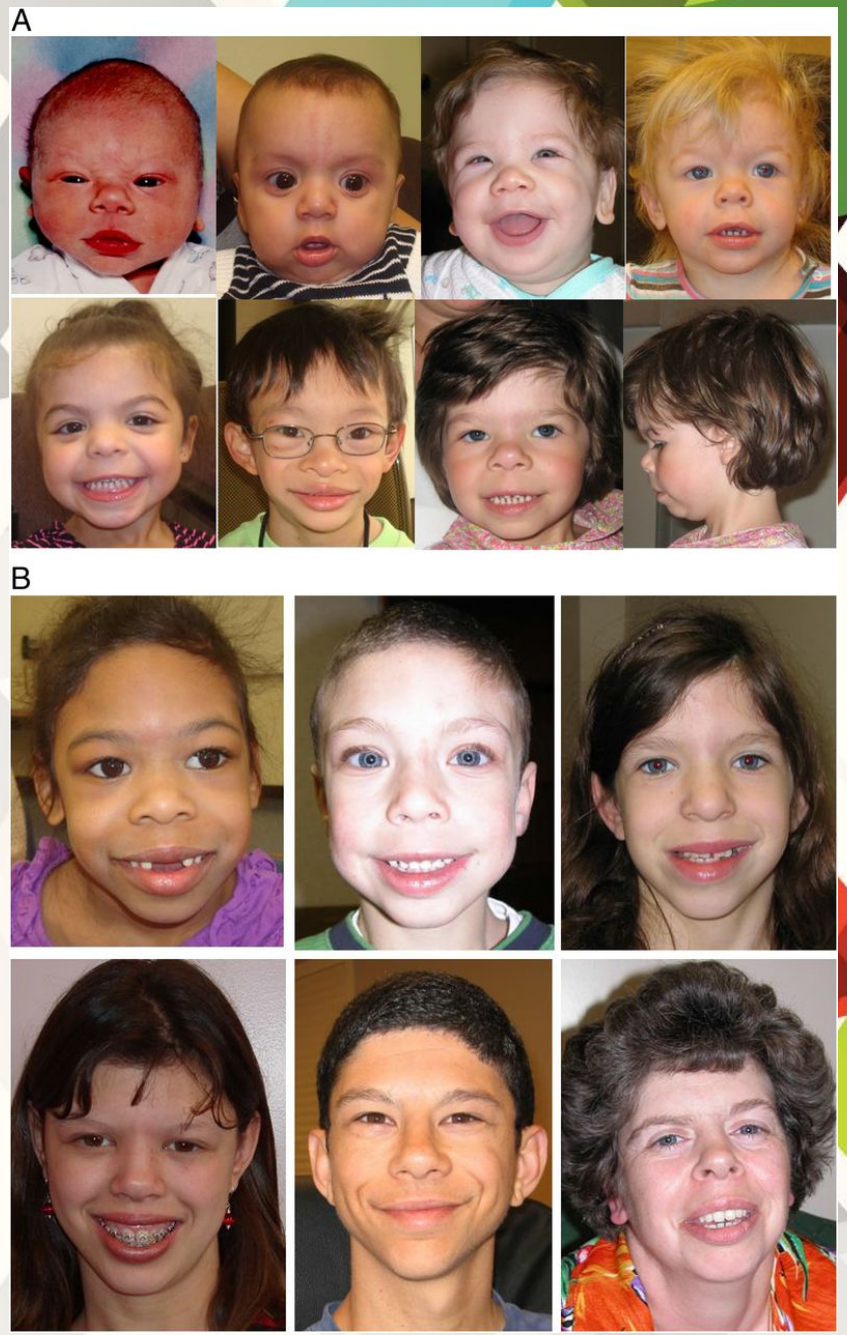


WILLIAMS SYNDROME

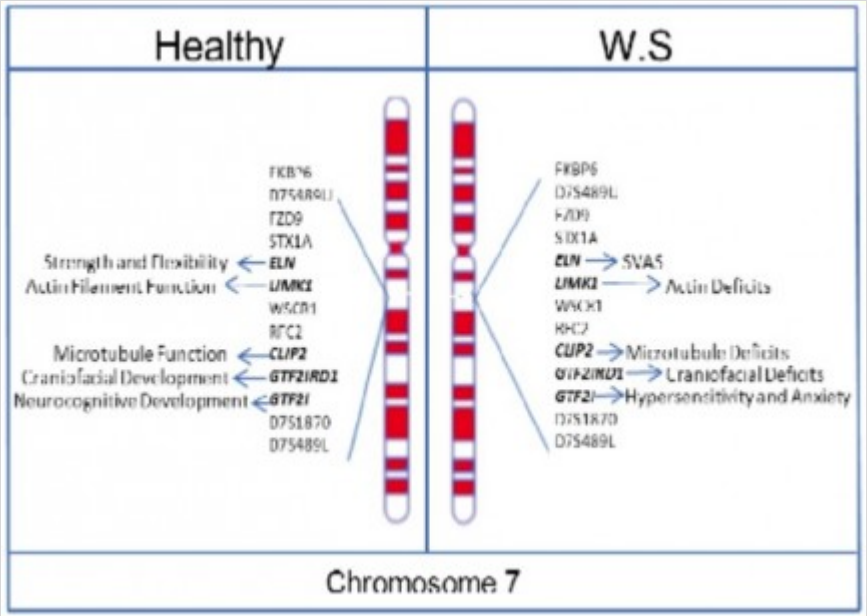
Aaron Goldberg, MD
UCI/CHOC Pediatric Residency Program

Learning Objectives

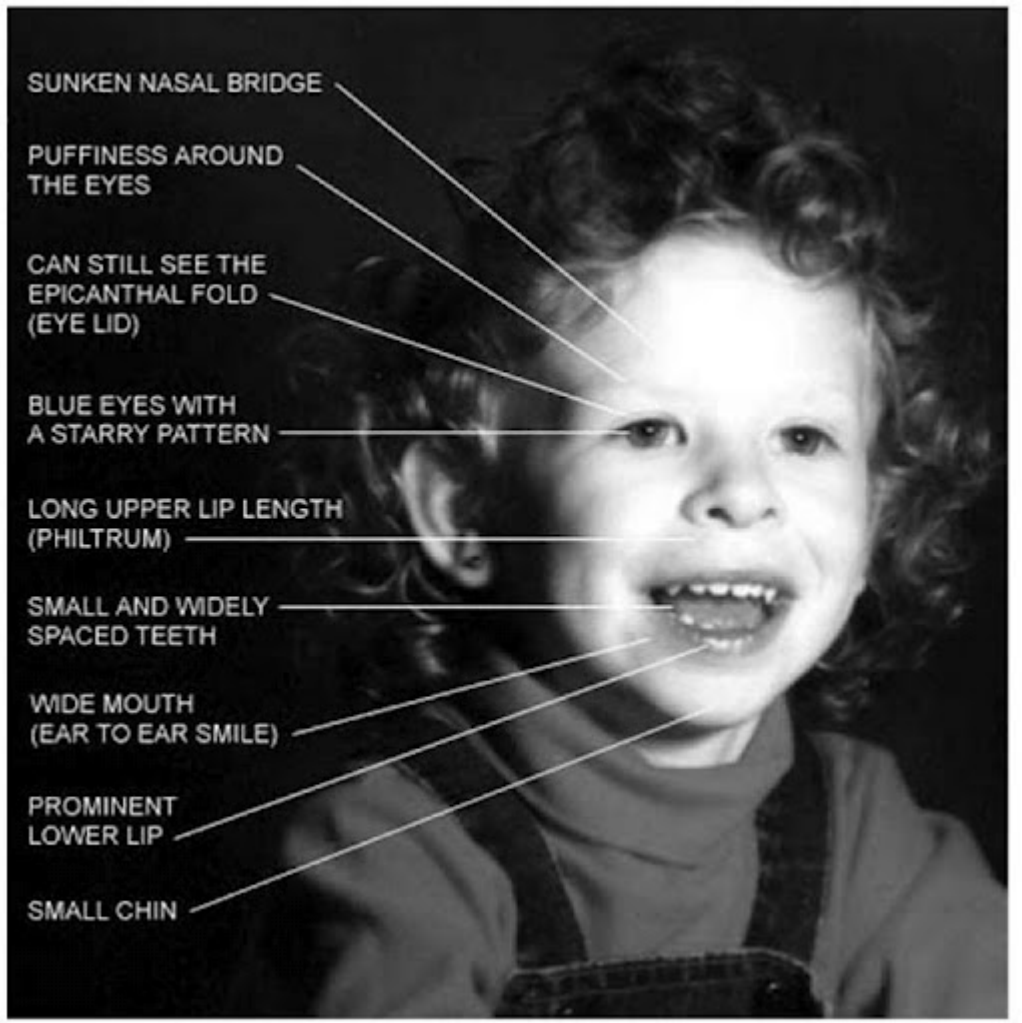
- Understand the genetic basis of Williams syndrome
- Be able to identify key clinical features of Williams Syndrome
- Know how Williams syndrome is diagnosed
- Know the basics of screening and health care supervision for children with Williams Syndrome

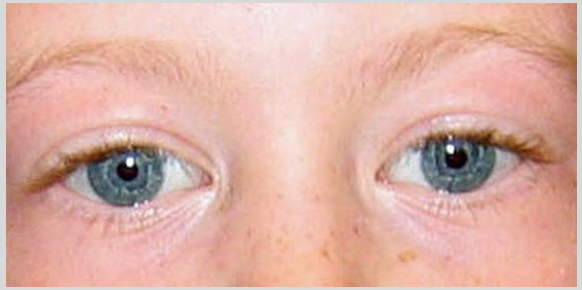
The Genetics

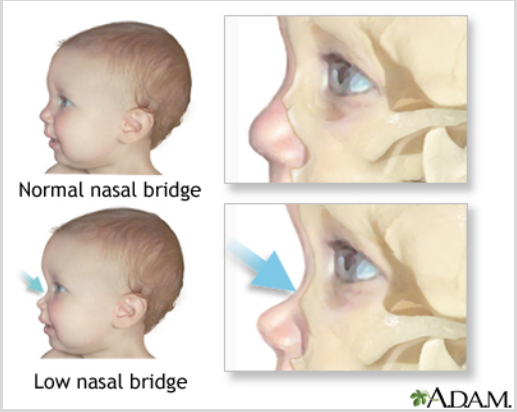
- 1 in approximately 10,000 live births
- Microdeletion of the long arm of chromosome 7 (7q11.23)
  - Includes 26 to 28 genes
  - Elastin gene lost in nearly all cases
- Most cases result from spontaneous microdeletion, with small number of cases having autosomal dominant inheritance



Facial Features: “Elfin facies”







Ears:

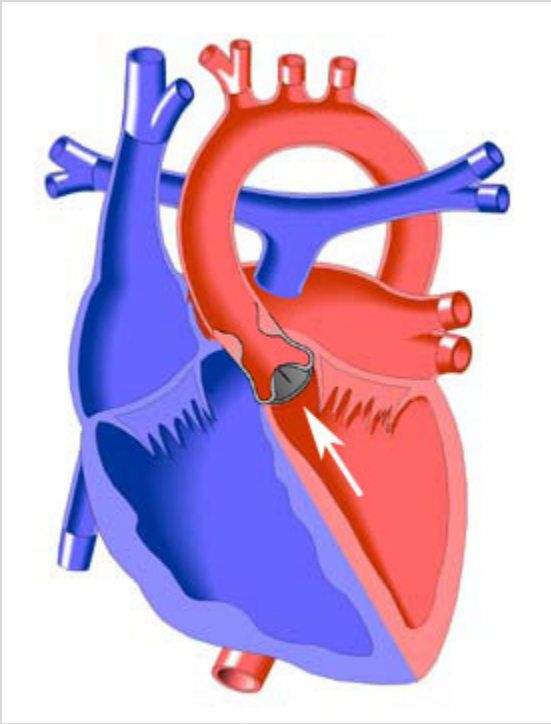
- Hyperacusis (sensitive to certain frequencies)
- Progressive sensorineural hearing loss
- Recurrent ear infections

Eyes:

- Starry pattern on iris (above)
- Strabismus

Heart, Hypercalcemia, Hyperflexible, Hernias

- Cardiovascular abnormalities (80%)
  - Supravalvar aortic stenosis (most common) or peripheral pulmonic stenosis
  - Hypertension (50%)
- Hypercalcemia
  - Idiopathic
  - Results in extended period of colic/irritability
  - Usually starts in infancy and resolves before 3 years old
- Joint hypermobility and/or contractures
- Umbilical and inguinal hernias



Growth

- Slightly lower to normal birth weight
- Slow weight gain
  - Feeding difficulties due to hypotonia, which typically resolve as child gets older
- Early puberty
- Overall growth delay, resulting in short stature

Development, Cognitive and Behavioral

- “Cocktail party” personality
  - Loquacious, gregarious, excel socially
- Developmental delay (predominantly language and motor)
  - Language – first words at 3 years old
  - Motor – 6 months delayed in young children
- Moderate intellectual disability (IQ 50-60)
- Impaired visuospatial constructive cognition
- Unusually good musical ability (20% with absolute or perfect pitch)

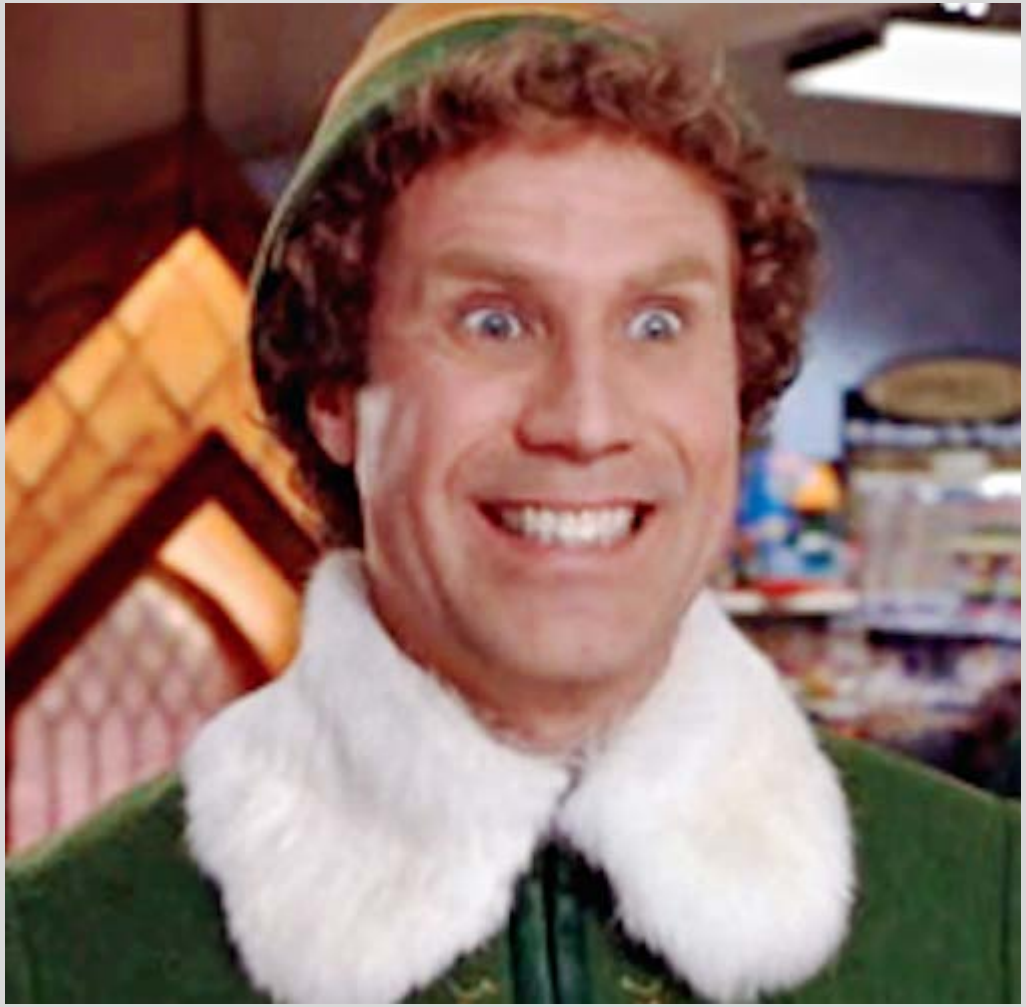
Diagnosis

- First identify physical and clinical features
- Confirm with either:
  - Chromosomal microarray (looks at all chromosomes)
  - FISH (Fluorescence in Situ Hybridization) probes targeted at identifying if 2 copies of elastin gene

Health Screening and Surveillance

- Plot growth parameters on Williams Syndrome-specific growth chart (each visit)
- Check blood pressure in both arms (each visit)
  - If aortic stenosis present, 3 limb BP and echo with cardiology every 3 months in 1st year, then every 1-2 years
- Check for inguinal hernia (each visit in first year, then annually)
- Evaluate for hypotonia, hyperreflexia, cerebellar signs, joint laxity (each visit in first year, then annually)
- In first year of life, discuss potential feeding issues, hypercalcemia (avoid Vitamin D), constipation (treat aggressively)
- Vision and hearing screening yearly
- Serum calcium levels every 4 months in 1st year of life, then every 4-6 mo until 2yo, then every 2 years
  - EKG yearly for prolonged QT surveillance
- Thyroid function tests yearly until 3yo, then every 2 years
- Renal/bladder ultrasound at diagnosis (possible malformations) and urinalysis yearly

William Ferrell is **Elf** (a mnemonic)



Bonus: William is 7 letters = chromosome 7

William Syndrome Feature	How it fits in the mnemonic
Elfin facies	Will Ferrell is an Elf
Hypersocial/friendly	This is his character's personality in the movie
Short stature	Elves are short
Cardiac (supravalvar aortic stenosis)	He had a big loving heart
Hypercalcemia	As an elf, he drank A LOT of milk

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