Williams-Beuren Syndrome

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Discovery of Williams Syndrome

- 1961 Dr. J. C. Williams treats four patients with distinct symptoms and features
- 1962 Dr. A. J. Beuren reports similar findings in three patients
- 1993 Dr. C. A. Morris discovers the genetic cause for the disease
Inheritance and Penetrance

- Autosomal dominant
- *De novo* contiguous deletion within the WBSCR
- Hemizygosity for the *ELN* gene
- 100% Penetrance
- 50% chance that a parent with Williams Syndrome will pass the mutated chromosome to their child
- Occurs in 1:7,500 births in Norway and 1:20,000 births in the U.S.
Cytogenetics of Williams Syndrome

- The WBSCR deletion is due to unequal crossing over between chromosome 7 homologs.
- WBSCR is flanked by low copy repeats.
- *ELN* gene intron contains large repetitive elements.
Diagnostic Testing

- Clinical diagnosis based on the contiguous gene deletion for the WBSCR encompassing the elastin gene \textit{ELN}
- Fluorescent in situ hybridization (FISH)
- Targeted mutation analysis
Clinical Descriptions

- Phenotypes can range
- Mental Retardation
- Predisposed to cardiovascular diseases
  - 75% exhibit SVAS
- Endocrine complications
- Difficulty with visuospatial construction
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Behavior and Speech

• They have the “cocktail party manner”
  – Social exuberance
  – Overly friendly
• Anxiety issues
• Attention deficit disorder (ADD)
• Mastery of the spoken language
  – Expressive language
• Link:
  http://www.youtube.com/watch?v=_qAxdWSgpA
Inspiration for “Wee Folk” of Legends

- Williams Syndrome may have inspired the creation fairies, elves, leprechauns, and other “wee folk” of fairy tales.
- “Elfin-like” facial features
- Affinity for music
- Great storytellers
Treatment

• No cure
• Special education programs, counseling
• Psychotropic medication
• Several treatments for hypercalcemia
• 30% individuals require cardiothoracic surgery
• Constantly monitor their health

| Interval/Age | Test/Measurement |
|-------------|-----------------|
| Annual      | •Medical evaluation  
              • Vision screening to monitor for refractive errors and strabismus  
              •Monitoring of blood pressure in both arms  
              •Measurement of calcium/creatinine ratio in a random spot urine and urinalysis |
| Every 2 years | •Serum concentration of calcium |
| Every 3 years | •Thyroid function and TSH level |
| Every 5 years | •Audiologic examination |
| Every 10 years | •Renal and bladder ultrasound examination |
| In adults    | •Oral glucose tolerance test (OGTT) starting at age 30 years to evaluate for diabetes mellitus 1  
              •Evaluation for mitral valve prolapse, aortic insufficiency, and arterial stenoses  
              •Evaluation for cataracts |
Works Cited

• Boucher, Geoff. "Could Syndrome Be Source of Folk Tale." *Los Angeles Times* [Los Angeles] 26 Aug. 1994. Print.

• *Genes and Disease. NCBI*. National Institutes of Health, 1998. Web. 20 Jan. 2012. <http://www.ncbi.nlm.nih.gov/books/NBK22183/>.

• Kniffin, Cassandra L. "Williams-Beuren Syndrome." *Online Mendelian Inheritance in Man*. Institute of Genetic Medicine, 24 Mar. 2011. Web. 20 Jan. 2012. <http://www.ncbi.nlm.nih.gov/omim>.

• Levitin, Daniel J., and Ursula Bellugi. "Musical Abilities in Individuals with Williams Syndrome." *Music Perception: An Interdisciplinary Journal* 14.4 (1998): 357-89. *JSTOR*. Web. 19 Jan. 2012. <http://www.jstor.org/stable/40300863>.

• Morris, Colleen A. "GeneReviews - NCBI Bookshelf." *Williams Syndrome*. University of Washington, 21 Apr. 2006. Web. 20 Jan. 2012. <http://www.ncbi.nlm.nih.gov/books/NBK1116/>.

• "What Is Williams Syndrome?" *Genetics Home Reference - Your Guide to Understanding Genetic Conditions*. U.S. National Library of Medicine, 16 Jan. 2012. Web. 20 Jan. 2012. <http://ghr.nlm.nih.gov/>.

• "Williams Syndrome." *GeneTests*. National Institutes of Health, 2012. Web. 20 Jan. 2012. <http://www.ncbi.nlm.nih.gov/sites/GeneTests/?db=GeneTest>.