Priapism: Current Concepts in Medical and Surgical Management

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Disclosure

- The author identifies no conflicts of interest associated with the presentation of this study.
- The study did not receive financial support from any pharmaceutical company.
- The presentation includes discussion of unlabeled, investigational use of a product not approved by the FDA.
Acknowledgments

- **Urology**
  - Biljana Musicki, Trinity Bivalacqua, Thomas Chang

- **Neuroscience**
  - Solomon Snyder, David Bredt, K. Joseph Hurt

- **Cardiology**
  - Charles Lowenstein, Hunter Champion, David Kass
Overview

- Evolution of the science and therapy of priapism
- Current perspectives on molecular mechanisms
- Available and potential clinical management strategies
Definition

“Priapism is a pathological condition of a penile erection that persists beyond or is unrelated to sexual stimulation.”

AFUD Thought Leader Panel, IJIR 5:S39, 2001
Significance of Priapism

- **Prevalence**
  - Afflicts 40% of males with sickle cell disease

- **Medical consequences**
  - May lead to permanent and irreversible erectile dysfunction and psychosocial debilitation

- **Under-management**
  - Obscure etiology and pathogenesis
Historical Treatments

- Warm baths
- Cold or hot packs
- Antibiotics
- Anticoagulants
- Tobacco enemas
- Camphorated mercurial ointment
- Leeches
- Trichloracetic acid
- Sedatives
- Hypnotics
- Anesthetics
- Dorsal artery ligation
- Perineal nerve transection
- Ischiocavernosus muscle division
- Penile amputation
- Corporal incision/aspiration

Burnett AL. J Urol 170: 26-34, 2003
Management Algorithm for Priapism

**PRIAPISM**

**History & Physical**

- Simultaneous treatment of any underlying disease (e.g., sickle cell disease)
- Cavernal Aspiration with Blood Gas or Doppler Ultrasound

**Ischemic**

- Aspiration with or without irrigation
- Phenylephrine
  - Distal Shunting
    - Repeat Distal or use Proximal Shunting

**Nonischemic**

- Observation
  - Arteriography & Embolization
  - Surgical Ligation

*Erection greater than 4 hours duration.
*Proceed upon treatment failure.
Management of Recurrent Priapism

- Presentations: sickle cell disease patient with “stuttering” priapism, “idiopathic”, neurologic disease
- Strategies:
  - Surveillance
  - Pharmacologic therapies (terbutaline, baclofen, digoxin, anti-androgens)
  - Standard veno-occlusive algorithms ready
There are currently no effective curative treatments for this disorder.

Current clinical management represents only reactive and frankly extreme circumventional interventions, which carry major complication risks.
Pathophysiologic Ignorance?

- What causes priapism?
- Who is most susceptible?
- What are predisposing factors?
- What is the evidence for a pathophysiologic mechanism?

Understanding the mechanisms involved in the pathogenesis of priapism is key to developing effective mechanism-based preventative and corrective therapies for the disorder.
Dysregulation Thesis

- Defective regulation of the functional state of the cavernosal tissue, favoring cavernosal tissue relaxation.
- Does not exclude mechanisms of classic hemodynamic disorders of priapism.
- Relevance to priapism variants.

Burnett AL. J Urol 170:26-34, 2003
PDE5 Dysregulation In Penile Erectile Tissue: Mechanism Of Priapism

- NOS3 -/- mice had enhanced erectile response to CNS.
- eNOS gene transfer to the NOS3-/- mouse penis resulted in neurogenic-mediated erectile responses similar to WT mice via an elevation of PDE5A expression/activity.

Thus, properly regulated PDE5 function under physiologically relevant NO signaling preserves normal erection physiology.

Therefore, if penile PDE5 expression is dysregulated priapism occurs.

Mechanism of Priapism

Champion HC, et al. PNAS 102: 1661-6, 2005
Low NO Bioavailability as a Basis for PDE5 Dysregulation

- Oxidative stress associated with ischemia?
- Endothelial adhesion molecule defects?
- Endothelial injury and cell loss?

Sludged erythrocytes do not solely explain the pathology of priapism in sickle cell disease.
Cycle of Pathogenic Factors: Cavernosal Tissue Level Mechanisms

Oxidative Stress
- Reactive Oxygen Species Generation
- Lipid Peroxidation

Anoxia
- Cytokine Induction
- Inflammatory Response

Priapism

NO Imbalance
- Constitutive Endothelial NO Bioactivity Decrease

Penile Vasculopathy
- PDE5 Dysregulation
- Rho-kinase Inactivation
Sequelae of Ischemia/Anoxia

- **Cellular**
  - Smooth muscle damage/apoptosis
  - Endothelial destruction
  - Fibrosis

- **Molecular**
  - Reactive oxygen species generation (oxidative stress)
  - Low nitric oxide bioavailability
  - Hypoxia-induced growth factors (e.g., TGF-β)
Dysregulatory Erection Physiology: Mechanisms at Multiple Control Levels

- Central and peripheral neurotransmission
- Paracrine agency
- Hormonal axis
Interim Summary: 
Hypothesis

Sickle Cell Disease

PDE5 Inhibitor Therapy

Penile Vasculature

Endothelial-NO

Priapism

Restore Normal Penile Vascular Homeostasis

?
Summary of PDE5 Inhibitor Therapeutic Response

<table>
<thead>
<tr>
<th>Patient</th>
<th>Etiology</th>
<th>Priapism (Baseline)</th>
<th>Priapism (On Treatment*)</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 yo</td>
<td>Hgb SS</td>
<td>3h, daily</td>
<td>Rare</td>
<td>15 mo</td>
</tr>
<tr>
<td>37 yo</td>
<td>Hgb SC</td>
<td>3h, daily</td>
<td>Rare</td>
<td>12 mo</td>
</tr>
<tr>
<td>22 yo</td>
<td>Hgb SS</td>
<td>&gt;4h (2x)</td>
<td>Rare</td>
<td>8 mo</td>
</tr>
<tr>
<td>22 yo</td>
<td>Idiopathic</td>
<td>5h, daily</td>
<td>Occasional</td>
<td>6 mo</td>
</tr>
<tr>
<td>35 yo</td>
<td>Idiopathic</td>
<td>&gt;4h (3x)</td>
<td>Occasional</td>
<td>4 mo</td>
</tr>
<tr>
<td>24 yo</td>
<td>Hgb SS</td>
<td>2h, 4x weekly</td>
<td>Unchanged</td>
<td>2 mo &amp; d/c’d</td>
</tr>
<tr>
<td>25 yo</td>
<td>Idiopathic</td>
<td>2h (5x)</td>
<td>Occasional</td>
<td>3 mo</td>
</tr>
</tbody>
</table>

Priapism improved in 6 of 7 patients after long-term, continuous use of PDE5 inhibitors.

* Sildenafil (25-50 mg po qd) or Tadalafil (10 mg po qod or 5 mg po qd)

Possible New Mechanisms

- $A_{2B}$ adenosine receptor-mediated\(^1\)
  - Adenosine deaminase deficiency
- Variable coding sequence protein A1 – mediated\(^2\)
  - Up-regulation of neurogenic ED gene

Proposed Therapeutic Strategies

- PDE5 downregulation
  - PDE5 inhibitors\(^1,2\)
- Adenosine deaminase deficiency
  - PEG-ADA (ADA enzyme therapy)\(^3\)

Priapism Management Algorithm

History & Physical Exam
Laboratory Values

>4 hrs duration

Ischemic Priapism

Phenylephrine

Distal Shunting

Proximal Shunting

Penile Prosthesis

Non-Ischemic Priapism

Aspiration & Irrigation

Observation

Arteriography & Embolization
Surgical Management of Ischemic Priapism: Guidelines

■ Indications
  ➢ Failed adequate trial of corporal aspiration and alpha-agonist administration

■ Preparation
  ➢ Documentation of baseline erectile function, duration of priapism, history of stuttering, and prior interventions
  ➢ Informed consent process
Surgical Shunting

- **Objection**
  - Re-establish outflow from the corpora cavernous bodies by creating a communication to the glans, corpus spongiosum, or a vein

- **Categories**
  - Percutaneous distal shunts
  - Open distal shunts
  - Open proximal shunts
  - Vein anastomoses (saphenous, superficial/deep dorsal)
Surgical “Distal” Shunt Options

Percutaneous Techniques

Surgical Techniques
Surgical “Proximal” Shunt Options

Quackles/Sacher

Grayhack
Conventional Management Using Shunts

- Attempt distal shunt first; technique based on surgeon familiarity
- If distal shunt fails (no patency, no reconstituted intracavernous blood flow), perform a proximal shunt
- If proximal shunt fails, perform a vein bypass procedure
What is the Success of Conventional Shunt Procedures?

- The efficacy of penile shunt surgery is controversial owing to the variability of success using these procedures.
- Penile shunt surgery does have usefulness to mitigate the pathologic effects associated with first-line treatment refractory presentations.
- Interest has pushed forward to re-evaluate surgical approaches and produce improvements in surgical techniques.
To create tunneling of the corpora cavernosa, a straight 20-24 urethral sound or dilator is inserted through each glans incision and advanced to the penile crura.

Clinical Series

- Clinical presentation
  - 13 patients with ischemic priapism, including 6 patients who had undergone unsuccessful distal or proximal shunt procedures

- Priapism resolution achieved
  - T-shunt alone: 6 patients
  - T-shunt with tunneling: 7 patients (3 of whom failed prior shunts)

- Erection recovery observed
  - 8 of 11 patients without preexistent ED

A cavernosal dilator (#7 Hegar) is retrogradely inserted through excised tunical windows of the distal corpora cavernosa after transglanular incision.

Burnett AL, Pierorazio PM. J Sex Med 6:1171-6, 2009
Clinical Series

- **Case 1**: 48 year old CA man with 2-day episode of priapism following trazodone use.
  - Underwent Winter shunt and corporal incision without resolution x 3 days (incomplete priapism resolution of 5 days duration)

- **Case 2**: 43 year old AA man with 24-hour episode of priapism.
  - Underwent Al-Ghorab shunt without resolution x 1 day (incomplete priapism resolution of 2 days duration)

- **Case 3**: 40 year old AA man with 72-hour episode of priapism.
  - Underwent Winter shunt without resolution x 3 days (incomplete priapism resolution of 6 days duration)

All 3 men underwent the corporal “snake” shunt with priapism resolution, with some erection recovery observed in cases 2 and 3.

Burnett AL, Pierorazio PM. J Sex Med 6:1171-6, 2009
Features and Advantages of Proximal Trans-Shunt Dilation

- Ensures a reliably patent shunt
- Applies a major penile venous system for blood evacuation (circumflex and deep dorsal vein egress)
- Restores intracavernous circulation
- Likely carries decreased complication rates (compared with proximal shunts)
- May permit erectile function recovery
- May reduce the eventuality of extensive penile fibrosis

*Distal penile shunt modifications may obviate the role of proximal penile shunt maneuvers.*
Role of Penile Prosthesis Surgery:
Recommendations of International Consultation on Sexual Medicine 2009

■ Indications
  - Failed aspiration and sympathomimetic intracavernous injection
  - Failed distal and proximal shunting
  - Presence of ischemia >36 hours
  - Management of confirmed ED (delayed setting)

■ Optional Procedures (to document corporal smooth muscle necrosis)
  - Magnetic Resonance Imaging prior to surgery
  - Corporal biopsy at surgery

Penile Prosthesis Management: Premises

- Overcome corporeal rigidity\(^1\)
  - Postulated advantage of semi-rigid prosthesis
- Limit long term anoxic injury and corporal fibrosis\(^2,3\)
- Lessen psychological trauma of repeated priapism episodes\(^4\)
- Decrease complication rates (by immediate insertion)\(^4,5\)
  - Potential opportunity for acute refractory presentations

5. Rees RW et al. BJU Int 90:893-7, 2002
Penile Prosthesis Management: Technical Considerations

- Corporectomy (sharp dissection and tissue excavation)\textsuperscript{1-3}
  - Pain management without prosthesis insertion as an additional possible indication
- Corporoscopic excavation\textsuperscript{4}
- Reimplantation (tissue expansion)\textsuperscript{5}
- Cylinder fixation\textsuperscript{5,6}

Conclusions

- Erectile tissue dysfunctional regulation constitutes a pathophysiologic mechanism for priapism.
- Corrective and/or preventative strategies for priapism will arise from further study of the molecular science of priapism.
- Clinical treatment refractory presentations of ischemic priapism merit consideration for surgical intervention.