# Cockayne Syndrome

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# Cs phenotypic spectrum

- Although there are 3 types (I, II, and III), there are common phenotypic characteristics:
  - Short stature and microcephaly
  - Premature aging
  - Intellectual disabilities
  - Photosensitivity
  - Eye abnormalities (cataracts, pigmentary retinopathy, etc.)
  - Impaired development of the nervous system
- CS Type I ("moderate" form):
  - Normal prenatal growth
  - Growth and developmental abnormalities by the 2nd year
  - Mean age of death is 12 years though some have lived to over 30

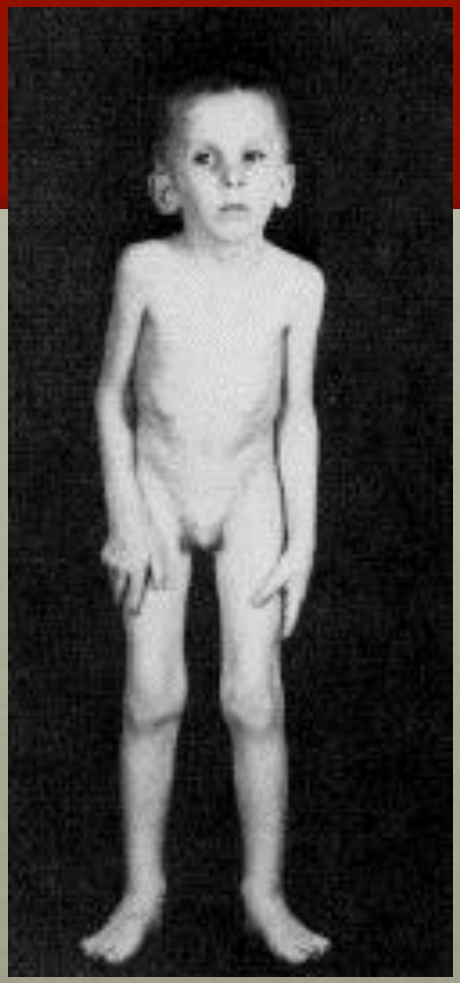
# Cs phenotypic spectrum continued

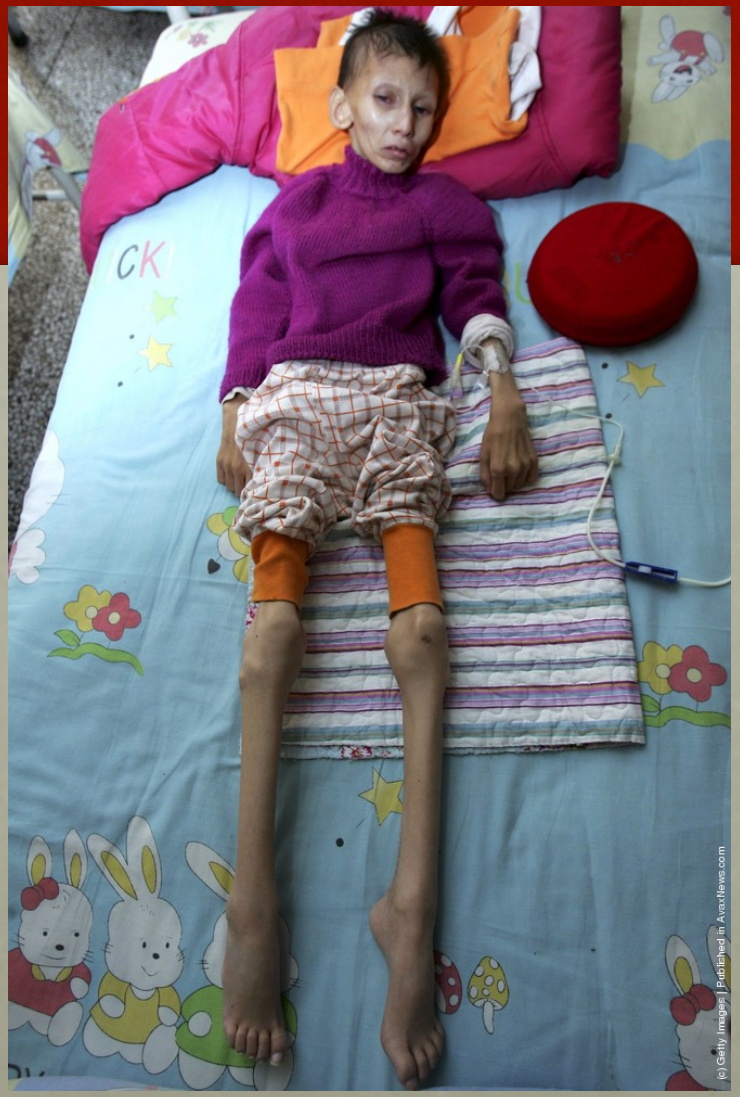
- CS Type II:
  - Growth failure is apparent at birth and/or neonatal period
  - Most severe out of all types
  - Many signs overlap with cerebro-oculo-facio-skeletal (COFS) syndrome and/or Pena-Shokeir syndrome type II
  - Death generally occurs after 7 years
- CS Type III:
  - Mild or late onset
  - Growth and cognitive function are “normal” and exceed those of CS type I; clinical features are associated with CS
- Xeroderma pigmentosum–CS (XP-CS):
  - A similar DNA repair disorder characterized by facial freckling and skin cancers (not found in CS)

# Classical diagnosis

- CS Type I:
  - Postnatal growth failure (<5$^{th}$ percentile by 2$^{nd}$ year)
  - Progressive microcephaly and neurologic dysfunction
    - Photosensitivity, eye atrophy, hearing loss, dental abnormalities (e.g. excessive caries)
- CS Type II:
  - Growth failure and little postnatal growth
  - Little or no postnatal neurologic development
  - Presence of congenital cataracts
- CS Type III:
  - Was recently confirmed as an additional type
  - Much more mild than the other 2 types and appears later in childhood

http://phobos.ramapo.edu/~pbagga/cs.JPG





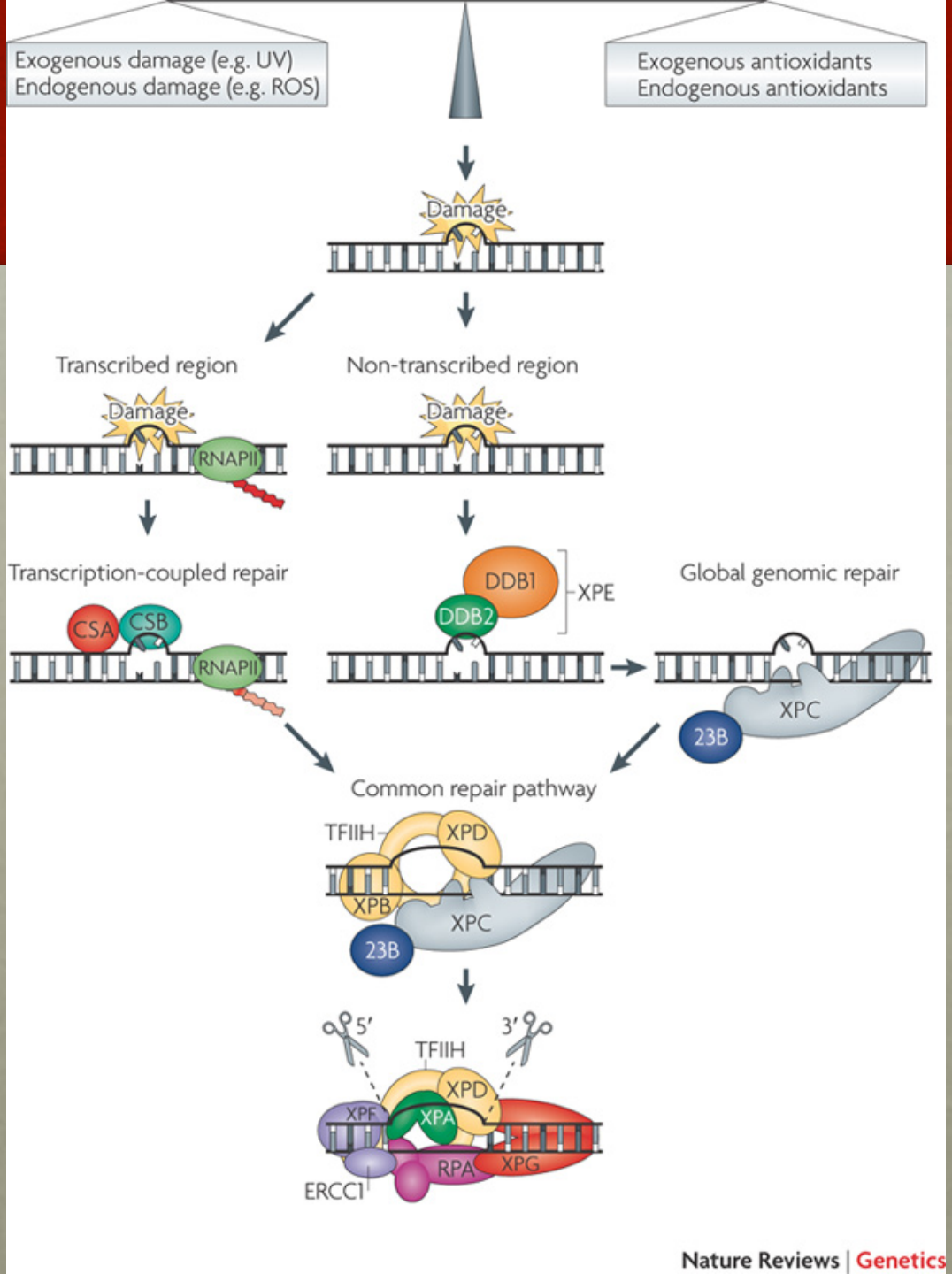
http://avaxnews.com/pictures/13467

Type II: http://cockaynesyndrome.net/main/MeettheKids/NathanPrantePrice.aspx

# ERcc6 and ercc8

| Gene Symbol | % of CS associated with this gene | Chromosomal Locus | CS Type |
|---|---|---|---|
| ERCC6 | 65% | 10q11.23 | CS Type II |
| ERCC8 | 35% | 5q12.1 | CS Type I |

- Autosomal recessive
- ERCC (excision repair cross-complementing rodent repair deficiency, complementation group 6/8)
  - Mutations cause for the proteins (CSA and CSB) to be defective in gene repair




http://www.nature.com/nrg/journal/v10/n11/images/nrg2663-i1.jpg

# Modern diagnostics

- DNA Repair Assay
- Complementation groups (research basis only)
- DNA sequence analysis
- Deletion/duplication analysis
- Carrier testing
- Prenatal diagnosis & preimplantation genetic diagnosis

# treatment

- Developmental education programs
- Physical therapy and ambulation-assisted devices
- G-tube (gastrostomy tube) feeding
- Management of hearing loss
- Sunscreen
- Sunglasses
- Aggressive dental care
- No cure or exceptionally effective treatment of the disease

# Bibliography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- http://www.ncbi.nlm.nih.gov/pubmed/10767341
- http://www.ncbi.nlm.nih.gov/gene/1161
- http://www.ncbi.nlm.nih.gov/gene/2074
- http://ghr.nlm.nih.gov/condition/cockayne-syndrome
- http://omim.org/entry/133540
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