

Pravin Rao, MD  
Assistant Professor of Urology  
Director of Male Reproductive Medicine and Surgery  
Johns Hopkins Hospital  
July 27, 2013  
**XXY AND FERTILITY**

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**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)

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**Assisted Reproductive Technologies (ART)**

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

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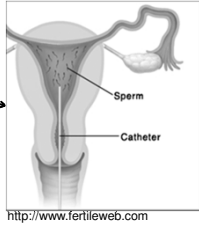
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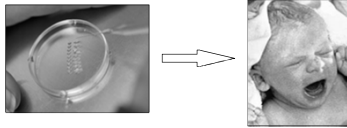
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Step toe, Edwards, Purdey, Br. J Ob/Gyn, 87:757, 1980

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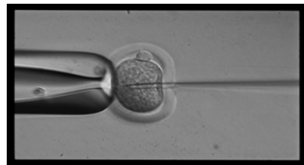
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Palermo, et al, Lancet, 340:17, 1992

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**XXY Fertility at a Glance**

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

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**XXY Fertility at a Glance**

- Questions (*What we don't know*):
  - Optimal time to 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)

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**The Johns Hopkins  
Klinefelter Syndrome Center**  
  
*Introduction and Concepts  
of the Multidisciplinary Clinic*

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**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

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**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.”

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**Outline:**

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

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**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

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### Outline:

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### The Team:

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

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

Pediatrics / Puberty:  
**David Cooke, M.D.**

Genetic Counseling:  
**Cathleen Lawson, MS, GSC**

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

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

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

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### David W. Cooke, M.D.

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

- Specialty in XXY
  - Management of puberty in XXY adolescents




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**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




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***Role in XXY Care***

- Evaluation of adults  $\geq 18$  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

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***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

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**Vinayak Kottoor, MD**

• Instructor, General Internal Medicine, Johns Hopkins Hospital

• Board Certification – Internal Medicine, Pediatrics, and Clinical Genetics



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*Role in XXY Care*

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

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*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.

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### Chris Kraft, Ph.D.

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




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### *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

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### Cathleen Lawson, MS

- Assistant Professor  
Department of GYN/OB
- Genetic counseling




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*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.

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**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




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*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

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*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

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Pravin Rao, MD

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




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*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

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*Research Questions / Interests:*

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

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**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

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## 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.

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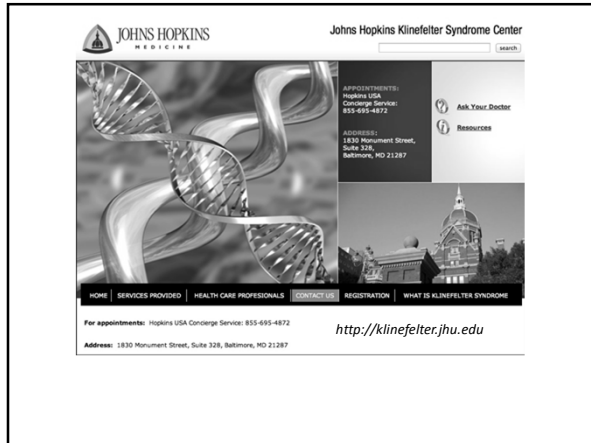
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