

Williams Syndrome



Deletion of chromosome 7q11.23

- Every human has 46 chromosomes
- 23 pairs - one from mother
one from father

Each person's DNA is like a text book

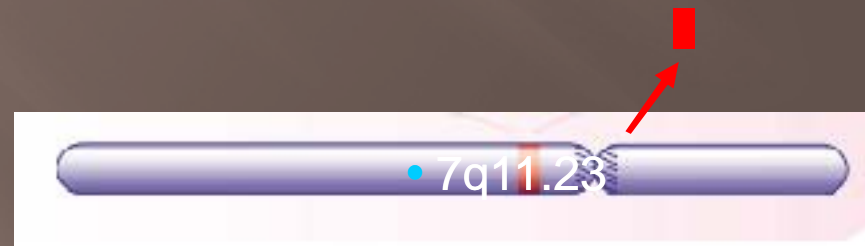
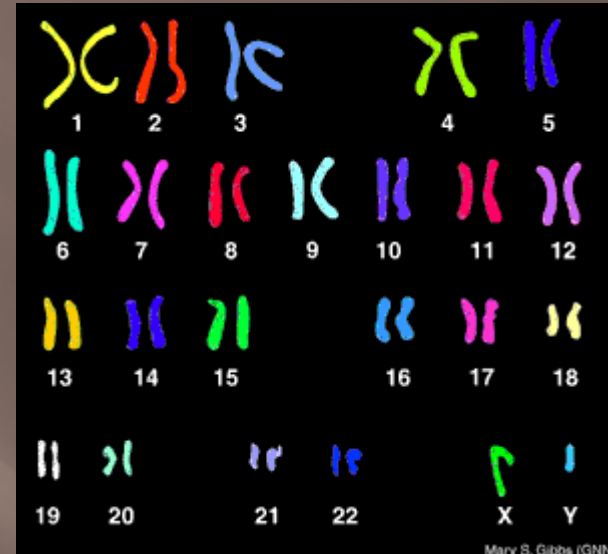
Each chapter in the book is a chromosome

Each gene is a word.

Individuals with WS are missing 28 words

In a 30,000 word book

p = short arm
q = long arm



Genes in the WS Critical Area

Name	Function
• ELN [Elastin] narrowing	<ul style="list-style-type: none">▪ Connective tissue scaffolding; Blood vessels▪ Skin -soft; early wrinkles▪ Bowel and bladder diverticula (pouches)
• WS TF	<ul style="list-style-type: none">▪ Facial appearance
• CYLN2	<ul style="list-style-type: none">▪ Growth• Facial Appearance?• Neurologic function
• GTF2IRD1	<ul style="list-style-type: none">▪ Facial appearance?▪ Visuo-spatial understanding (cognition)
• GTF2I	<ul style="list-style-type: none">▪ ?Social behaviors - gaze; - attention to strangers



Longer deletions: typical WS plus

- seizures & severe mental retardation

Shorter deletions: lack some typical WS features;
non-verbal skills often better

Williams syndrome

1 in 10,000 births - 5000 with WS in South Africa.

26-28 genes deleted on chromosome #7...
contiguous gene syndrome

Common Characteristics :



- ♦ Characteristic facial appearance - individuals appear related if side by side but also retain family resemblance
- ♦ Feeding difficulty - poor suck/swallow; sensory issues
 - ♦ Low birth-weight / slow weight gain - failure to thrive
 - ♦ Irritability (severe colic during infancy)
- ♦ Heart and blood vessel problems

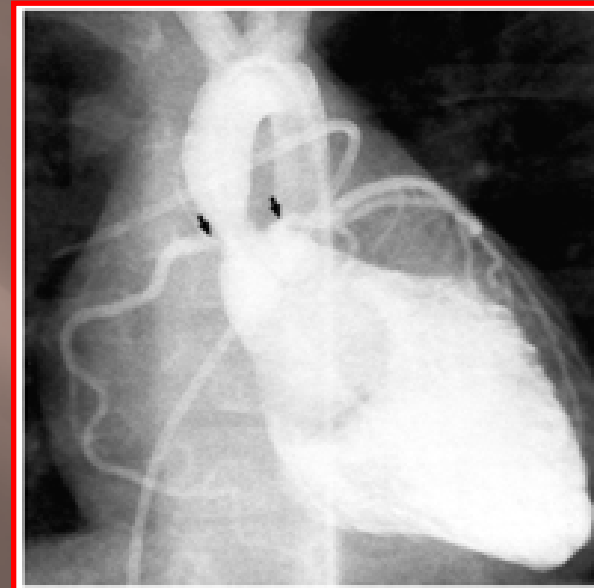
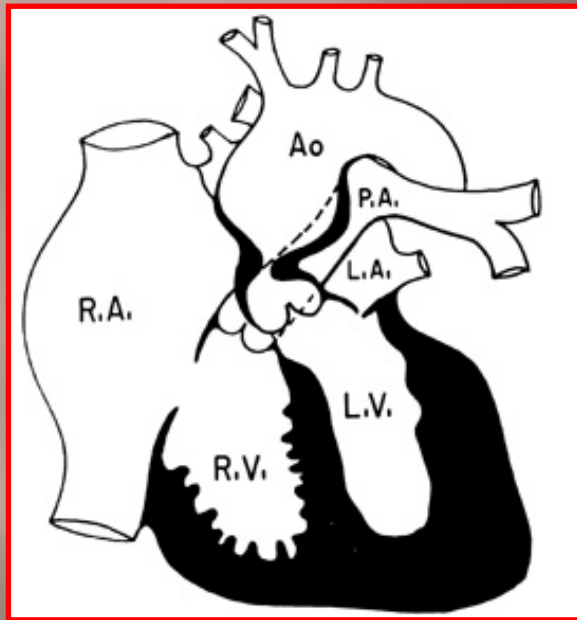
Cardiovascular Issues in Williams Syndrome

- Supra Valvular Aortic Stenosis - never gets better but can be stabilized
- Peripheral pulmonary stenosis - often resolves on its own
- Coronary Artery Stenosis
- Carotid Artery Stenosis
- Mesenteric Artery Stenosis - stomach pain
- Renal Artery Stenosis - hypertension



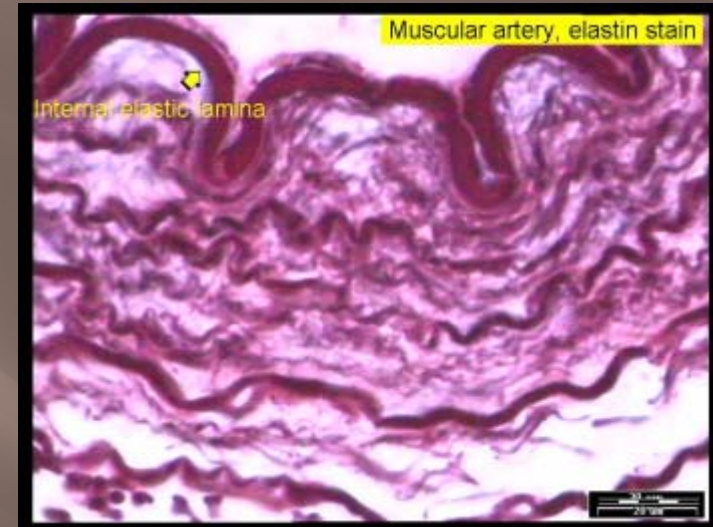
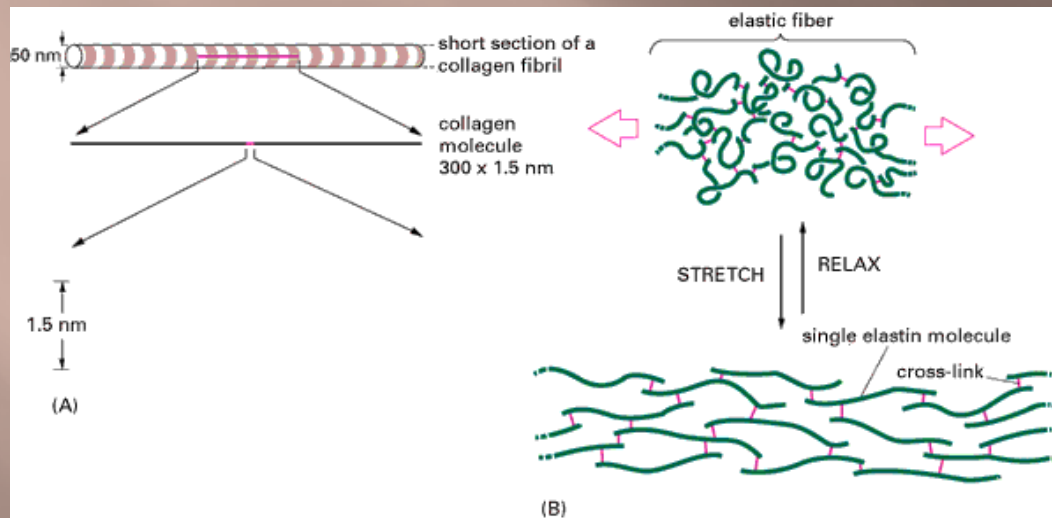
Cardiovascular issues usually appear in first decade of life. Most surgical intervention before age 5

Cardiovascular Disease : SVAS



Supra valvular aortic stenosis

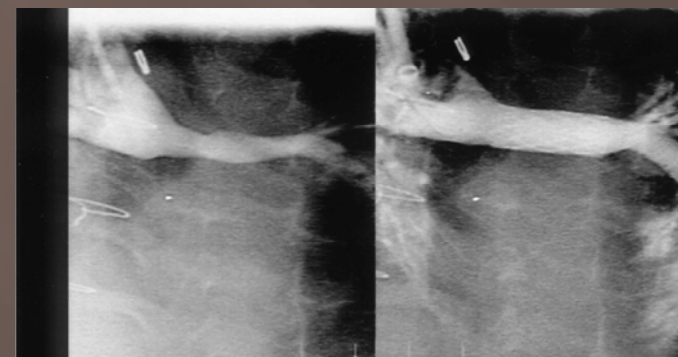
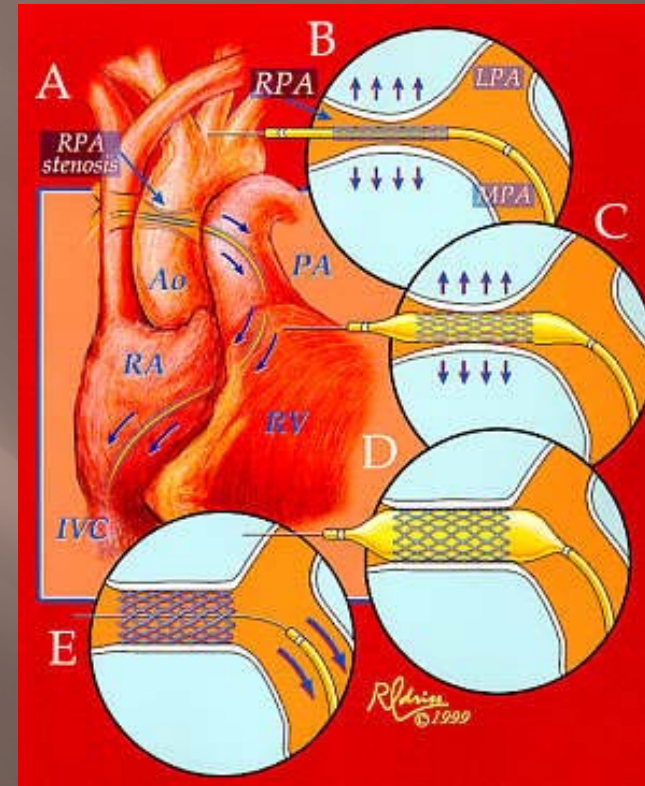
Cardiovascular Disease



Decreased manufacture of elastin leads to smooth muscle overgrowth and inelastic arterial walls.

Pulmonary Stenosis

- **Cardiac catheterization:**
- balloon angioplasty ± stent(s)
- **Surgery**
-patch repairs



Cardiovascular Procedures



WS patients often need sedation or general anesthesia for both cardiac and non-cardiac procedures:

echo, MRI, cardiac cath, cardiac surgery, ENT surgery, orthopedic, endoscopy, etc.

- Echo & EKG give good info re: SVAS, SVPS, RVH, LVH, but that may not be enough.
- Difficult to assess the coronaries without more invasive testing (ie: cardiac cath)
- Newer cardiac imaging techniques (CTA, MRI) may allow more accurate coronary anatomy assessment

Other Medical Issues

Infancy and early childhood

- GI
 - gastro-esophageal reflux (GER)
 - constipation
 - feeding difficulties
- CNS
 - low tone;
 - developmental delays
- Hypercalcemia • 15/100 children



WS: Medical Aspects in Childhood

- ▣ **Gastro-intestinal tract (GI)**
 - Gastro-esophageal reflux (GERD)
- ▣ Persistent feeding problems:
 - inability to chew and swallow coarser textured foods
 - Rx: Feeding specialist/speech therapist
- Constipation → diverticula



Williams syndrome: Medical Issues

Constipation

Untreated/chronic:

→ diverticula → diverticulitis

Rx: Fiber in diet

No sodas

Cut down on starch

Miralax (PEG); Mineral oil

Toilet routine (older child)



Medical Issues in childhood

■ Sleep

- Difficulties in falling and staying asleep - common
- Sleep study (polysomnography) - significantly higher periodic limb movements in sleep (PLMS) - *restless legs*
 - Woke up many more times during the night - less time spent sleeping during "sleep" periods
- This may worsen symptoms of ADHD

Rx: *Clonazepam* ?- significant improvements in sleep and behavior

Clonopin ?

Melatonin ?



WS Medical Issues in childhood

■ Puberty in WS:

- Menarche (first menstrual period):
average in USA - 10.3 yr;
UK - 11.2 +/- 1.3yr
- Precocious puberty - rare
- Accommodate to menstruation
without many problems
- Sexual desires - prevalent
contraception



Medical Issues in Childhood: anesthesia

Does anesthesia carry a greater risk of death in WS?

- Sudden death
 - ◆ at times - occurs with anesthesia
 - ◆ at times - unrelated
- No evidence that a deleted gene in the WS region causes malignant hyperthermia
- Linked to condition of the heart & coronary arteries:
 - ◆ if the aorta and /or the pulmonary arteries are narrow (stenosis),
 - ◆ the heart has to work harder to push out the blood
 - ◆ heart wall becomes thickened (hypertrophy), but eventually may fail to work properly

Medical Issues in Childhood

- ▣ Chiari I “malformation” (sequence?)
Stenosis of the brain stem

headaches, vertigo, tinnitus, diplopia,
contractures and decreased muscle strength.
- ▣ Surgical decompression may relieve symptoms

Seizures - rare

- deletions larger than usual
- infantile spasms
- usually with severe mental retardation

Medical Issues in Teens & Adults



- Decreased energy
- Scoliosis/Lordosis/
Kyphosis
- Thrombosis
- Weight gain/Diabetes
- Anxiety/depression
- Gastrointestinal issues
 - Diverticulitis
 - Diverticulosis



Treatment for Medical Issues

- ▣ WS Multispecialty Clinic
- ▣ Integrated, anticipatory care by medical staff
- ▣ Expertise in cardiology, genetics, developmental pediatrics, physical, occupational, and speech therapies, nutrition and feeding, behavioral pediatrics, ophthalmology, orthopedics, dentistry, psychiatry, gynecology, neurology, and neuroradiology.
- ▣ Relevant evaluations at 1-3 year intervals, depending on age and medical needs, during a 1-2 day outpatient visit.

Individuals with Williams Syndrome

Uniquely Challenged;
Uniquely blessed...

Eager to make a difference
in a changing world

