New England Pediatric Sickle Cell Consortium

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Management of Priapism in Sickle Cell Disease

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Disclaimer Statement:

- Hospital clinical pathways are designed to assist clinicians by providing an analytical framework for the diagnosis and treatment of specific medical problems. They may be used for patient education and to assist in planning future care. They are not intended to replace a physician's judgment or to establish a protocol for all patients with a particular condition. The ultimate decision regarding the care of any patient should be made in respect to the individual circumstances presented by the patient.
- Any specific medications and dosing must always be reviewed carefully for each patient in view of any history of drug allergy or adverse reactions.
- This document was based on available research and clinical experience at time of its compilation.
- The following protocol is a regional guideline, and may be adapted by individual institutions as needed.

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PRIAPISM

Inclusion: Males with sickle cell disease of all genotypes.

I. Introduction

Definition:

- Priapism: A sustained, painful and unwanted erection [1] usually unrelated to sexual activity [2].
- Stuttering Priapism: recurrent episodes lasting minutes to < 3hours [1] and may herald a prolonged event.
- Prolonged Priapism: Longer than 3 hours [1]

Incidence/Prevalence: Estimated prevalence figures in US are broad. Priapism has been reported responsible for between 2-5% of admissions to hospital [3, 4] in a pediatric population, whereas retrospective data from adult males suggests 30-45% have suffered this complication at least once [5, 6]. Prevalence by age 20 has been reported to be as high as 75-89% [7, 8]. May occur in children as young as 3 y.o.

Pathophysiology: In sickle cell anemia, priapism is considered a low-flow / ischemic type. The precise mechanism is unclear, however it is assumed that decreased oxygen tension in the turgid corpus cavernosa leads to enhanced sickling and blockage of the venous outflow from the penis through the dorsal penile vein [1, 7]. Recurrent or prolonged priapism can result in corpus cavernosal fibrosis and erectile dysfunction, the incidence of which is inversely correlated to the duration of priapism [9]. Venous stasis leads to further oxygen extraction acidosis and a vicious circle of sickling and inflammation, which if not broken may lead to fibrosis and erectile dysfunction.

Triggers: Sexual arousal/ prolonged intercourse, fever, cold exposure, nocturnal tumescence (REM sleep), full bladder, dehydration, alcohol, cocaine and testosterone have all been implicated [1, 7, 10, 11].

Protective Factors: Increased HbF%.

Counseling and Psychosocial Aspects: Lack of awareness of this sickle related complication and embarrassment to discuss an acute event represent leading to under-recognition and under-treatment and are a significant hurdle to appropriate care. In order to raise awareness and decrease anxiety or embarrassment of the subject, priapism must be discussed at each Health Maintenance visit. Boys and their parents must be educated that prolonged priapism is a urological emergency [1].

II. Evaluation and Management of Acute Priapism

Prompt institution of supportive medical therapy (IVF, analgesia) and adjunctive procedures such as corporeal aspiration +/- injection of vasoactive medications is beneficial. [7] Goal of management is pain relief, detumescence and preservation of erectile function. There are few clinical trials, mostly anecdotal reports and small case series.

A. Outpatient

1. Pre-Hospital / Home Treatment [2, 7, 8, 12]:
   - Increased fluids.
   - Urination.
   - Oral pain medications.
   - Warm baths / soaks.
   - Gentle exercise.
   - Oral pseudoephedrine for patients with previous history of priapism.

When to Seek Medical Attention
   - 1st episode of priapism or
   - Recurrent priapism with any of:
     - Inability to void,
     - Severe pain,
     - No improvement with home treatment within 2 hours.

2. Emergency Department Evaluation & Treatment
   - History: Onset, frequency and duration of current and previous episodes. Pain, dysuria, frequency, discharge. Association with sleep, sexual activity, or masturbation. Response to previous therapy. Associated symptoms: dehydration, pain elsewhere, trauma, obstructive sleep apnea
   - Physical Exam: VS and hydration status. Size and degree of penile tumescence/turgor. Bicorporeal (corpus cavernosa only) or tricorporeal (includes corpora and glans).
   - IV hydration (10mL/kg bolus and 100-150% maintenance)
   - Analgesia (careful use of opiods to avoid urinary retention)
   - Supplemental O_2 to keep SaO_2 >92%
   - Pseudoephedrine (if not already given at home)
   - Laboratory: CBC, reticulocyte count, urinalysis +/- culture. Type & screen.
   - PRN catheterization if difficulty voiding.
   - Imaging not usually needed, unless history of trauma.
   - Never use ice packs or ice water enemas in patients with sickle cell anemia associated priapism.
   - Consult urology if no relief within 3 hours of the onset of symptoms. Goal of urology consult is penile aspiration/irrigation with epinephrine.

3. Emergency Department Discharge Criteria
   - Able to void.
   - Penis more flaccid (swelling and/or edema may be present for several weeks)
   - Pain controllable on PO medications.
   - Consider addition of pseudoephedrine (See dosing in Appendix).

4. Aspiration and Irrigation [8, 13]
   - Conscious sedation is appropriate.
   - Local anesthesia (1% lidocaine).
   - 23G needle inserted into corpus cavernosa on 3-way stopcock. Aspirate with 10mL syringe.
   - Irrigate with 10mL of 1:1,000,000 epinepherine solution (1mL of 1:1,000 in 1L of NS) while aspirating into 10mL syringe on 3-way stopcock until detumescence. (Alternative is a dilute solution of phenylepherine).
   - Withdraw needle and apply firm pressure for 5 minutes.
   - May repeat 3-4 times.
   - Admit for observation if aspiration and irrigation required.

B. Inpatient

1. Symptomatic
   - Fluids and analgesia (IV and/or PO)
   - Supplemental O_2 to keep SaO_2 >92%
   - PRN catheterization if unable to void
   - May need to keep patient NPO if possibility of line placement for erythrocytapheresis/exchange transfusion.

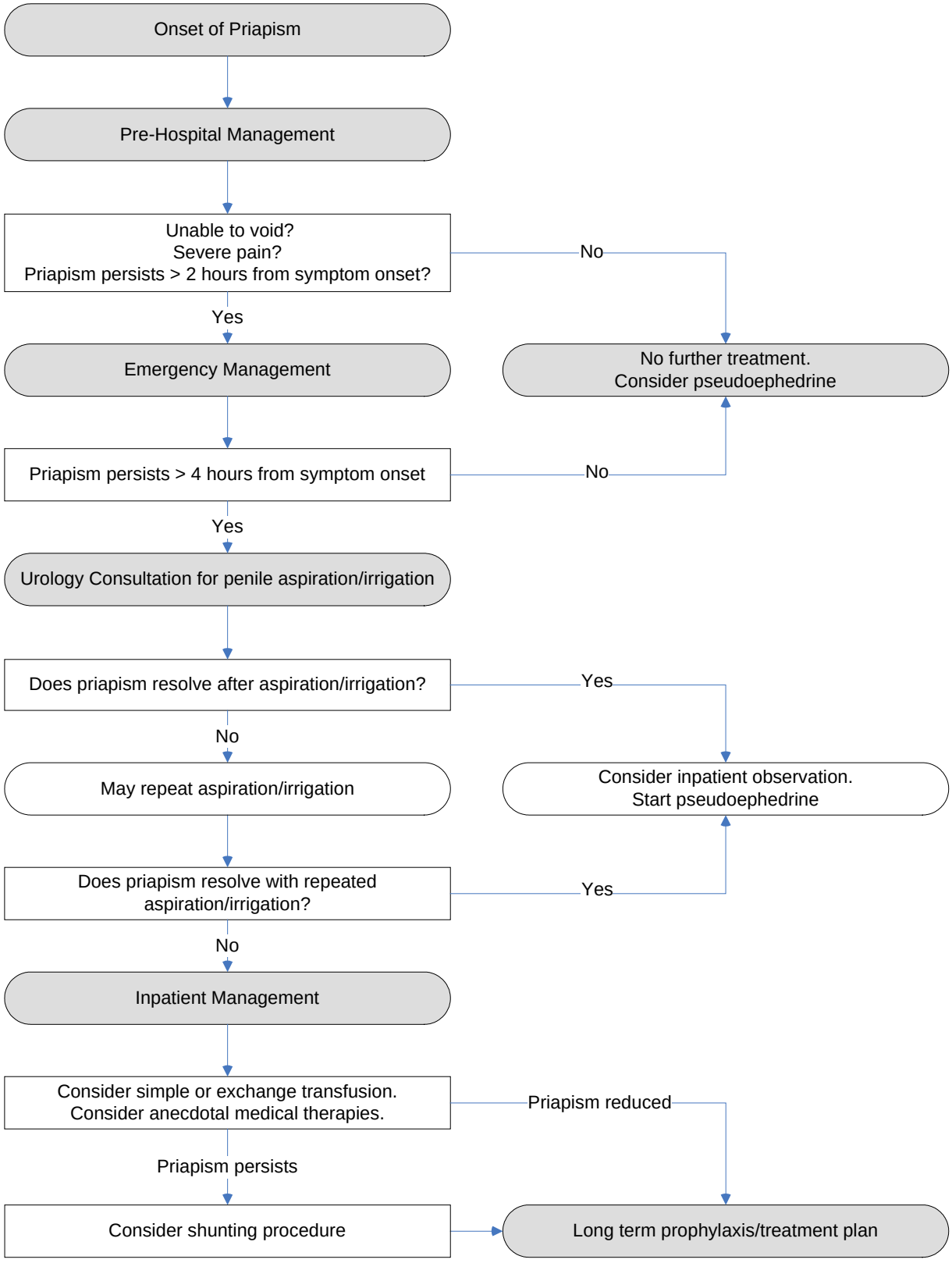
2. Pharmacological
   - Pseudoephedrine (See dosing in Appendix) [8]

3. Transfusion
   - Unclear if simple transfusion has any role, but do not transfuse Hb > 10g/dL/Hct > 30%. Transfusion may be appropriate prior to surgical intervention.
   - If no response to initial aspiration/irrigation, exchange transfusion or erythrocytapheresis has been shown to be effective in small series [14, 15] although not universally effective [16]. Goal final Hb 10g/dL and HbS% 30%.
   - There has been a reported association of SCA, priapism exchange transfusion and neurologic events (headache, seizure, obtundation, or stroke) called ASPEN syndrome [17, 18]. Therefore observe for neurological symptoms post exchange transfusion.

4. Urological
   - If not already performed, penile aspiration and irrigation with dilute epinephrine or phenylepherine may need to be repeated periodically.
   - Without detumescence after 24hours of medical therapy (supportive care, aspiration, irrigation and transfusions), surgical intervention/shunting may need to be performed.
   - Winter Shunt: a shunt is created between the corpus cavernosa and the glans penis allowing blood to drain into the uninvolved corpus spongiosa [19, 20]. Usually performed by inserting needles longitudinally through the glans into the corpus cavernosa, thus creating a fenestration in the fibrous albuginea.
   - If percutaneous shunting fails, open shunts between the corpus cavernosa and the corpus spongiosum, dorsal vein or saphenous vein have been described.
   - Complications of surgical intervention include infection, stricture, fistula and high risk of impotence.

5. Discharge Criteria
   - Able to void.
   - Penis more flaccid (swelling and/or edema may be present for several weeks)
   - Pain controllable on PO medications.
   - Consider addition of pseudoephedrine (See dosing in Appendix).

Flowchart for Evaluation and Management of Acute Priapism



III. Evaluation and Management of Chronic Priapism

Long-term management of patients with recurrent priapism requires collaboration between hematologists and urologists.

For all patients: Patient/family education, keeping pseudoephedrine in the home

If recurrent and/or severe: short term transfusion therapy (6-12months) has been recommended [1] though not clearly efficacious.

Other pharmacological approaches that have been described anecdotally or in small series:

- Hydroxyurea [12, 21, 22]
- Alpha-adrenergic agonists: Etileferine [23-26]
- Beta-adrenergic agents: Terbutaline [27]
- Pseudoephedrine [8]
- Sildenafil [28]
- GnRH antagonists (Leuprolide) [29]
- Stilbestrol [30]
- Hydralazine [31]

None of these has been tested in a randomized clinical trial with pediatric/adolescent sickle cell patients.

IV: Appendix

Pseudoephedrine dosing

< 12 y.o. 4mg/kg q24hours divided q6,

> 12 y.o. 30-60 mg/dose q6 hours (may convert to longer acting preparation)

Preparations of Pseudoephedrine

Sudafed 24 hour tablets	(240 mg)
Sudafed 12 hour tablets	(120 mg)
Sudafed tablets	(30 mg)
Children's Sudafed Chewables	(15 mg)
Children's Sudafed Liquid	(15mg/5ml)

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