WERNER SYNDROME

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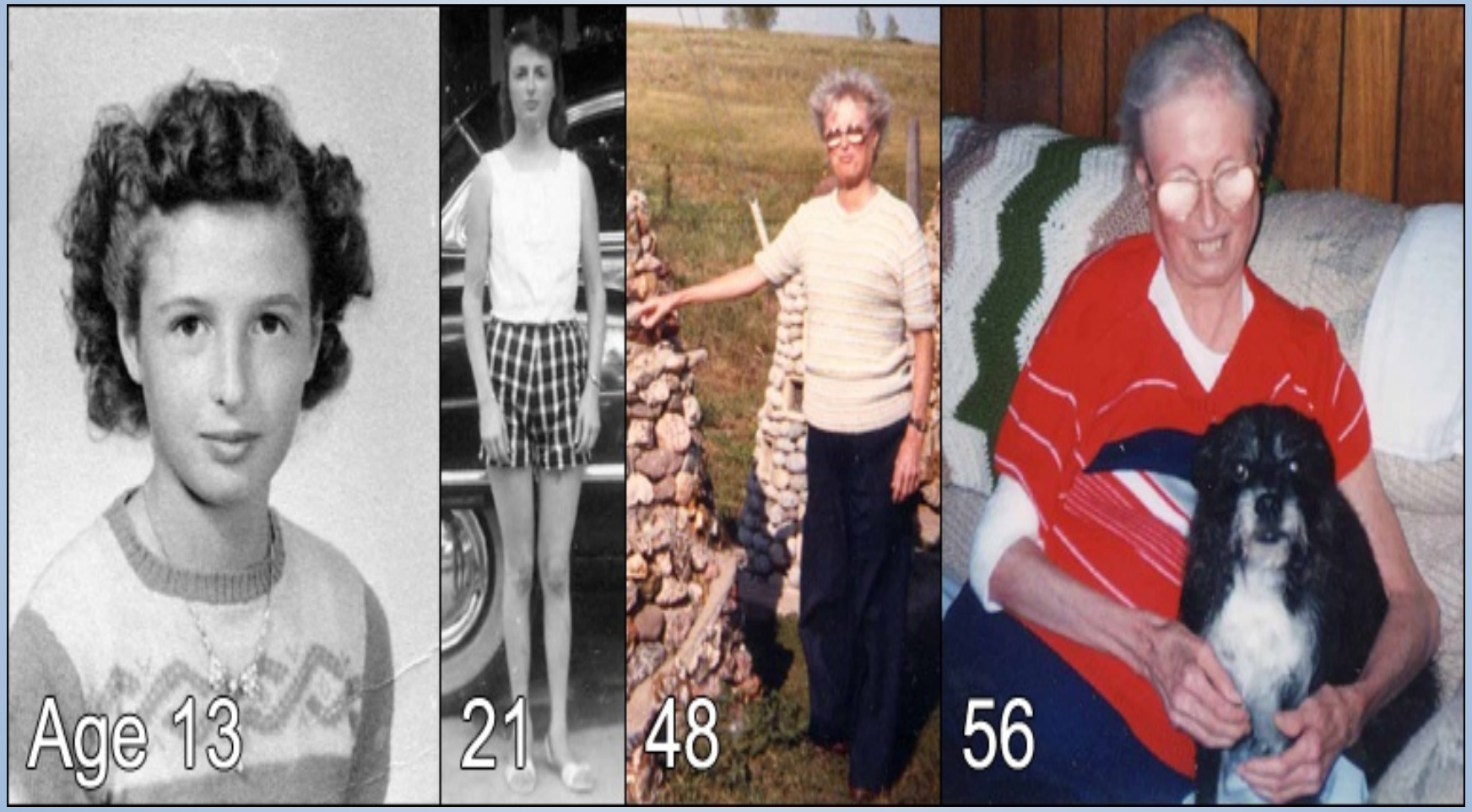
What is Werner Syndrome

- Rare aging disease (adult progeria)
- Stunted growth
- Abnormal fat deposition
- Decreased fertility
- Susceptibility to normal aging disorders
  - Cataracts
  - Graying and thinning of hair
  - Arthrosclerosis
  - Osteoporosis
  - Cancer


Age 13
21
48
56

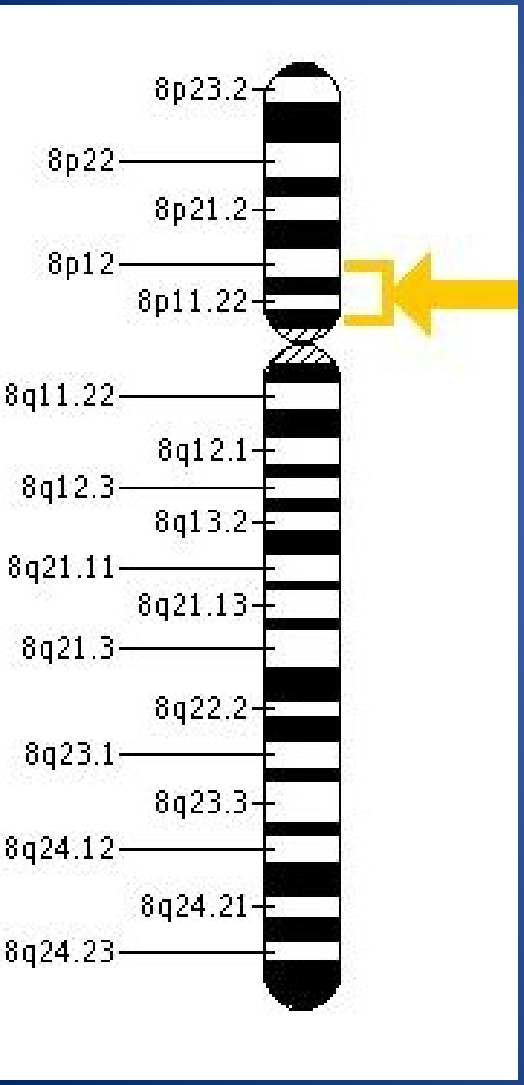
Classical Diagnosis

- Based on observation of physical symptoms
  - Individual may notice skin problems and visit a dermatologist
  - A probable diagnosis can be made once at least 3 of the physical signs manifest
- A urine test can confirm whether a patient has the disease if other symptoms are present
  - Tests the amount of hyaluronic acid
  - Low specificity

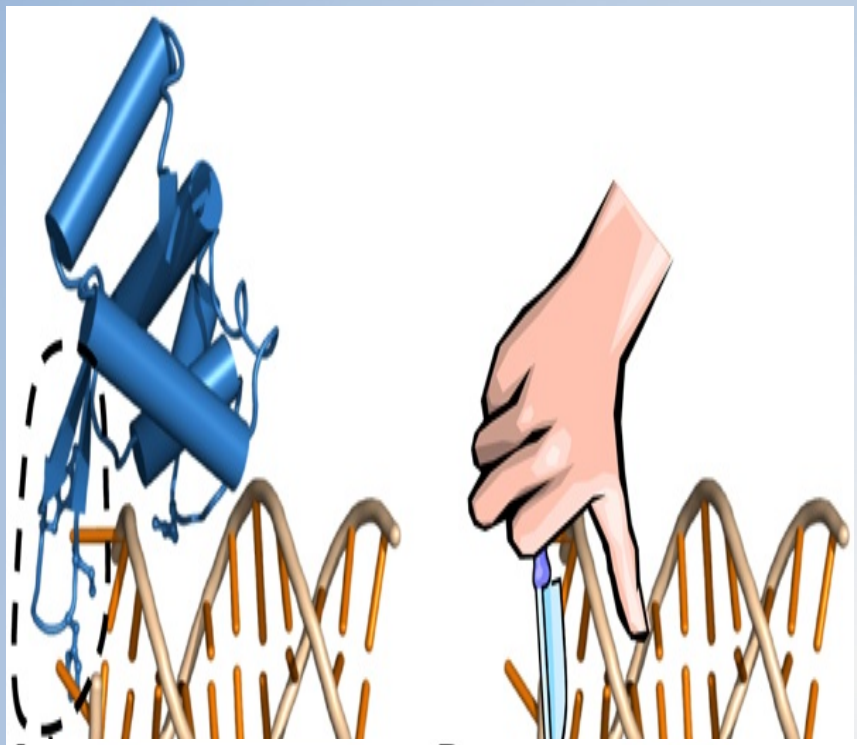
Treatment

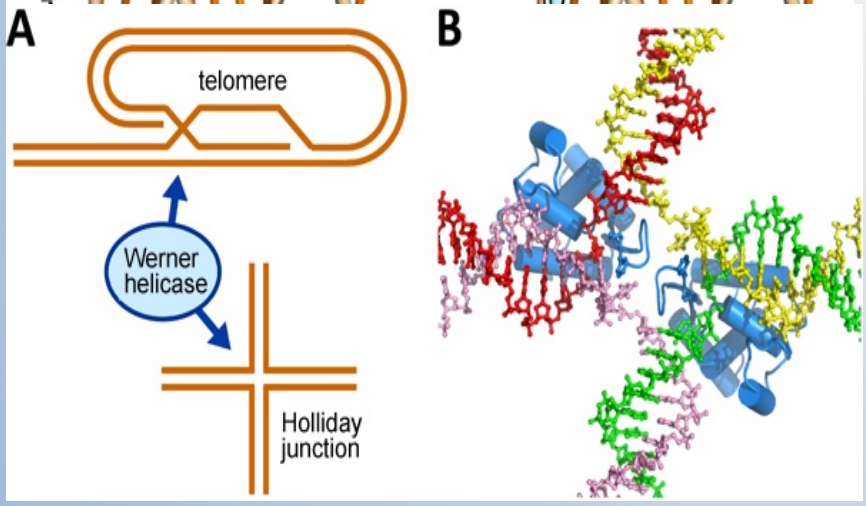
- Based on relieving the symptoms
  - Removal of cataracts
  - Lipid profiling to determine cholesterol levels
  - Annual screening for type 2 diabetes and cancer
    - Monitor nutrition, exercise, and sun exposure to help prevent the onset of these secondary complications
  - Normal treatment for all complications

Gene Details



- WRN gene located on Chromosome 8
  - About 140,000 base pairs long
- It is involved in DNA maintenance and repair
  - Codes for the Werner protein, which acts as a helicase AND as an exonuclease
- More than 70 mutations in the WRN gene, most code for a nonfunctional protein
  - 90% of people diagnosed with Werner syndrome have a mutation in this gene





Details

- Unlike most other helicases, the structure of the Werner protein allows it to unwind **Telomeres**.
- Telomeres play a critical role in aging

Application of Genetic Knowledge

- In the US, the main laboratory offering clinical tests is at the University of Washington
  - Sequence analysis of the entire coding sequence
  - Protein analysis
  - Carrier testing
- Gene counseling
- Little Urgency to offering clinical treatment for the disease directly because of its rarity. Treating the symptoms is ‘easier’

Road to a Cure

- 2009 mouse model for Werner Syndrome
  - Vitamin C maintained the integrity of DNA in heart and liver
    - Improved metabolism and decreased inflammation in tissue
    - Phosphorylation of stress markers in the liver
  - This has no effect on healthy mice
- Elongation of shortened Telomeres
  - (2007) Added telomerase prevents the lack of a functional Werner protein to stop DNA Damage

Sources

- Genetics Home Reference – Werner Syndrome
- NCBI – Gene tests – Werner Syndrome
- Kitano, Dr. Ken. Nara Institute of Science and Technology, Helicase Activity of Werner Protein. Feb 11, 2010.
- NCBI – Gene Reviews – WRN Gene
- The FASEB Journal. Vitamin C Restores Healthy Aging in Mouse Model for Werner Syndrome. Sep 9, 2009