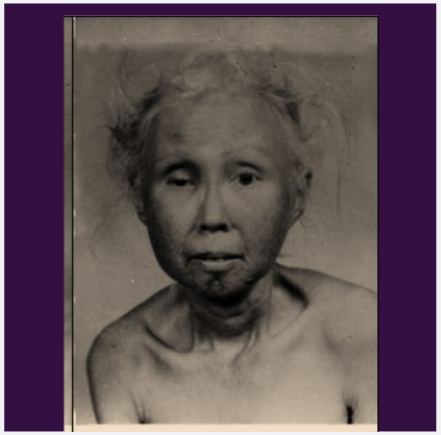
# WERNER SYNDROME



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# + Symptoms

## -Cardinal signs & symptoms

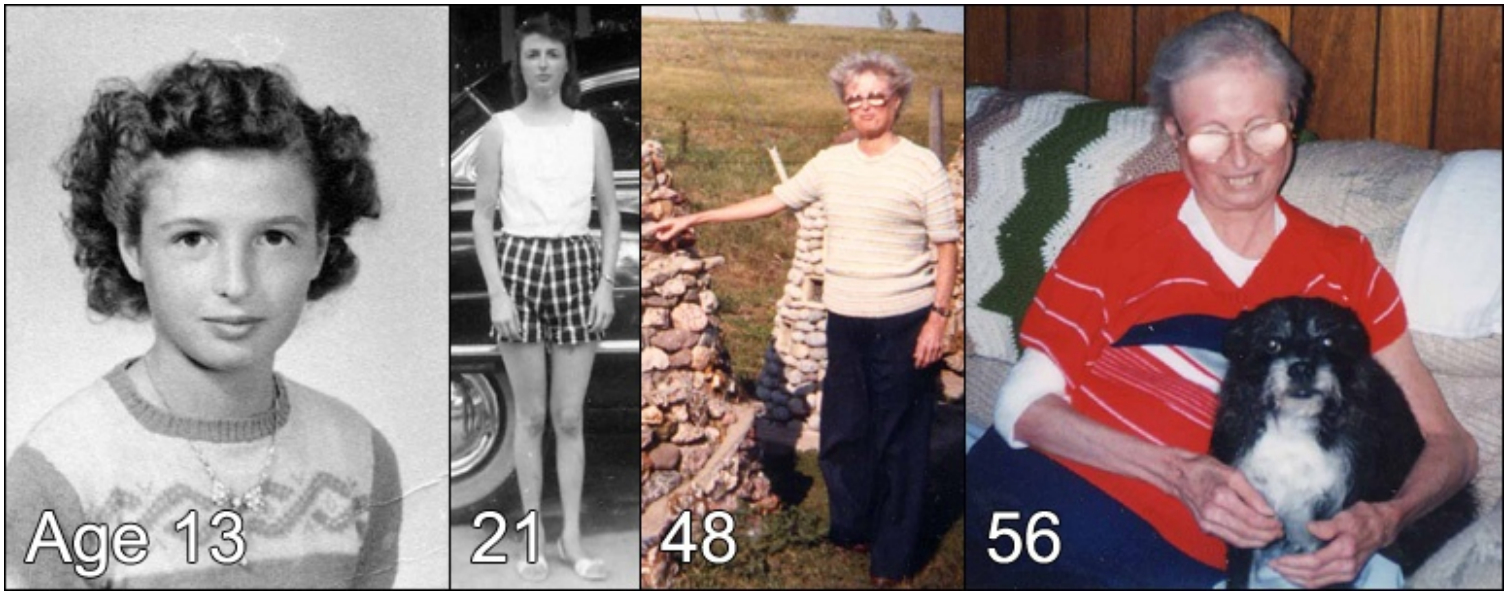
- Bilateral cataracts
- Characteristic skin (ulceration, tight skin, pigmentary alterations)
- "Bird-like" facial features (nasal bridge seems pinched)
- Short stature (lack of growth spurt during teen years)
- Premature graying/thinning of scalp hair
- Inherited: third cousin or closer, or affected sibling

## -Further/Secondary signs & symptoms:

- Type 2 diabetes, osteoporosis, flat feet, atherosclerocis, secondary sexual underdevelopment and diminished infertility

# Diagnosis

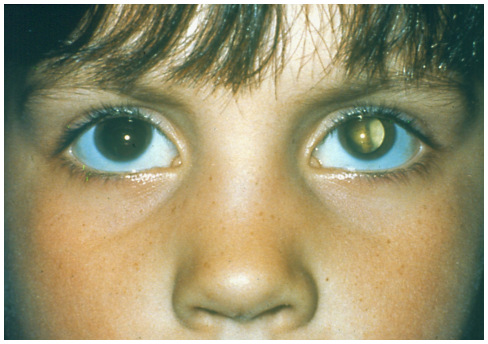
- **Definite:** all cardinal signs present + 2 others
- **Probable**: first 3 cardinal signs + any 2 others
- **Possible**: cataracts or dermatologic alterations + any 4 others
- **Exclusion:** cardinal signs + further symptoms before age 10 (except for short stature)



# Treatment

- *No specific treatment to cure disease*

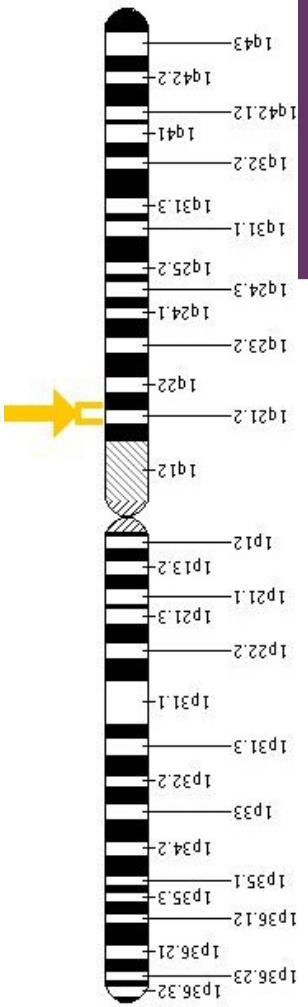
-Treatment addresses symptoms:



- Aggressive treatment of **skin ulcers**
- Control **type 2 diabetes**
- Cholesterol-lowering drugs if needed
- Surgery for **ocular cataracts**
- Prevention of Secondary Complications:
  - Avoidance of  smoking, excess weight, & inactivity (increase the risk of **atherosclerosis**)
  - Skin care

# Molecular Genetics of WS

- Gene: WRN
  - Only gene associated with Werner Syndrome
  - Located in short arm of chromosome 8 at position 12
  - Codes for Werner protein that is a **member of the DNA helicases family**
    - Helicases unwind DNA structures for DNA repair or replication
  - N-terminal region of the protein has **exonuclease activity**
    - Exonucleases trim broken ends of damaged DNA
  - Werner protein is needed to **maintain genomic stability** (DNA repair via unwinding or digesting intermediate DNA structures)
    - *Note- a mutation would thus easily lead to cancer*
    - *Stop codon, insertions or deletions → frame shift mutations*
  - **Recent finding:** needed to maintain DNA ends (telomeres)
    - *Telomere dysfunction → genomic instability →cancer*



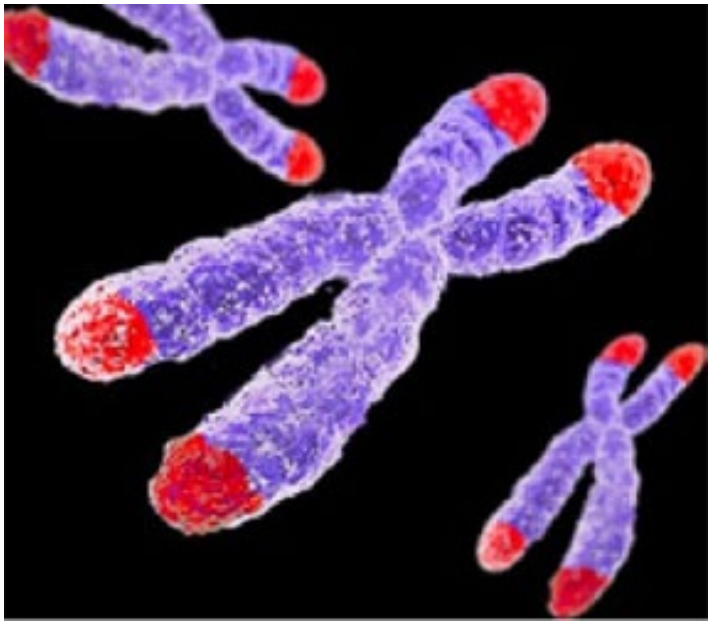
# Genetic Diagnosis/Testing

- Carrier testing for WRN mutations is not offered- not clinically available

- Research Testing:
  - Sequence Analysis- of WRN coding region to detect mutations
    - Results- 90% of individuals with Werner's Syndrome showed mutations in the WRN gene
  - Western Blot Analysis- determines the effect of the mutation on the WRN protein
    - Results- majority of affected individuals with WRN mutations → absence of protein
  - Preimplantation Genetic Diagnosis- available for families with affected relatives
  - FISH Sequencing- found absence of protective telomeres in WS patients

# Novel Genetic Therapy

- Therapy found while seeking to understand relationship between aging & cancer(2007)
  - Elongation of short telomeres via **telomerase**
  - Study added functional copy of WRN gene or a gene encoding telomerase to WS cells= equally abolished mutations/DNA damage
  - Researchers predict cancer in old people has the same basis
- Treatment is very limited
- (2011) Aging is accompanied by a decrease in WRN gene expression in human blood cells



# References


- Genetics Home Reference: WRN gene
- OMIM: Werner Syndrome
- Gene Review
- Genes and Diseases
- "FISH-ing for links between cancer and aging." *Salk Institute for Biological Studies. (2007)*
- Polosak, J. "Aging is Accompanied by a Progressive Decrease of Expression of the WRN Gene in Human Blood Mononuclear Cells." *PubMed. (2011)*