DESPITE THE COMMON COMPLAINT, EACH PATIENT COMES AS AN INDIVIDUAL, WITH UNIQUE EXPECTATIONS

My special interest

Counseling patients prior to major pelvic surgery with high risk of erectile dysfunction

Supporting patients through their journey to regain their sexual function after surgery – “penile rehabilitation”
ERECTILE DYSFUNCTION

Definition:

Persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance

But..... What does this actually mean to the patient?

Does it get hard, and stay hard enough to satisfy the sexual needs of the patient (and the partner)
Patients believe ED would not be recognized as a medical problem

Patients fear that discussing sexuality may embarrass their doctors

44% of men attending urologists have ED but fail to mention it - most are too embarrassed

Marwick C. JAMA 1999;281:2173–2174
# ASIAN PREVALENCE OF ED

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Region</th>
<th>Prevalence of ED (age group in years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khoo et al./2008¹</td>
<td>Malaysia</td>
<td>70.1% in men &gt;50 years of age</td>
</tr>
<tr>
<td>Quek et al./2008²</td>
<td>Malaysia</td>
<td>41.6% in men &gt;20 years of age</td>
</tr>
<tr>
<td>Li et al./2005³</td>
<td>Malaysia</td>
<td>59% in men of 50–80 years of age</td>
</tr>
<tr>
<td>Masumori et al./1999⁴</td>
<td>Japan</td>
<td>15% (40–49), 23% (50–59), 39% (60–69), 71% (70–79)</td>
</tr>
<tr>
<td>Kongkanand et al. /2000⁵</td>
<td>Thailand</td>
<td>7% (40–49), 22% (50–59), 49% (60–69)</td>
</tr>
<tr>
<td>Moreira et al. /2006⁶</td>
<td>Korea</td>
<td>32% in men of 40–80 years</td>
</tr>
</tbody>
</table>

Predicted increase
In prevalence of ED by 2025

Worldwide prevalence will increase from
152 million men in 1995 to 322 million men in 2025

Aytac IA et al. BJU Int 1999; 84: 50-56.
ED is linked to serious health problems!

ERECTILE DYSFUNCTION: NARROWING OF BLOOD VESSELS

- 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.)

<table>
<thead>
<tr>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penile artery</td>
<td>Coronary artery</td>
</tr>
<tr>
<td>1-2 mm</td>
<td>3-4 mm</td>
</tr>
<tr>
<td>ED</td>
<td>Angina infarction</td>
</tr>
</tbody>
</table>

ERECTILE DYSFUNCTION

Cardiovascular risk

- Men with organic ED should have their cardiac risk factors addressed
- ED is significantly associated with cardiovascular risk factors. These include:
  - hypertension
  - raised cholesterol (hyperlipidaemia)
  - diabetes
  - smoking
- There is a degree of cardiac risk associated with sexual activity, so it is crucial to assess the CV risk
  - The risk is small (~1% for myocardial infarction) and low compared with many other risks most patients will encounter (e.g. watching football)

ERECTILE DYSFUNCTION

Princeton II evaluation algorithm

ERECTILE DYSFUNCTION

Diabetes
- 20-85% of men with diabetes suffer from ED (ranging from mild to complete)
- ED was three times more common in diabetic men vs nondiabetic men
- ED occurs earlier in men with diabetes compared with men who do not have diabetes
- The risk of ED increases:
  - The longer diabetes is present
  - If the condition is inadequately controlled (raised blood glucose and HbA1c)
ERECTILE DYSFUNCTION

Prostate

- Men with enlarged prostates can also suffer from erection problems
  - ED is underdiagnosed in patients consulting urologists for benign prostatic hyperplasia
- ED is very often seen after radical prostatectomy for prostate cancer
  - 44-75% of patients

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 health care providers:
  - Empathize and communicate effectively with sufferers
  - Appreciate the value of appropriate treatment

DIAGNOSIS AND TREATMENT OF ED

Diagnosis of ED

- Basic workup includes:
  - Medical history
  - Psychological history
  - Sexual history
  - Physical examination
  - Laboratory tests
- Medical and psychological histories should be taken for both patients and their partners
Patient with erectile dysfunction (self-reported)

Medical and psychosexual history
(use of validated instruments, eg IIEF)

- Identify other than ED sexual problems
- Identify common causes of ED
- Identify reversible risk factors for ED
- Assess psychosocial status

Focused physical examination

- Penile deformities
- Prostatic disease
- Signs of hypogonadism
- Cardiovascular and neurological issues

Laboratory tests

- Glucose-lipid profile (if not assessed in the past 12 months)
- Total testosterone (morning sample) If available: bio-available or free testosterone (instead of total)

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>
Clinical approaches to treatment of ED
DIAGNOSIS AND TREATMENT OF ED

First-line treatment: Oral treatment – PDE5 inhibitors

- PDE5 inhibitors are recommended as the preferred pharmacotherapy for ED
- PDE5i is a class of vasodilators that work on the nitric oxide-cGMP mechanism to help restore natural erectile function in the presence of sexual stimulation
- Efficacy is defined by rigidity sufficient for vaginal penetration
- Sildenafil citrate (Viagra) was the first licensed oral medication for ED, receiving marketing authorization in 1998
- Vardenafil (Levitra) and tadalafil (Cialis) received marketing authorization in 2003

Efficacy evaluation during placebo-controlled studies
SILDENAFIL EFFICACY

24-week dose-response study: Ability to achieve erection
Percent increase from baseline in response to IIEF Q3: “When you attempted sexual intercourse, how often were you able to penetrate your partner?”

The results were derived from a 24-week, dose-response, placebo-controlled study with 501 patients completing evaluation.

24-week dose-response study: Maintenance of erection

Percent increase from baseline in response to IIEF Q4: “During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?”

The results were derived from a 24-week, dose-response, placebo-controlled study with 501 patients completing evaluation.

## SILDENAFIL EFFICACY

### Discontinuations

<table>
<thead>
<tr>
<th>Variable</th>
<th>24-week dose-response study number of men (percent)</th>
<th>Placebo (n=216)</th>
<th>Sildenafil 25 mg (n=102)</th>
<th>Sildenafil 50 mg (n=107)</th>
<th>Sildenafil 100 mg (n=107)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for discontinuation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All causes</td>
<td></td>
<td>36 (17)</td>
<td>15 (15)</td>
<td>8 (7)</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Treatment-related adverse effect</td>
<td></td>
<td>1 (&lt;1)</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Insufficient response</td>
<td></td>
<td>11 (5)</td>
<td>3 (3)</td>
<td>2 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Other*</td>
<td></td>
<td>24 (11)</td>
<td>11 (11)</td>
<td>5 (5)</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Adverse effect**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td>14 (6)</td>
<td>14 (14)</td>
<td>23 (21)</td>
<td>32 (30)</td>
</tr>
<tr>
<td>Flushing</td>
<td></td>
<td>3 (1)</td>
<td>13 (13)</td>
<td>29 (27)</td>
<td>21 (20)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td></td>
<td>3 (1)</td>
<td>3 (3)</td>
<td>12 (11)</td>
<td>17 (16)</td>
</tr>
<tr>
<td>Rhinitis</td>
<td></td>
<td>4 (2)</td>
<td>1 (1)</td>
<td>3 (3)</td>
<td>12 (11)</td>
</tr>
<tr>
<td>Visual disturbance***</td>
<td></td>
<td>1 (&lt;1)</td>
<td>2 (2)</td>
<td>6 (6)</td>
<td>10 (9)</td>
</tr>
</tbody>
</table>

*Other reasons for discontinuation included protocol violations, not returning for follow-up, adverse effects not related to treatment, withdrawal of consent, and other reasons.

**The adverse effects listed are those that occurred in 5% or more of any treatment group.

***The visual disturbances reported were changes in the perception of color hue or brightness.

SILDENAFIL EFFICACY

12-week evaluation of sildenafil in the treatment of ED of various etiologies

Objective: To determine the efficacy and safety of fixed-dose sildenafil in patients with ED of various etiologies.

Study design: 12-week, double-blind, placebo-controlled, fixed-dose study.

Patients: 514 men (ages 19 to 79) with ED and co-morbid conditions including genitourinary procedures, essential hypertension, diabetes mellitus, BPH, depression, or ischemic heart disease.

SILDENAFIL EFFICACY

12-week evaluation of patient/partner satisfaction with sildenafil in the treatment of ED

**Objective:** To assess the efficacy and safety of sildenafil in men with erectile dysfunction and patient and partner satisfaction with treatment using EDITS.

**Study design:** 12-week, multicenter, double-blind, placebo-controlled, parallel-group, flexible-dose study.

**Patients:** 247 men (ages 31 to 81) with ED and co-morbid conditions including essential hypertension, diabetes, hypercholesterolemia, hyperlipidemia, and prostatic hyperplasia.

SILDENAFIL EFFICACY

12-week fixed-dose study: Patient/partner responses to IIEF questionnaire

Mean scores at baseline and at the end of double-blind treatment

Patient responses to IIEF Q3, Q4, Q7

*P<.001 compared with placebo

**SILDENAFIL EFFICACY**

12-week fixed-dose study: Patient/partner responses to IIEF questionnaire

Mean scores at baseline and at the end of double-blind treatment

Partner responses to IIEF Q1, Q2, Q3

- Baseline
- Placebo, 12 weeks
- Sildenafil, 12 weeks

*P<.001 compared with placebo

SILDENAFIL EFFICACY

Analysis of pooled data from sildenafil double-blind studies in ED patients with co-morbidities

Objective: To evaluate findings from 11 double-blind, placebo-controlled, flexible-dose (taken as needed) sildenafil studies.

Study design: Four-week baseline period and a 12-week, double-blind, placebo-controlled study.

Patient: 2,667 patients (ages 23 to 89) with ED and co-morbid conditions including diabetes, ischemic heart disease, peripheral vascular disease, post-radical prostatectomy, hypertension, depression, or concomitant use of antihypertensive or antidepressant medications.
SILDENAFIL EFFICACY

Analysis of pooled data from sildenafil double-blind studies in ED patients with co-morbidities

**Dosage:** Patients were randomized to an initial dose of 50 mg sildenafil or matching placebo. Dose could be increased to 100 mg or decreased to 25 mg based on efficacy or tolerability.

**Efficacy parameters for the 11 pooled studies:** Patients were asked to respond to question 3 (achieving an erection) and question 4 (maintaining erections) of the IIEF questionnaire. A global efficacy question (whether treatment improved erections) was asked at the end of treatment. In 6 of the 11 studies, patients were asked to keep an event log of sexual activity.
SILDENAFIL EFFICACY

Results from 11 pooled double-blind studies:
Patient responses to IIEF Q3

Overall baseline mean score and least squares mean (±) SE scores at end of treatment for IIEF question 3 (ability to achieve erections)

Results from 11 pooled double-blind studies:
Patient responses to IIEF Q4
Overall baseline mean score and least squares mean (±) SE scores at end of treatment for IIEF question 4 (ability to maintain erections)

ENDOTRIAL study

EVALUATION OF EFFICACY IN THE TREATMENT OF ED AMONG SILDENAFIL, TADALAFIL, AND VARDENAFIL (ENDOTRIAL STUDY)
**SILDENAFIL EFFICACY**

Within-subject mean change from baseline for IIEF: International Index of Erectile Function question 15

Primary outcome showing statistical equivalence for all four PDE5i (Data for IIEF questions 1-5 not shown)

A spontaneous, open-label, randomized, multicenter, crossover study. The protocol consisted of a four-week washout period, followed by an eight-week treatment period. Data for primary efficacy were available for 77 out of 100 patients.

# THE TIMING FOR SEX ACCORDING TO MEDICATION

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sildenafil, 100 mg</th>
<th>Tadalafil, 20 mg</th>
<th>Vardenafil, 20 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to maximum effect</td>
<td>0.8-1 hours</td>
<td>2 hours</td>
<td>0.9 hours</td>
</tr>
<tr>
<td>Half-life of drug</td>
<td>2.6-3.7 hours</td>
<td>17.5 hours</td>
<td>3.9 hours</td>
</tr>
</tbody>
</table>
General side effects
# SILDENAFIL SAFETY

## Reported adverse reactions

Medically important adverse reactions reported during clinical trials or post-marketing surveillance

<table>
<thead>
<tr>
<th><strong>Very common</strong> (≥10% of patients)</th>
<th><strong>Uncommon</strong> (≥0.1% to &lt;1% of patients)</th>
<th><strong>Rare</strong> (≥0.01% to &lt;0.1% of patients)</th>
<th><strong>Incidence not known</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Headache</td>
<td>• Somnolence</td>
<td>• Hypersensitivity reactions</td>
<td>• Transient ischemic attack</td>
</tr>
<tr>
<td>• Dizziness</td>
<td>• Hypoaesthesia</td>
<td>• Atrial fibrillation</td>
<td>• Unstable angina</td>
</tr>
<tr>
<td>• Visual disorders</td>
<td>• Conjunctival disorders</td>
<td>• Myocardial infarction</td>
<td>• Ventricular arrhythmia</td>
</tr>
<tr>
<td>• Visual color distortion</td>
<td>• Eye disorders</td>
<td>• Cerebrovascular accident</td>
<td>• Sudden cardiac death</td>
</tr>
<tr>
<td>• Flushing</td>
<td>• Lacrimation disorders</td>
<td>• Hypertension</td>
<td>• Seizure</td>
</tr>
<tr>
<td>• Nasal congestion</td>
<td>• Vertigo</td>
<td>• Hypotension</td>
<td>• Seizure recurrence</td>
</tr>
<tr>
<td>• Dyspepsia</td>
<td>• Tinnitus</td>
<td>• Syncope</td>
<td>• Non-arteritic anterior ischemic optic neuropathy (NAION)</td>
</tr>
<tr>
<td></td>
<td>• Vomiting</td>
<td>• Sudden deafness</td>
<td>• Retinal vascular occlusion</td>
</tr>
<tr>
<td></td>
<td>• Nausea</td>
<td>• Epistaxis</td>
<td>• Visual field defect</td>
</tr>
<tr>
<td></td>
<td>• Dry mouth</td>
<td></td>
<td>• Priapism</td>
</tr>
<tr>
<td></td>
<td>• Palpitations</td>
<td></td>
<td>• Prolonged erection</td>
</tr>
<tr>
<td></td>
<td>• Increased heart rate (by investigation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Tachycardia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Skin rash</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Myalgia</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>• Chest pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Fatigue</td>
<td></td>
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</tr>
</tbody>
</table>

* Reported through post-marketing surveillance so incidence unknown.
IMPACT OF TREATMENT ON SELF-ESTEEM AND CONFIDENCE IN THE ED PATIENT

- Men with ED experience low rates of confidence
- Treatment with a PDE5 inhibitor has been associated with an increase in self-esteem and confidence in patients with ED
- From both patient and partner perspectives, satisfaction with ED treatment plays a critical role in maintaining long-term therapy for ED