The American Association for Klinefelter Syndrome Information and Support

Here we come!

The 2001 AAKSIS National Conference
Friday, August 3 thru Sunday, August 5
at the Philadelphia Airport Marriott Hotel
One Arrivals Road
Philadelphia, Pennsylvania 19153

There is still time to reserve a spot at the AAKSIS conference. AAKSIS has planned the most ambitious meeting ever to address issues relating to Klinefelter Syndrome. Highlights of this year’s meeting include: updates on NIMH’s ongoing brain studies; medical management of Klinefelter Syndrome; related health issues for 47XXY adults; medical issues of 47XXY for boys and adolescents; early childhood developmental findings in 47XXY; psychiatric and emotional issues that can be related to 47XXY; anger management issues in the adolescent; gynecomastia and its treatment…… and much more. Support, discussion, and networking groups for parents of young children, parents of adolescents, adult XXY’s, XXY wives and significant others, and gay and bisexual adult XXY’s.

(Please note: We also welcome and encourage any and all variations of this condition such as XXYY, XXXY, XYY, etc. to join us at this conference and the AAKSIS organization.)

Genetic Diagnosis in Adulthood—A Case Report

Carl V Tyler Jr MD; Paul A. Kungl MD; and Laura A. Green PhD
Cleveland, Ohio (Reprinted with permission)

While family physicians may readily entertain genetic diagnoses in their pediatric patients, they may fail to consider such diagnoses in their adult patients. We present the case of a man with recurrent leg ulcers who was recognized as hypogonadal and was ultimately given the diagnosis of Klinefelter’s syndrome (XXY) at age 47. Although there is no primary treatment for XXY, significant associated conditions, including osteoporosis and testosterone deficiency, can be ameliorated. We review the clinical condition of XXY at various ages and summarize age-specific interventions. We discuss the importance of genetic diagnosis throughout the life span.

Key Words. Family practice; genetics; hypogonadism; genetic screening. (J Fam Pract 1998; 47:227-230)

With continued progress in clinical genetics, family physicians can assist in the recognition and diagnosis of genetic conditions in their patients. At present, the incidence of single gene disorders at birth is estimated to be 1 in 100; that of chromosomal disorders is estimated to be 1 in 150.1 Many adults with genetic conditions grew up before their disorder had been characterized, or before the means to diagnose the condition were developed. The following case study illustrates the potential benefits and complexities involved in genetic diagnosis in adulthood.

CASE REPORT

A 47-year-old man was hospitalized with deep venous thrombosis of the left leg 3 weeks after arthroscopic knee surgery. He had a 10-year history of recurrent venous stasis ulcers. While on hospital rounds, the attending physician observed that the patient had a boyish-looking face with a paucity of facial hair, which prompted speculation about possible hypogonadism.

Further evaluation of his eunuchoid facial appearance was performed after hospital discharge. The patient was six feet tall and weighed 270 pounds. He had gynecomastia a penis 2 1/2 cm in length, and small testicles measuring 1 cm by 2 cm. Hypogonadism was confirmed by laboratory testing, with free testosterone 0.24 nmol/L (5.5-11.5) and total testosterone of 0.52 nmol/L (10.4-30.8). This was clarified as hypergonadotrophic hypogonadism by follicle stimulating hormone (FSH) level of 26.7 mIU/mL and leutenizing hormone (LH) level of 10.3 mIU/ml. Chromosomal karyotype revealed 47,XXY pattern.

See page 3
AAKSIS
2945 West Farwell Ave.
Chicago, Illinois 60645-2925

AAKSIS is a non-profit, volunteer organization dedicated to meeting the need and challenges of the 47XXY/Klinefelter Syndrome community.

Directors
Roberta Rappaport, President
Margaret Garvin, Vice President
Michael Schwarz, Treasurer
Dalene Basden, Minority Outreach
Daniel Becker
Wendy Becker
Virginia Cover
Mary Davidson, The Genetic Alliance
Preston Garvin
J. Giedd, M.D.
Vaughn Hambley
Wolfram E. Nolten, M.D.
Stefan Schwarz

KaleidoScope is a publication of AAKSIS, the American Association for Klinefelter Syndrome Information and Support.

AAKSIS is a non-profit organization dedicated to promoting understanding and awareness of 47XXY/Klinefelter Syndrome and to the support of individuals and families affected by this condition.

KaleidoScope is published three times a year and is free to members of AAKSIS. Articles in this newsletter may not be reprinted without permission from the editor. Inquiries can be made to: Margaret Garvin, Editor 7109 Stilson Court Columbus, Ohio 43235 email: XXYnetohio@aol.com

AAXS Announces Newest Board Member

Virginia Cover, MSW, MBA was recently appointed to the AAKSIS Board of Directors. Ginnie has been a healthcare administrator for 20 years and currently serves as Executive Director of Mid-Suffolk Pediatrics, a group practice of 27 pediatricians on Long Island, New York.

Active in special education advocacy, Ginnie was recently a member of her school district’s task force to expand inclusion programs in its secondary schools. She is also a volunteer with the newly created Cody Center for Autism and Developmental Disabilities at the State University of New York—Stoney Brook. Currently they are developing a series of continuing education programs in developmental disabilities for pediatricians.

Ginnie and her husband, Albert, live on Long Island. They are the parents of two sons. Their oldest is a junior at the University of Michigan. Their younger son was diagnosed 47XXY prenatally and began receiving early intervention services at 15 months. He is an avid violinist and chess player.
Cont. from page 1

Testosterone replacement was instituted with two 2.5 mg transdermal patches, applied nightly. After 3 months of therapy, the patient noted no significant changes in energy level, strength, mood, or sleep requirements. He did note increased libido and increased frequency of erections occurring with sexual fantasy.

Because of the XXY diagnosis, bone-mineral density testing was performed and revealed osteopenia of the fourth lumbar vertebra and of the femoral neck of the left hip. He began treatment with calcium 1500 mg daily, vitamin D 400 IU daily, and osteoclast inhibition therapy with alendronate 10 mg daily.

Psychosocial information relevant to the XXY diagnosis was obtained over subsequent office visits. The patient had been married twice; each marriage lasted less than 1 year. The second marriage ended 17 years ago because of his wife’s drug use and marital infidelity. His second wife bore a son during their marriage. After the divorce she and the child moved out of state and the patient has had infrequent contact with his son. The patient had always wondered about the boy’s true paternity but continued to pay child support. The XXY diagnosis forced him to confront the issue of the boy’s paternity once again. He ultimately decided to keep his XXY diagnosis from his ex-wife and their son, but would consider disclosing it if she ever requested an increase in the child support payments.

Within the past year he had been involved in another heterosexual relationship. After he developed difficulties in maintaining erections, the couple ceased the physical aspects of their relationship, but maintained their friendship. This occurred prior to the XXY diagnosis. The patient was hopeful that testosterone replacement therapy would improve his sexual functioning and allow a resumption of the sexual relationship.

During the office visits following diagnostic disclosure, the primary physician was surprised at the calm acceptance the patient exhibited toward the diagnosis. He expressed no shame or guilt, but was relieved that medical diagnosis provided an explanation for his vague sense of feeling “different” from other persons. The patient found information about XXY obtained by his physician from the internet extremely helpful in understanding his condition.

Additional developmental and psychoeducational history was obtained during a conjoint meeting with the patient and his widowed mother. His mother recalled no developmental delays or guilt that in some way she had caused his son’s condition. She was relieved to learn that they each privately questioned his son’s condition. She was relieved to learn that XXY occurs sporadically, unrelated to maternal antenatal behaviors.

Over the next year, the patient has maintained good psychological adjustment to his diagnosis. He has declined any intensive psychological evaluation or support. As evidence of his low bone-mineral density, a minor fall resulted in a fracture of his patella, requiring intraoperative repair. He has had no recurrence of leg ulcers since beginning the testosterone supplement.

TABLE 1

Recognition, Diagnosis, and Management of XXY

<table>
<thead>
<tr>
<th>Recognition, by age</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toddler</td>
<td>Developmental speech delay</td>
</tr>
</tbody>
</table>
| Grade school             | Learning disabilities, "problems with immediate memory, auditory processing"
|                          | Attention Deficit Disorder                    |
| Adolescent               | Gynecomastia                                  |
|                          | Psychosocial maladjustment                    |
| Adult                    | Persisting Infertility                         |
|                          | Small testes                                  |
| Diagnosis, by test       | Results                                       |
| Serum testosterone       | Decreased or normal                           |
| Serum FSH                | Elevated                                      |
| Serum LH                 | Normal to elevated                            |
| Karyotype                | 90% have classic XXY                         |
| Management, by problem   | Comments                                      |
| Testosterone deficiency  | Replace with transdermal testosterone; adjust dosage according to serum testosterone levels |
| Risk for osteoporosis    | Screen with bone-mineral density test; assure optimal calcium and vitamin D intake |
| Risk for breast cancer   | Instruct in breast self-exam                  |
| Risk for autoimmune disorders | Screen for diabetes mellitus and hypothyroidism |

FSH denotes follicle-stimulating hormone; LH luteinizing hormone.
**DISCUSSION**

Approximately 1 in 500 males have the XXY chromosomal complement. As with many chromosomal conditions, the phenotypic expression on XXY is variable. The full syndrome identified by Dr. Harry Klinefelter (gynecomastia, testicular atrophy, azoospermia, and sparse facial and body hair) is not found in the majority of XXY males. For this reason, the term “XXY males” has replaced the term “Klinefelter’s syndrome.”

As in our patient, XXY males may not be diagnosed as such until adulthood, if at all. The family physician needs to recognize features of XXY that might present at different ages. Table I summarizes in a developmental fashion the recognition, diagnosis, and management of XXY.

The most consistent physical feature of XXY is small testes, typically measuring less than 2 cm to 3 cm in their longest axis. Phallus size may also be decreased. Diminished pubic and facial hair is common. They have a diminished upper-to-lower segment ratio (crown-to-pubis height is less than pubis-to-floor height).

The laboratory evaluation of an adult suspected to be XXY begins with determination of serum testosterone, FSH, and LH. Since the degree of Leydig cell damage in XXY is variable, serum testosterone and virilization in some individuals may be normal. More consistently, the FSH level is elevated. Chromosomal confirmation of XXY is important to distinguish variant syndromes from pure XXY. These variants include 46,XY/47,XXX; 46,XXXXY; and 46,XX males, termed sex-reversal syndrome. 3

Characteristically, most XXY males are azoospermic and infertile. However, XXY males should not assume they are infertile without semen analysis. Mosaic individuals with 46,XY/47,XXX have variable phenotypic expression; some have preserved testicular function. 4

XXY males suffer an increased risk for autoimmune disorders, including type I diabetes, autoimmune thyroiditis, and systemic breast cancer (estimated 20- to 50-fold). 5 There also appears to be an association with lymphoma, leukemia, bladder cancer, and primary mediastinal germ cell tumors. As in our patient, XXY males are predisposed to leg ulcers. 6, 7 Physicians need to consider XXY in young men who present with chronic leg ulcers. 8

Adults with XXY should undergo bone-mineral density testing because of the increased risk for osteoporosis, although in early adulthood, bone-mineral density may be normal. 9 Testosterone replacement alone may not normalize low bone-mineral density. 10

XXY males should be offered testosterone replacement at the onset of puberty. Testosterone replacement will promote the development of muscle mass, strength, and facial and body hair. It may assist, with psychological adjustment through improved body image as well and mood enhancement. 11

Options for testosterone replacement now include transdermal products, as well as earlier oral and intramuscular forms. The transdermal products eliminate the nonphysiologic hormonal peaks and troughs associated with the other forms. Not surprisingly, some patients report fewer mood swings associated with the transdermal products. 12

Regardless of age at diagnosis, XXY males should be evaluated for the presence of specific learning disabilities and for negative self-appraisal. Psychoeducational assessment is available through public school systems for any school-age child. Adults can be evaluated through hospital-based learning clinics or by psychologists, learning specialists, and speech therapists in outpatient settings. Comprehensive psychoeducational evaluation for XXY males should include tests of genetic intelligence, academic achievement, oral and written language, and memory and auditory processing. Identification of specific learning disabilities can lead to individualized educational programming and occupational training at any age.

According to Francis Collins, director of the National Human Genome Research Institute, “...the responsibilities for use and interpretation of genetic tests increasingly will fall to primary care clinicians.” 13 Although we have had the ability to detect XXY by chromosomal karyotyping for several decades, this case exemplifies the expanding role that primary care physicians will be playing in the identification of genetic conditions, the utilization of genetic tests, and the medical care of persons with genetic conditions. As caregivers for patients throughout their life spans, family physicians need to consider the possibility of genetic conditions in patients of all ages, not only their pediatric patients. For this reason, it is important to familiarize oneself with the more common genetic diagnoses that may evade diagnosis in childhood, such as Fragile X, Marfan syndrome, and neurofibromatosis.

A recent survey assessed the knowledge of primary care physicians regarding medical genetics and genetic tests. One-third of respondents failed to correctly identify the mode of inheritance from a pedigree. The authors of this survey recommended that curriculum planners specifically ensure that primary care resident physicians become skilled in the interpretation of probabilistic results and the counseling of patients. 14

There is some evidence that commercially available gene tests are not fully understood by those physicians who order them. For example, in a nationwide sample of physicians who ordered adenomatous

![TABLE 2](http://www.medhelp.org/www/agsq.htm)

**Internet Addresses of Genetic Resources for Patients and Families**

- http://www.pcnetcom/~orphan/ (National Organization for Rare Disorders)
- http://www.familyvillage.wisc.edu/coffee.htm (The Family Village Coffee Shop)
- http://www.waisman.wisc.edu/~rowley/mums/home.html (MUMS National Parent-to-Parent Program)
polyposis coli gene testing (for a genetic mutation associated with colorectal cancer), telephone interviews by the commercial laboratory performing the test revealed that 31% of physicians misinterpreted the test result.

XXY resembles many other genetic conditions in its variable phenotypic expression of physical, cognitive and behavioral characteristics. Family physicians may be less familiar with the cognitive and behavioral aspects of genetic disorders compared to the medical aspects. In the case of XXY family physicians are probably more familiar with the associated features of hypogonadism and infertility and less familiar with the associated learning and psychosocial difficulties. The Internet can be a valuable tool for supplementing purely medical sources of information. Through the Internet, patients with genetic conditions, their families, and their primary care physicians can locate relevant lay and professional organizations obtain patient education materials written in clear, nontechnical language, and link with other persons and families with the same condition (Table 2).

Much of the literature advising physicians about how to “break bad news” sensitively is readily applicable to the context of disclosing a genetic disorder. Patient response to diagnostic disclosure may range from grateful relief from anxiety and uncertainty to intense feelings of guilt or shame. Table 3 summarizes tactics that family physicians might employ in alleviating guilt or reducing shame when disclosing a genetic diagnosis.

Physicians may need to self-examine their attitudes toward persons with genetic conditions. They need to identify their patients’ strengths and competencies, as well as their limitations and health risks.

In our patient, earlier genetic diagnosis may have prevented osteoprotic fracture, recurrent leg ulcers, and financial exploitation related to misattributed paternity. Less tangible, though no less important, benefits of diagnosis included the psychological sense of closure provided to our patient, and the though no less important, benefits of diagnosis included the psychological sense of closure provided to our patient, and the knowledge that genotypic screening can aid in recognizing and treating conditions. They need to identify their patients’ strengths and competencies, as well as their limitations and health risks.

In our patient, earlier genetic diagnosis may have prevented osteoprotic fracture, recurrent leg ulcers, and financial exploitation related to misattributed paternity. Less tangible, though no less important, benefits of diagnosis included the psychological sense of closure provided to our patient, and the relief of his mother’s guilt that she somehow caused his condition. Although earlier diagnosis is ideal, benefits can be accrued when genetic diagnoses are made well into adulthood. Family physicians need to recognize the value in making such diagnoses throughout the life span.

Table 3

Counseling Strategies Relating to Genetic Diagnosis

<table>
<thead>
<tr>
<th>Guilt-Alleviating Tactics</th>
<th>Shame-Reducing Tactics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use professional authority: “You took all the necessary precautions.”</td>
<td>Develop a working alliance which is nonjudgmental and accepting</td>
</tr>
<tr>
<td>Normalize patients feelings: “Others in your position would feel similarly.”</td>
<td>Evoke feelings and respond empathetically</td>
</tr>
<tr>
<td>Reframe perceptions and actions to ones with less distressful meanings</td>
<td>Accentuate the positive: identify strengths and competencies</td>
</tr>
<tr>
<td>Limit liability: “You are responsible for A, but not B.”</td>
<td>Reward with praise</td>
</tr>
</tbody>
</table>


We thank Carla Kungl, MA, for her assistance in the preparation of this manuscript; Kathryn Gaughan, for her secretarial assistance.

**DISTINGUISHED PRESENTERS**

- **Mary Davidson MSW**  
  Executive Director of the Alliance of Genetic Support Groups, Washington, DC, and currently represents consumers and families on the Secretary’s Advisory Committee on Genetic Testing.
- **Daniel Davis PhD**  
  Psychologist specializing adolescent and adult issues. Author of “The Aggressive Adolescent: Clinical and Forensic Issues.” Consultant with Columbus Children’s Hospital Guidance Center and an Associate Professor at Ohio State University, Columbus, Ohio
- **Jay Giedd MD**  
  Chief of the Brain Imaging Unit, National Institute of Mental Health, Child Psychiatry Branch, Bethesda, MD where he conducts research on the biological basis of behavioral, cognitive, and emotional disorders of children. Currently he is using MRI to explore brain development in Klinefelter Syndrome.
- **Wolfram Nolten MD**  
  Endocrinologist and currently Associate Professor of Medicine, Division of Endocrinology, Diabetes, and Metabolism, University of Wisconsin Medical School, Madison, Wisconsin. Frequent presenter on various aspects of Klinefelter Syndrome and one of the founding members of AAKSIS
- **Jefferson Prince MD**  
  Child Psychiatry, Massachusetts General Hospital, Boston, Massachusetts
- **Arturo Rolla MD**  
  Endocrinologist, Beth Israel Deaconess Hospital, Associate Professor, Harvard Medical School, Boston, Massachusetts
- **Carole Samango-Sprouse ED D**  
  Director of Infant and Child Studies, Dept of Medical Genetics, Children’s National Medical Center. Director of the Neurodevelopmental Diagnostic Center for Young Children, Davidsonville, Maryland. Author of over thirty-five articles on the neurocognitive capabilities of atypical children
- **Stephen Woodside JD**  
  Trial attorney with a special interest in Educational Law
- **Tammie Weaver MA**  
  Speech Pathologist, Good Shepherd Rehabilitation, Allentown, Pennsylvania
- **Lois Walden, RN BSN**  
  Northwest Hospital Center, Baltimore, MD. Member of the Community Education Department. Writes "Stress Busters" for the LifeBridge Health Newsletter. Frequent presenter on a variety of health subjects, including "Laughter in Medicine--Humor and Health"
- **William Zipf MD**  
  Pediatric Endocrinologist, Ohio State University/Children’s Hospital Medical Center. Head of Central Ohio Pediatric Endocrinology, Columbus, Ohio.
- **Robert Bock**  
  Journalist, NIH, and author of the booklet, “Understanding Klinefelter Syndrome.” Featured luncheon speaker and recipient of the AAKSIS Achievement Award in Publications.

**Update to our list of presenters**

Michael A. Bermant, MD---Board Certified Plastic Surgeon, Chester, Virginia. Expert in gynecomastia and male breast Reduction issues. Will explore the problem, surgical excision and liposuction contouring. Has been designing lectures and producing printed material for more than 25 years to help the public learn about Plastic & Cosmetic Surgery.

---

**The American Association for Klinefelter Syndrome Information and Support and the 2001 National Conference Committee gratefully acknowledges the financial support provided by**

**UNIMED & ALZA**

Their generous support makes it possible for AAKSIS to present an outstanding program of speakers for our second national conference.

---

**Conference Fees**

Effective until July 20, 2001:

<table>
<thead>
<tr>
<th></th>
<th>AAKSIS MEMBERS</th>
<th>NON-MEMBERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>single</td>
<td>$110</td>
<td>$135</td>
</tr>
<tr>
<td>couple</td>
<td>$190</td>
<td>$215</td>
</tr>
<tr>
<td>Each additional family member</td>
<td>$60</td>
<td></td>
</tr>
</tbody>
</table>

After July 20, 2001:

<table>
<thead>
<tr>
<th></th>
<th>AAKSIS MEMBERS</th>
<th>NON-MEMBERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>single</td>
<td>$135</td>
<td>$160</td>
</tr>
<tr>
<td>couple</td>
<td>$215</td>
<td>$240</td>
</tr>
<tr>
<td>Each family additional family member</td>
<td>$85.</td>
<td></td>
</tr>
</tbody>
</table>

Questions? Call the AAKSIS Hotline (888) 466-KSIS (5747)
The Betsy Ross House, home of America's most famous seamstress, hosts an array of family activities. With colonial magic, singers, and other fun activities, the courtyard seating and adjacent stage of the Betsy Ross House is a great spot for a midday picnic lunch break. The kids will love the quaint home of America's flag-maker with the unique gifts and toys of the gift shop. And the stage is always alive with short plays and demonstrations of colonial activities!

At the African American Museum in Philadelphia, you’ll see “Why Samana?” where Africans make an incredibly difficult decision—do they struggle for equality in the colonies or head to Haiti for a new life?

The noble story of “Haym Solomon, A Remarkable Man” is told at the National Museum of American Jewish History. This colonial merchant helped finance America’s Revolutionary War but was never repaid.

If you stop into Atwater Kent Museum or Elfreth’s Alley, you can enjoy the light performance of Circa 1780, which compares our lives to life in the 18th century.
I recommend a Philly Cheesesteak!
If bugs are your thing, this is the place to see at at 8046 Frankford Avenue in Northeast Philadelphia.

**Insectarium**: Famous science museum, with Planetarium, Omniverse and Futures Center. Giant walk-through model of the human heart.

**Franklin Institute**: Famous science museum, with Planetarium, Omniverse and Futures Center. Giant walk-through model of the human heart.

With attractions such as Twiddlebug Land, the Count's Fount, Teeny Tiny Tidal Waves and the mildly thrilling Vapor Trail, a coaster that's just right for wee folks and the big people who love them, where else could you be but **SESAME PLACE**. **Location**: 100 Sesame Road Langhome, PA 19407

**Trendy Shopping Area**: The Shops at Liberty Place, with upscale specialty shops and a huge food court. 16th to 17th and Chestnut Streets, phone 215-851-9055.

**Performing Arts**

**The Philadelphia Orchestra** performs in summer at Fairmount Park.

**The Opera Company of Philadelphia** performs at the Academy of Music (Broad and Locust).


**Merriam Theater** (Broadway shows)

**Society Hill Playhouse** (off-Broadway shows)

**PHILADELPHIA**
"The City That Loves You Back"

**Outdoor Markets**: The Italian Market, fresh produce, meats, household goods and clothing. Also The Reading Terminal Market, produce, foodstuffs and eateries (Amish, Asian, Greek, Mexican). Adjacent to the Convention Center.

7109 Stilson Ct
Columbus, Ohio 43235