Pravin Rao, MD
Assistant Professor of Urology
Director of Male Reproductive Medicine and Surgery
Johns Hopkins Hospital

July 27, 2013

XXY AND FERTILITY

XXY Fertility at a Glance

• ~ 5% have few sperm (Require A.R.T.)
• ~ 95% have zero sperm (Azoospermia)
• Sperm retrieval techniques
  – Mapping
  – TESE (Testicular sperm extraction)
  – microTESE (Microdissection TESE)

Assisted Reproductive Technologies (ART)

• Performed by Reproductive Endocrinologists
• ART Options:
  - IUI
  - IVF
  - ICSI
Assisted Reproductive Technologies (ART)

- Performed by Reproductive Endocrinologists
- ART Options:
  - IUI
  - IVF
  - ICSI


Assisted Reproductive Technologies (ART)

- Performed by Reproductive Endocrinologists
- ART Options:
  - IUI
  - IVF
  - ICSI

XXY Fertility at a Glance

- Hormone therapy - May increase or decrease sperm production:
  - Testosterone
  - Anastrozole
  - Clomiphene Citrate
  - hCG
  - hMG / rFSH

XXY Fertility at a Glance

- Questions (What we don’t know):
  - Optimal time for sperm collection / retrieval procedures
  - Predictors for successful sperm retrieval
  - Optimal hormone treatment schedule for fertility preservation
  - Role for new and improved hormone modulators

(More on Infertility at 1:30pm session)
The Johns Hopkins Klinefelter Syndrome Center

Introduction and Concepts
of the Multidisciplinary Clinic

Harry Klinefelter, MD
• Johns Hopkins School of Medicine 1937
• Johns Hopkins Residency 1940
• Massachusetts General Hospital 1941-1942
  – Worked under Fuller Albright
• Armed Forces 1943-1946
• Johns Hopkins Faculty 1947-1988

Harry Klinefelter, MD
• 1942, described “gynecomastia, aspermatogenesis without aleydigism, and increased excretion of follicle-stimulating hormone.”

  “These patients often have an entirely normal appearance save for their small testes, and I am sure many escape detection.”
Outline:

• Goals of the Center
• The Team
• The Multidisciplinary Approach

Goals of the Center:

– Develop standardized testing procedures for this population
– Develop treatment guidelines for men with sex chromosomal disorders
– Expand the scientific knowledge on the diagnosis, pathophysiology and treatment of the syndrome
Outline:

• Goals of the Center

• The Team

• The Multidisciplinary Approach

The Team:

Adult Endocrinology:
Adrian Dobs, M.D., M.H.S.

Pediatrics / Puberty:
David Cooke, M.D.

Urology (Infertility, Sexual function):
Pravin Rao, M.D.

Neuropsychology (Cognition, Mood):
Cynthia Munro, Ph.D., ABPP(CN)

Primary Care (Preventive / General):
Vinayak Kottoor, M.D.

Genetic Counseling:
Cathleen Lawson, MS, GSC

Psychology (Gender identity, Sexuality):
Chris Kraft, Ph.D.

David W. Cooke, M.D.

• Clinical Director, Pediatric Endocrinology, Johns Hopkins University School of Medicine

• Specialty in XXY
  • Management of puberty in XXY adolescents
Adrian Dobs, M.D., M.H.S.

- Professor of Medicine, Division of Endocrinology, Diabetes and Metabolism
- Vice-chair, Department of Medicine
- Specialty – Testosterone replacement therapies, Osteoporosis, Diabetes

Role in XXY Care

- Evaluation of adults ≥18 years of age and older
  - Review of medical history and physical examination to determine sex hormonal status
  - Interpretation of hormone blood tests
  - Determination of any complications of low testosterone such as osteoporosis or diabetes
- Testosterone treatment
  - Discussion of need for treatment
  - Assist in the decision on the testosterone options
  - Plan appropriate follow-up

Research Questions / Interests:

- Complications of testosterone deficiency in men with KS
- Sex hormones in men with chronic diseases, such as diabetes and cancer
- Understanding the benefits of testosterone treatment in men with KS
Vinayak Kottoor, MD

- Instructor, General Internal Medicine, Johns Hopkins Hospital
- Board Certification – Internal Medicine, Pediatrics, and Clinical Genetics

Role in XXY Care

- Primary-care / General-medical-care concerns:
  - Pediatric to Adult care transitioning
  - Preventive care concerns

Research Questions / Interests:

- Ways in which genetic diagnoses inform the provision of primary care.
- Provider education in the incorporation of genetic principles into medical care.
Chris Kraft, Ph.D.

- Co-clinical director, Johns Hopkins Sexual Behaviors Consultation Unit
- Gender identity and sexual functioning

Role in XXY Care

Psychological Support:

- Identity and sexuality
  - Gender identity concerns
  - Body/genital image concerns
  - Sexual functioning
  - Sexual relationships
- Psychotherapy
  - Mood disorders
  - Addictive behaviors
  - Family Therapy

Cathleen Lawson, MS

- Assistant Professor
  Department of GYN/OB
- Genetic counseling
Role in XXY Care

• Provide genetic counseling to assist with
  – Education about inheritance, testing, management, resources and research
  – Adaptation to diagnosis
  – Reproductive decision-making

• Genetic counseling is appropriate for parents of a child with XXY and for adults with XXY.

Cynthia Munro, Ph.D., ABPP(CN)

• Associate Professor of Psychiatry, Division of Medical Psychology, Johns Hopkins Hospital

• Board certified in clinical neuropsychology

• Specialty in XXY – Influence of hormones on cognition and mood; social aspects of the XXY diagnosis to men and their families

Role in XXY Care

• Neuropsychological assessment of adolescents and adults
  – Extensive record review
  – Clinical interview
  – Formal assessment of cognition, adaptive functioning, psychiatric symptoms, and personality characteristics
  – Diagnostic formulation
  – Treatment recommendations, with specific referrals if requested

• Patient and family education
Research Questions / Interests:

- Determination of characteristics that are specific to KS rather than co-incident with KS
- Cognitive and emotional effects of testosterone treatment in men with and without psychiatric (e.g., mood) disorders

Pravin Rao, MD

- Director, Male Reproductive Medicine and Surgery, Johns Hopkins Hospital
- Specialty in XXY:
  - Infertility
  - Sexual Function

Role in XXY Care

- Navigate Fertility Considerations of Hormones:
  - Effects of medications on sperm production
  - Timing with surgical intervention
  - Fertility preservation approaches
- Retrieval Procedures:
  - micro TESE (Sperm Retrieval for ART)
  - Tissue for Stem Cell Preservation
Research Questions / Interests:

• Timing of hormonal interventions
• Age/Timing of surgical intervention
• Medical optimization before attempted sperm retrieval

Outline:

• Goals of the Center
• The Team
• The Multidisciplinary Approach

Multi-disciplinary Approach

• Patients are scheduled through Hopkins USA
• Priority scheduling so that XXY patients can see all relevant specialists within the same week if possible
• After one specialist sees a patient, he or she communicates any relevant information (need to order additional tests, etc.) to the other members of the center who will also be seeing the patient
Multi-disciplinary Approach

- After all examinations are completed, specialists who have seen a particular patient have a conference to discuss their results and how they may relate to each others’ treatment recommendations

- Patients get written reports that can be shared with their treating physicians

- Differences in care between adults and children.