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Wiedemann-Rautenstrauch Syndrome: A Brief Synopsis

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Abstract

Wiedemann-Rautenstrauch syndrome is a genetic condition that is a type of progeria, characterized by premature aging. Wiedemann-Rautenstrauch syndrome is a rare disorder with only three dozen cases since its first diagnosis in 1979. The syndrome is the result of a mutation within POLR3A gene that is responsible for the coding of the large subunit of RNA polymerase III. Mutation to this gene leads to the production of abnormal proteins systems resulting in a faulty RNA polymerase III. How the mutations in the POLR3A gene cause the observable symptoms of Wiedemann-Rautenstrauch syndrome is currently under investigation. The condition itself displays as an inherited autosomal recessive pattern, indicating that both copies of the gene in each cell are affected. Current treatment is directed toward the specific symptoms that are apparent in each individual and often requires a team of specialists due to its diverse nature. We will present the molecular mechanism and developmental progression of Wiedemann-Rautenstrauch syndrome as well as potential therapeutic targets for treatment.



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Wiedemann-Rautenstrauch Syndrome: A Brief Synopsis

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Definition A genetic disorder that is characterized by an aged appearance at birth (progeria), with growth delays before and after birth, and a deficiency or absence in a layer of fat below the skin.

Diagnosis In most patients, WRS is diagnosed shortly after birth, based upon thorough clinical evaluation and identification of characteristic physical findings such as: short stature, characteristic craniofacial and skeletal malformations, and absence or deficiency of subcutaneous fat. In some cases, specialized tests may also be conducted to detect abnormalities of cranial bones. In addition, it is possible that CAT, MRI, and/or other specialized tests may reveal widespread loss of myelin sheath within the white matter of the brain (pure sudanophilic leukodystrophy) or other abnormalities as described above.

Management The treatment of this syndrome is generally directed towards specific symptoms that the individual is experiencing. There is not a treatment that will cure the syndrome instead they are supportive and symptomatic. This will usually be carried out by a team of specialists including, but not limited:

- Physical therapist
- Neurologist
- Genetic counselor
- Physician



Antenatal diagnosis In some cases, growth disability, macrocephaly and/or other characteristic findings of WRS may be detected prenatally by ultrasound.

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Clinical Description People who have this syndrome:

- Do not grow or gain weight at an expected rate
- Facial features that make them appear older (larger head, triangular face with prominent forehead, pointed chin, lower set ears, lower eyelids)
- Translucent skin with no fat underneath it
- Little to no hair on their head



Etiology The syndrome is caused by a mutation in a gene known as POLR3A. When this gene is not mutated it works to provide instructions for making the largest subunit of RNA polymerase III. The mutation causes abnormal formation of the large subunit which ultimately leads to the impaired ability to synthesize RNA. This condition is inherited in an autosomal recessive pattern.



Prognosis This is a rare genetic disorder that leads to a decreased life expectancy in affected individuals. The life expectancy and severity of this syndrome both vary from case to case. There are some children who live into their teens or twenties but this is not common.

Epidemiology WRS is an extremely rare disease that appears to affect males and females equally. WRS has been observed in various ethnic and racial groups. The disorder was initially described as a distinct entity in 1979 (Wiedemann HR) based upon observation of two unrelated individuals as well as previous reports of two affected sisters in 1977 (Rautenstrauch T). More than 35 affected individuals have been reported in the medical literature to date.

Differential Diagnosis Hutchinson-Gilford progeria syndrome, De Barys syndrome, Hallerman-Streiff syndrome, Cockayne syndrome

References: Pivnick, Eniko K. "Wiedemann Rautenstrauch Syndrome." *NORD (National Organization for Rare Disorders)*, Health Science Center, rarediseases.org/rare-diseases/wiedemann-rautenstrauch-syndrome/ "Wiedemann-Rautenstrauch Syndrome - Genetics Home Reference - NIH." *U.S. National Library of Medicine*, National Institutes of Health, ghr.nlm.nih.gov/condition/wiedemann-rautenstrauch-syndrome#diagnosis.