38th Annual Meeting

SSSA 2025
Philadelphia PA

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My Sotos syndrome story

MEETINGS OF THE SSSA

~~1988 Arizona~~
~~1989 Texas~~
~~1990 St. Louis, MO~~
~~1991 Boston (officially the SSSA)~~
~~1992 St. Louis, MO~~
1993 Phoenix, AZ
1994 Chicago, IL
1995 Boca Raton, FL
1996 Santa Barbara, CA
~~1997 Detroit, MI~~
1998 Washington D.C.
1999 Seattle, WA
2000 Toronto, Ontario, CA
2001 Atlanta, GA
2002 Colorado Springs, CO
2003 Chicago, IL
2004 Calgary, Alberta, CA
2005 San Antonio, Texas
2006 Anaheim, CA
2007 Omaha, NE

MEETINGS OF THE SSSA

2008 Niagara Falls, Ontario, CA
2009 Salt Lake City, UT
2010 Arlington, TX
2011 Williamsburg, VA
2012 Vancouver, British Columbia, CA
2013 Minneapolis, MN
2014 Little Rock, AR
2015 Orlando, FL
2016 Portland, OR
2017 Kansas City, MO
2018 Montreal, Quebec
2019 Boston MA
2020 Virtual
2021 Virtual
2022 Virtual
2023 Redondo Beach, CA
2024 Denver CO
2025 Philadelphia PA

Past

Current

Sotos Syndrome

We have a diagnosis

Now what?

Diagnostic Issues in Sotos Syndrome

Accuracy from the beginning

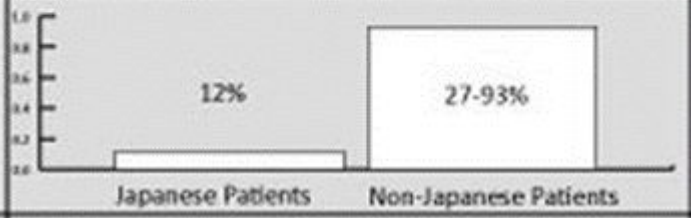
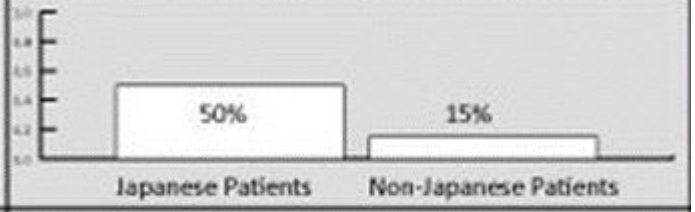
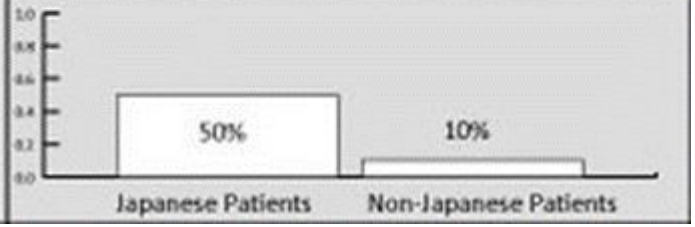
Speed is good, but accuracy is everything
- Wyatt Earp

Making the diagnosis … Clinically

- The "strict criteria" proposed for a diagnosis of Sotos syndrome requires that the individual have at least three of the following:
  - Facial appearance: large head, tall narrow skull, wide set down-slanting eyes, flat-bridged nose, high arched palate, early eruption of teeth (often by 3 months of age), thin hair, pointed chin, prominent forehead, and the appearance of a receding hairline.
  - Birth length above the 90th percentile
  - Bone age above the 90th percentile
  - Early verbal and motor delays

Types of Genetic Changes That Cause Sotos Syndrome

Genetic Tests

Test Method	Mutants Detected	Detection Frequency
Sequence analysis/ mutation scanning	Sequence variants	
Deletion/ duplication analysis	5q35 microdeletion of *NSD1* and *NSD1* partial deletions	
FISH	5q35 microdeletion of *NSD1*	

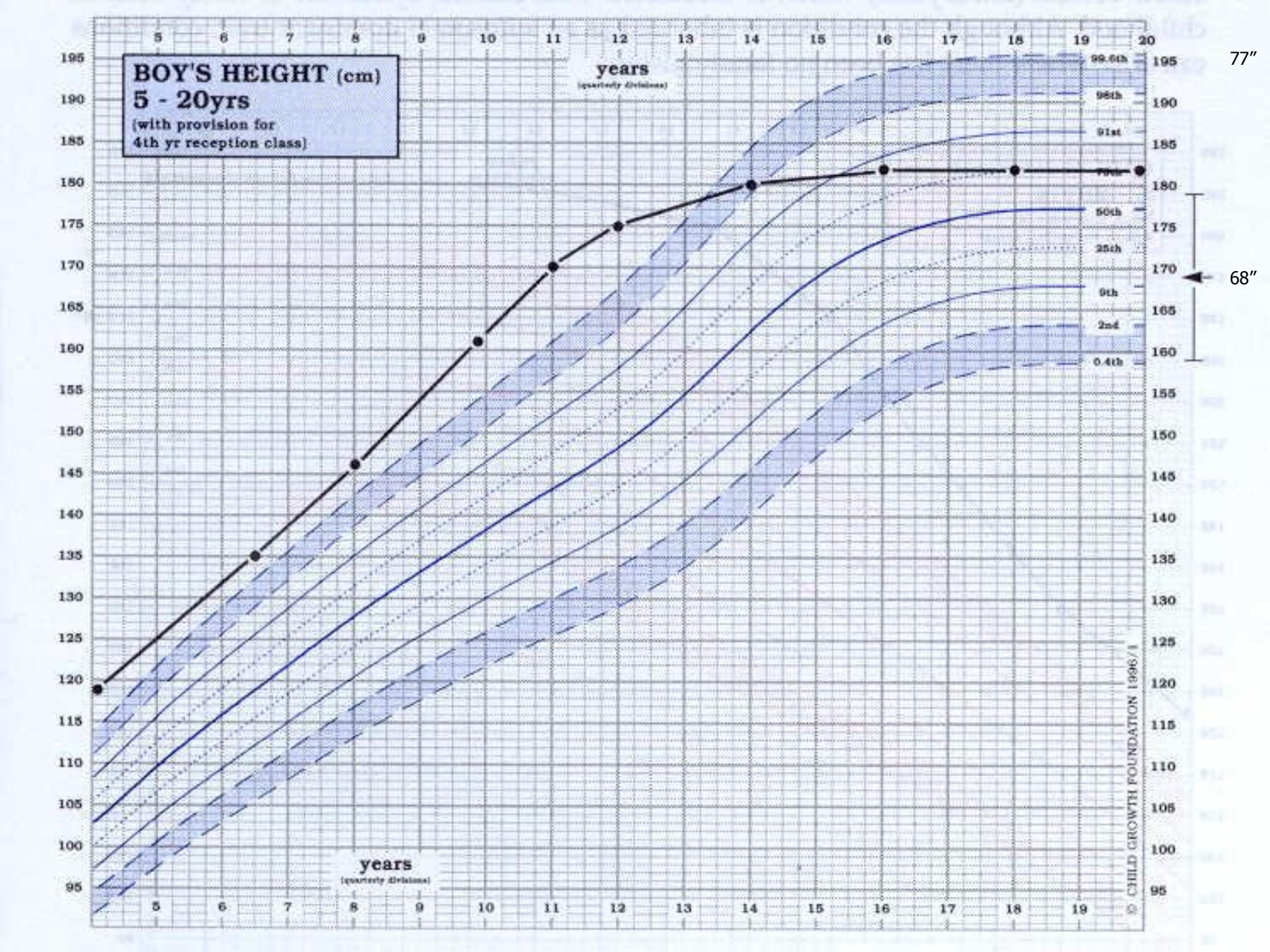
So why's a diagnosis important?

- Etiology (cause)
- Pathophysiology (mechanism)
- Natural history (collective wisdom)
- Genetics (familial implications)
- Targeted treatments (current and future)

We Have a Diagnosis – Now What?

- 10 often asked questions

1. What about their size?


BOY'S HEIGHT (cm)
5 - 20yrs
(with provision for
4th yr reception class)
years
(quarterly divisions)
years
(quarterly divisions)
99.6th
98th
91st
75th
50th
25th
9th
2nd
0.4th
77″
68″
© CHILD GROWTH FOUNDATION 1996

Endocrine Issues in Sotos syndrome

- Final adult height does not end up as big as it might seem early on
- True precocious puberty is rare
- Monitor thyroid functions

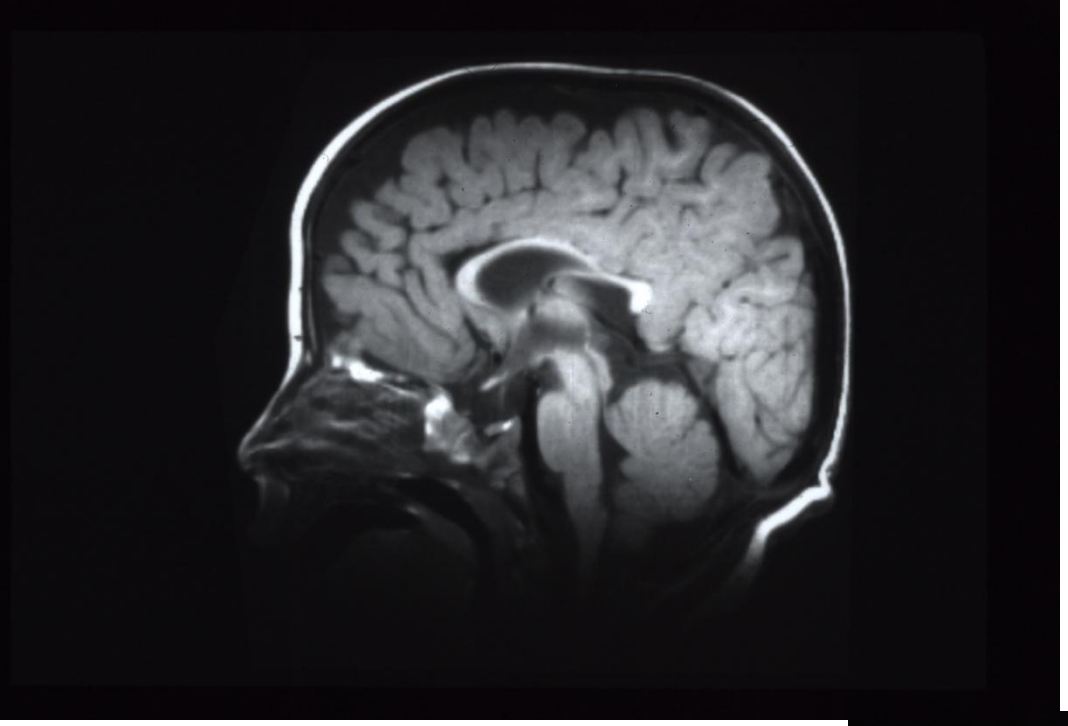
Sotos Syndrome
Final Height Predictions

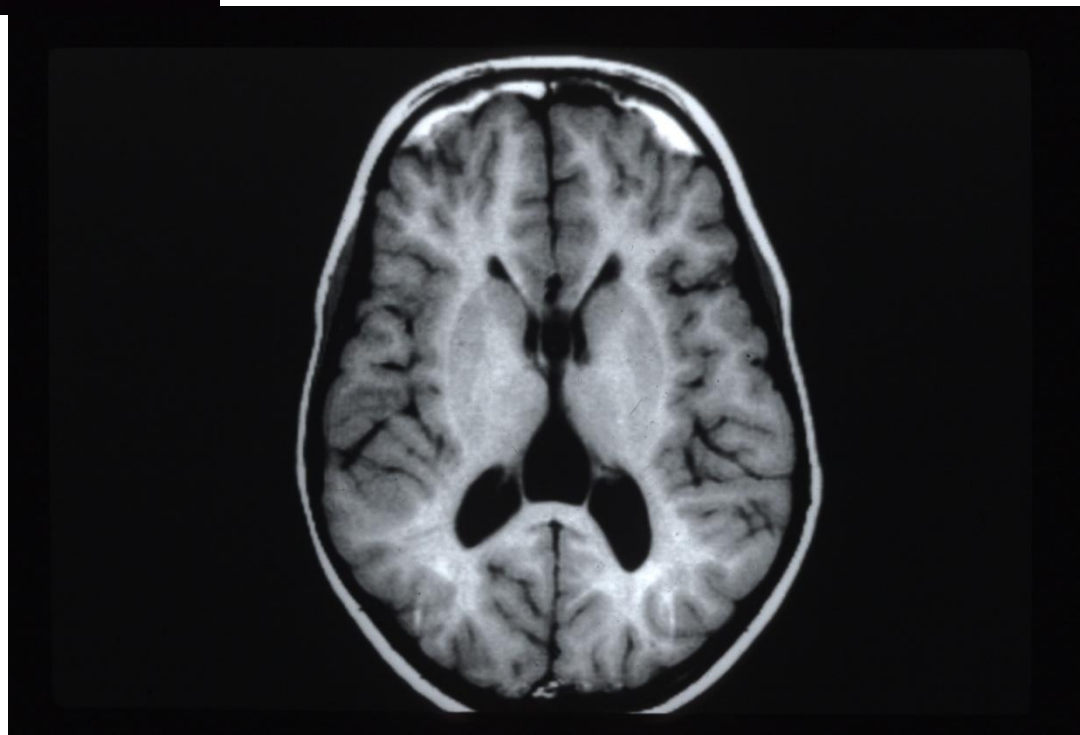
- Females
  - mean 8 cm (3”) greater than predicted FH
- Males
  - mean 13.6 cm (5 ¼”) greater than predicted FH

2. Do I have to worry about the head size?

Brain MRIs and Sotos syndrome

- Children with Sotos syndrome do not have severe brain malformations.
- However, they usually have extra fluid on the surface of the brain, enlarged ventricles and absence or reduced size of the corpus callosum.
- The brain itself is a normal size for the body size
- The extra fluid, which fills up the space inside the skull, is not "hydrocephalus, although some people have used that term.



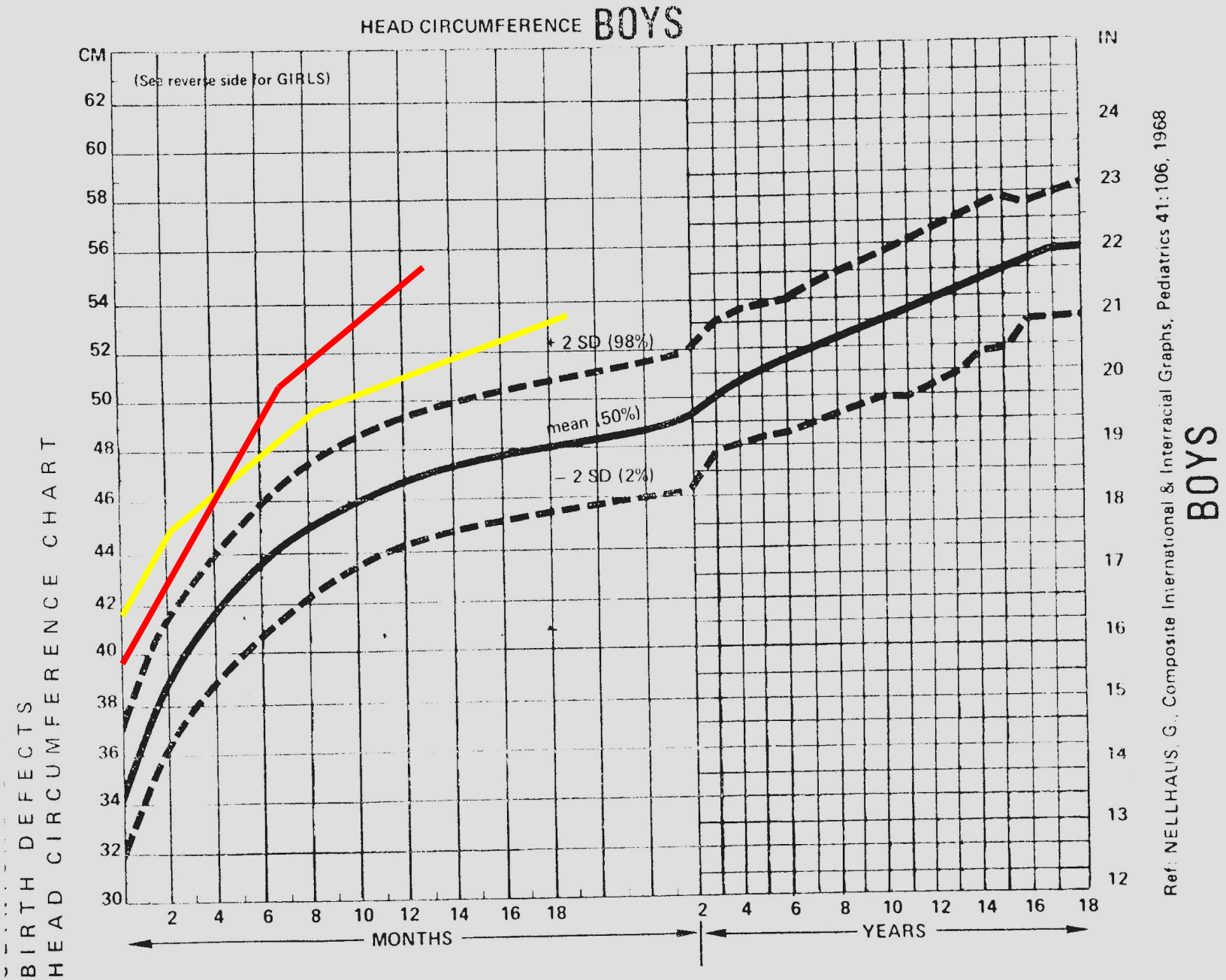


Care Must Be Taken in the Interpretation of MRIs

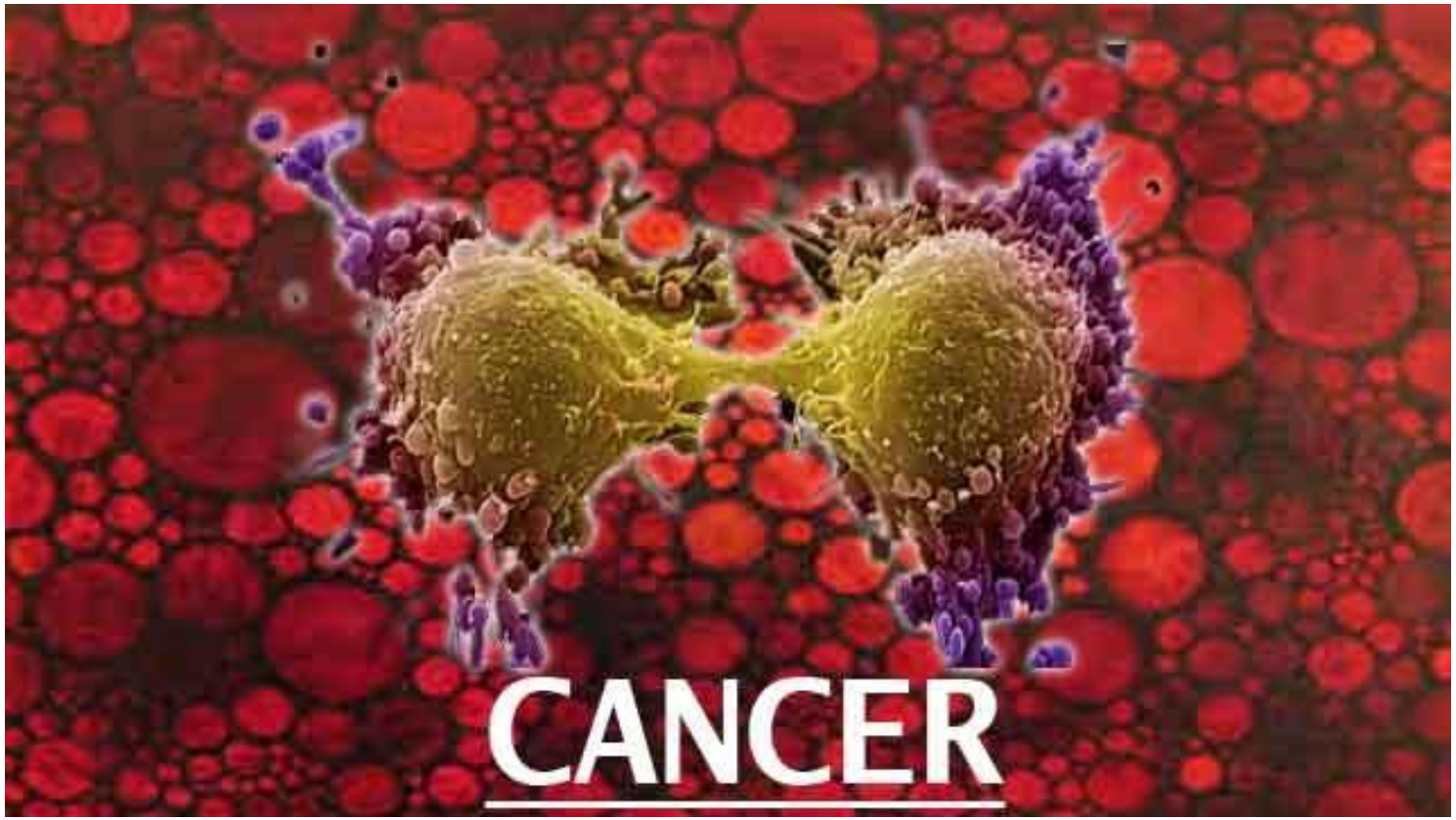
- Pay attention to symptoms
- Monitor head circumference
- Know the 'normal' MRI findings of Sotos syndrome
- Most do not have hydrocephalus

Do we need to an MRI if one has not already been done?

- Often the children will have had an MRI because of the large head size and the concern over hydrocephalus
- No need to do a scan for diagnostics
  - Though not one of the 4 key criteria, additional diagnostic evidence can be provided by the brain MRI scan.
  - Not nearly as important with the advent of gene testing
- May want to do a scan if the brain growth pattern is concerning


HEAD CIRCUMFERENCE BOYS
(See reverse side for GIRLS)
CM
62
60
58
56
54
52
50
48
46
44
42
40
38
36
34
32
30
IN
24
23
22
21
20
19
18
17
16
15
14
13
12
+ 2 SD (98%)
mean (50%)
– 2 SD (2%)
2 4 6 8 10 12 14 16 18
MONTHS
2 4 6 8 10 12 14 16 18
YEARS
BIRTH DEFECTS
HEAD CIRCUMFERENCE CHART
Ref: NELLHAUS G., Composite International & Interracial Graphs, Pediatrics 41:106, 1968
BOYS

3. What about cancer?



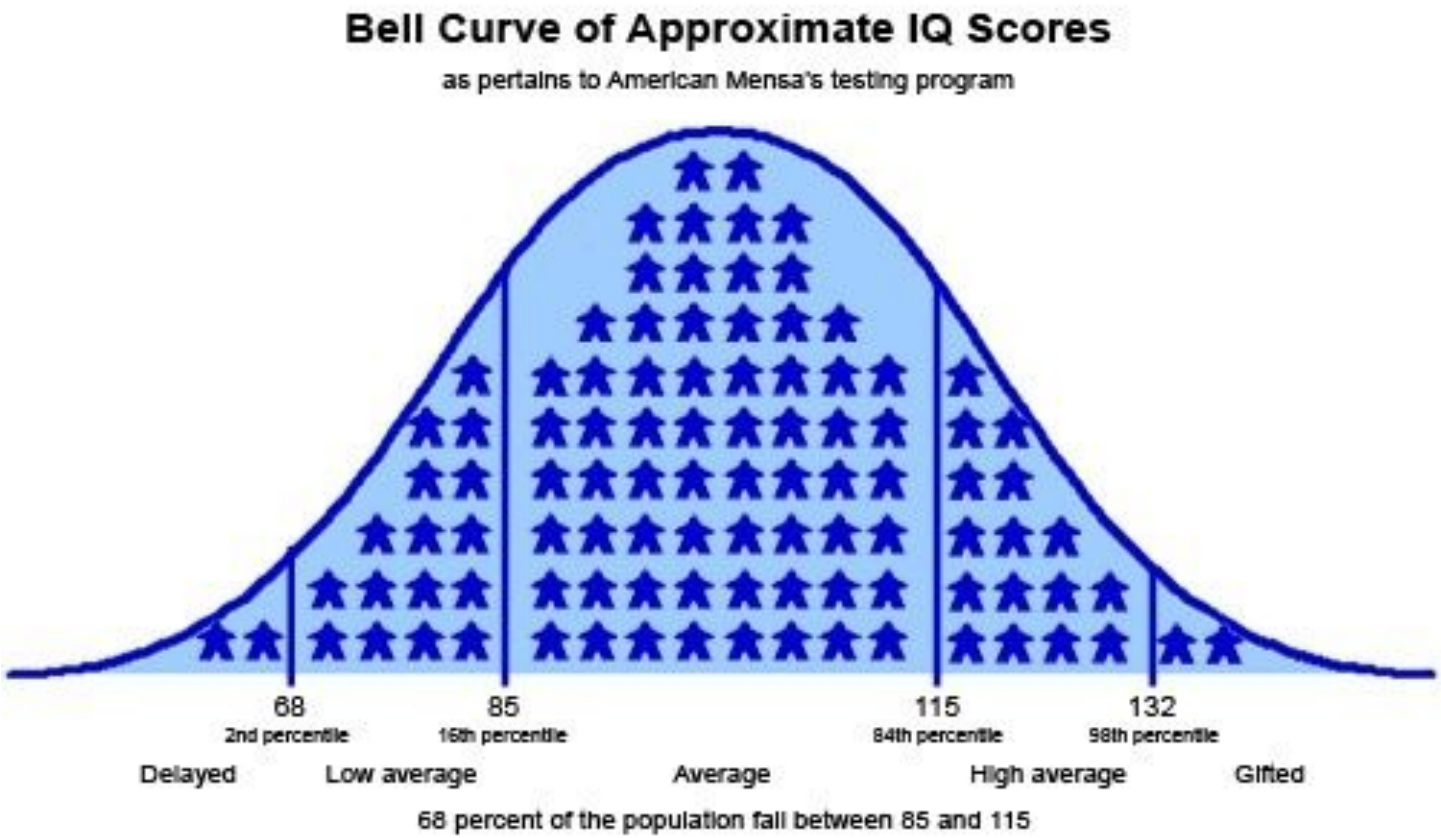
The cancer incidence rate in Sotos syndrome:

- Rare
  - Early reports inaccurate
- Tumors have occured in 1-3% of young adults with Sotos syndrome
  - UK study 1/40 (2.5%) by age 24
  - Series from Hersch et al 1991 (<2%)
  - 60.4 per 100,000 in the 25- to 29-year-old population;
  - 3 cases out of over 300 (1%)
  - 1/3 for a lifetime (same as general population)
- Reported sacrococcygeal teratoma, neuroblastoma, presacral ganglioma, acute lymphoblastic leukemia (ALL) and small cell lung cancer

Cancer Screening

- Cancer screening is not recommended.
- The level of risk does not warrant routine screening,
  - Wilms tumor risk is not significantly increased and routine renal ultrasound examination is not indicated [Scott et al 2006].
  - Screening for neuroblastoma has not been shown to decrease mortality and can lead to false-positive results [Schilling et al 2002].
  - The absolute risk of sacrococcygeal teratoma is low (~1%) [Tatton-Brown et al 2005b, Tatton-Brown & Rahman 2007].

4. Can we predict what the overall development is going to be like?



Developmental Delays

- Concerns over development in Sotos syndrome are one of the most commonly posed questions.
- No developmental problems are specific to Sotos syndrome
  - i.e. hypotonia in Sotos syndrome is treated the same as in any other child

Monitoring Development

- Developmental quotient (DQ)
  - Compares skills to age matched peers
  - Little to no prognostic value
- Intelligence quotient (IQ)
  - A test that tries to assess learning potential
  - No perfect test

Pediatric Neuropsychology

What is assessed?

- Intelligence
- Achievement skills
- Attention / Executive Functioning
- Learning & Memory
- Language
- Sensory & Sensory Motor
- Motor
- Behavioral, Emotional, & Social Functioning

Key Principles of Development

- Development is not a foot race
- Few predictive tools
  - Reported IQ range in Sotos syndrome is 20 – 120
  - Given wide range of outcomes, flexibility is needed
- Natural history of neuro-development in Sotos

A somewhat unique feature of Sotos syndrome lies in the "natural history" of this condition. In contrast to most other conditions with neurodevelopmental delays, the early developmental delays seen in patients with Sotos syndrome are poorly correlated with long term outcomes; e.g. the developmental pace typically gets better

Look Around

5. They say the muscle tone is low, but this child is really strong

Hypotonia

- Universal in Sotos syndrome
- Low muscle tone
  - Not the same as strength

Consequences of hypotonia

- 'Floppy baby'
- Delayed motor development
  - Problems over-coming gravity
- Loose (hyperflexible) joints
  - Not a CTD
- Oro-motor problems
  - Protruding tongue
  - Drooling
  - Problems with feeding / swallowing
- Frequent infections (not immune deficiency)
  - Ear infections
  - Colds, bronchitis

Hypotonia

- Generally improves with time
- Probably never completely goes away
- Therapies
  - Physical therapy
  - Occupational / speech therapy
  - Orthotics
  - Sugeries

6. Behavioral changes?

3 General Stages

- Early childhood
  - Tantrums (meltdowns), frustration behaviors, aggression, impulsivity
- Later childhood
  - ADHD, phobias, obsessions / compulsions, adherence to routines
- Young adults
  - Disrupted socialization, anxiety, depression

Sotos Syndrome and Socialization

- Persistently socially naïve
  - Intuitive social rules - are not
- Problems understanding personal space
- Difficulty with peers
  - Relate better to younger kids and adults than peers
- Struggle with unfamiliar settings

Autism and Sotos syndrome

- Many persons with Sotos syndrome will have autistic-like behaviors
  - Lots of sensory issues
- A few people with Sotos syndrome will meet the diagnostic criteria for autism
- Treatments are the same – but have to be individualized

Which therapies to use?

- Consider risks / side effects
- Look for reputable documentation of efficacy
- Seek input from trusted health care professionals
- Talk to other families
- If it isn’t working stop it
- Customize for your child

7. The speech pathologist and audiologist are confused. What gives?

Speech-Language

Auditory Processing

Causes of Speech Problems in Sotos syndrome

- Cognition
- Social impairments
- Hypotonia
- Mechanical (high arched palate, small jaws)
- Oro-motor dis-coordination
- Auditory processing

Any of the above, in any combination!

Characteristics of Speech and Language in Sotos Syndrome

- Expressive language impairments
  - Reduced variety of words
  - Shorter sentences
  - Simplified grammar
- Sound production impairments
  - Create their own linguistic 'rules'

Speech-language characteristics of children with Sotos syndrome. Ball LJ, Sullivan MD, Dulany S, Stading K, Schaefer GB. Am J Med Genet 136A:363 - 367, 2005

Characteristics of Speech and Language in Sotos Syndrome

- Voice differences
  - Hoarseness, hypernasal, pitch changes
- Social – pragmatic differences
  - Monotone speech
  - Difficulty initiating topics
  - Reading social clues
  - (just because you can make your sounds OK doesn't mean your communication is functional)
- Stuttering (dysfluency)
  - Later onset than typical (even into adolescence)

Speech-language characteristics of children with Sotos syndrome. Ball LJ, Sullivan MD, Dulany S, Stading K, Schaefer GB. Am J Med Genet 136A:363 - 367, 2005

Auditory Processing

- Auditory Processing Disorder (APD) is a neurological defect that affects how the brain processes spoken language. This makes it difficult for the child to process verbal instructions or even to filter out background noise in the classroom.
- There's no clear agreed-to definition of Auditory Processing Disorder, but there seems to be agreement on these points:
  - There is a breakdown in receiving, remembering, understanding, and using auditory information.
  - Hearing ability is adequate.
  - There is a neurological basis.
  - The child’s ability to listen is impaired.

Auditory Processing

- Changes in auditory processing have been suggested in many children with Sotos syndrome
- 2014 SSSA meeting (Arkansas)
  - Auditory processing differences are common in Sotos children (maybe 40%)
  - Pattern likely somewhat unique

Augmentative and Alternative Communication (AAC)

- See Lauren's talk

8. Every time I turn around I read about something else to worry about. What's real and what's not?

Important Clinical Genetic Concepts

- Genotype does not define phenotype
- That is, you can not predict what a particular person with Sotos syndrome is going to experience or not experience based on the genetic test results.

Important Clinical Genetic Concepts

- The Sotos gene (NSD1) is only one of 22,000 genes that a person has.
  - Even if it has a change, this does not 'trump' the way the other genes work.
- A person with Sotos syndrome will still have all of the other genetic traits and predispositions that are inherited from the parents.
  - Sotos syndrome does not define the child!

Important Clinical Genetic Concept

- Each person with Sotos syndrome will not exhibit every reported trait.
- They have an increased threshold for developing certain problems, but everyone's baseline threshold is different.
- It is sort of like a buffet line ….

What's on the buffet line?

- Common features
  - Overgrowth
  - Macrocephaly
  - Low muscle tone
  - Speech /language problems
  - Facial changes
  - Developmental delays
- Less common features
  - Seizures
  - Heart problems
  - Kidney / bladder problems
  - Gastrointestinal problems
  - Vision / hearing problems
  - Scoliosis

Seizures

- Seizures (30 - 50%)
  - can appear in many forms
- Some forms are subtle
  - e.g. absence seizures
- Temperature control problems may exacerbate seizures
  - “febrile seizures” (actually seizures associated with fevers) 50%

Feeding and Swallowing

- Multiple contributors to feeding and swallowing problems
  - Hypotonia
  - High arched palate
  - Oro-motor dis-coordination
  - Texture hypersensitivity
  - Gastro-esophageal reflux
  - Other esophageal dysfunction

GI problems

- Constipation
- Functional mega-colon
- Food intolerances

Skeletal Problems

- Scoliosis

Does _____ occur with Sotos?

- Commonly reported associations (in handbook, articles)
- Other things not reported??
- Chance occurrence of 2 rare events
- Listen to the mom's group

Watch for 'stuff'

If it ain't broke, don't fix it

- The following are appropriate at times of clinical evaluations:
  - Thorough history to identify known clinical sequelae of Sotos syndrome
  - Examination for curvature of the spine
  - Cardiac auscultation
  - Blood pressure measurement
  - Referral for audiologic assessment if hearing is a concern or if the child has had many upper respiratory tract infections
  - Referral to an ophthalmologist if strabismus or other problem with vision is suspected
  - Urine dipstick to investigate quiescent urine infection
  - Referral to the appropriate clinical specialist if problems are identified

9. Everything seems so negative, what can we celebrate?

Toileting

- 50% resolve per year if uncomplicated
- Diagnostic evaluation after "too long"
  - UTI's for wetting
  - Mega-colon for stooling
  - Tethered cord / Chiari malformation for one or both
- Behavioral interventions
  - Awareness training
  - Distractibility
- Medications as needed

Drivers License

- Not age dependent, but skill readiness
  - Skills achievement check list
  - Co-pilot / navigator activities
  - Trial runs
  - Professional evaluations

Other major milestones

- Solo travel
  - Planes, trains and automobiles
- Employment
- College
- Independent living
- Marriage

Should I let them _____ ?

- The key issue is the individual (cap)abilities of the person.
- Strengths / weaknesses assessment
  - Parents insight
  - Quantitative tools

10. OK, so what I am missing?

Puberty

- (Early) normal, not precocious
- Pre-signs
  - Girls = breast buds
  - Boys = testicular enlargement
- Preparation / anticipation

Sexuality Issues

- Self discovery
- Dating
- Sexual activity
- Protection
  - STDs
  - Abuse
- Reproduction

Sexuality

- People with Sotos syndrome are just people … all of us are sexual beings
- Don’t be freaked

Career Planning

- As in most things, must be individualized
- Must figure in
  - Cognition
  - Social skills
  - Temperament
  - Anxiety
  - Personal preference
    - Many seem to have a great affinity for working with younger children or older adults

Life without mom and dad

- Residence
  - Group home options
  - Talk to siblings / other relatives
- Safe storage of important documents
- Wills / trusts

Longevity

- No evidence that person with Sotos syndrome have a shortened life expectancy
- I am aware of several individuals over 60 years old

There is very little that the diagnosis of Sotos syndrome keeps people from doing

- We know there are people with Sotos syndrome who
  - Have driver's licenses
  - Got to college and graduate
  - Have 'real' jobs
  - Travel all over the world by themselves
  - Live by themselves
  - Get married
  - Have their own children

What to do with all of the information?

- Resources
  - SSSA, handbook, DVD
- Annual meetings
  - Networking, updates, look around
- Local geneticist
- Medical advisory board
- Other parents

The Long Look

- There is every reason to be hopeful for a long, healthy, happy life for persons with Sotos syndrome