Let’s Talk Turner!

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Disclosures

- Neither Dr. Dowlut-McElroy nor Dr. McDonough have anything to disclose
Objectives

- Understand the use of hormone replacement therapy in girls with Turner Syndrome from pubertal induction through adulthood
- Review options for building a family for girls with Turner Syndrome including the assessment of ovarian reserve and the use of assisted reproductive technology
- Comprehend the life-long impact of the diagnosis of Turner Syndrome on girls and their families
History & Epidemiology

- First described by Henry Turner in 1938
- In 1964 was determined to be due to a chromosomal abnormality
- TS affects approximately 1 in 2500 live births
- Much more among pregnancies that end in miscarriage/stillbirth

Bondy CA. J Clin Endocrinol Metab 2007;92:10–25
Diagnosis

- Classic physical features AND complete or partial absence of second X chromosome (± cell line mosaicism)
- Women with 45,X karyotype but without physical features are not considered to have TS
Diagnosis

- Presentation
  - Intrauterine
  - At Birth
  - In Peds Endocrinology
  - In Gynecology
Diagnosis: Intrauterine

- Abnormal maternal serum screening
- Ultrasound
  - Increased nuchal translucency
  - Cystic Hygroma
  - Cardiac anomalies (coarctation of aorta ± left-sided defects)
  - Renal anomalies, Polyhydramios, Oligohydramios, IUGR
- Prenatal diagnosis must include karyotype

Bondy CA. J Clin Endocrinol Metab 2007;92:10–25
Physicians and Genetic Counsellors should be involved in post-dx counselling

TS is a spectrum, and symptoms are variable at birth

Include discussion on IQ, learning disabilities, ability to function independently

Bondy CA. J Clin Endocrinol Metab 2007;92:10–25
Diagnosis: Genetics

- Degree of mosaicism prenatally is not predictive of severity of TS phenotype
- Karyotype should be repeated in all cases
- 30 cell karyotype recommended by ACMG
- Testing for Y chromosome material

Bondy CA. J Clin Endocrinol Metab 2007;92:10–25
Davenport ML. Growth Horm IGF Res 2006;16(Suppl):91-97
Diagnosis: At Birth

- Lymphedema
- Nuchal folds, low hairline
- Left-sided cardiac anomalies
- Failure to Thrive
- Horseshoe kidneys
- If not diagnosed at birth, dx may be delayed for years
Diagnosis: Genetics

- Degree of mosaicism prenatally is not predictive of severity of TS phenotype
- Mosaicism present in 20-30%
- Karyotype should be reevaluated in all cases
Physical Exam Findings

- Classic Phenotype
  - Short Stature
  - Webbed neck, low hair line
  - Wide spaced nipples
  - Cubitus valgus
  - Hypoplastic nails
Diagnosis: At Peds Endo

- **Short Stature**
  - Almost universal feature of girls with TS
  - Due to haploinsufficiency of SHOX gene
Diagnosis: At Gyn

- Delayed Puberty/Primary Amenorrhea
  - Hypergonadotrophic Hypogonadism
    - Elevated FSH level
    - Decreased Estradiol level
    - Ultrasound: uterus present
Associated Findings: Cardiology

- Left-sided heart defects
  - Coarctation of the aorta & BAV are most common
- Aortic dissection
  - Risk requires aggressive BP management
- HTN present in 25-40%
- Screening (by a Peds Cardiologist familiar with TS)
  - 2D Echo & EKG at diagnosis
  - Cardiac MRI when able to undergo without sedation

Bondy CA. J Clin Endocrinol Metab 2007;92:10–25
Sybert VP. Pediatrics 1998;101(1)
Associated Findings: GU

- Urinary tract malformations present 30-40%
  - Collecting System (20%)
  - Horseshoe kidneys (10%)
  - Other positional anomalies (5%)

- Renal U/S should be performed at diagnosis

Davenport ML. Growth Horm IGF Res 2006;16(Suppl):91-97
Associated Findings: Learning

- Normal intelligence
- Struggle with non-verbal & visuospatial skills
- Difficulty with problem solving (math)
- Gross motor deficits
- Psychoeducational testing & IEP
- Excel at verbal skills (but not always social cues)

Rovet J. Child Neuropsychol 2004;10:262-279
Associated Findings: H&S

- Hearing problems & ear malformations are common in TS
- Frequent Otitis Media
- Conductive and progressive sensorineural hearing loss

Associated Findings: Vision

- Epicanthal folds, hypertelorism & upward slanting palpebral fissures
- Strabismus and farsightedness (25-35%)
- Peds Ophtho starting at 18 months

Davenport ML. Growth Horm IGF Res 2006;16(Suppl):91-97
Chrousos GA. Ophthalmology 1984;91:926-928
Associated Findings: Dental

- High arched palate and small mandible
- Higher rate of root resorption
- Initial visit to Peds Dentist by 2 years

Davenport ML. Growth Horm IGF Res 2006;16(Suppl):91-97
Associated Findings: Autoimmunity

- Increased risk for autoimmune disease
  - Hypothyroidism: 24%
  - Hyperthyroidism: 2-3%
  - Celiac Disease: 4-6%

Davenport ML. Growth Horm IGF Res 2006;16(Suppl):91-97
Primary Ovarian Insufficiency (POI)

- Most common genetic cause is TS
- ~ 90% of girls with TS develop POI

Sullivan SD. Fertil Steril 2016;106(7):1588-1599
Bondy CA. J Clin Endocrinol Metab 2007;92:10–25
**Associated Findings: POI**

- **46,XX**
  - 4 million germ cells at 21 wk GA → 2 million germ cells at birth → 400,000 at puberty
  - Loss via apoptosis

- **45,XO**
  - Increased apoptosis
  - Normal germ cells early gestation → significantly decreased by mid gestation

Associated Findings: POI

- Mosaic karyotype (46XX, 45X)
  - Larger # oocytes at birth
  - May allow for spontaneous puberty/menarche
- Spontaneous puberty
  - 30% of girls with TS
  - ALL are at risk of POI

Associated Findings: POI

- Health Complications of POI
  - Decreased BMD
    - Increased fracture risk
  - Infertility
  - Sexual Dysfunction

Sullivan SD. Fertil Steril 2016;106(7):1588-1599
SHORT STATURE
Growth Issues

- Use of TS Growth Chart
  - Controversial
  - GH therapy impacts growth, so should they be plotted on standard curve?

Rieser P, Davenport M. Houston, TX: TSS of the United States; 2002
Growth Therapy

- Untreated
  - > 50% will be below 5th percentile by 2 years
  - Average height 143 cm (4 feet 8 inches)
  - Rarely exceed 150 cm (4 feet 11 inches)
  - Average height of a woman in the US: 163 cm (5 feet 4.5 inches)

Lyon AJ. Arch Dis Child 1985;60:932-935
Growth Therapy

- Growth Hormone
  - Canadian GH Advisory Committee (2005)
    - Girls treated for mean of 5.7 years were 7.2 cm taller than control group
  - Davenport et. Al (2007)
    - Starting GH between 9 months & 4 years
    - Mean height SDS increased 1.1 (near avg non-TS girls) vs decline 0.5 SDS in non-treated girls
Growth Hormone Risks

- Wooten et al. (2008) study of 5520 girls w/ TS
  - Scoliosis (0.39%)
  - Diabetes (0.19%)
  - Serious cardiac events (0.32%)
  - Increased Intracranial hypertension (0.23%)
  - SCFE (0.24%)
  - No AE of GH on cardiac size or aortic diameter or CV function were found
Growth Therapy

- Growth Hormone Therapy
  - Ideal age to start treatment is unknown
    - Controversy over prophylactic tx vs waiting for growth failure
  - Follow-up with Peds Endo every 3-6 months
  - D/C when growth velocity slows to < 2 cm/year
- Oxandrolone (rare cases)
Growth Therapy

- Improvements in 8-10 inches with at least 6 years of GH therapy
- One of the major reasons we delay estrogen initiation
- Higher dose, earlier GH to allow early E2?

Sas TC. JCEM 1999;84:4607-4612
PUBERTAL INDUCTION
ADOLESCENCE TO MENARCHE
Goal of Estrogen Replacement

- Normalize secondary sexual characteristics
  - Breast size/shape
  - Uterine size/shape for possible reproductive function
  - Bone growth and mineral accrual
  - CV Function
  - Brain Development

Davenport ML. Growth Horm IGF Res 2006;16(Suppl):91-97
Timing of Replacement

- Choice of estrogen, dose, and modes of delivery are imperative
- Need to allow E2 initiation at a normal(ish) age, but to still allow maximum height accrual

Davenport ML. Growth Horm IGF Res 2006;16(Suppl):91-97
Approach to Replacement

- Transdermal Application
  - Patch (preferred) or gel
  - Only form that achieves natural levels of estradiol in the blood

- Conjugated Equine Estrogen
  - Contains multiple estrogens, progestins & androgens

Ankarberg-Lindgren C. JCEM 2001;86:3039-3044
Approach to Replacement

- Oral Administration
  - Undergoes extensive hepatic first-pass metabolism (converted to estrone)
  - Cause increased resistance to APC and decrease ATIII leading to increased thrombosis risk
  - Can cause GH resistance, decreasing IGF-1 & BP3
  - Increase TG enrichment of LDL and HDL proteins, making them more atherogenic

Ankarberg-Lindgren C. JCEM 2001;86:3039-3044
Approach to Replacement

- Nabhan et al. (2009)
  - Randomized to PO conjugated estrogen or transdermal estrogen for 1 year
  - No differences were found in GV, IGF-1, or Lipid Profile
  - Transdermal group did have significantly greater increases in spine BMD and uterine growth

Nabhan ZM. JCEM 2009;94:2009-2014
Consider initiation of puberty at 11-12 years if no spontaneous breast development

<table>
<thead>
<tr>
<th>Months</th>
<th>E2 (pg/mL)</th>
<th>E2 Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3-4</td>
<td>0.1 mcg/kg</td>
<td>Matrix patch (PM to AM)</td>
</tr>
<tr>
<td>6</td>
<td>3-4</td>
<td>0.1 mcg/kg</td>
<td>Change twice weekly</td>
</tr>
<tr>
<td>12</td>
<td>6-8</td>
<td>0.2 mcg/kg</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>~12</td>
<td>12.5 mcg</td>
<td>E2 levels below this are believed to accelerate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>growth more than bone maturation</td>
</tr>
<tr>
<td>24</td>
<td>~25</td>
<td>25 mcg</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>~37</td>
<td>37.5 mcg</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>~50</td>
<td>50 mcg</td>
<td>Start Progestins</td>
</tr>
<tr>
<td>42</td>
<td>~75</td>
<td>75 mcg</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>50-150</td>
<td>100 mcg</td>
<td>Typical adult dose</td>
</tr>
</tbody>
</table>

Davenport ML. Growth Horm IGF Res 2006;16(Suppl):91-97
HORMONE REPLACEMENT
MENARCHE TO MENOPAUSE
Hormone Replacement Therapy

- Age
- Methods
- Risks and Benefits
- Compliance
Hormone Replacement Therapy

- TS/POI = Pathologic state of estrogen deficiency
- Replacement of hormones that would normally be present

Sullivan SD. Fertil Steril 2016;106(7):1588-1599
Hormone Replacement Therapy

- Optimal formulation, dosage, method of administration and time to initiate progesterone are controversial

- Rare condition → difficult to accumulate evidenced-based data → extrapolations from postmenopausal HRT → recommendations based on expert opinion

Gravholt CH. Endocrine 2017;55(2):329-330
Hormone Replacement Therapy

- Goal: Physiologic HRT that ameliorates health risks of POI (fracture risk, cardiovascular health)

Sullivan SD. Fertil Steril 2016;106(7):1588-1599
## Clinical Practice Guideline (2007)

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Age specific suggestions</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 to 16</td>
<td>Begin cyclic progesterone after 2 years of estrogen or when breakthrough bleeding occurs</td>
<td>Best option: oral micronized progesterone 200mg/d on day 20 to 30 of monthly cycle or day 100-120 of 3 month cycle</td>
</tr>
<tr>
<td>14 to 30</td>
<td>Continue full doses until at least age 30 because normally estrogen levels are higher between age 15 and 30</td>
<td>Some women may prefer using oral or transdermal contraceptive for HRT; monitor endometrial thickness</td>
</tr>
<tr>
<td>30 - 50</td>
<td>Lowest estrogen dose to providing full protection against osteoporosis is 0.625 CEE* or equivalent</td>
<td>Monitor osteoporosis risk factors, diet, exercise; obtain BMD and begin regular screening MMG by age 45</td>
</tr>
<tr>
<td>&gt;50</td>
<td>Decision on estrogen use based on same considerations as for other postmenopausal women</td>
<td>Consider new HRT options; recommendations may need updating</td>
</tr>
</tbody>
</table>

Bondy CA. J Clin Endocrinol Metab 2007;92:10–25
Transdermal vs Oral Estrogen

- Randomized trial of 20 girls with TS (all karyotypes)
  - Ages 13 to 20 years (mean 17.7 ± 0.4)
  - Comparison 20 normally menstruating girls (mean age 16.8 ± 0.4)
  - Lose dose oral micronized estradiol (0.5 mg) and bi-weekly
    transdermal E$_2$ (0.0375 mg) with 2 week washout period in
    between versus high dose oral micronized estradiol (2.0 mg)
    and bi-weekly transdermal E$_2$ (0.075 mg)

Taboada M. L Clin Endocrinol Metab 2011;96(11):3502-3510
Transdermal vs Oral Estrogen

- Randomized trial of 20 girls with TS
  - Transdermal E₂ results in concentrations closer to normal
  - Long-term metabolic effects unknown in TS

<table>
<thead>
<tr>
<th>Route/Dose</th>
<th>Mean E₂ Level (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Mean Follicular &amp; Luteal)</td>
<td>96 ± 11</td>
</tr>
<tr>
<td>Oral: 0.5 mg E₂</td>
<td>18 ± 2.1</td>
</tr>
<tr>
<td>Transdermal: 0.0375 mg E₂</td>
<td>38 ± 13</td>
</tr>
<tr>
<td>Oral: 2 mg E₂</td>
<td>46 ± 15</td>
</tr>
<tr>
<td>Transdermal: 0.075 mg E₂</td>
<td>114 ± 31</td>
</tr>
</tbody>
</table>

Taboada M. L Clin Endocrinol Metab 2011;96(11):3502-3510
Transdermal vs Oral Estrogen

- Advantages of transdermal estrogen
  - Avoid first pass liver effect
  - Lower risk VTE [Estrogen and Thromboembolism Risk] study postmenopausal women
    - OR for oral E<sub>2</sub> was 4.2 (95% CI 1.5 – 11.6)
    - OR for transdermal E<sub>2</sub> was 0.9 (95% CI 0.4 – 2.1)

Sullivan SD. Fertil Steril 2016;106(7):1588-1599
Canonico M. Circulation 2007;115:840-845
Transdermal HRT vs Oral cOCP (Effect on BMD)

- RCT cross-over trial in women with POI (including TS)
  - 18 completed study; 7 with TS
  - Mean age 27 years (Range 19-39 years)
  - 4 week cycle transdermal E₂ (100-150μg/d) plus cyclic progesterone (oral or vaginal) vs combined OCP (30μg EE and 1.5 mg norethisterone) daily for 3 weeks per month
  - DEXA at baseline and after each 12 month period

Crofton PM. Clin Endocrinol (oxf) 2010;73:707-14
Transdermal HRT vs Oral cOCP (Effect on BMD)

- RCT cross-over trial in in women with POI (including TS)
  - No significant change in femoral neck or hip BMD z-scores with either group in response to either regimen
  - Transdermal E$_2$ regimen resulted in improvement in lumbar spine BMD z-scores whereas cOCP regimen did not [+$0.17$ (CI +0.07 to +0.27), $p = 0.003$]

Crofton PM. Clin Endocrinol (oxf) 2010;73:707-14
Oral HRT vs. cOCP
(Effect on BMD)

- RCT in women with POI
  - 36 completed study
  - Age range 18-44 years
  - No treatment vs. HRT (Estradiol 2mg/day with levonorgestrel 75mcg for 12 day/month) vs. cOCP (EE 30mcg and levonorgestrel 150mcg for 21d with 7d break)
  - DEXA at baseline, 6, 12 and 24 months

Cartwright B. J Clin Endocrinol Metab 2016;101:3497-505
Oral HRT vs. cOCP (Effect on BMD)

- At lumbar spine
  - With no treatment: drop in BMD at 12 and 24 months
  - With HRT: significant increase at all time points [+0.050 (CI 0.007-0.092, p=0.025)]
  - With cOCP: no significant change in BMD

Cartwright B. J Clin Endocrinol Metab 2016;101:3497-505
Oral HRT vs. cOCP (Cardiovascular Effects)

- RCT crossover trial in women with POI
  - 18 completed study
  - Age range 19 to 30 years
  - EE 30μg and norethisterone 1.5mg/d for 3 weeks with 1 week pill-free vs. 4 week cycle transdermal E₂ (100-150μg/d) plus cyclic progesterone (oral or vaginal) for 12 month period

Langrish JP. Hypertension 2009;53:805-11
Oral HRT vs. cOCP
(Cardiovascular Effects)

- RCT crossover trial in women with POI
  - Physiologic HRT
    - Associated with lower BP (p<0.0001) for both SBP & DBP and differed from cOCP at 3 (p<0.05), 6 (p<0.05) and 12 months (p<0.01)
    - Associated with better renal function; reduced serum creatinine (p=0.015)
    - Reduced activation of renin-angiotensin-aldosterone system; reduced plasma Ang II (p=0.007) without affecting plasma aldosterone concentrations

Langrish JP. Hypertension 2009;53:805-11
HRT Method and Benefits

- **cOCP**
  - Provide “supraphysiologic” levels of estrogens and progestins to suppress ovulation
  - More steroid hormone necessary to replace ovarian production
  - “Pill-free” week results in regular temporary estrogen-deficient state

Sullivan SD. Fertil Steril 2016;106(7):1588-1599
HRT Method and Benefits

- Physiologic HRT is more effective in maintaining bone health than combined OCPs in women with TS/POI
- Transdermal vs. oral delivery of ERT considering risk factors
- More prospective, long-term trials including assessment of fracture events and cardiovascular health are needed

Sullivan SD. Fertil Steril 2016;106(7):1588-1599
Cintron D. Endocrine 2017;55(2):366-375
Compliance with HRT

- HRT crucial in reaching maximal peak bone mass in TS during adolescence and early adulthood
- HRT important in maintaining BMD in later adulthood
- When adjusted for size, women that have received appropriate estrogen treatment usually have normal BMD in trabecular bone, e.g. the spine

Trolle C. Endocrine 2012;41:200-219
Bondy CA. J Clin Endocrinol Metab 2007;92:10–25
Compliance with HRT

- Adherence rates 54% to 70%
- Education about importance of HRT major predictive factor of adherence

Hanton L. J Womens Health (Larhmt) 2003;12(10):971-977
Hormone Replacement Therapy

- Pathologic state of estrogen deficiency
- Replacement of hormones that would normally be present
- Physiologic HRT can ameliorate many health risks of POI

Sullivan SD. Fertil Steril 2016;106(7):1588-1599
Fertility

- When to discuss?
- AMH
- Fertility Strategies
When to discuss?

- Identify girls with residual ovarian follicles during childhood/adolescence → opportunity for fertility preservation.
- Depleted ovarian reserve before adulthood
- Mosaics: varying ovarian function for varying time before POI
Anti-Müllerian Hormone (AMH)

- Best endocrine marker of number of small antral follicles in ovaries
- Can be used as marker of ovarian function in girls with TS

Hagen CP. J Clin Endocrinol Metab 2010;95:5003
Anti-Müllerian Hormone (AMH)

- Cross-sectional study of 270 girls with karyotype proven TS
  - Ages 0 to 20 years
    - 21.9% had detectable serum AMH
    - Level correlates with karyotype
      - 77% of TS girls with karyotype 45,X/46,XX
      - 25% with ‘other’ karyotypes
      - Only 10% of 45,X

Visser JA. Hum Reprod 2013; 28:1899
Anti-Müllerian Hormone (AMH)

- Longitudinal study of serum AMH levels in 926 healthy women and 172 with TS
  - AMH stable from 8 to 25 years
  - Levels associated with spontaneous or lack of puberty/menarche
  - AMH as screening test for POI in TS: AMH < 8pmol/L sensitivity 96%, specificity 86%

Hagen CP. J Clin Endocrinol Metab 2010;95:5003
Fertility Preservation Strategies

- Oocyte Cryopreservation
- Embryo Cryopreservation
- Ovarian Tissue Cryopreservation
- Adoption
Oocyte Cryopreservation

- Proven fertility option in adults
- Success reported in girls with TS

Oktay K. Fertil Steril 2010; 94:753.e715
Huang JY. Hum Reprod 2008;23:336
Oocyte Cryopreservation

- Case Report (2008)
  - 16 year old 45X(20%)/46XX(80%)
  - Spontaneous menses
  - Basal FSH 9.8 IU/L, LH 1.4 IU/L, E2 119 pmol/L
  - Laparoscopic ovarian wedge resection → follicle aspiration → IVM
  - 8 IVM oocytes cryopreserved

Huang JY. Hum Reprod 2008;23:336
Oocyte Cryopreservation

- Ovarian stimulation → monitor with serial abdominal ultrasound and serum estradiol levels → trigger oocyte maturation → transvaginal oocyte retrieval under general anesthesia

Oktay K. Fertil Steril 2010; 94:753.e715
### Oocyte Cryopreservation

<table>
<thead>
<tr>
<th></th>
<th>45X/47XXX</th>
<th>46XX/45X</th>
<th>46XX/45X</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>13</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td><strong>Spontaneous menarche</strong></td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td><strong>AMH (ng/ml)</strong></td>
<td>1.59</td>
<td>0.9/1.7</td>
<td>0.76</td>
</tr>
<tr>
<td><strong>FSH (mIU/ml)</strong></td>
<td>5.7</td>
<td>5.3</td>
<td>5.6</td>
</tr>
<tr>
<td><strong>Antral follicle count</strong></td>
<td>6</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td><strong>Oocytes retrieved</strong></td>
<td>19</td>
<td>11/7</td>
<td>16</td>
</tr>
<tr>
<td><strong>Mature oocytes</strong></td>
<td>9 + 1(IVM)</td>
<td>8/4</td>
<td>7 + 5(IVM)</td>
</tr>
</tbody>
</table>

Oocyte Cryopreservation

- Possibility of aneuploidy $\rightarrow$ pre-implantation genetic testing of resulting embryos
- Unknown efficacy in girls with TS

Embryo Cryopreservation

- Live birth rates higher and may be comparable to rates achieved with fresh embryo transfers
- Limited applicability for adolescents with TS (requires access to sperm)

Ovarian Tissue Cryopreservation

- Experimental
- Adequate ovarian reserve but cannot wait for maturity to undergo oocyte cryopreservation
- Surgical removal or part of or entire ovary

Ovarian Tissue Cryopreservation

- Laparoscopic harvest of ovarian cortex (harbors primordial follicles) → cryopreservation → thaw → autotransplantation (pelvis, forearm, lower abdominal wall)

More than 40 total pregnancies reported thus far; only 1 from ovarian tissue harvested as a child

13 year old post pubertal, premenarcheal
- Sickle-cell anemia; hematopoetic stem cell transplantation from matched sibling donor
- Tissue thawed and transplanted 10 years later
- Spontaneous pregnancy > 2 years post transplantation

Demeestere I. Hum Reprod 2015; 30:2107
Ovarian Tissue Cryopreservation

- Evidence for long-term survival of cryopreserved ovarian tissue and ability to restore fertility
- Data on efficacy lacking in girls with TS
- Possibility of aneuploidy → pre-implantation genetic testing of resulting embryos

Demeestere I., Hum Reprod 2015; 30:2107
Life-Long: Pediatrics

- Social Development
  - Non-verbal learning disabilities common
  - Difficulty making/keeping friends
  - Trouble picking up on social cues
  - Less mature than similar aged peers

Rovert J. Child Neuropsychol 2004;10:262-279
Impact on parents

- Sadness (95%), Ashamed (56%), Guilt (29%) immediately after diagnosis
- Conversations regarding fertility/child birth (90% said it was difficult to cope with)

Slijper FME. Netherlands 1998;142(39):2150-4
Partnering and Sexuality

- Women with TS more frequently live alone

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time 1: Study Start</th>
<th>Time 2: 6 years later</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>80</td>
<td>56</td>
</tr>
<tr>
<td>Age (mean ± SD) yrs</td>
<td>34.4 ± 11.7</td>
<td>40.6 ± 11.1</td>
</tr>
<tr>
<td>Live alone</td>
<td>37 (46%)</td>
<td>28 (50%)</td>
</tr>
<tr>
<td>Live with partner</td>
<td>31 (39%)</td>
<td>19 (34%)</td>
</tr>
<tr>
<td>Live with parents</td>
<td>12 (15%)</td>
<td>--</td>
</tr>
</tbody>
</table>

Fjermestad. Clinical Endocrinology 2016;85:423-429
Naess EE. Clinical Endocrinology 2010;72:678-684
Partnering and Sexuality
- Those with partner equally satisfied with family and intimate relationships as controls
- Fewer sex partners, less confident as sexual partners

Fjermestad. Clinical Endocrinology 2016;85:423-429
Naess EE. Clinical Endocrinology 2010;72:678-684
Partnering and Sexuality

– Having regular partner associated with increased sexual activity among women with TS (N=26)
### Partnering and Sexuality

- Height associated with sexual activity

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Sexually Active (n=13)</th>
<th>Sexually Inactive (n=13)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD) years</td>
<td>37.2 ± 7.6</td>
<td>36.3 ± 7.7</td>
<td>NS</td>
</tr>
<tr>
<td>Height (mean ± SD) cm</td>
<td>152 ± 8.7</td>
<td>146 ± 5.6</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Ros C. Am J of Obstetr Gynecol 2013;208:484-486
Life-Long Impact

Patient & Family Experience Video

https://youtu.be/YUDgpaw24b8
Thank you!

- Questions?