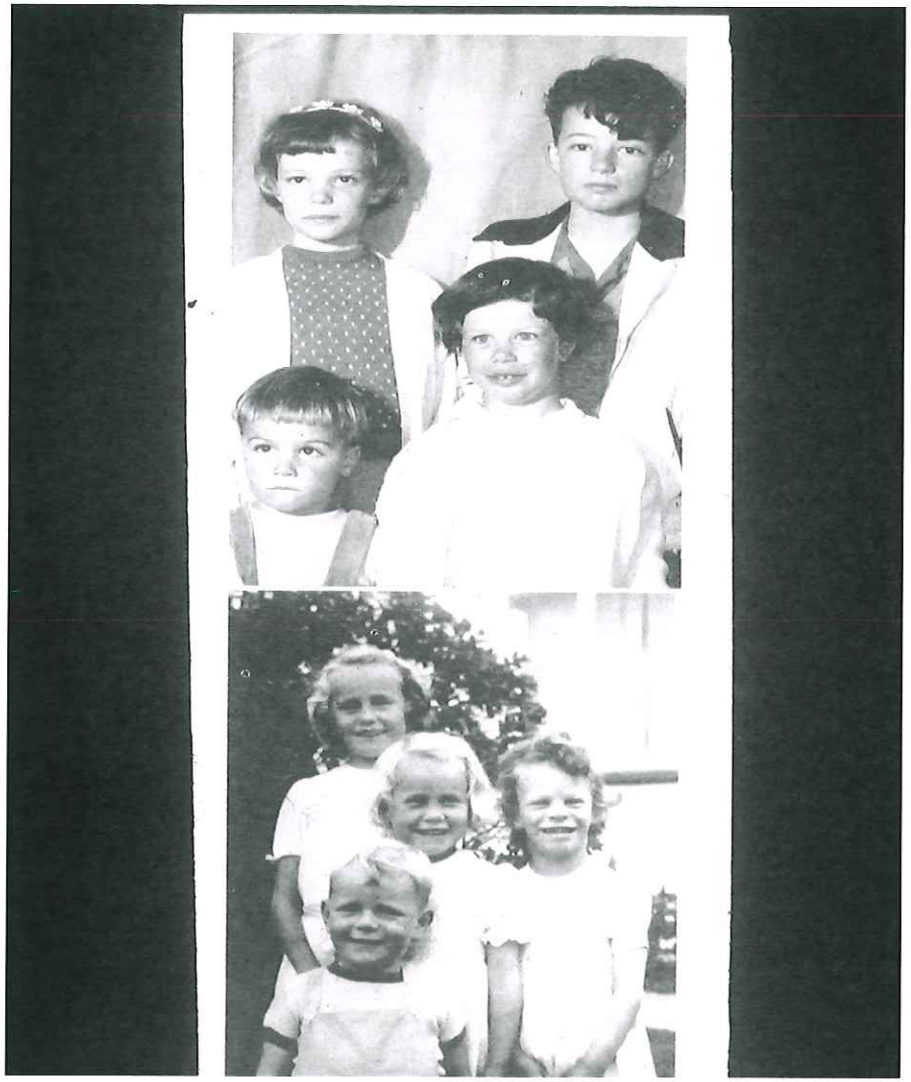
Overview of Williams syndrome

Barbara R Pober, MD
Geneticist, Massachusetts General Hospital
Boston, MA.

Pober BR, NEJM
362(3); 239-252:2010

Conflicts of Interest

- WSA supports the WS Registry (www.williams-syndrome.org/registry)
  - housed at MGH and run under my supervision
  - I receive no salary support from the WSA



JCP Williams (1961)

Circulation

American Heart Association.

Supravalvular Aortic Stenosis

J. C. P. WILLIAMS, B. G. BARRATT-BOYES and J. B. LOWE

Circulation. 1961;24:1311-1318
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Williams syndrome (WS)

OMIM # 194050

- **Unique multi system developmental disorder**
  - Characteristic physical features& medical problems
  - Distinctive cognitive, personality, & behavioral profile
- **~1/10,000 individuals**

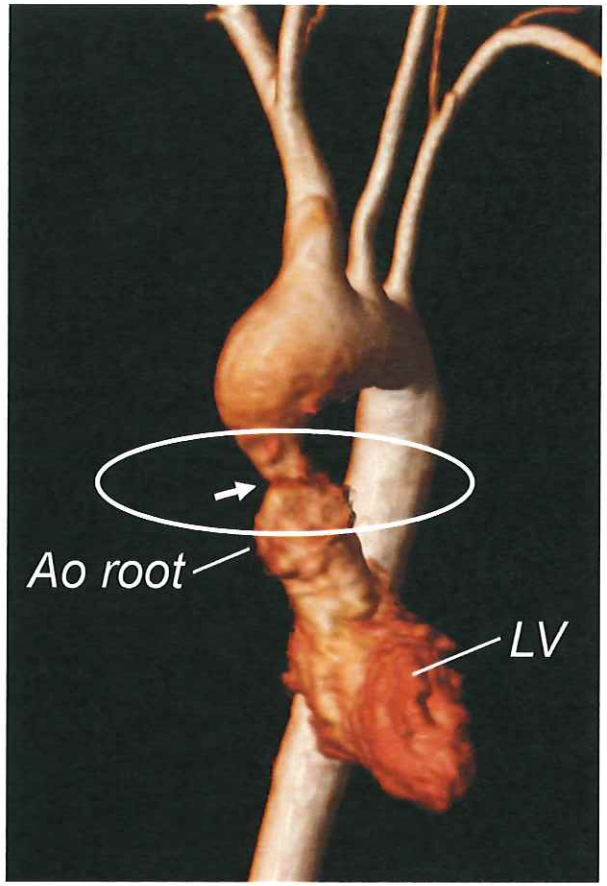
Auditory, ENT
Cardiovascular
Development, Cognitive
Dental
Endocrine
Gastrointestinal, Weight
Genitourinary
Miscellaneous
Musculoskeletal
Neurologic
Ophthalmologic
Personality, Behavior, Emotional well-being
Skin, Integument

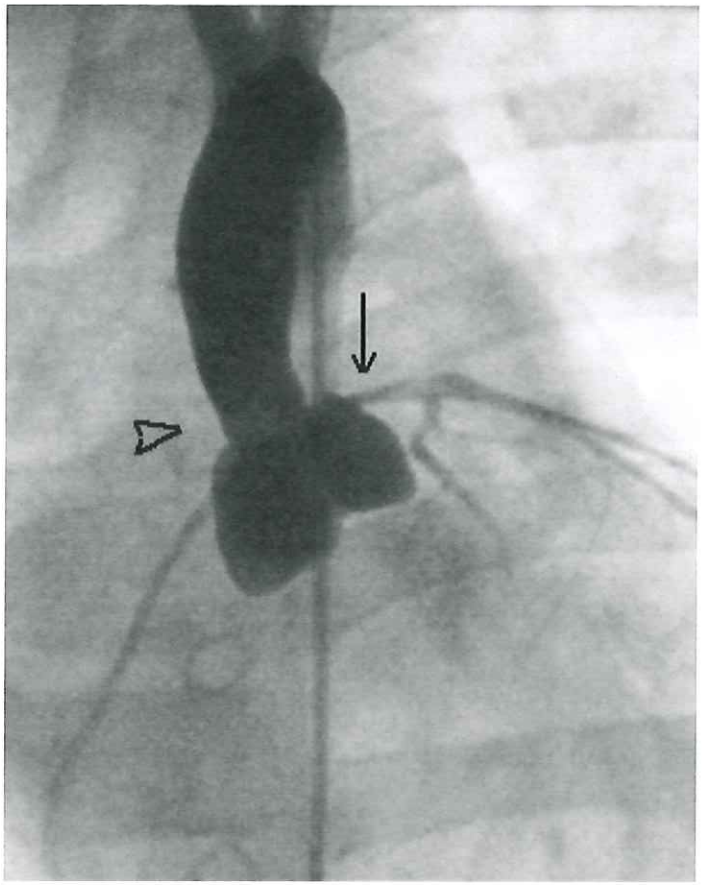
Lengthy list of POTENTIAL Problems

- No single individual with WS develops all these problems!

Auditory, ENT	"Hyperacusis" / Mild to moderate high tone SNHL / Ear wax
Cardiovascular	Vascular stenoses / Hypertension / Valve abnormalities / QTc prolongation / Stroke / Sudden death, anesthesia concerns
Development, Cognitive	Global cognitive impairment / Characteristic pattern of strengths & weaknesses ("WBS cognitive profile")
Dental	Poor dental hygiene / Abn shaped teeth / Malocclusion / Hypodontia
Endocrine	IGT, diabetes mellitus / Osteopenia & osteoporosis / (Subclinical) Hypothyroidism / Hypercalcemia
Gastrointestinal, Weight	Weight gain / Constipation / GER / Abdominal pain of ?etiology / Diverticular disease / Celiac disease
Genitourinary	Voiding frequency, urgency, enuresis / Structural renal anomalies / Bladder diverticuli / Nephrocalcinosis / Recurrent UTI
Miscellaneous	Short stature / Sleep dysregulation
Musculoskeletal	Joint laxity / Joint contractures / Spinal curvatures
Neurologic	Hypotonia / Hyperreflexia / Cerebellar findings /Chiari, type 1
Ophthalmologic	Altered visual acuity / Reduced stereopsis / Cataract / Glaucoma
Personality, Behavior, Emotional well-being	Impulsivity/short attention span ("ADHD") / Anxiety + Phobias / Obsessive compulsive traits / Dysthymia / Friendly personality → vulnerable to inappropriate advances or sexual abuse / "Psychosis"
Skin, Integument	Soft skin with ?premature aging / Premature graying of hair / Inguinal & other hernias

Supravalvar Aortic Stenosis (SVAS)

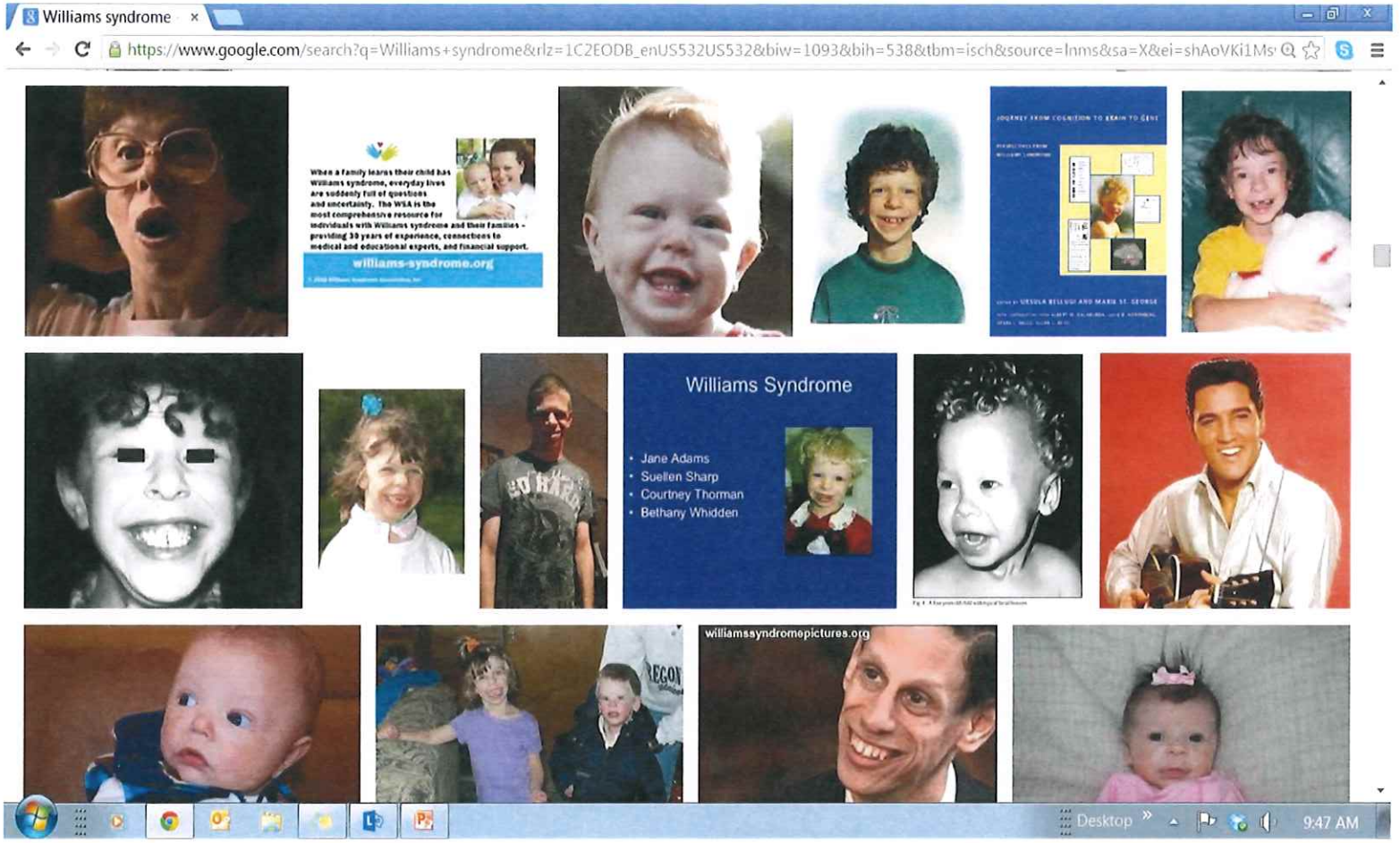




Pober, Johnson + Urban. *J. Clin. Invest.* **118**:1606–1615 (2008).

Glucose status in WS

- Majority (50-60%) of adults have abnormal glucose tolerance on standard oral glucose tolerance testing
  - Prediabetes
  - mild Diabetes Mellitus (DM)

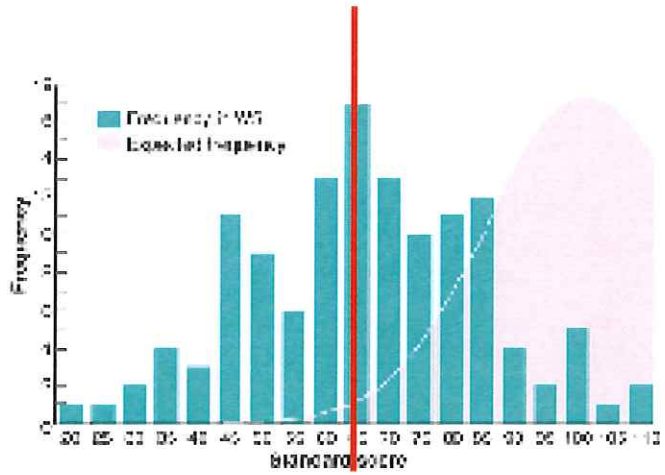

Williams syndrome
https://www.google.com/search?q=Williams+syndrome&rlz=1C2EODB_enUS532US532&biw=1093&bih=538&tbm=isch&source=lnms&sa=X&ei=shAoVKi1Ms
When a family learns their child has Williams syndrome, everyday lives are suddenly full of questions and uncertainty. The WSA is the most comprehensive resource for individuals with Williams syndrome and their families - providing 30 years of experience, connections to medical and educational experts, and financial support.
williams-syndrome.org
Williams Syndrome
Jane Adams
Suellen Sharp
Courtney Thorman
Bethany Whidden
williamssyndromepictures.org
Desktop
9:47 AM

Behavioral Features

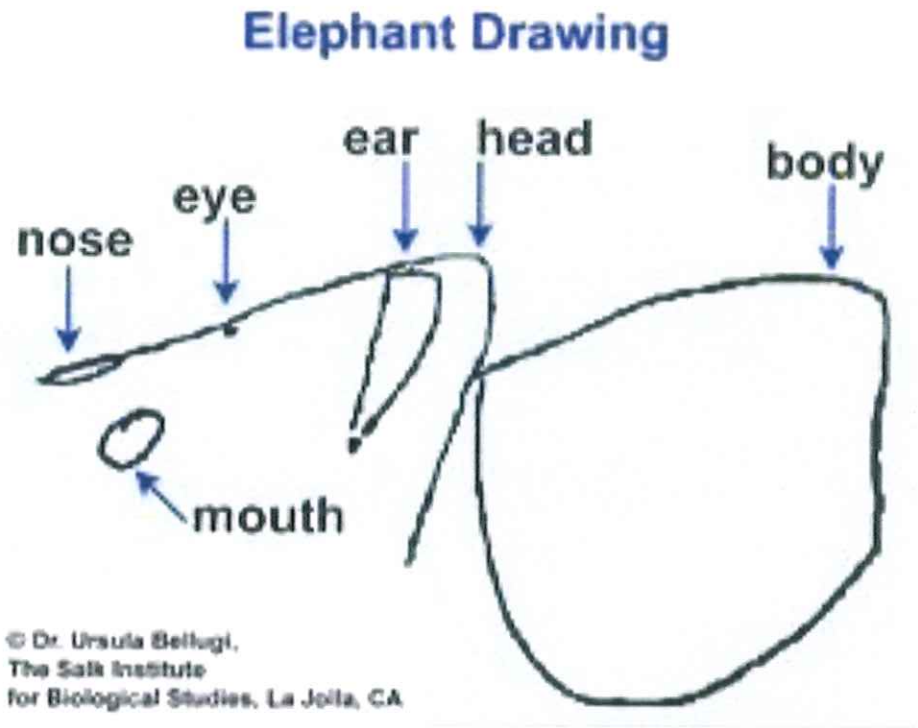
- Engaging, Charming
- Empathic, Sensitive, Affectionate
- Musical
- Hyper/sociability - Outgoing, Disinhibited
- Attention problems, Hyperactivity
- Phobias
- Perseverative
- Anxiety, anxiety, anxiety
- Dysthymic / Depressed
- Socially isolated

WS Cognitive Profile

- Global cognitive impairment
- Mean Full Scale IQ = 55 - 65
- Most function in mild-moderate intellectual disability range



Verbal High, Spatial Low

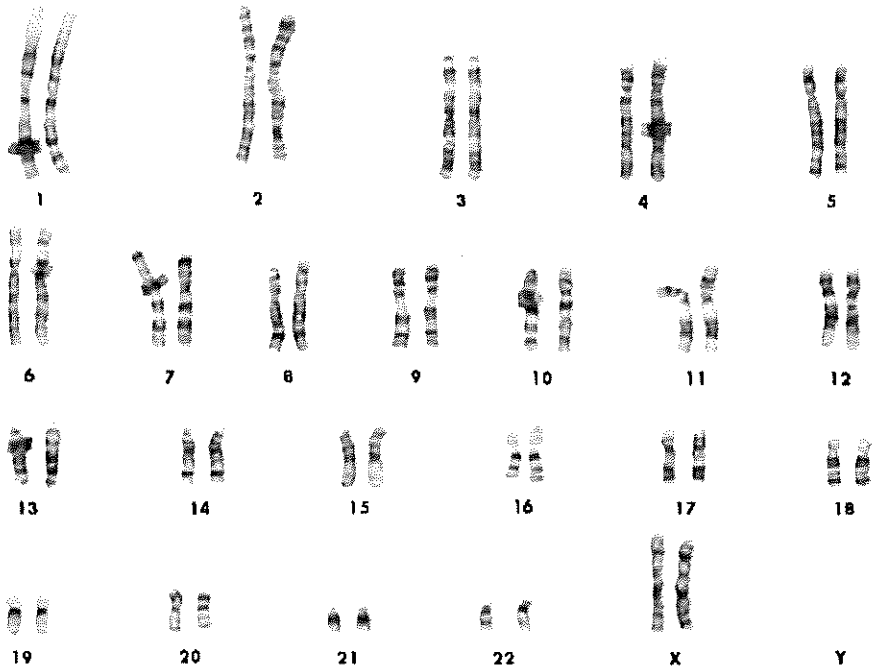


- AND WHAT AN ELEPHANT IS. It is one of the animals. And what the elephant does, it lives in the jungle. It can also live in the zoo. And what it has, it has long grey ears, fan ears, ears that can blow in the wind. It has a long trunk that can pick up grass or pick up hay… If they're in a bad mood it can be terrible..If the elephant gets mad, it could stomp; it could charge. Sometimes elephants can charge like a bull can charge. They have big long tusks. They can damage a car. It could be dangerous. You don't want an elephant as a pet. You want a cat or a dog or a bird.

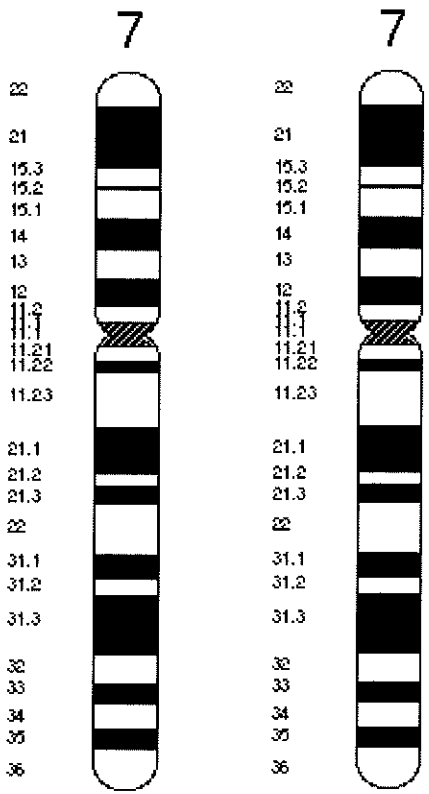
What causes WS?

Is it a genetic disorder?

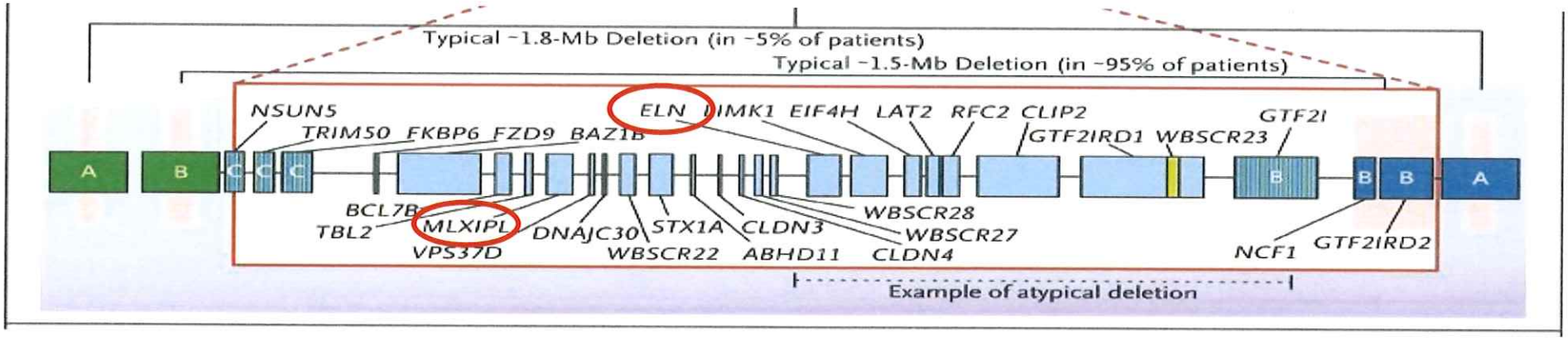
Normal chromosomes in WS



WS: microdeletion disorder w/ loss 26-28 genes



Mechanism of Underlying SVAS or DM



- Due to deletion of a chromosome 7 gene
- Deletion of elastin (ELN) gene → SVAS
- Deletion of MLXIPL (ChREBP) may → DM

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Impact of Williams syndrome

- Present at birth and lasts a lifetime
  - Never "outgrow" Williams syndrome
  - (Misconception that WS is a childhood or pediatric disorder)
- Likely to develop various medical problems over the lifespan
  - More medications, surgeries, doctor's visits
  - (Huge financial + emotional burden to family)
- Intellectual and emotional disability
  - Unable to navigate medical system, manage own health care, live independently, hold a competitive job
- Treatment is supportive, not curative

Challenges Transitioning from Pediatric to Adult Medical Providers

- Pediatricians may hand over care adult providers unfamiliar with the special healthcare needs of these patients.
- This can result in over-referral to many different medical specialists which, in turn, → fragmentation of care.
- Poor transition results in decreased quality health care.

Possible Solutions Transitioning from Pediatric to Adult Medical Providers

The Maastricht model

- "a special outpatient clinic has been developed at the academic hospital in Maastricht, the Netherlands.
- …clinic is primarily aimed at providing quality healthcare for adult patients with ID and/or genetic syndromes in general.
- (The clinic is run by a) clinical geneticist and a medical doctor specialized in treating persons with ID."

Schrander-Stumpel CTRM, et al. Healthcare transition in persons with intellectual disabilities: General issues, the Maastricht model, and Prader–Willi syndrome. Am J Med Genet Part C Semin Med Genet 145C:241–247.

RESEARCH REVIEW

AMERICAN JOURNAL OF medical genetics PART A

Healthcare Transition in Patients With Rare Genetic Disorders With and Without Developmental Disability: Neurofibromatosis 1 and Williams–Beuren Syndrome

Andrea Van Lierde,[1] Francesca Menni,[1] Maria Francesca Bedeschi,[2] Federica Natacci,[2] Sophie Guez,[1] Paola Vizziello,[3] Maria Antonella Costantino,[3] Faustina Lalatta,[2] and Susanna Esposito[1]*

[1]Pediatric Clinic 1, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

[2]Genetic Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

[3]Child and Adolescent Neuropsychiatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

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- Create Centers of Expertise [CE] - "Regional or national multidisciplinary facilities specialized in groups of Rare Diseases and housed in University-based or tertiary care hospitals…….thus overcoming the limited experience of professionals confronted with very rare conditions"

TABLE III. Requirements for Meeting the Healthcare Needs of RD-Affected Patients at Transition

Expert multidisciplinary team
Availability of dedicated areas
Availability and accessibility of social worker, psychologist, vocational counselor, legal assistance, interpreter, trained nurses, and administrative personnel
Training and education of the transition team
Partnership/joint meetings with adult multispecialist team
Dedicated care/transition coordinator acting as a link to the community
Coordination and information sharing with primary care providers
Telephone time/dedicated lines for patients, families, and primary care providers
Links and collaboration with patient associations
Links and collaboration with other national and international CEs
Capacity to produce and adhere to good practice evidence-based guidelines for RD care in children and adults
Capacity of implementing outcome measures and quality control

CEs, centers of expertise.

Suggested Strategies

- "continuing medical education (CME) programs"
  - needs of adults with Rare Diseases (RDs), with or without developmental and intellectual disabilities, how to communicate with them….."
- "group discussions between medical students & RD pts and their families"
- "training of adult psychologists & psychiatrists [AND MDs!] in life-span developmental psychology and the management of psychiatric problems"
- "financial support to individual CEs allocated on the basis of quality of care evaluations"
- "questionnaires asking patients and their families to evaluate their degree of satisfaction and make suggestions for improvement"

SUMMARY

- Williams syndrome as an example of a rare disorder with ID
  - Medical & Genetic aspects
- Impact of having Williams syndrome
  - Transition from pediatric to adult medical care
- Shared suggestions from two European groups on how to provide better care for adults with rare disorders.
  - ???Support advanced training in CT for a healthcare provider to specialize in treating persons with ID/RD??