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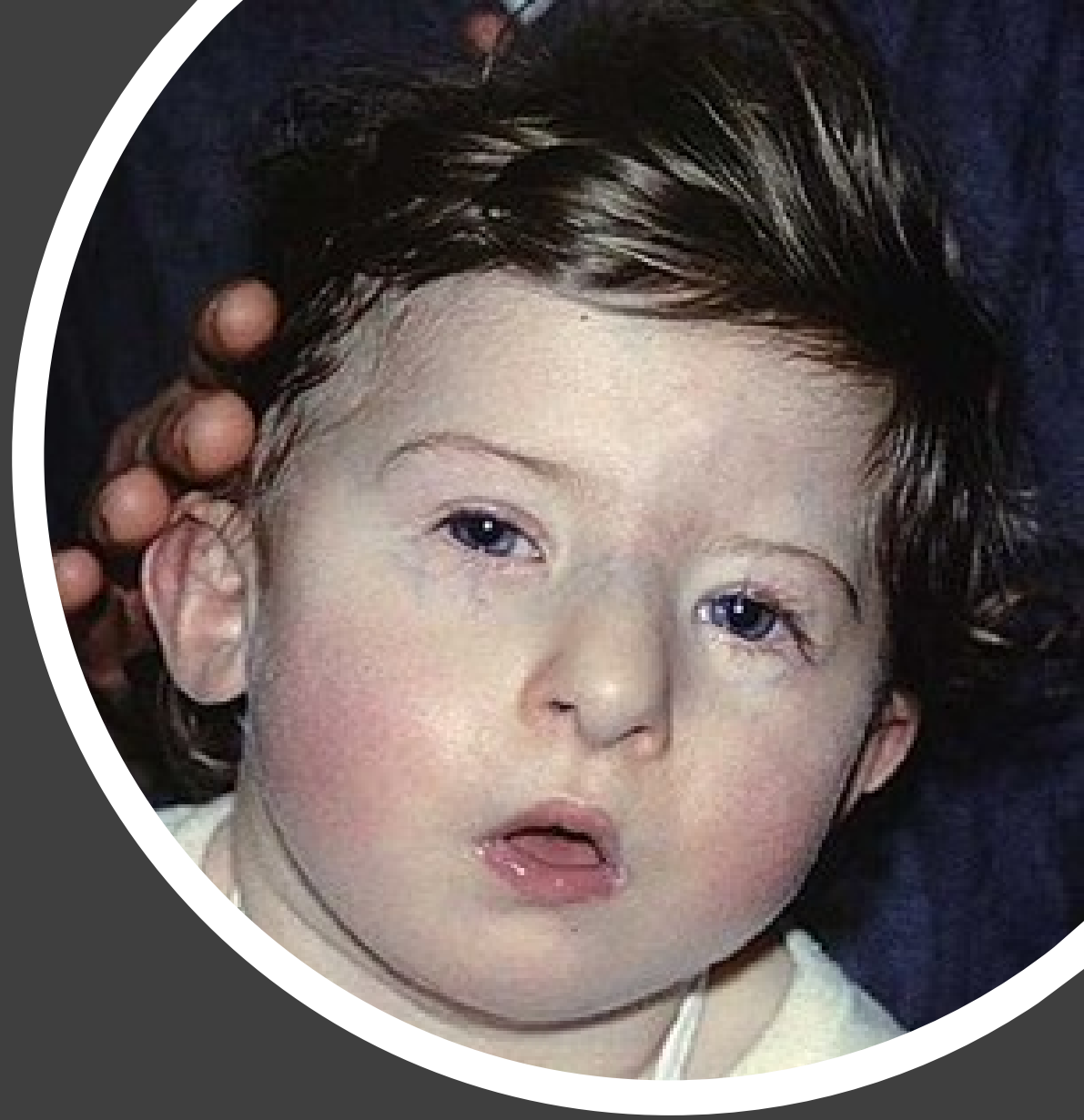
DiGeorge syndrome

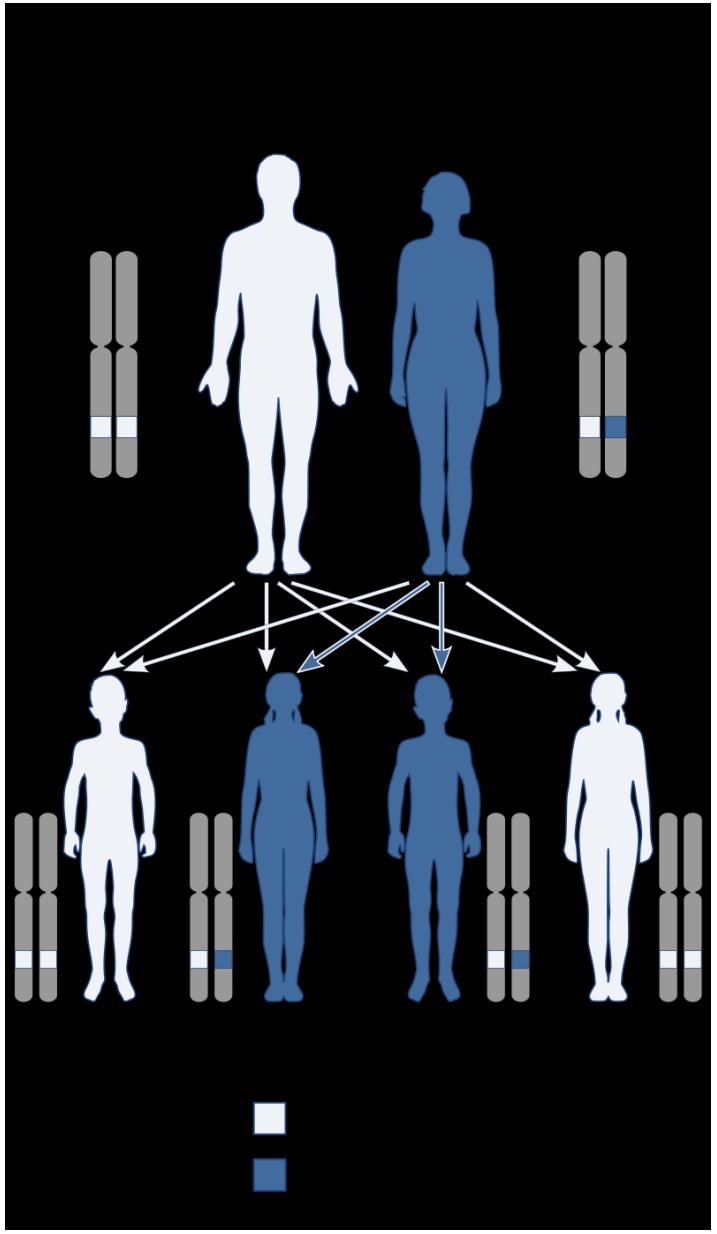
History

- Also known as:
  - 22q11.2 deletion syndrome
  - Velocardiofacial syndrome
- First described in 1968 by Angelo DiGeorge.
- The underlying genetics were found in 1981.



Epidemiology

- DiGeorge syndrome affects one in 2000-4000 live births.
- Probably underdiagnosed due to some individuals having very few and mild symptoms – and therefore not diagnosed
- It is one of the most common causes of intellectual disability due to a genetic deletion syndrome.



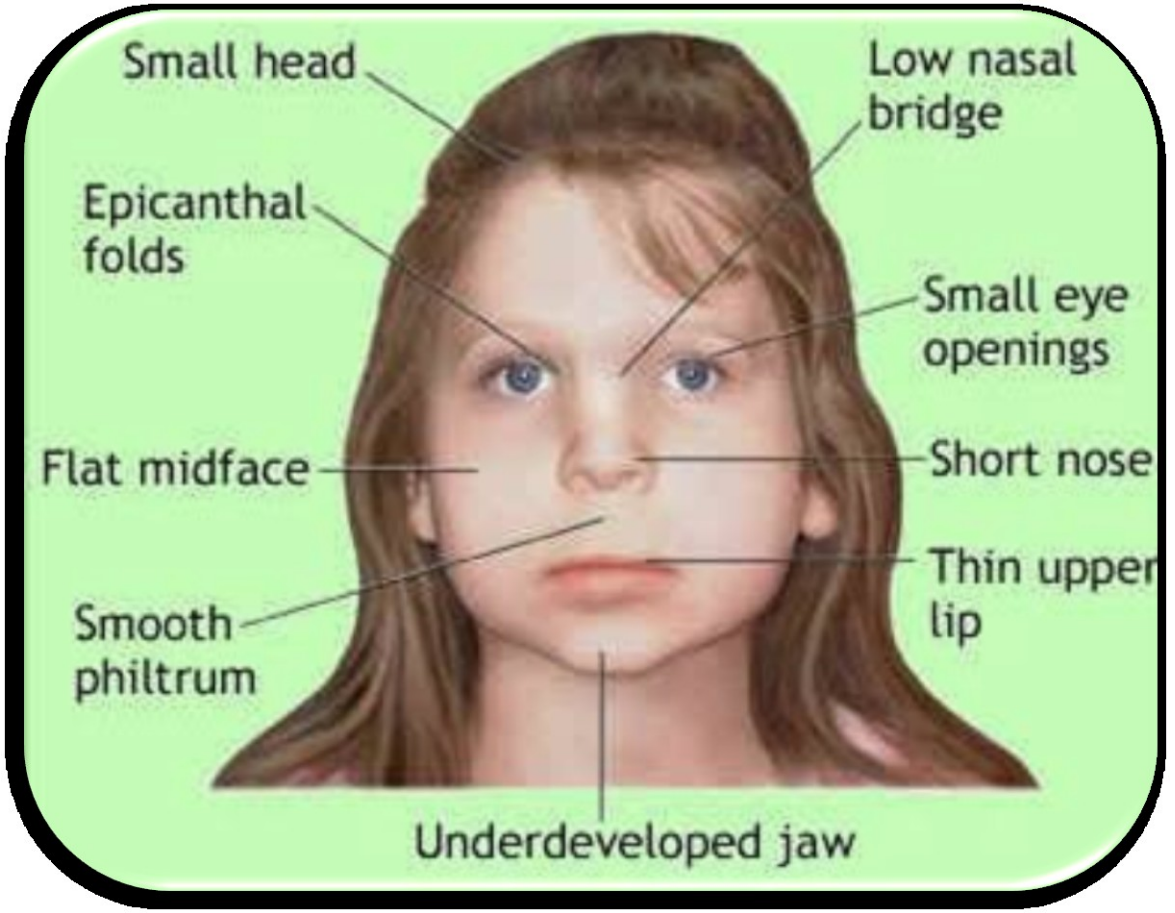
Etiology

- Caused by the deletion of a small segment of chromosome 22
  - Typically deletion of 30-50 genes
  - 22q11.2 (long arm of chromosome 22, region 1, band 1, sub-band 2)
  - Very rarely due to deletions on short arm of chromosome 10
- Autosomal dominant
- 90% due to new mutation
- 10% inherited from parents
- **=> hypoplasia of 2nd & 3rd pharyngeal pouch derivates**

- Very wide register of symptoms – due to incomplete penetrance

Symptoms

- Birth defects
  - Congenital heart disease (40%) w. cyanosis
  - Cleft palate (due to neuromuscular problems) (50%)
- Thymic hypoplasia - **recurrent infections** & **autoimmune disorders** due to altered T-cell response
- Parathyroid gland dysfunction – low PTH & **hypocalcemia**
- Kidney- & GIT problems
- Hearing loss (both sensorineural & conductive)

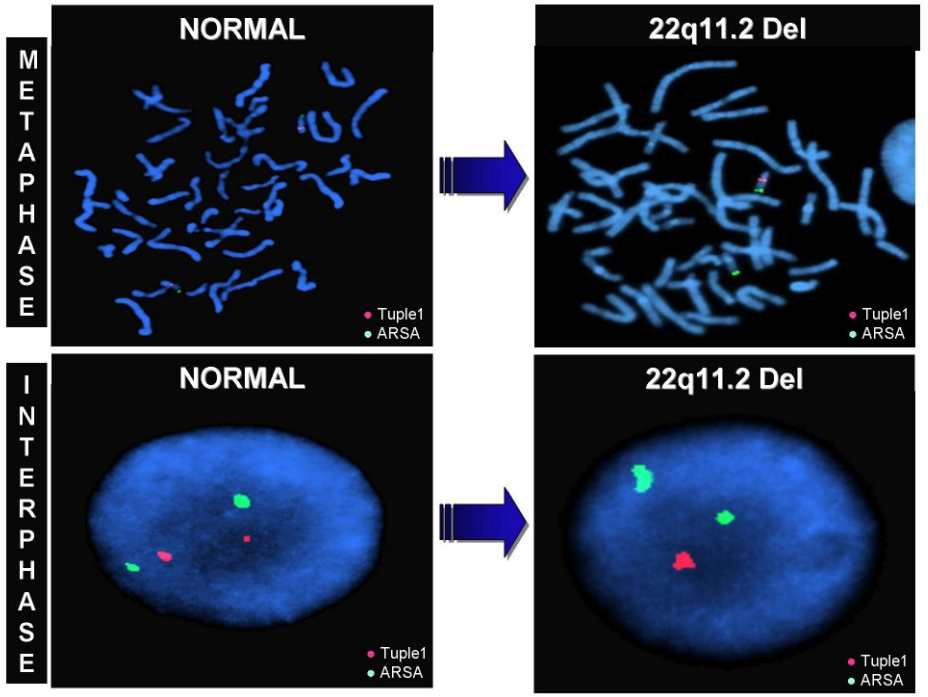


Cognitive- & psychiatric impairments

- Usually below borderline normal IQ
  - Learning difficulties in 90%
- Speech & language
  - Hypernasality, articulation errors & delayed vocabulary aquisition
- Autism-like behavior (severe hypocalcemia in early childhood)
- ADHD
- Seizures
- High risk of schizophrenia (25%) & psychosis
- High risk of early onset Parkinson's Disease

Diagnosis

- Diagnosis can be difficult due to great variability of symptoms and phenotypes between individuals.
- Fluorescence in situ hybridization (FISH) is able to detect microdeletions that standard karyotyping miss.
- Newer methods of analysis which can detect atypical deletions (not detected by FISH):
  - Multiplex ligation-dependent probe amplification assay (MLPA)
  - Quantitative polymerase chain reaction (qPCR)



Treatment

- No cure is known for DiGeorge syndrome.
- Although there is no cure, treatment can improve symptoms. The key is to identify each of the associated features and manage each using the best available treatments.
  - E.g., cardiac surgery is often required for congenital heart abnormalities. Hypoparathyroidism causing hypocalcemia often requires lifelong vitamin D and calcium supplements, etc..

Sources

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- https://en.wikipedia.org/wiki/DiGeorge_syndrome