Managing Erectile Dysfunction

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Objectives

1. Review physiologic mechanism of erection
2. Discuss medical management of ED
3. Discuss surgical management of ED
Male Sexual Dysfunctions:

1. Arousal disorder
2. Erectile dysfunction *
3. Emission failure
4. Premature / delayed ejaculation
5. Prolonged refractory period
Definition:

Erectile Dysfunction is the:

“…consistent inability to obtain or maintain an erection satisfactory for sexual function.”

NIH consensus in JAMA, 1993
Prevalence:

Massachusetts Male Aging Study

- Complete
- Moderate
- Minimal

Prevalence in Population (%)

Age of Respondents

Prevalence:

![Graph showing prevalence of ED-related factors vs age]

- Age
- Diabetes
- Hypertension
- Smoking
- Depression
- Hyperlipidemia

% ED prevalence vs Age (years)
Risk Factors:

Massachusetts Male Aging Study

ED is associated with:

• Age
• Diabetes
• Hypertension
• Heart Disease
• Smoking
• Depression
• Obesity
• Medications

Anatomy

Corpora Cavernosa

- key structures mediating erection are the paired corpora cavernosa
- fused distally in midline
- separate proximally to attach to ischial tuberosity
- thick tunica albuginea surrounds erectile tissue
Anatomy

Corpora Cavernosa

- aorta, common iliac, internal iliac arteries
- internal iliac-arteries exit pelvis as paired pudendal aa.
- pudendal gives rise to common penile, urethral, corporal arteries
- paired corporal aa. ultimately supply blood to erectile tissue
Anatomy

Corpora Cavernosa

- specialized vascular beds
- multiple endothelial-lined vascular spaces (*lacunae*)
- walls of vascular spaces contain smooth muscle
- allows contraction and expansion of lacunae
- parasympathetic NS innervation
Anatomy

Corpora Cavernosa

- corporal smooth muscle relaxation leads to vasodilation
- blood flow into penis increases
- vascular spaces engorge
- fibrous tunica albuginea permits rigidity as vascular tissue engorges
- vascular and/or tunical disease etiologic in 70% cases of ED
Corpora Cavernosa

- fibrotic disease involving tunica albuginea termed **Peyronie’s Disease**
- multifactorial etiology
- results in variable degrees of penile deformity, palpable plaque
- 20% associated with ED
- presence or absence of Peyronie’s disease significantly impacts therapeutic options
# Categorizing ED:

<table>
<thead>
<tr>
<th>Categorization</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vasculogenic (70%)</strong></td>
<td>diabetes, hypertension, Peyronies disease, hypercholesterolemia, hyperlipidemia, post-surgical</td>
</tr>
<tr>
<td><strong>Pharmacologic (10%)</strong></td>
<td>antihypertensives, antidepressants, ETOH, GnRH agonists, 5-alpha reductase inhibitors, antiandrogens</td>
</tr>
<tr>
<td><strong>Neurogenic (10%)</strong></td>
<td>spinal cord injury, diabetes, multiple sclerosis, CVA</td>
</tr>
<tr>
<td><strong>Endocrinologic (5%)</strong></td>
<td>hypogonadism, hypopituitarism, prolactinoma, hypothalamic disorders</td>
</tr>
<tr>
<td><strong>Psychogenic (5%)</strong></td>
<td>depression, stress, psychosis, anxiety</td>
</tr>
</tbody>
</table>
Neurophysiology:

Nitric Oxide

- nitric oxide is the most important NT mediating erection (*parasympathetic*)
- following arousal, cavernous nerves release NO into synapses on smooth muscle
- NO leads to increase in intracellular cGMP
Neurophysiology:

Nitric Oxide

- cGMP causes smooth muscle relaxation, and, vascular space engorgement
- *erection results from corporal smooth muscle relaxation (vasodilation)*

![Diagram showing the role of NO in erection](image-url)
Neurophysiology:

Nitric Oxide

- PDE-5 is present in corporal smooth muscle cells
- PDE-5 degrades active cGMP to inactive 5-GMP
- as cGMP levels decrease, smooth muscle tone returns to resting, contracted state
Neurophysiology:

Nitric Oxide

• vascular spaces become devoid of blood
• penis becomes flaccid
• detumescence results from corporal smooth muscle contraction (vasoconstriction)
Neurophysiology:

PDE-5 inhibitors

- slow cGMP degradation and prolong its effects:
  - penile smooth muscle remains relaxed
  - vascular spaces remain engorged
  - penis remains erect

- oral PDE-5 inhibitors are current first line therapy for managing ED
Neurophysiology:

VIP, PGE-1, papaverine

- cAMP can induce corporal smooth muscle relaxation
- cAMP degraded by cAMP specific PDE
- cAMP pathway is of secondary importance to NO pathway in mediating erection
- VIP, PGE-1, phentolamine, and papaverine can stimulate cAMP formation and induce erection
Management of ED

1. Pharmacologic Agents
   a. Oral agents
      • sildenafil
      • vardenafil
      • tadalafil
   b. Transurethral suppository (PGE-1)
   c. Intracorporal injection
      • PGE-1
      • papaverine
      • phentolamine

2. Mechanical Devices
   a. Vacuum erection device (VED)
   b. Penile prosthesis
PDE-5 Inhibitors:

PDE-5 inhibitors:

- PDE-5 predominates in the corporal tissue
- Other PDE’s exist:
  - PDE-1  vascular, brain, heart
  - PDE-3  heart
  - PDE-6  retina
  - PDE-11 heart, testis, pituitary
- PDE-5 inhibitors:
  - Sildenafil  *(Viagra)*
  - Vardenafil  *(Levitra)*
  - Tadalafil  *(Cialis)*
# PDE-5 Inhibitors:

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>t1/2 (hours)</th>
<th>dose (mg)</th>
<th>Dosing interval (hours)</th>
<th>Side effects (result from stimulation of extracorporeal PDE’s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sildenafil *</td>
<td>(Viagra)</td>
<td>3.8</td>
<td>25, 50, 100</td>
<td>Q 24</td>
<td>facial flushing, HA, dyspepsia, color vision disturbance</td>
</tr>
<tr>
<td>vardenafil **</td>
<td>(Levitra)</td>
<td>4.7</td>
<td>10, 20</td>
<td>Q 24</td>
<td>facial flushing, HA, hypotension, prolongation QT interval</td>
</tr>
<tr>
<td>tadalafil ***</td>
<td>(Cialis)</td>
<td>17.5</td>
<td>10, 20, 5</td>
<td>Q 72 Q 24</td>
<td>HA, dyspepsia, myalgia</td>
</tr>
</tbody>
</table>

* * * contraindicated with nitrates  
* * ** contraindicated with alpha-blockers  
*** contraindicated with alpha-blockers except tamsulosin (Flomax)
PDE-5 Inhibitors:

- PDE-5 inhibitors have had enormous impact in treatment of ED
- currently considered 1st line treatment for ED
- overall effectiveness reported 60-70% *
- many men are reluctant to discuss ED issues:
  - embarrassment
  - feelings of inadequacy
  - perception that ED is not a medical problem
  - lack of knowledge that effective therapy exists
  - fear of invasive testing
- if initial trial of PDE-5 inhibitor is ineffective, subsequent trial of alternate PDE-5 inhibitor less likely to succeed
- consider Urology consultation if initial PDE-5 inhibitor fails

* J Urol. 2001
Transurethral Suppository

PGE-1 (*MUSE*)

- 250, 500, 750, 1000 mcg
- q 24 hour dosing
- side effects:
  - hypotension
  - penile aching
  - urethral bleeding
- efficacy 40%
Intracorporal Injection

PGE-1 (*Cavarject*)
- 10-40 mcg
- q 24 hour dosing
- efficacy 80%
- side effects:
  - *penile aching*
  - *hematoma*
  - *priapism*
  - *Peyronie’s*

PGE-1, phentolamine, papaverine (*Trimix*)
PGE-1, phentolamine (*Bimix*)
Vacuum Erection Device (VED)

- mechanically created vacuum draws blood into corpora
- constricting ring necessary to maintain “erection”
- advantages:
  - safe
  - simple
  - reusable
  - safe for anticoagulants
Vacuum Erection Device (VED)

- disadvantages:
  - cumbersome
  - ring uncomfortable
  - limited ejaculation
  - only “erect” distal to ring
  - hematoma
  - tourniquet effect

- many models available with price ranges of $20 - $400
Inflatable Penile Prosthesis (IPP)

• surgically implanted device
• 2 hour surgical procedure
• < 24 hour hospitalization
• advantages:
  ✓ reliable
  ✓ spontaneous
  ✓ no paraphernalia
  ✓ no daily use limitations
  ✓ highest satisfaction rates
  ✓ cost effective
  ✓ corrects penile deformity
Inflatable Penile Prosthesis (IPP)

- disadvantages:
  - device failure
  - erosion
  - infection
  - auto-inflation
  - SST deformity
  - perceived penile shortening

- highest long-term couple satisfaction rates

- still covered by Medicare…
Summary:

1. Numerous therapeutic options are available for patients suffering from erectile dysfunction.

2. While oral PDE-5 inhibitors serve as first line therapy for most patients with ED, approximately 1/3 of patients can be expected to fail.

3. Consider Urology referral if initial trial of PDE-5 inhibitor is not successful, contraindicated, or if problematic Peyronie’s Disease is present.