, 1st line	SE: Dry ejaculation, Hypotension, Priapism, Floppy iris syndrome
5-ARIs Finasteride, Dutasteride	IPSS: - 3-5 pts Flow: + 1.5 to 2 ml/s	Reduces prostate volume 20-30%, 6 months lag	SE: ED
Combination Therapy AB+5-ARI (CombAT, MTOPS)	IPSS: - 5-8 pts Flow: + 2-3 ml/s	Superior for larger glands > 60 gms	SE: ED, Hypotension
PDE 5 inhibitors Tadalafil 5mg	IPSS: - 3-5pts Flow: modest	Concomitant ED	SE: Headaches, Flushing
Anti- Cholinergic therapy Oxybutynin, Mirbegon		Detrusor overactivity	SE: Increases risk of retention when PVR > 250

Haile ES, Sotimehin AE, Gill BC. Medical management of benign prostatic hyperplasia. Cleve Clin J Med. 2024 Mar 1;91(3):163-170. doi: 10.3949/ccjm.91a.23027. PMID: 38429006.

BPH

Management

- Indications for surgery
  - Worsening IPSS/ Bothersome symptoms on medical therapy
  - Urine Retention
  - Recurrent UTI
  - Bladder stones
  - Recurrent Haematuria
  - Worsening renal function
  - Bilateral hydronephrosis
  - Adverse reaction of alpha blocker therapy

Take home messages

BPH- Association with metabolic syndrome and management

- Luts is prevalent in aging men (50% in 60 year old)
- Up to 50% of men with LUTS have MetS
- Untreated MetS accelerates progression of BPH & severity of LUTS
- Manage metabolic syndrome
- Manage BPH with lifestyle modifications, medical therapy or surgery when indicated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HAEMATURIA

DR SHANNON MCGRATH

OVERVIEW

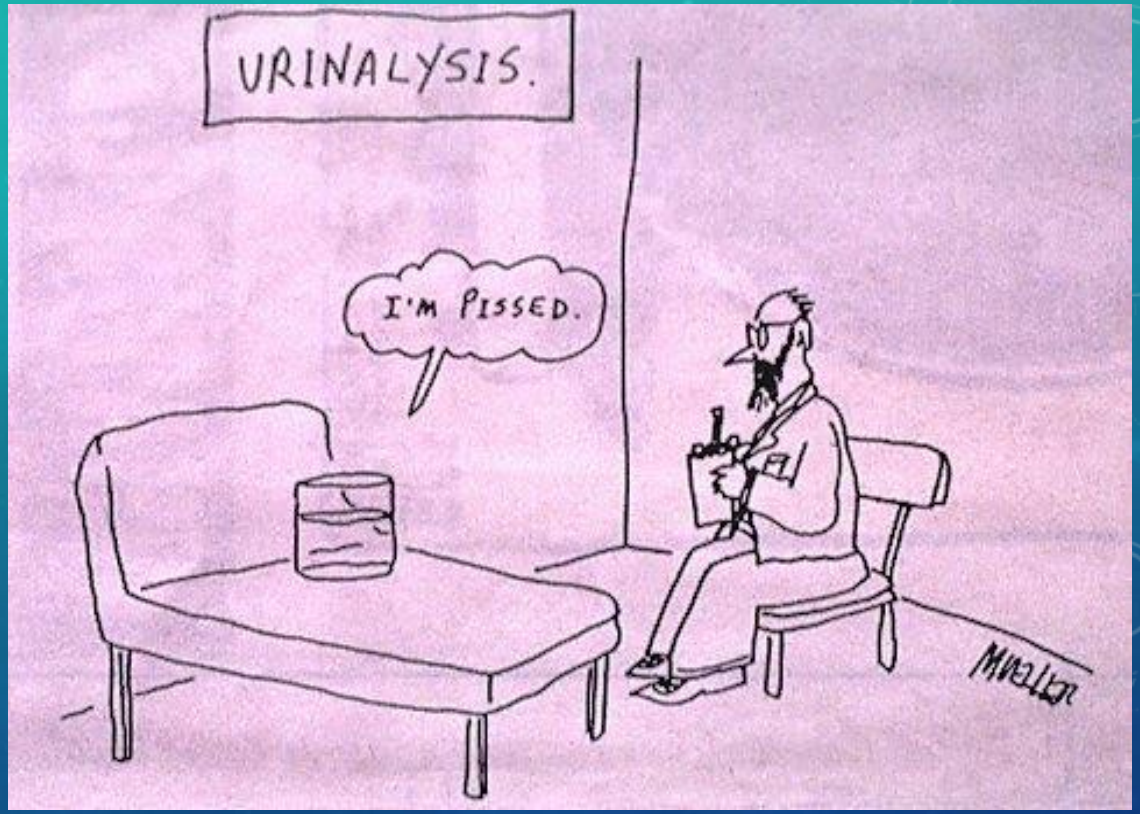
- Definition – presence of blood in urine
- Microscopic vs macroscopic
- Microscopic – 3 to 10 RBC's per HPF
- Dipstick – detection of haem (1 or 2 rbc's)

- Macroscopic haematuria - VISIBLE
- False positives- myoglobin
- Beetroot , rifampicin, severely jaundiced, severely concentrated urine

HAEMATURIA

- Microscopic haematuria => ~4% risk of cancer
- Macroscopic haematuria => ~25% risk of cancer

- Initial haematuria – suggests disease of urethra, prostate, bladder neck
- Terminal haematuria – suggests bladder disease
- Total haematuria – suggests possible upper tract disease


URINALYSIS.
I'M PISSED.

WHO TO REFER

Criteria for referral to public hospital specialist clinic services

- Any visible haematuria.
- Persistent microscopic haematuria: at least 2 episodes confirmed through midstream specimen of urine collected at least a week apart.
- Microscopic or macroscopic haematuria in the absence of a urinary tract infection.

CAUSES

- **INFECTIONS**
- **STONES**
- **CANCERS**

Others

- Trauma
- Catheterisation
- Inflammation
- BPH
- Vascular malformations
- Medication (cyclophosphamide, BCG)

Renal

- IgA nephropathy
- Glomerulonephritis
- Congenital - medullary sponge kidneys

EVALUATION & ASSESSMENT

- History
  - Micro vs macro
  - Painful vs painless
  - Associated urinary Sx/flank pain
  - Smoker
  - Anticoagulation
  - FHx – malignancy, lynch syndrome
  - Infections
  - IDC etc
  - Radiation exposure
  - Medical exposures
  - Occupational exposures (hair dyes, paints, leather, rubber)

- Examination
  - Genitourinary examination + DRE
  - Abdominal examination

HIGH RISK FACTORS

- AGE
- Smoking
- Occupational exposure
- Pelvic radiation
- Medications – (bex powder, cyclophophamide)
- Recurrent urinary tract infections
- Chronic indwelling catheter/foreign body
- Other: lynch syndrome

INVESTIGATIONS

Serum

- FBE
- UEC
- Coagulation profile
- *PSA

Urine

- Dipstick/UA
- MC&S
- *Urine Cytology x3
  - Second urination of the day
- *Cx Bladder

Imaging

•CT KUB – stones

•CT Urogram/IVP (delayed phase contrast)

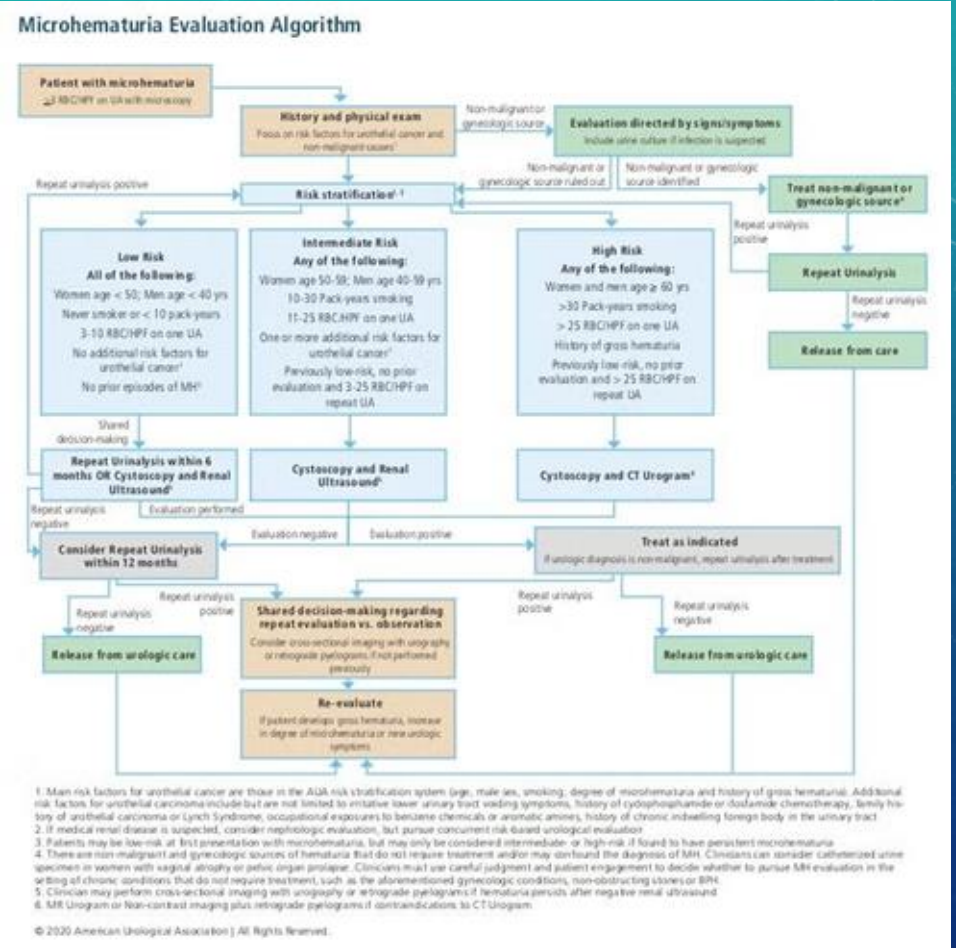
•Looking for malignancy – renal, ureteric or bladder

- Cystoscopy/Ureteropyeloscopy +/- retrograde pyelogram

•Ultrasound renal tract

- (45% - 90% depending on the stone's size and location)

RISK STRATIFICATION



REFERRAL

Information to be included in the referral

Information that must be provided:

- Midstream urine microscopy culture sensitivities.
- Creatinine and electrolytes.
- Urinary tract ultrasound or CT intravenous pyelogram results.

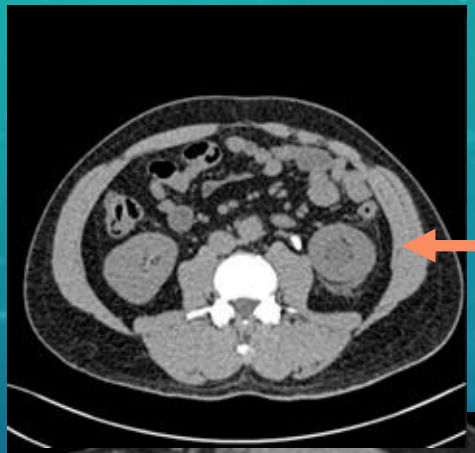
Provide if available:

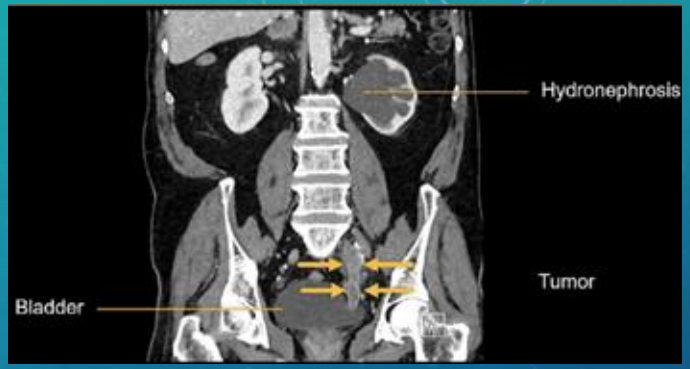
- Urine cytology results.

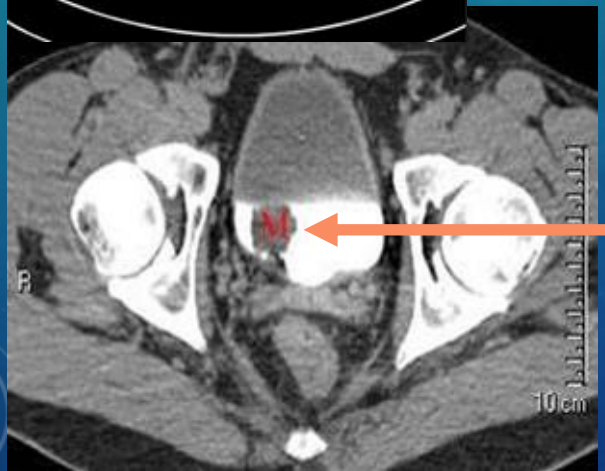
WHAT DO WE DO?

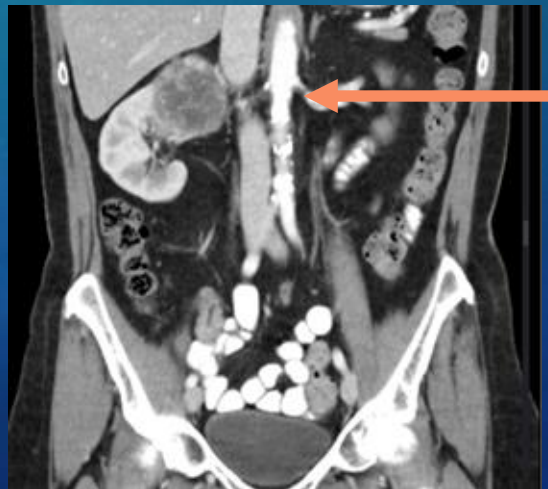
- Cystoscopy
  - Biopsy
- Retrograde pyelogram +/- Washings
- Ureteropyeloscopy + proceed (biopsy, lithotripsy, etc)
- Prostate cancer screening/ BPH evaluation

CT UROGRAM/IVP

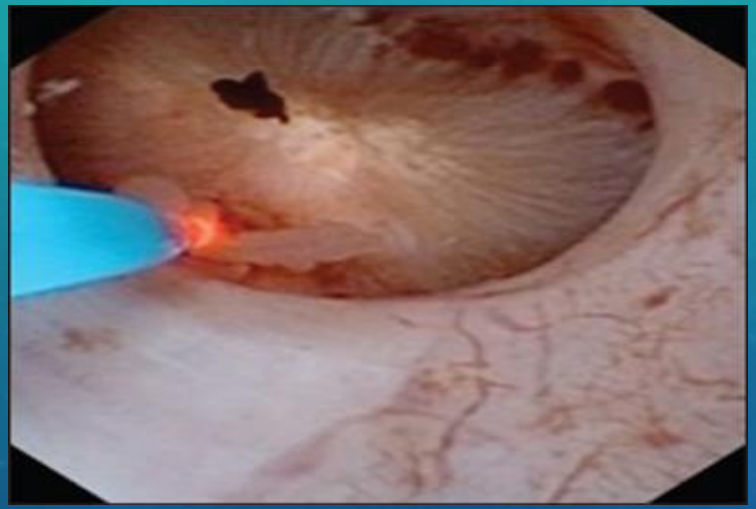


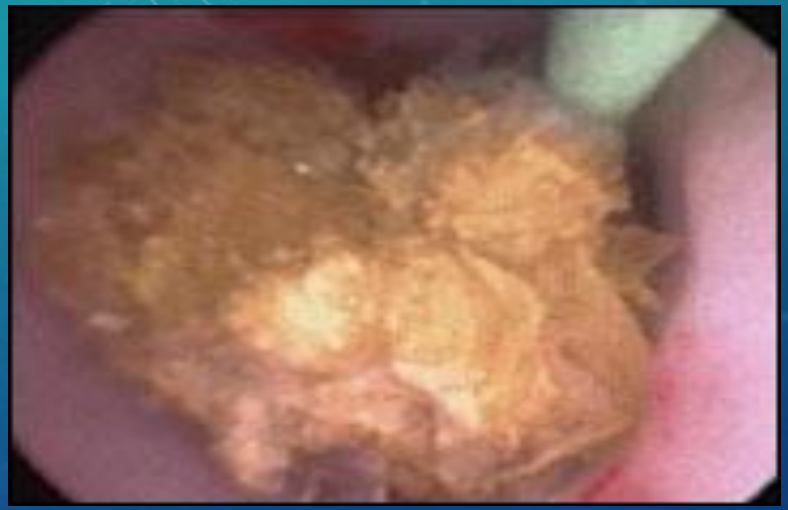






URETEROPYELOSCOPY



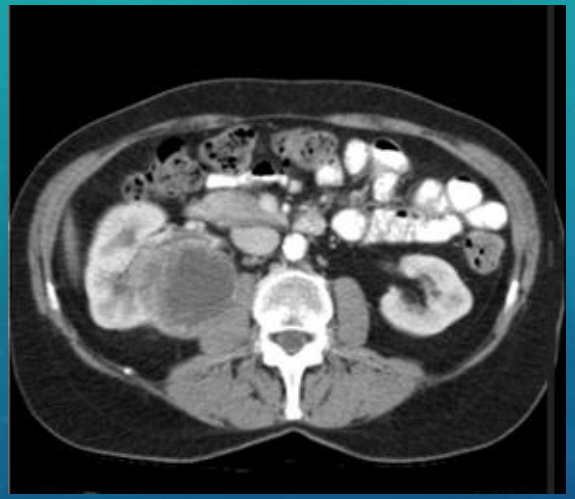


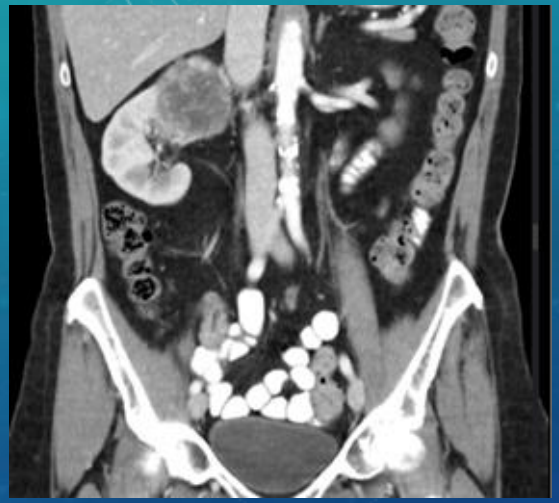
CASE 1

- 64M p/w right flank pain this morning – 10/10 radiating to groin
- 2x episodes frank haematuria
- HTN, CABGs (18 years ago – on aspirin), obesity
- Ex-smoker
- DDx:

- Ix:
- Bloods: FBE, UEC, coagulation
- UA – Blood +++, nitrites -; leuks -
- Urine MC&S negative
- CT KUB
- CT IVP

IMAGING



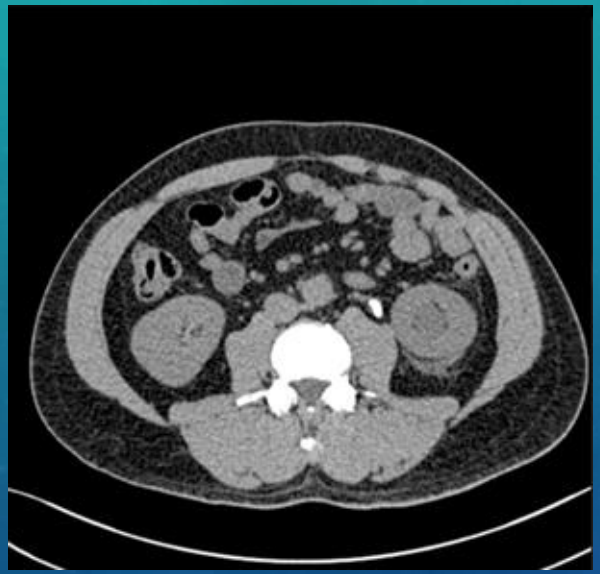


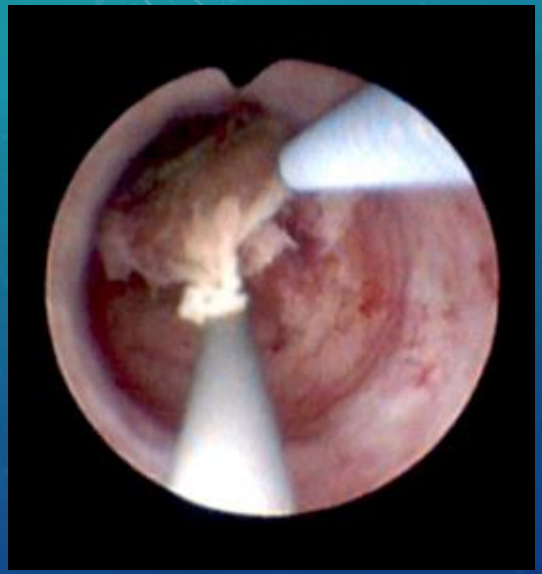
CASE 2

- 57M Left flank pain radiating to groin
- Smoker
- No other Hx
- DDx:

- Ix:
- Bloods – FBE, UEC, coagulation
- Urine dipstick – Blood +; leuks -; nitrites -
- Urine MC&S - negative
- Urine cytology
- CT Urogram
- Retrograde pyelogram
- Cystoscopy/Ureteroscopy

INVESTIGATIONS



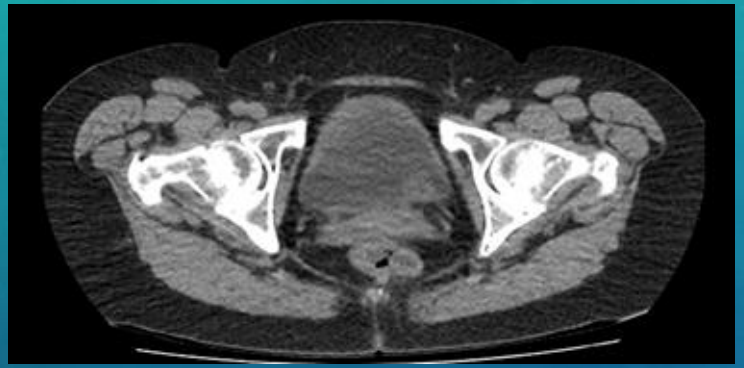


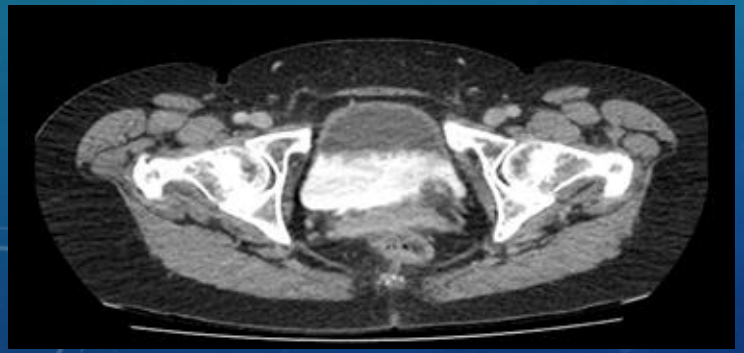
CASE 3

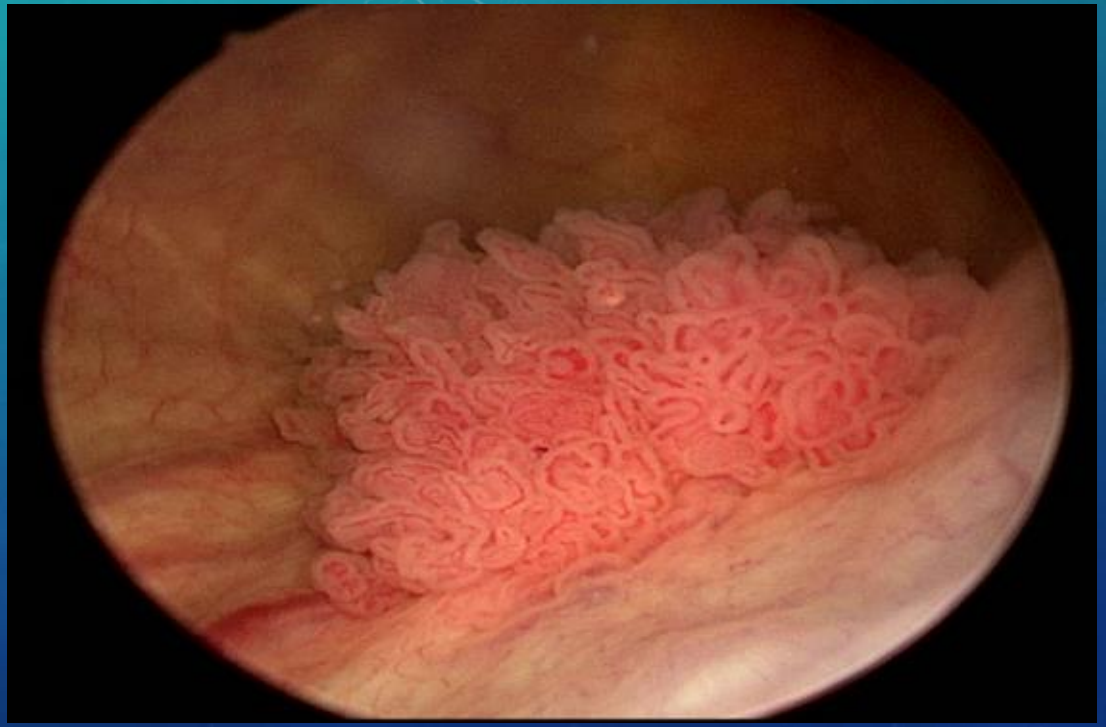
- 64F dysuria, frank haematuria
- HTN, gastritis, passive smoker, hairdresser
- DDx:

- Ix:
- Bloods – FBE, UEC, coagulation
- Urine dipstick – Blood +; leuks -; nitrites -
- Urine MC&S - negative
- Urine cytology
- CT IVP
- Cystoscopy + Biopsy

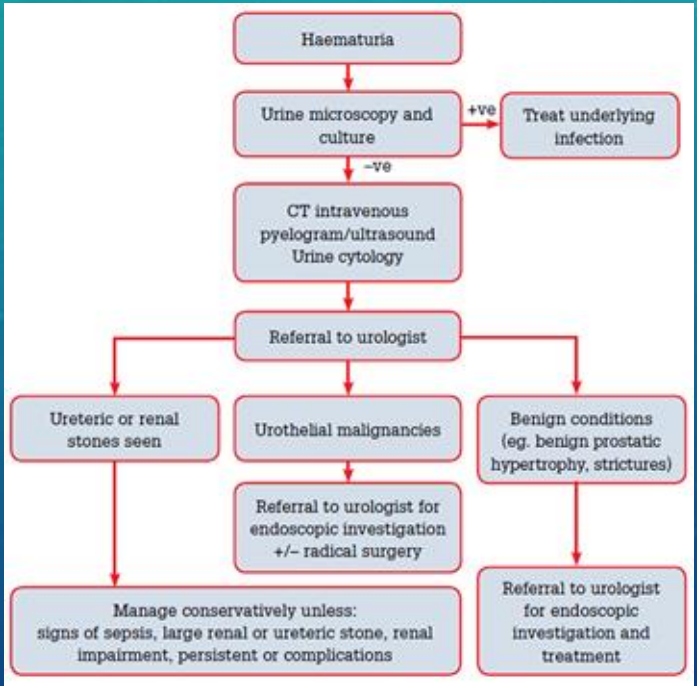
INVESTIGATIONS







SUMMARY


Haematuria
Urine microscopy and culture
+ve
Treat underlying infection
–ve
CT intravenous pyelogram/ultrasound
Urine cytology
Referral to urologist
Ureteric or renal stones seen
Urothelial malignancies
Benign conditions (eg. benign prostatic hypertrophy, strictures)
Referral to urologist for endoscopic investigation +/– radical surgery
Manage conservatively unless: signs of sepsis, large renal or ureteric stone, renal impairment, persistent or complications
Referral to urologist for endoscopic investigation and treatment

SUMMARY FOR MICROHAEMATURIA

- Negative haematuria evaluation => shared decision as to whether repeat urinalysis required
- Persistent microHU => refer to nephrologist for evaluation of renal causes.
- MicroHU => develop new macroHU => re-evaluation should be considered

UROLOGY

- Other resources:

https://www1.racgp.org.au/ajgp/2021/july/haematuria-in-the-general-practice-setting

RESOURCES

AUA microhaematuria guidelines 2024

- https://www.auanet.org/guidelines-and-quality/guidelines/microhematuria

AFP

- https://www.racgp.org.au/afp/2013/march/macroscopic-haematuria

AJGP Website

- https://www1.racgp.org.au/ajgp/2021/july/haematuria-in-the-general-practice-setting

Images from radiopedia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Advanced Prostate Cancer in General Practice

- Recognition
- Management
- Prognosis
- Oncological red flags

Presented by Dr. Matthew Farag
Phone: (03) 9522 9886
Fax: (03) 9823 5211
Healthlink (EDI): matturol
Email: info@matthewfaragurology.com.au

Objectives

- Recognise presentations of advanced prostate cancer
- Modern staging and terminology
- Identify emergencies and urgent referrals
- Optimise community-based management and shared care
  - GP
  - Urologist/ oncologist/ radiation oncologist/ palliative care/ allied health/ prostate cancer nurse

Epidemiology

- Most common male malignancy in Australia
- Advanced disease may present de novo or after recurrence
- Despite being advanced, earlier recognition can still improve survival and quality of life

Prognosis

Prognostic Group	Typical Features	Approximate Median Survival*
Favourable metastatic disease	Low-volume bone metastases, good ECOG performance status, strong PSA response to ADT	Often **>5 years** with modern therapy
Intermediate prognosis	Multiple bone metastases, rising PSA burden, preserved performance status	Approximately **3–5 years**
High-volume metastatic disease	Extensive skeletal metastases and/or bulky nodal disease	Approximately **2–4 years**
Visceral metastatic disease	Liver or lung metastases	Typically **shorter survival** than bone-only disease
Metastatic castration-resistant prostate cancer (mCRPC)	Progression despite ADT, requiring second-line systemic therapy	Often **2–3 years**, variable with treatment response
mCRPC with frailty / poor performance status	Significant weight loss, functional decline, extensive disease burden	Often **<2 years**

*Approximate survival estimates based on contemporary EAU-aligned data in the era of PSMA PET staging, treatment intensification (abiraterone, enzalutamide, apalutamide, docetaxel), and multidisciplinary care. Outcomes vary substantially depending on disease biology, comorbidities and treatment response.

Terminology

- Locally advanced disease
- Metastatic hormone-sensitive prostate cancer (mHSPC)
  - Can be diagnosed de-novo
- Metastatic castration-resistant prostate cancer (mCRPC)
  - Usually after systemic treatment
- Biochemical recurrence after treatment
  - After curative treatment

Biochemical Recurrence after Treatment

Factor	Prognostic significance
PSA doubling time (PSADT)	Strongest predictor of metastasis & mortality; PSADT <6–9 months = high risk
Time to BCR	Early recurrence (<1–2 yrs) = more aggressive disease
Grade Group (especially 4–5)	Independent predictor of systemic progression
Pathological stage (SVI, EPE, nodal disease)	Strong structural risk marker
Post-RT vs post-RP setting	Post-RT BCR generally higher heterogeneity and later detection burden
Absolute PSA level at recurrence	Higher PSA at recurrence correlates with worse outcomes

Biochemical Recurrence after Treatment

BCR risk category	PSA kinetics / timing	Key prognostic features	Risk of metastasis	Prostate cancer-specific mortality risk	Clinical implication
Low-risk BCR	PSADT >15 months AND recurrence >3 years post-treatment	*Indolent biology*	<10–15% at 10 yrs	<5%	Observation or delayed salvage often appropriate
Intermediate-risk BCR	PSADT 9–15 months OR recurrence 1–3 years	*Mixed biology*	~20–40% at 10 yrs	~10–20%	Early salvage RT often beneficial
High-risk BCR	PSADT <9 months OR recurrence <1 year OR GG4–5	*Aggressive systemic potential*	>50–70% at 10 yrs	20–40%	Treat as systemic-risk disease even if imaging negative

Common Presentations in General Practice

- LUTS and urinary obstruction
- Bone pain or pathological fracture
- Fatigue, anaemia, weight loss
- Renal impairment from obstruction
- Rising PSA after prior treatment

Red Flags Requiring Urgent Referral

- Severe back pain
- Neurological symptoms or leg weakness
- Urinary retention
- Macroscopic haematuria with clots
- Acute kidney injury / hydronephrosis
- Rapid PSA rise
- (Family History/ BRCA)

Spinal Cord Compression

- Oncological emergency
- Symptoms: weakness, sensory change, incontinence
- Urgent MRI spine required

- Immediate specialist discussion essential/ referral to hospital/ Steroids +/- radiation +/- neurosurgical interventiion

Case Study

- 74-year-old male with younger brother treated for prostate cancer

Initial GP Investigations

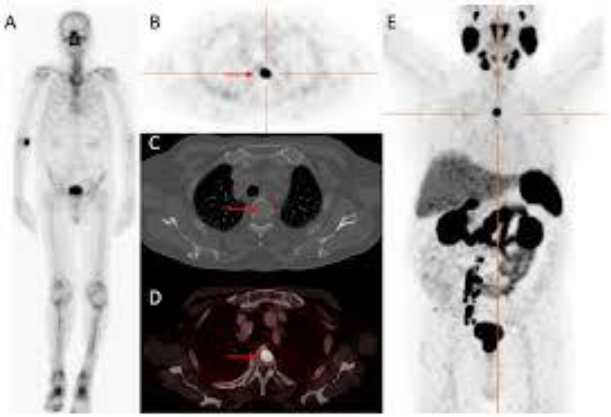
- PSA and DRE
- FBC, UEC, ALP
- Urinalysis and urine culture
- Renal tract imaging if obstruction suspected

- Bone scan/ CT CAP

Case Study

- 74-year-old male with younger brother treated for prostate cancer

- DRE* bilateral nodules
- PSA 180
- CT CAP/ bone scan: bone lesions, pelvic lymphadenopathy, lung nodules, bilateral moderate hydronephrosis



Role of MRI and PSMA PET

- MRI important for local staging/ localised disease
  - Guiding local treatment

- PSMA PET increasingly standard for staging and recurrence
  - Improves detection of metastatic disease (biochemical recurrence)

Management Prinicples

- Metastatic disease requires multidisciplinary care

- *Sequential life-prolonging systemic therapy*

Management

- Metastatic disease requires multidisciplinary care

Disease state	Definition	Key biology	Clinical importance
mHSPC (metastatic hormone-sensitive PCa)	Metastatic disease, no castration resistance	Androgen-driven	***Most important survival-impacting treatment window***
mCRPC	Progression despite castrate testosterone (<50 ng/dL or <1.7 nmol/L)	Androgen-independent clones emerge	Systemic sequential therapies required

Androgen Deprivation Therapy (ADT)

- Foundation of treatment in advanced disease
- LHRH agonists and antagonists commonly used
- Side effects include metabolic syndrome and osteoporosis
- GP role critical in chronic disease monitoring

Management

Treatment component	Options	Evidence-based role	Key outcome impact
Androgen deprivation therapy (ADT)	LHRH agonist/antagonist or orchiectomy	Backbone therapy	Symptom control + survival benefit
Androgen receptor pathway inhibitor (ARPI)	Abiraterone, enzalutamide, apalutamide, darolutamide	***Standard of care early add-on in most patients***	↑ overall survival (OS ~30–40% relative reduction in death in trials)
Chemotherapy	Docetaxel	Best for high-volume / fit patients	OS benefit, especially high-volume disease
Triplet therapy (selected patients)	ADT + docetaxel + abiraterone or darolutamide	High-volume, fit patients	Maximal OS benefit in high-risk disease

Management

Disease burden	Definition	Preferred approach
Low-volume	Limited bone mets, no visceral disease	ADT + ARPI (preferred)
High-volume	Visceral mets OR ≥4 bone mets with ≥1 outside spine/pelvis	ADT + docetaxel ± ARPI (triplet often considered)

Local treatment (selected cases)

Therapy	Indication	Evidence
Prostate radiotherapy	Low-volume mHSPC	Survival benefit (STAMPEDE Arm H)
Metastasis-directed therapy (SBRT)	Oligometastatic disease (3–5 lesions)	Delays progression, not yet definitive OS benefit

Metastatic Castration-Resistant Prostate Cancer

Treatment class	Options	Use case	Key benefit
Continue ADT	Always maintained	Castrate testosterone	Prevents flare
Second-line ARPI (if not used earlier)	Enzalutamide, abiraterone	If naïve to prior ARPI	Symptom + OS benefit
Chemotherapy	Docetaxel → Cabazitaxel	Progression after ARPI or docetaxel	OS benefit in resistant disease
Radioligand therapy	^{177}Lu-PSMA-617	PSMA-positive disease post-ARPI/chemo	OS + QoL improvement
PARP inhibitors	Olaparib, rucaparib	BRCA1/2 or HRR mutations	Targeted survival benefit
Immunotherapy	Pembrolizumab	MSI-high / TMB-high (rare)	Durable responses in subset

Bone Health

- High fracture risk in advanced disease
- Consider calcium and vitamin D
- DEXA scans often indicated
- Denosumab or bisphosphonates in selected patients

Bone Health

Intervention	Indication	Benefit
Denosumab or zoledronic acid	mCRPC with bone metastases	↓ skeletal-related events
Calcium + vitamin D	With antiresorptives	Prevent hypocalcaemia
Palliative radiotherapy	Bone pain / spinal risk	Rapid pain control
Spinal decompression / steroids	Cord compression	Emergency intervention
Analgesia ladder	Pain management	QoL improvement

Managing Treatment Toxicities

- Monitor blood pressure, diabetes and lipids
- Assess falls risk and frailty
- *Screen for depression and fatigue*
- Manage LUTS and sexual dysfunction supportively

Palliative Care Integration

- Early integration improves quality of life
- Pain management is essential
- Advanced care planning should be encouraged

Recap: When to Contact Urology Urgently

- Spinal cord compression symptoms
- Hydronephrosis or urinary obstruction
- Macroscopic haematuria with clot retention
- Severe uncontrolled bone pain
- Rapid clinical deterioration

Key GP Take Home Messages

- Recognise oncological red flags early
- ADT requires long-term metabolic monitoring
- Management = *Sequential life-prolonging systemic therapy*
- Bone health is key
- Multidisciplinary shared care improves outcomes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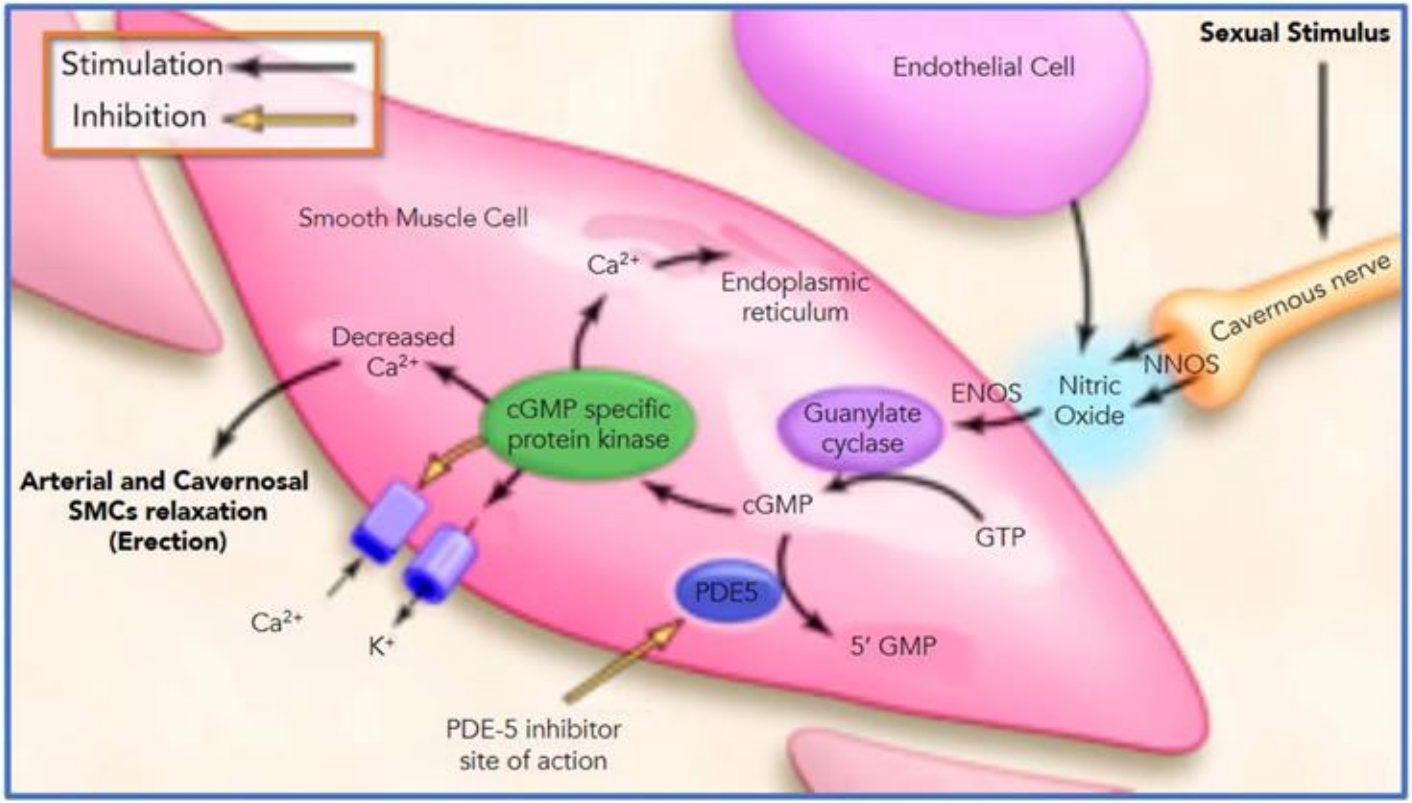
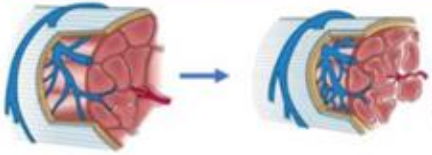
Beyond the Blue Pill
The New Era of ED Treatment

A/Prof Homi Zargar





Reduction in NO Synthesis
Impaired Neurogenic Dilatation
Impaired Endothelium Dependent Dilatation
Increased Vasoconstriction

→ Erectile Dysfunction

Key Concept: The Veno-Occlusive Mechanism

- The erection is maintained not just by arterial inflow, but by **trapping blood within the corpora**. The tunica albuginea acts as a natural tourniquet. Damage to this mechanism (e.g., Peyronie's disease, diabetes-related fibrosis) causes venous leak — a common reason for PDE5i failure.

Introduction to Erectile Dysfunction

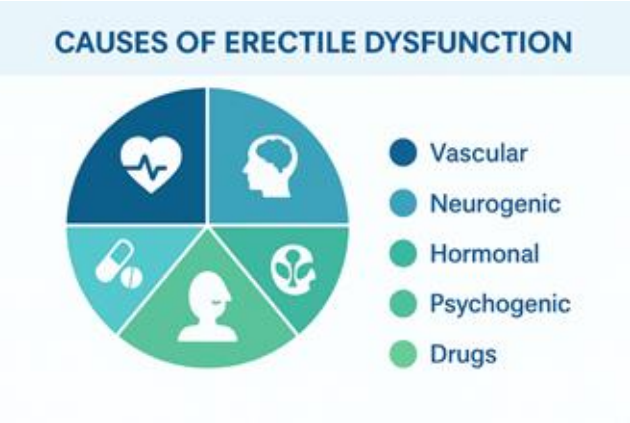
- Persistent inability to achieve/maintain erection for satisfactory intercourse
- Affects up to 50% of men over 50
- Impacts quality of life, relationships, and mental health

Age Group	Estimated Prevalence	Clinical Context
40–49 years	~20%	Often early vascular disease or psychogenic
50–59 years	~35%	Increasing metabolic and vascular contributors
60–69 years	~50%	Mixed aetiology — organic predominates
70–79 years	~65–70%	Multifactorial — comorbidities accumulate
80+ years	~75–80%	Often accepted but still treatable

- The Massachusetts Male Aging Study (MMAS) demonstrated that the probability of complete ED triples between ages 40 and 70.
    - However, age alone does not cause ED — it is the accumulation of vascular risk factors that drives the condition.
    - A healthy 70-year-old may have better erectile function than an unhealthy 50-year-old.

Causes of ED

- Vascular (atherosclerosis, diabetes, hypertension)
- Neurogenic (spinal injury, pelvic surgery)
- Hormonal (low testosterone, thyroid disease)
- Iatrogenic/Drug-related (antidepressants, antihypertensives)
- Psychogenic (stress, anxiety, depression)



Pathophysiology of ED

Category	Mechanism	Key Features
Vasculogenic	Reduced arterial inflow or impaired veno-occlusion	Most common (70–80%). Gradual onset. Associated with CV risk factors.
Neurogenic	Impaired nerve signalling	Diabetes, MS, post-prostatectomy. May respond to ICI better than PDE5i.
Hormonal	Testosterone deficiency, hyperprolactinaemia	Reduced libido often prominent. Check morning testosterone.
Psychogenic	Performance anxiety, depression, relationship conflict	Sudden onset, situational, preserved morning erections.
Drug-induced	Medication side effects	Temporal relationship with medication change.
Mixed	Combination of the above	**Most common clinical presentation.**

ED as a Marker of Cardiovascular Disease

- ED and coronary artery disease (CAD) share identical risk factors
    - diabetes
    - Hypertension
    - Dyslipidaemia
    - Obesity
    - Smoking
    - sedentary lifestyle
  - The penile arteries (1–2 mm diameter) develop atherosclerosis **before** the larger coronary arteries (3–4 mm), making ED a sentinel symptom of systemic vascular disease.

ED precedes a major cardiovascular event (MI, stroke) by an average of **3–5 years**. A man presenting with new-onset ED and no cardiac history should be considered for cardiovascular risk assessment as a matter of clinical priority.

Think: "ED today, MI in 3–5 years"

Risk Factor	Relative Risk Increase	Notes
Diabetes mellitus	3–4× increased risk	Both vascular and neurogenic mechanisms; onset 10–15 years earlier
Hypertension	1.5–2× increased risk	Both disease and treatment (beta-blockers, thiazides) contribute
Dyslipidaemia	1.5× increased risk	Endothelial dysfunction; statins may be protective
Obesity (BMI >30)	1.5–3× increased risk	Hypogonadism, inflammation, metabolic syndrome
Smoking	1.5–2× increased risk	Direct endothelial toxicity; dose-dependent
Depression	2–3× increased risk	Both cause and consequence; bidirectional relationship
Sedentary lifestyle	1.5× increased risk	Exercise is independently protective

Medication contributing to ED

- **Medication-Induced ED**

Medication Class	Examples	Mechanism
Beta-blockers	Atenolol, metoprolol	Reduced sympathetic tone, ? central effects
Thiazide diuretics	Hydrochlorothiazide, indapamide	Reduced penile blood flow, zinc depletion
SSRIs/SNRIs	Sertraline, venlafaxine	Serotonergic inhibition of ejaculation and arousal
Spironolactone	—	Anti-androgen effects
5-alpha-reductase inhibitors	Finasteride, dutasteride	Reduced DHT; sexual side effects in 5–8%
Opioids	Oxycodone, tramadol	Hypogonadotropic hypogonadism
Antiandrogens / ADT	GnRH agonists/antagonists	Testosterone suppression

Common Pitfalls

Attributing ED solely to age — "It's just your age" misses treatable vascular disease

Failing to check medications — beta-blockers and SSRIs are commonly overlooked contributors

Common Pitfalls

Not screening for depression — ED and depression are bidirectional; treating one often improves the other

Ignoring relationship context — ED rarely exists in a relational vacuum; partner dynamics matter

Impact on Relationships and Mental Health

- ED has a profound effect beyond the physical impact.

Impact on Relationships and Mental Health

Reduced self-esteem and confidence in up to 70% of affected men

Relationship strain and avoidance of intimacy

Increased rates of anxiety, depression, and social withdrawal

Partner distress — often under-recognised

Addressing ED is not just about restoring erections — it is about restoring quality of life, relational health, and psychological wellbeing.

Psychogenic vs Organic ED

Feature	Psychogenic	Organic
Onset	Sudden	Gradual
Morning erections	Preserved	Absent/reduced
Situational	Yes	Consistent
Masturbation	Often preserved	Impaired
Libido	Usually normal	May be reduced
Age	Typically <40	Typically >50

Assessment of ED

- History: sexual, medical, psychosocial
- Examination: cardiovascular, neurological, genital
- Questionnaires: IIEF-5
- Investigations: glucose, lipids, testosterone, PSA

Question	Clinical Significance
When did it start?	Sudden onset → psychogenic or medication-related. Gradual → organic.
Do you get morning erections?	Preserved → suggests psychogenic component. Absent → organic.
Can you achieve erection with masturbation?	Situational preservation → psychogenic overlay likely.
Can you achieve but not maintain?	Venous leak pattern — may indicate Peyronie's or corporal fibrosis.
Is it consistent or situation-specific?	Partner-specific or context-specific → psychogenic.

Libido Assessment

Reduced libido suggests hormonal aetiology (hypogonadism, hyperprolactinaemia) or depression.

Libido and erection are driven by different pathways — testosterone drives desire, while NO/cGMP drives the vascular erection.

Relationship Context

- Ask sensitively about relationship quality, partner health, frequency of sexual activity, and any recent changes (new partner, conflict, separation).
- Partner involvement in management often improves outcomes.

Cardiovascular Symptom Screen

- Exertional chest pain or dyspnoea
- Previous MI, stroke, or PVD
- Known diabetes, hypertension, dyslipidaemia
- Exercise capacity (can he climb 2 flights of stairs without symptoms?)

Medication Review

- Systematically review all medications. Key culprits: beta-blockers, thiazide diuretics, SSRIs/SNRIs, spironolactone, 5-alpha-reductase inhibitors, opioids, antiandrogens, antipsychotics.

Screening for Performance Anxiety

- Ask: *"Do you find that thinking about whether it will work actually makes it harder?"* This normalises the experience and identifies the anxiety-ED cycle.

Examination

System	What to Assess	Significance
Cardiovascular	BP, heart rate, peripheral pulses, BMI, waist circumference	Vascular risk stratification
Genital	Penile plaque (Peyronie's), phimosis, hypospadias	Structural causes of ED
Testicular	Size, consistency, masses	Small soft testes → hypogonadism
Secondary sex characteristics	Body hair, gynaecomastia, muscle mass	Signs of androgen deficiency
DRE	Prostate size, nodules (if indicated)	BPH, prostate cancer screening context

Don't Skip the Genital Exam

- Many GPs examine everything except the genitals.
  - Peyronie's disease (palpable dorsal plaque) is present in 5–10% of men with ED and changes management significantly.
  - A simple examination takes 30 seconds and can identify treatable structural pathology.

SHIM Score

Score	Severity	Clinical Implication
22–25	No erectile dysfunction	Reassurance; consider other causes of sexual dissatisfaction
17–21	Mild ED	Lifestyle modification ± on-demand PDE5i
12–16	Mild to moderate ED	PDE5i trial (on-demand or daily); address modifiable risk factors
8–11	Moderate ED	Optimised PDE5i; consider combination therapy; specialist referral if no response
5–7	Severe ED	Early specialist referral; consider second-line therapies; ICI or prosthesis discussion

Investigation	When to Order	Clinical Rationale
Fasting glucose / HbA1c	All patients	Diabetes is the single strongest risk factor for ED
Lipid profile	All patients	Cardiovascular risk stratification
Morning testosterone	All patients (fasting, before 10 AM)	Hypogonadism found in 20–40% of ED patients
LH, FSH	If testosterone low	Differentiate primary vs secondary hypogonadism
Prolactin	If testosterone low or libido markedly reduced	Exclude prolactinoma
TFTs	If clinical suspicion	Both hypo- and hyperthyroidism can cause ED
PSA	If testosterone replacement considered (>40 yrs)	Baseline before testosterone replacement therapy (TRT) initiation
FBC, renal function, LFTs	Baseline	General health assessment, CKD as contributor

Common Pitfalls

Not asking about morning erections — the single most useful question in differentiating psychogenic from organic

Ordering afternoon testosterone — leads to falsely low results and unnecessary treatment

Skipping the medication review — changing a beta-blocker to an ACE inhibitor may resolve the ED entirely

Common Pitfalls

Not assessing cardiovascular fitness — PDE5i safety depends on cardiac functional capacity

Forgetting to ask about recreational drugs — cannabis, cocaine, anabolic steroids all affect erectile function

MCQ 1

A 52-year-old man presents with new-onset erectile dysfunction. He has no cardiac history but has hypertension and a BMI of 32. What is the most important clinical implication of his ED?

A. He should be referred immediately for penile Doppler ultrasound

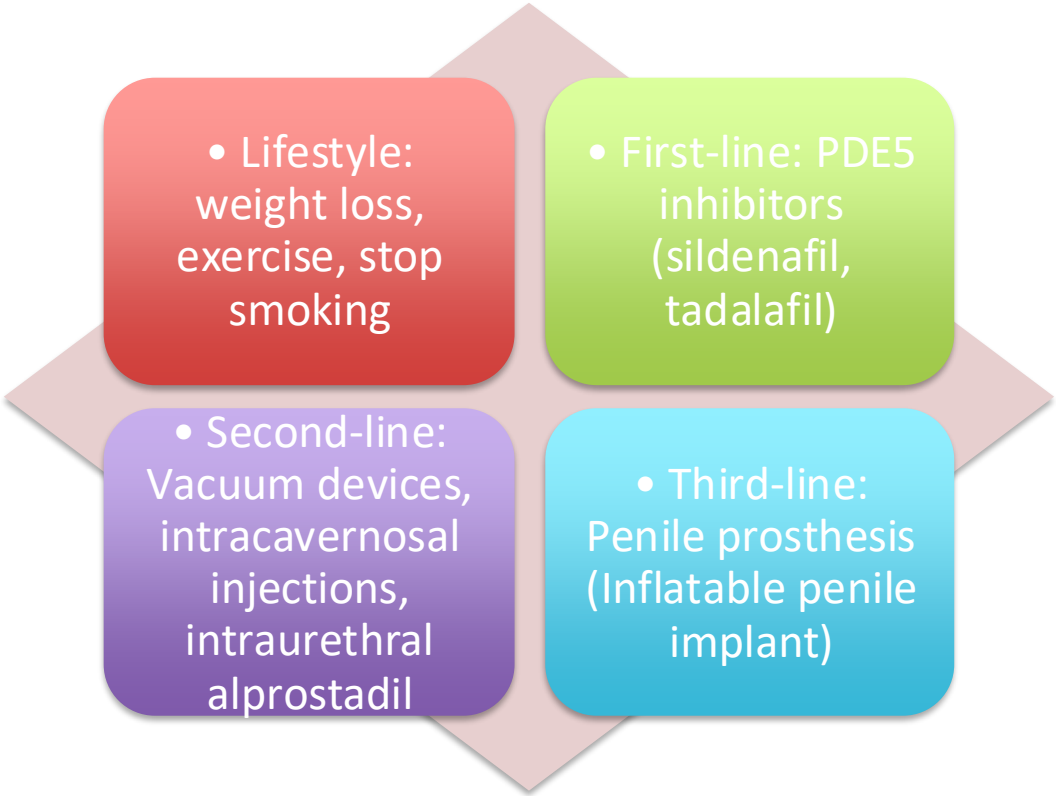
B. His ED is likely psychogenic given his age

C.ED may be an early marker of systemic cardiovascular disease and warrants cardiovascular risk assessment

D. He should avoid all sexual activity until cardiac clearance is obtained

A 52-year-old man presents with new-onset erectile dysfunction. He has no cardiac history but has hypertension and a BMI of 32. What is the most important clinical implication of his ED?

Management Spectrum



First-Line Medical Therapy: PDE5 Inhibitors

Mechanism of Action

PDE5 inhibitors block the degradation of cyclic GMP (cGMP) in the corpus cavernosum smooth muscle, amplifying the nitric oxide–mediated relaxation pathway. They **do not initiate erections** — sexual stimulation is still required to release NO and trigger the cascade.

First-Line Medical Therapy: PDE5 Inhibitors

Drug	Brand	Onset	Duration	Food Effect	Approx. Cost (Aus)	PBS Status
Sildenafil	Viagra / generics	30–60 min	4–6 hours	Delayed by fatty meals	$5–10/tablet (generic)	Not PBS listed for ED
Tadalafil	Cialis / generics	30–60 min	**Up to 36 hours**	No food effect	$5–12/tablet (generic)	Not PBS listed for ED
Vardenafil	Levitra	25–60 min	4–6 hours	Delayed by fatty meals	$15–25/tablet	Not PBS listed
Avanafil	Spedra	**15–30 min**	6–12 hours	Minimal food effect	$18–30/tablet	Not PBS listed

Choosing Between PDE5 Inhibitors

- **On-Demand Use**
  - **Sildenafil** — Best established evidence base, cheapest generic option. Good first choice. Advise taking on an empty stomach for reliable onset.
  - **Tadalafil** — The "weekend pill." 36-hour window removes pressure to time sexual activity. Preferred by couples who value spontaneity. Can also be taken on-demand at 10–20 mg.

Choosing Between PDE5 Inhibitors

- **On-Demand Use**
  - **Vardenafil** — Similar profile to sildenafil. Some evidence of efficacy in difficult-to-treat populations (post-prostatectomy). Available as orodispersible tablet.
  - **Avanafil (Spedra)** — Fastest onset (15 min in some men). Most selective for PDE5 → potentially fewer visual/flushing side effects. Useful when rapid onset matters. Higher cost limits routine use.

Daily Dosing: Tadalafil 5 mg

- Daily low-dose tadalafil (2.5–5 mg) provides **continuous PDE5 inhibition**, enabling spontaneous sexual activity at any time.

Daily Dosing: Tadalafil 5 mg

- It is particularly suited for:
  - Men with frequent sexual activity (≥2x/week)
  - Men with concurrent LUTS/BPH (TGA-approved dual indication)
  - Men with significant performance anxiety around "timing the pill"
  - Post-prostatectomy penile rehabilitation protocols
- **Cost:** Daily tadalafil 5 mg generic costs approximately $150–200/month — a significant ongoing expense that should be discussed.

Side Effect	Frequency	Notes
Headache	10–15%	Most common; usually diminishes with continued use
Flushing	10%	Facial/neck warmth; benign
Nasal congestion	5–10%	Due to nasal mucosal vasodilation
Dyspepsia	5–10%	More common with sildenafil; take with small meal
Visual disturbance (blue tinge)	3% (sildenafil)	Due to cross-reactivity with PDE6 in retina — less with tadalafil/avanafil
Myalgia / back pain	5–6% (tadalafil)	Unique to tadalafil due to PDE11 cross-reactivity; usually resolves in 48 hrs
Priapism	Very rare	Counsel patients: erection >4 hours → ED presentation
Non-arteritic anterior ischaemic optic neuropathy (NAION)	Extremely rare	Controversial causal link; counsel patients with prior NAION or crowded optic disc

Absolute Contraindications

Concurrent nitrate therapy (GTN spray, isosorbide mononitrate/dinitrate, amyl nitrite) — risk of profound hypotension

Recent MI or stroke (<6 months) without cardiology clearance

Severe aortic stenosis or **hypertrophic obstructive cardiomyopathy (HOCM)**

Absolute Contraindications

Hypotension (BP <90/50 mmHg)

Alpha-blocker use — relative contraindication; if required, use tadalafil with caution and separate dosing by 4+ hours. Tamsulosin is safest alpha-blocker to combine.

Lifestyle Modification — The Foundation

Medication works best alongside lifestyle change. Evidence-based interventions:

Weight loss — 5–10% weight reduction improves erectile function (Esposito et al., JAMA 2004)

Exercise — 150 min/week moderate aerobic exercise equivalent to PDE5i effect in mild ED

Smoking cessation — Direct endothelial toxin; improvement seen within months of quitting

Lifestyle Modification — The Foundation

Alcohol moderation — >14 units/week associated with ED; acute intoxication causes transient ED

Mediterranean diet — Associated with improved endothelial function and lower ED prevalence

Pelvic floor exercises — Emerging evidence for pelvic floor physiotherapy in ED (Dorey et al.)

Combination Therapies — Limited Role

Combining PDE5 inhibitors with other ED treatments is sometimes attempted but has **limited evidence and increased risk**:

PDE5i + ICI — Can be considered in refractory cases (e.g., post-radical prostatectomy) under specialist supervision. Risk of priapism increases.

PDE5i + VED — Reasonable combination; PDE5i improves arterial inflow, VED provides mechanical engorgement. Low risk.

Combination Therapies — Limited Role

PDE5i + testosterone replacement — Appropriate when hypogonadism coexists. Normalising testosterone may improve PDE5i response in non-responders. Evidence supports this combination.

Dual PDE5i use — Never combine two PDE5 inhibitors.

In general, combination therapies should be **specialist-initiated**. The GP role is to optimise single-agent therapy and refer when it fails.

The 6-Attempt Rule

- PDE5 inhibitors should be trialled for **at least 6 separate attempts** at adequate dose before declaring treatment failure.
  - Many men abandon therapy after 1–2 unsuccessful attempts. Counsel patients that the first few doses may not produce the best response —
  - efficacy often improves with repeated use and comfort with the medication.
  - Ensure correct technique: adequate sexual stimulation, empty stomach (for sildenafil), and realistic expectations.

Emerging: SPONTAN® — Vardenafil Nasal Spray

SPONTAN® (vardenafil HCl nasal spray 2.5 mg per 130 µL) is a first-in-class nasal spray formulation of vardenafil manufactured in Australia.

The recommended dose is 5 mg (two sprays).

Property	SPONTAN® Nasal Spray	Oral Vardenafil
Onset	Peak concentration in as little as **9 minutes**	25–60 minutes
Average onset	**12 minutes**	~56 minutes
Dose	5 mg (half the standard oral dose)	10–20 mg
Food effect	Not affected by food intake	Delayed by fatty meals
Bioavailability	Higher (bypasses first-pass metabolism)	~15% oral bioavailability
TGA status	Not ARTG-listed; accessible via TGA Special Access Scheme	Approved
Approximate cost	~$250 per unit	$15–25/tablet

Why Nasal Delivery Matters

SPONTAN® aims to address the key reasons men discontinue oral PDE5 inhibitors:

Speed: 470% faster peak concentration than oral tablets — closer to "on-demand" spontaneity

Lower dose required: Half the oral dose achieves similar effectiveness, potentially reducing side effects

No food interaction: Nasal absorption bypasses the gastrointestinal tract entirely

Delivery consistency: More predictable absorption compared to oral tablets affected by food/alcohol

Counselling Points for PDE5i Prescribing

- Take on an **empty stomach** (sildenafil/vardenafil) — fatty food delays absorption by up to 1 hour

Counselling Points for PDE5i Prescribing

- Allow **adequate time** — don't take and immediately attempt intercourse

Counselling Points for PDE5i Prescribing

- **Sexual stimulation is required** — these are not aphrodisiacs

Counselling Points for PDE5i Prescribing

- Try at **least 6 times** before concluding it doesn't work
  - Start at **standard dose** (sildenafil 50 mg, tadalafil 10 mg) — titrate up if needed

Counselling Points for PDE5i Prescribing

Discuss **cost** — patients may not fill scripts they can't afford

Reassure about **safety** — side effects are usually mild and transient

Erectile Dysfunction (ED)

Vacuum Erection Device

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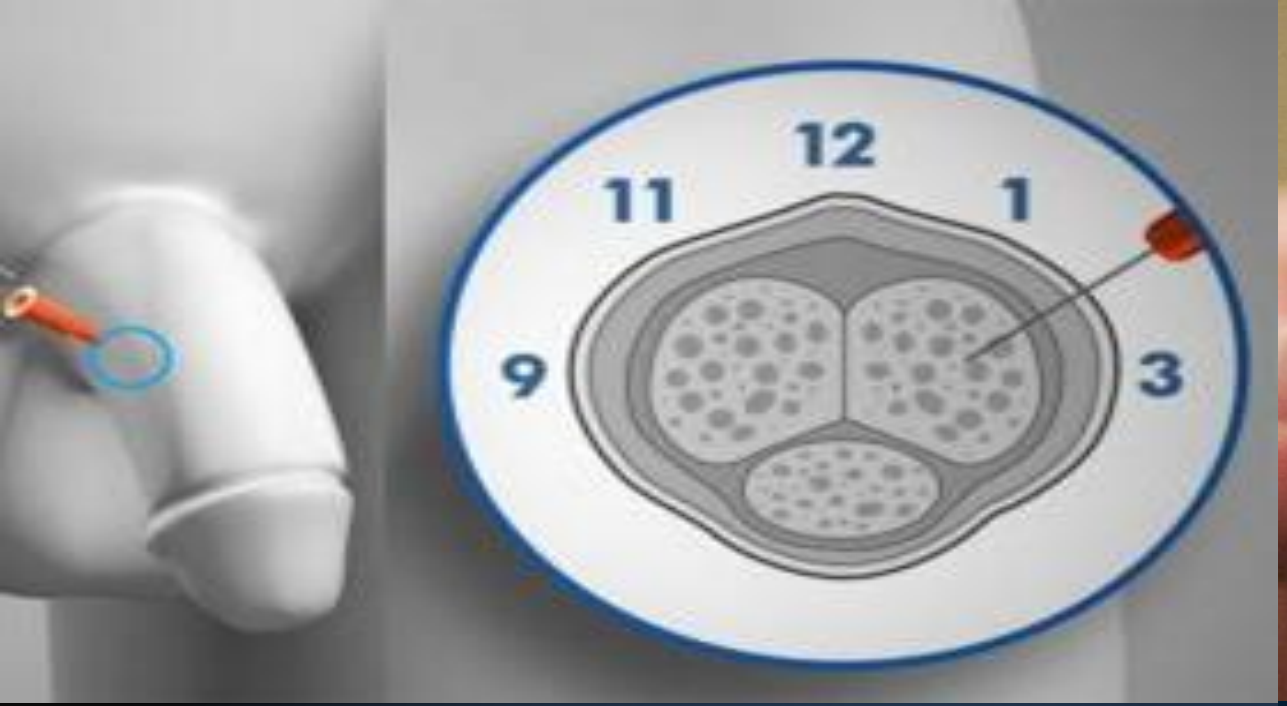
Intracavernosal Injection (ICI) Therapy

- ICI therapy involves self-injection of a vasoactive agent directly into the corpus cavernosum, bypassing the NO/cGMP pathway entirely. It is the most effective non-surgical treatment for ED.

Alprostadil (PGE1)	**Prostaglandin E1**	**Caverject Caverject Dual Chamber**	70–80%	**$30–50/injection**
Alprostadil (PGE1)	Prostaglandin E1	Prostin VR (off-label)	70–80%	$15–25/ampoule
Bi-mix	Papaverine + Phentolamine	Compounded	60–70%	$8–15/injection (compounded)
Tri-mix	Papaverine + Phentolamine + Alprostadil	Compounded	**85–95%**	$10–20/injection (compounded)


12
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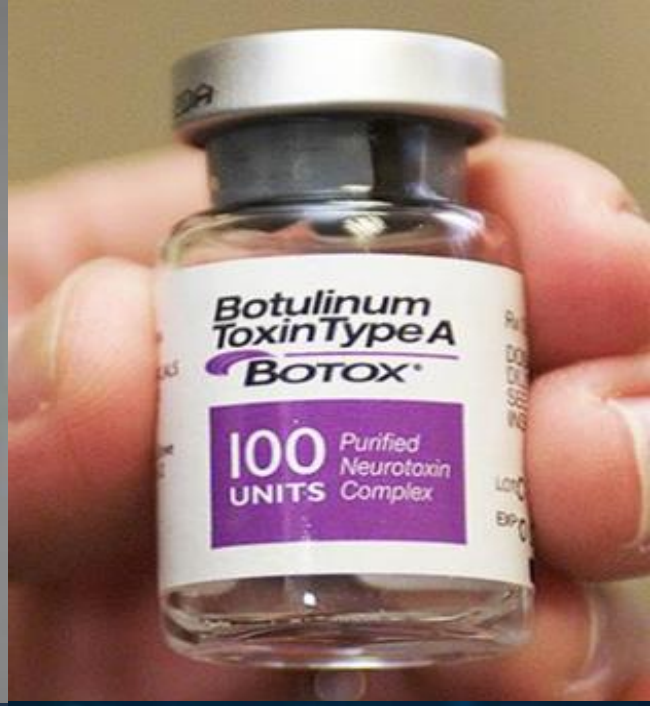
Botulinum Toxin Type A
BOTOX
100 UNITS
Purified Neurotoxin Complex


CLINICAL TRIAL

Clinical Pearl: Choosing an ICI Formulation

Start with Caverject (alprostadil) — TGA-approved, well-studied, dual-chamber device is user-friendly. Best for initial trial under medical supervision.

Upgrade to Tri-mix — if alprostadil alone is insufficient, causes excessive pain (aching is common with PGE1), or if cost is a barrier. Tri-mix uses lower doses of each component, reducing side effects while improving efficacy.

Bi-mix — reasonable budget option but lacks the prostaglandin component that provides the most physiological erection quality.

Prostin VR — same drug as Caverject at lower cost, but less convenient. Suitable for experienced patients comfortable with vial/syringe preparation.

Side Effect	Frequency	Management
Penile pain/aching	30–50% (alprostadil)	Worse with PGE1; less with tri-mix. Usually diminishes over time. Consider switching to tri-mix if persistent.
Priapism (>4 hours)	1–3%	**Urological emergency.** Higher risk with bi-mix. Counsel: ED presentation, aspiration + phenylephrine by treating doctor.
Penile fibrosis/nodules	5–10% long-term	Rotate injection sites (alternating sides). Avoid repeated injection into same spot. May necessitate switching to prosthesis.
Haematoma/bruising	5–10%	Technique-related; compress injection site for 3 minutes post-injection.
Dizziness/hypotension	Rare	More common with higher-dose tri-mix. Remain seated/lying for 10 min after injection.

Priapism Risk & Management

- Priapism (erection lasting >4 hours) is a **urological emergency**. Patients must be counselled:
- Present to ED if erection persists >4 hours
- Never exceed prescribed dose
- Never inject more than once in 24 hours
- Dose titration should be performed under medical supervision — the first injection is always done in-clinic
- Risk: ~1–3% per injection with alprostadil; higher with bi-mix/tri-mix if not titrated carefully.

ICI Dropout & Practical Considerations

- ICI therapy has a high efficacy rate but also a high dropout rate (~50% at 2 years).
- Reasons include:
    - needle anxiety
    - pain at injection site,
    - loss of spontaneity and partner discomfort with the process.

ICI Dropout & Practical Considerations

- Adequate training and ongoing support are essential.
- Consider: auto-injector devices for needle-phobic patients, involvement of the partner in training, and regular follow-up to address concerns early.

MCQ 2

Which drug class is first-line in ED management?

A) Alpha-blockers

B) PDE5 inhibitors

C) Antidepressants

D) Testosterone only

Which drug class is first-line in ED management?

Surgical Options

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Penile implants

- Malleable implant
- Designed for those who have dexterity issues
- Concealable
- Natural feel
- Inflatable penile implant
  - Natural look and feel during intercourse
  - Offers spontaneity
  - Completely concealed
  - Maintains an erection for as long as you want.

Malleable Implant Animation

Features of an Inflatable Penile Implant

- Penile implants have been used for 40yrs[13] and are a long-term option for a man suffering from ED.
- Considered highly effective and reliable the penile implant has helped nearly 500,000 men[14] return to an active and satisfying sex life.
- Patients report 97% satisfaction rates with a penile implant.[15]

Inflatable Penile Implant Animation

Patient & Partner Satisfaction

In one study of 200 patients and 120 partners[18]:

- **98%** of patients reported their erections to be excellent or satisfactory following surgery
- **92%** of patients reported sexual activity with the implant to be excellent or satisfactory
- **96%** of partners reported sexual activity with the implant to be excellent or satisfactory
- **95%** of patients reported no change or better orgasms following surgery

Risks of a Penile Implant

•As with any medical device, complications can occur. The penile implant requires manual skill to use: some risks include but are limited to device malfunction and post operative pain.

- Side effects include but are not limited to:
  - Natural or spontaneous erections as well as other interventional treatment options will no longer be possible.
  - Infection, in which case the implant may need to be removed
  - Penis may become shorter curved or scarred
  - Pain typical associated with the healing process
  - Swelling or bruising
  - Mechanical failure of the implant

💡Key Facts for GPs

Satisfaction: 90–95% patient satisfaction, 85–90% partner satisfaction — highest of any ED treatment

Irreversibility: Implantation destroys the natural erectile tissue. This is a **one-way decision**. Patients must understand that other treatments will no longer be possible.

Key Facts for GPs

Infection risk: ~1–2% with antibiotic-coated devices. Higher in diabetes, revision surgery, immunosuppression.

Mechanical survival: Modern 3-piece devices have 85–90% mechanical survival at 10 years.

Wait time: Significant public hospital waiting lists in Australia.

- Private surgery $15,000–25,000+

Referral Triggers

PDE5i failure after adequate trial (6+ attempts at maximum dose)

Contraindication to PDE5i therapy (nitrate use)

Suspected Peyronie's disease (penile curvature/plaque)

Referral Triggers

- Young man (<40) with no vascular risk factors — may warrant Doppler investigation
- Post-radical prostatectomy ED not responding to rehabilitation
- Patient interest in ICI, prosthesis, or surgical options
- Suspected hormonal cause with complex endocrine picture

MCQ 3

Gold-standard surgical treatment for severe ED?

A) Vacuum pump

B) Intracavernosal injections

C) Inflatable penile prosthesis

D) Urethral suppositories

Gold-standard surgical treatment for severe ED?

Take-Home Messages

- ED is common, treatable, and often a marker of systemic vascular disease

- Management is stepwise: lifestyle → PDE5i → devices/injections → prosthesis

- GPs play a key role in screening for comorbidities and initiating treatment

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