Erectile Dysfunction (ED)

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Why are we doing this talk?

• ED is very common

• ED is often under-diagnosed

• ED affects quality of life

• ED can be a marker to underlying cardiovascular diseases
HCPs:

- May be the first to see a patient with ED
- Prescribe/dispense to the majority of patients with diabetes, heart disease, and hypertension; key risk factors for ED
1. Definition and Statistics
2. Pathophysiology
3. Risk Factors / Causes
4. Evaluation and Management
5. Mechanism of Action of PDE5 inhibitors
6. Take home messages
Definition and Statistics of ED
What is ED?

- Erectile Dysfunction is defined as the consistent inability to achieve and/or maintain an erection sufficient for *satisfactory* sexual activity

- ED is the most thoroughly studied sexual dysfunction in men and the most common sexual complaint of men presenting to healthcare providers

- In talking to patients, it is better to refer to their symptoms as ‘erection problems’
  - ‘Erectile dysfunction’ and ‘erection problems’ are both preferable terms to ‘impotence’, which, when used colloquially, has emotive or derogatory implications
Erectile Dysfunction (ED)

THE MALE LIFE CYCLE

FROM 13 To 31

FROM 31 To 41

FROM 41 TO 49

FROM 50 TO 59

FROM 59 To 64

FROM 65 Onwards
Man’s sexual chemistry

- At 20 thrice weekly
- At 30 tries weekly
- At 40 tries weakly
- At 50 tries and tries
- At 60 tries and cries
- At 70 tries and dies!

YOU DIDN'T SAVE ANYTHING FOR RETIREMENT DID YOU??
Prevalence

• The reluctance of many men to admit to suffering from erection problems causes difficulties in determining its prevalence

• Worldwide prevalence of ED is between 10% and 20%, and it is strongly correlated with aging
  – Among younger men, 8% of 20- to 29-year-olds and 11% of men ages 30-39 experience ED
  – Approximately 52% of men ages 40-70 experience ED
  – 71% of men over 70 experience ED

• This may be due to:
  – Increased incidence of diseases that cause ED
  – Use of treatments that can cause ED

• Estimated prevalence for 2025 = 300M men worldwide

### ED in men over 55 years

<table>
<thead>
<tr>
<th>Age</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>&gt;55</td>
<td>47%</td>
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<tr>
<td>&gt;75</td>
<td>78%</td>
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<tr>
<td>+ Diabetes</td>
<td>50%</td>
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<tr>
<td>+ Hypertension</td>
<td>34%</td>
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Pathophysiology of ED
Erection is a final common pathway of the integrative synchronized action of:

- Psychological
- Neuronal
- Hormonal
- Vascular and cavernous smooth muscle
Mechanism of an Erection

- Erection begins with sensory and mental stimulation
- Impulses from the brain travels down the spinal column
- Impulses from the nerves in the penis relax the smooth muscles in the paired corpora carvenosa
- When the impulses causes the muscle relaxation, blood flow into the spaces in the corpus spongiosum and
- The pressure makes the penis to swell out
- The membranes surrounding the corpora carvenosa then trap the blood in the penis and maintain the erection
- The size of the erect penis is 14-16cm long
• The penis needs blood flow
• Flow goes better through larger vessels
• Vasodilatation turns smaller vessels into larger vessels
• Erections need \textit{vasodilatation}
Mechanism of an Erection

- The penis needs erectile tissue and rigidity
- Sexual response is mediated through nerves
- The brain controls and coordinates nerves

CNS

Erection
Causes of ED
ED is multifactorial

- Drugs and other modifiable factors
- Conditions associated with increasing age
- Peyronie’s disease and other structural abnormalities of the penis
- Vascular disorders
- Cardiovascular disease
- Neurological disorders
- Surgery and trauma
- Endocrine disorders
- Renal disease
- HIV and antiretroviral drugs

Causes of ED

Psychogenic causes:

• Depression
• Anxiety
• Studies have shown that up to 50% of men diagnosed with 1st episode of depression at > 40yrs have ED
Erectile Dysfunction

Medications associated with ED

<table>
<thead>
<tr>
<th>Cardiovascular drugs</th>
<th>Psychotropic drugs</th>
<th>Recreational drugs</th>
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<tbody>
<tr>
<td>Thiazide diuretics</td>
<td>Major tranquillizers</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>Anxiolytics and hypnotics</td>
<td>Marijuana</td>
</tr>
<tr>
<td></td>
<td>Selective serotonin reuptake inhibitors</td>
<td>Amphetamines</td>
</tr>
<tr>
<td>Centrally acting agents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Metyldopa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Clonidine, reserpine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Ganglion blockers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid lowering agents</td>
<td></td>
<td></td>
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<tr>
<td>ACE inhibitors</td>
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</tbody>
</table>

Spironolactone blocks testosterone synthesis and competitively binds to androgen receptors

Decreases libido and causes impotence through elevation of serum prolactin and blocking of androgen receptors

<table>
<thead>
<tr>
<th>Others</th>
<th>Endocrine drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimetidine and ranitidine</td>
<td>Antiandrogens</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Oestrogens</td>
</tr>
</tbody>
</table>

Development of a peripheral autonomic neuropathy, and behavioral changes

Heroin

Risk factors for ED

Age
Smoking (without co-morbidity)
Diabetes
Heart disease
Depression
Hypertension
Obesity
Physical inactivity
HIV

Definition of Metabolic Syndrome

Abdominal obesity
- Women - waist circumference ≥ 80 cm
- Men – waist circumference ≥ 94 cm

High triglycerides > 1.7 mmol/L

Low HDL cholesterol
- < 1.0 mmol/L in men
- < 1.3 mmol/L in women

Elevated BP > 130/85 mm Hg or on treatment

Fasting glucose > 5.6 mmol/L

The metabolic syndrome is characterized by a constellation of risk factors in one individual and increases the risk for CVD at any given LDL-C level.
ED is linked to serious health problems


*P<0.0001
The Link between ED and Cardiovascular Disease

ED often occurs before other vascular diseases

The artery size theory

- ED manifests earlier than cardiovascular disease because the smaller penile arteries reach critical narrowing, with insufficient blood flow, earlier than larger vessels

(Threshold for symptom development is 50% lumen.)

Early

- Penile artery
  - 1-2 mm
  - ED

Late

- Coronary artery
  - 3-4 mm
  - Angina infarction
- Carotid artery
  - 5-7 mm
  - Stroke
- Femoral artery
  - 6-8 mm
  - Claudication

Footnotes

Erectile Dysfunction

Endothelial dysfunction, ED, and CVD

• ED and CVD share aetiologies as well as pathophysiology (endothelial dysfunction), and evidence suggests that the degree of ED correlates with severity of CVD

• ED may be a predictive symptom of CVD in otherwise asymptomatic patients
  – ED may precede a cardiovascular event by as much as five years in otherwise asymptomatic patients

• A man with ED and no cardiac symptoms is a cardiac (or vascular) patient until proven otherwise
Erectile Dysfunction

Impact on quality of life

- Men with ED experience low self-esteem, diminished confidence, and relationship problems

- Partners often have feelings of rejection, unattractiveness, and guilt

- Improvements in erection hardness with ED oral treatment have shown to improve satisfaction with sex life, love and romance, and overall health

- An awareness of the impact of ED on quality of life (QoL) can help healthcare providers:
  - Empathize and communicate effectively with sufferers
  - Appreciate the value of appropriate treatment

Diagnosis and Treatment of ED
Few men approach a healthcare professional about their sexual problems.

- 13% spoke to their doctor
- 8% spoke to a pharmacist
- 3% spoke to a psychiatrist or psychologist

59% of the men think that doctors should routinely ask patients about their sexual function.¹
Evaluation and Management of ED

• Early detection – often the pharmacist/primary care clinicians may be a first point of contact

• Cardiac risk assessment – refer the patient to a physician/doctor

• Directed investigations (e.g. psychiatric, testosterone levels, prostate check)

• Partner interaction

• Rigorous follow-up

• Specialist referral when necessary
Physical examination
Assessment of erection problems by validated tools

- Clinical trials use a number of self-assessment methods to quantify ED and treatment response, including:
  - **IIEF: International Index of Erectile Function**, 15 items in five domains and the abbreviated five-item SHIM: Sexual Health Inventory for Men questionnaires
  - **EHS: Erection Hardness Score**, four-point scale grading the hardness of the erection
  - **QEQ: Quality of Erection Questionnaire**, six-question, patient-reported outcome measure for evaluating satisfaction with the quality of erections in terms of hardness, onset, and duration
  - **SEAR: Self-Esteem and Relationship Questionnaire**, the 14-item SEAR questionnaire is a brief, self-administered, disease-specific scale for assessing the relevant psychosocial manifestations of ED, specifically patient-reported outcomes of self-esteem, confidence, and relationships
Erection Hardness Score

• The EHS is a robust, validated, single-item patient-reported outcome for evaluating erection hardness
  – Improvements in erection hardness have correlated with a restoration of confidence in the ED patient

• You can educate sufferers to use the EHS to assess the severity of their ED

• An expert panel defined the maximum score 4 as the main goal in the treatment of ED

<table>
<thead>
<tr>
<th>EHS 1</th>
<th>EHS 2</th>
<th>EHS 3</th>
<th>EHS 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penis is larger but not hard</td>
<td>Penis is hard, but not hard enough for penetration</td>
<td>Penis is hard enough for penetration, but not completely hard</td>
<td>Penis is completely hard and fully rigid</td>
</tr>
</tbody>
</table>

Erection Hardness Score (EHS)

<table>
<thead>
<tr>
<th>IIEF</th>
<th>Severe ED 6 - 10</th>
<th>Moderate ED 11 - 21</th>
<th>Mild ED 22 - 25</th>
<th>No ED 26 - 30</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Penis is larger</td>
<td>Penis is hard</td>
<td>Penis is hard</td>
<td>Penis is</td>
</tr>
<tr>
<td></td>
<td>but not hard</td>
<td>but not hard</td>
<td>enough for</td>
<td>completely</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>penetration</td>
<td>hard and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>but not</td>
<td>fully rigid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>completely</td>
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<tr>
<td></td>
<td></td>
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<td>hard</td>
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Rigidity is Important to Patients - Mullhall et al.

- Optimal Erection Hardness
  - Confidence/Self-Esteem
  - Sexual Satisfaction
  - ED Treatment Success

A shift from EHS Grade 3 at baseline to EHS Grade 4 at the EOT is accompanied by significant improvements in intercourse and relationship satisfaction.

An international panel of experts convened to evaluate data from clinical trials involving > 10,000 men with ED, concerning the role of erection hardness in defining the response to treatment with PDE5 therapy.

Tools – International Index of Erectile Function (IIEF), Self-Esteem and Relationship Questionnaire (SEAR) and Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS Index scores)

Mulhall J, et al. 2007
Studies also show ...

Studies show that erection hardness is important to patients

A total of 307 men were randomised to sildenafil or placebo

EHS 3 or 4 had increased by 40% for sildenafil vs. 11% for placebo (p<0.0001)

Improvement in function, emotional well-being, and satisfaction was greatest in men with completely hard erections and correlated positively with other measures of hardness

(Kadioglu A. et al. 2007)
Drug Therapy in ED Management
Treatment for ED!

• Main drugs (PDE5 inhibitors)
  – (Sildenafil)
  – (Vardenafil)
  – (Tadalafil)

• Accounts for 95% of all ethical Erectile Dysfunction Rx!

• Combination approach with counseling for psychological factors.
Alternative treatments
Concerns About Other Therapies in ED Management

What are alternative treatments?

• An alternative treatment is a “health treatment that is not classified as standard Western medical practice”

• Alternative supplements may include:
  – herbal medicines
  – nutritional supplements
  – acupuncture
What are herbal supplements?

- Herbal supplements may be called many things:
  - herbal medicines
  - plant preparations
  - nutritional supplements
  - alternative medicines
  - complementary medicines
  - traditional medicines

What are some herbal supplements for ED?

- Asian ginseng
- Ginkgo biloba
Some herbal products contain PDE5 inhibitors

- Twenty-six herbal products were tested by the US FDA laboratory for the presence of known PDE5 inhibitors or previously identified synthetic analogues
  - Synthetic analogues include sildenafil citrate, tadalafil, vardenafil hydrochloride trihydrate, methisosildenafil, homosildenafil, piperidenafil, thiosildenafil, and thiomethisosildenafil
- Fifteen of 26 of the “herbal” products actually contained a PDE5 inhibitor or analogue

Take Home Messages

• Worldwide, the prevalence of sexual dysfunction is high, but only a small proportion of individuals complaining seek medical attention\(^1\)

• By restoring erections, confidence can be restored\(^2\)

• Patient/couple–centric approach for ED treatment is recommended for achieving optimal erection hardness and treatment satisfaction

Take Home Messages

• ED, CVD, diabetes, and depression are strongly linked\(^1\)

• They share a common denominator – endothelial dysfunction\(^2\)

• Associated risk factors include smoking and obesity\(^2,3\)

• The psychological impact of ED may result in depression and deterioration in relationships\(^4,5\)
