Sexual Health Outcomes Improvement in SCD: A Matter of Health Policy?

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Overview

- Urgency of the problem and need for better solutions
- New perspectives on clinical management
- Improving outcomes: How it will get done

Significance of the Problem: Population Statistics

- 0.27% (1:365) of African-Americans (as much as 120,000 individuals) have sickle cell disease (SCD)[1]
- As much as 42% of males with SCD are afflicted by priapism[2-5]
- Actuarial probability of an individual with SCD experiencing priapism by 20 years of age is 89%

Priapism is a prevalent condition in the context of a specific population.

1. Hassell KL. Am J Prev Med 38 (4S):S512-21, 2010
2. Emond AM et al. Arch Intern Med 140:1434-7, 1980
3. Fowler JE Jr et al. J Urol 145:65-8-, 1991
4. Mantadakis E et al. J Pediatr Hematol Oncol 21:518-22, 1999
5. Adeyoju AB et al. BJU Int 90:898-902, 2002

Significance of the Problem: Health Economics

- Cost of health care for priapism in patients with SCD is unknown
- Medical expenditures for patients with SCD in general are substantial
  - 6- and 11- fold that of children without SCD enrolled in Medicaid and private insurance programs[1]
  - Lifetime cost averages $460,151 per patient with SCD[2]
- All figures of costs are likely underestimates when one considers financial losses associated with reduced quality of life, uncompensated care, lost productivity, and premature mortality for this population of patients

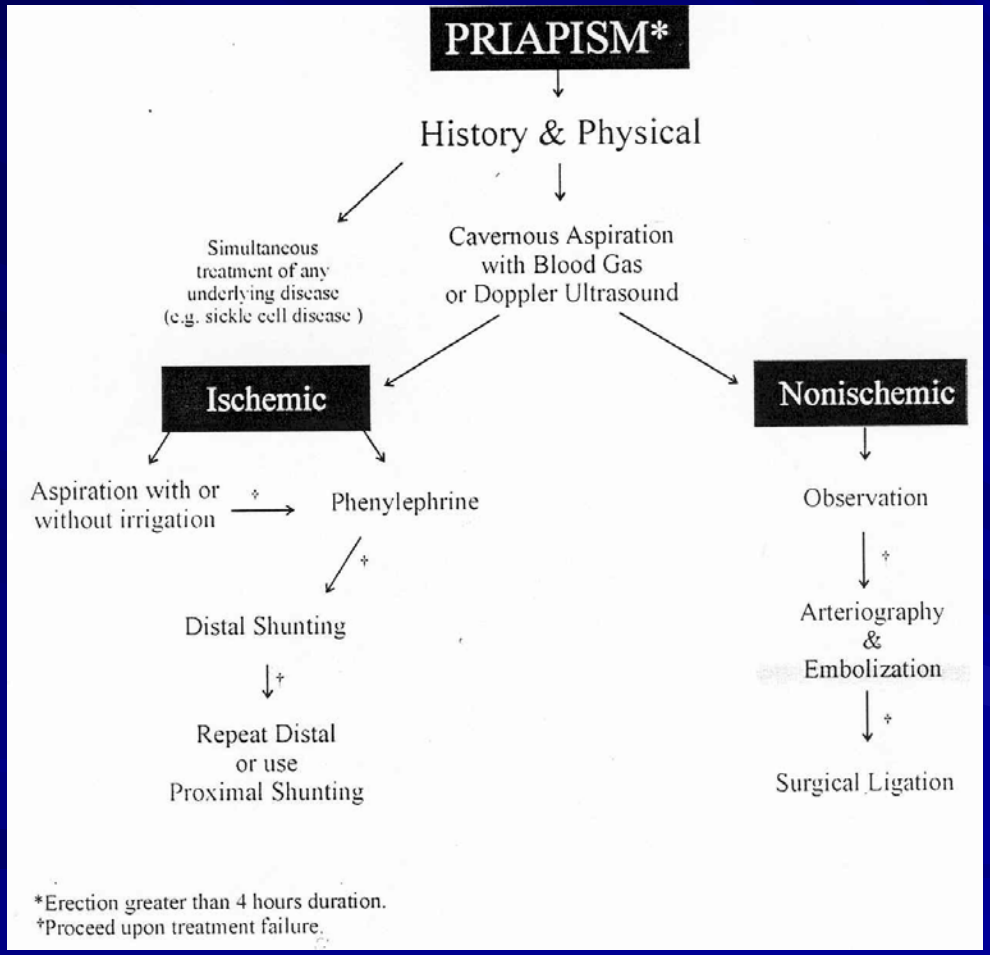
1. Amendah DD et al. Am J Prev Med 38 (4S):S550-6, 2010
2. Kauf TL et al. Am J Hematol 84:323-7, 2009

Significance of the Problem: Patient-Reported Health Burden

- Erectile impairment
  - 29% develop ED and 24% are unable to perform sexual intercourse satisfactorily[1]
- Psychosocial debilitation
  - One-third of boys report priapism as the worst complication of their disorder[2]

1. Adeyoju AB et al. BJU Int 90:898-902, 2002
2. Mantadakis E et al. J Pediatr Hematol Oncol 21:518-22, 1999

Management Algorithm for Priapism



Current Clinical Management Principles

Precept:	**Prompt recognition**
Approach:	**Reaction**
Actions:	**Serial procedures**
Objective:	**Resolution**

Revised Clinical Management Scheme

Precept:	**Prompt recognition**	→	**Universal precaution**
Approach:	**Reaction**	→	**Prevention**
Actions:	**Serial procedures**	→	**"Mechanism-specific" therapies**
Objective:	**Resolution**	→	**Functional preservation**

The future of priapism management calls for comprehensive, preventative care based on scientifically studied and supported interventions that maximally preserve intact erectile ability.

Keys to "Getting It Done"

- Scientific discovery
- Public health policy
- Medical consensus statements/guidelines

PDE5 Dysregulation

Adenosine Deaminase Deficiency

Opiorphin Overexpression

Molecular Mechanisms of Recurrent Ischemic Priapism in Sickle Cell Disease

Others?

Nitric Oxide/ Oxidative Stress Imbalance

Bivalacqua TJ, Burnett AL. Curr Urol Rep 7:497-502, 2006
Yuan J et al. Asian J Androl 10:88-101, 2008
Broderick GA et al. J Sex Med 7:476-500, 2010

Future Therapeutic Advances: Bench to Bedside

- Scientific discovery valued and supported
- Translational approach for advancing therapeutics
- Rigorous assessments are needed and ideally done (randomized, controlled clinical trials)

Priapism Prevention Program for Patients with Sickle Cell Disease: An Example

- Programs: NIH/NHLBI, Comprehensive Sickle Cell Centers (U54)
  - Collaboration with hematology group at Johns Hopkins Hospital
- Research Plan
  - Clinical trial component
    - Randomized, double-blind, placebo-controlled trial (sildenafil 50mg daily v. placebo)
    - Evaluations include priapism/erection questionnaires, Rigiscan monitoring
  - Mechanistic study component
    - Evaluations include biomarkers of inflammation, oxidative stress and endothelial function/dysfunction

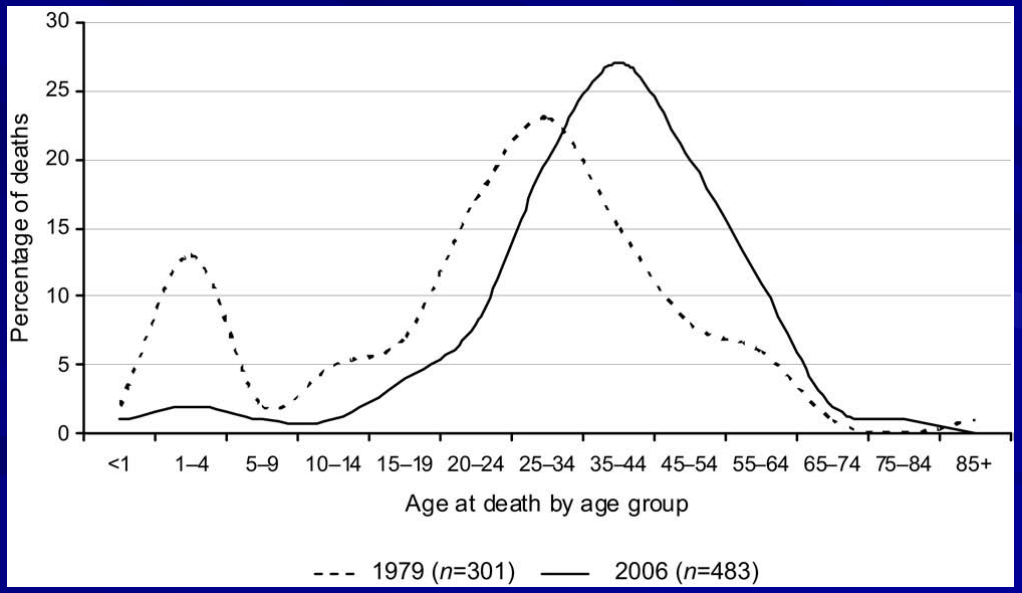
Public Health Policy: Prevention Strategies

- Primary Prevention (preventing the disease from occurring)
  - Carrier screening
  - Genetic counseling
- Secondary Prevention (providing early detection and preclinical intervention)
  - Newborn screening
  - Penicillin prophylaxis
  - Parental education
- Tertiary Prevention (minimizing the effects of the disease)
  - Blood transfusions
  - Daily folic acid supplementation
  - Analgesic administration
  - Bone marrow transplantation??
  - Gene therapy??

Olney RS. Am J Prev Med 16:116-21, 1999
Grosse SD et al. Applied Health Econ Health Policy 4:239-47, 2005

Impact of Prevention Strategies

- Key Developments
  - 92nd Congress of the U.S. enacted the national Sickle Cell Anemia Control Act of 1972
  - This law called for grant support for voluntary screening and counseling programs
  - Federal agency guidelines followed, e.g., NIH publications on SCD treatment, CDC standards for hemoglobinopathy laboratories
- Effectiveness measured (decreased morbidity and mortality rates from SCD)



Olney RS. Am J Prev Med 16:116-21, 1999
Hassell KL. Am J Prev Med 38 (4S):S512-21, 2010

SCD Life Expectancy and Treatment Highlights

Year	Life Expectancy, y	Advances
1949		Sickling of red blood cells attributed to hemoglobinopathy
1970	10–12	National Association for Sickle Cell Disease established (presently, Sickle Cell Disease Association of America)
1972		National Sickle Cell Anemia Control Act passed, funding 15 comprehensive sickle cell centers
1975		First statewide newborn screening implemented
1978		Cooperative Study of Sickle Cell Disease begun
1980	20–22	
1986		Prophylactic penicillin proven effective in preventing pneumococcal infection
1990	30–35	
1995		Hydroxyurea treatment found to decrease complications in adults
1996		Bone marrow transplantation found effective at curing sickle cell disease
1997		Stroke Prevention Trial study demonstrates effectiveness of screening and transfusion therapy
2000	40–45	Heptavalent pneumococcal vaccine introduced
2001		Corrected SCD in transgenic mouse model by gene therapy
2004		Sickle Cell Treatment Act[47] passed, providing funding for 40 sickle cell disease treatment centers, the establishment of a National Coordinating Center, and federal matched funds for genetic counseling and education

Smith LA et al. Pediatrics 117:1763-70, 2006

Gaps Persist in Public and Private Funding

Variable	SCD	Cystic Fibrosis
US prevalence[a]	80 000	30 000
Federal support		
NIH fiscal-year 2004 funding, in millions of dollars[b]	90	128
NIH funding per person with disease, $	1125	4267
No. of federal grants		
No. of grants funded in 1968[c]	22	65
No. of grants funded in 1972, after Sickle Cell Anemia Control Act[d]	215	80
No. of grants funded in 2004	331	459
Private philanthropic support, $		
Cystic Fibrosis Foundation 2003 annual revenue[e]		152 231 000
Sickle Cell Disease Association of America 2003 annual revenue,[f]	498 577	
Revenue per person affected with disease	6	5074
Total NIH and private support, in millions, $	90.4	280.2
Total support per person affected with disease, $	1130	9340

Smith LA et al. Pediatrics 117:1763-70, 2006

Health Policy Recommendations

- Increase the function of the established 40 SCD treatment centers (National Coordinating Center)
  - Coordination and distribution of data
  - Implementation of best practices
  - Development of educational materials and model protocols for the prevention and treatment of SCD
- Enhance the diffusion of clinical advances (Health Resources and Services Administration)
  - Employment of the clinical patient registry, for collection and dissemination of data on clinical care and outcomes
- Promote the funding priority for the implementation of equity and quality of scientific advances in clinical care for SCD (NIH and the Agency for Healthcare Research and Quality)

Smith LA et al. Pediatrics 117:1763-70, 2006

Conclusions

- Interventions designed to reduce priapism, as for all SCD complications, may reduce the significant economic and individual health burden of the disease.
- New clinical management schemes that acknowledge the prevalence of priapism in SCD and rationally provide "tertiary" prevention offer the best opportunities for erection preservation and general health maintenance.
- Sexual medicine specialists must galvanize the urologic community, the AUA, other medical organizations, societal health groups, and government agencies, to support efforts to advance the scientific field, enact public health initiatives, and derive guidelines for the effective management of priapism.