22q11.2 Microdeletions

DiGeorge and Velo-cardial-facial (VCF) Conditions

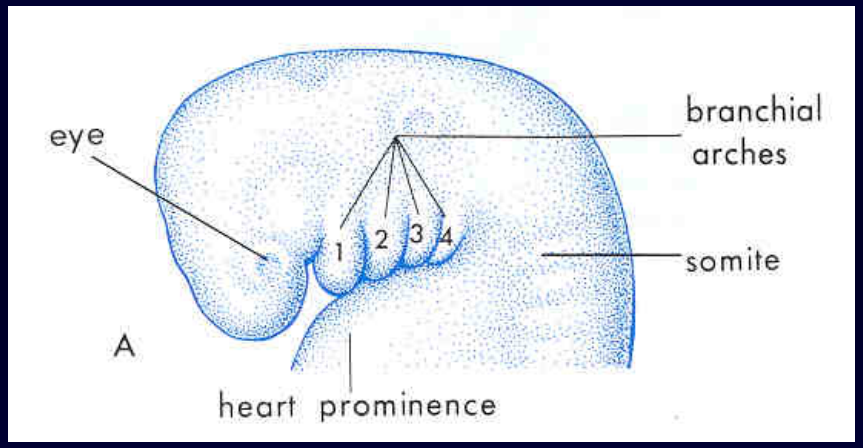
- May have a 1/4000 newborn prevalence.
- Very important cause of neonatal morbidity and of childhood learning delay.
- Deletion not detectable by routine G-banded chromosome study
- Variable clinical presentations, including near normal development. The two classical presentations (DiGeorge and VCF syndromes) are reviewed here.

DiGeorge Syndrome

- Variable facial dysmorphism, Pierre Robin sequence, cleft palate
- Thymic hypoplasia with T-cell deficit
- Hypocalcemia, seizures
- Cardiac defects:
  - Interrupted aortic arch
  - Tuncus arteriosus
  - Tetralogy of Fallot
  - Double outlet RV
  - Pulmonary atresia
- 22q11.2 deletion, detectable by chromosome microarray or FISH testing.

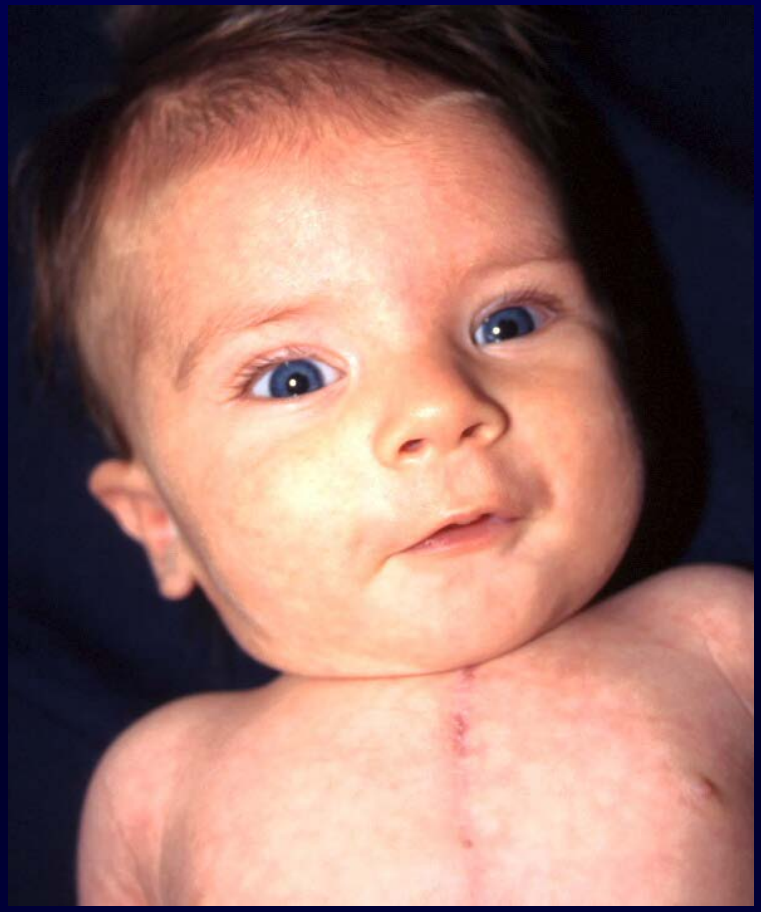
DiGeorge Sequence

3rd and 4th pouch and 4th arch defects

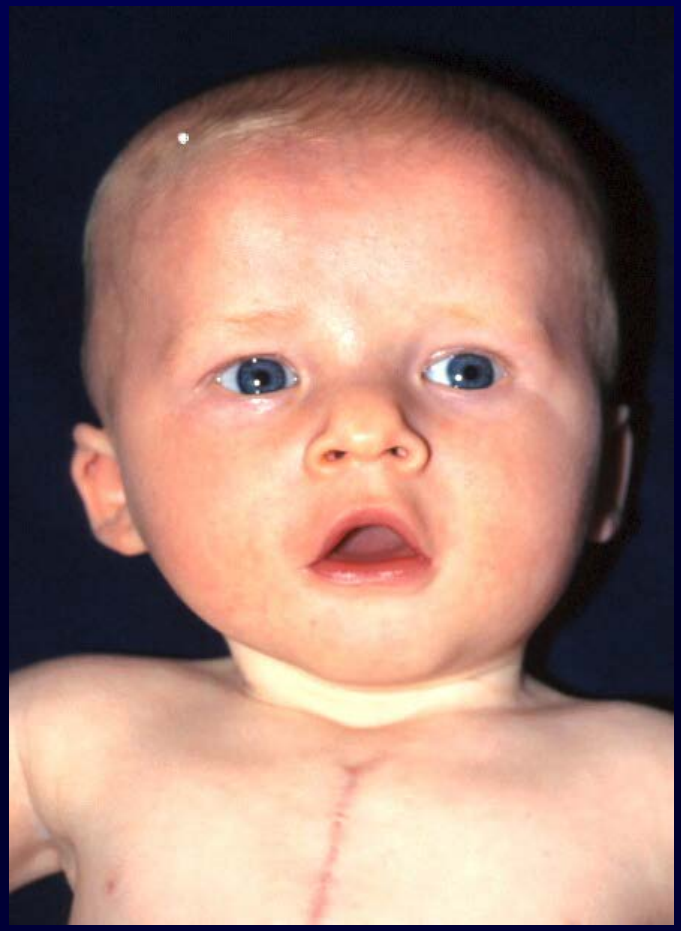


- **Thymus**
  - T-cell deficiency
  - absent thymus
- **Parathyroids**
  - severe hypocalcemia
- **Cardiovascular**
  - conotruncal heart defects
  - interrupted aortic arch

Sadler: Medical Embryology,1990



A



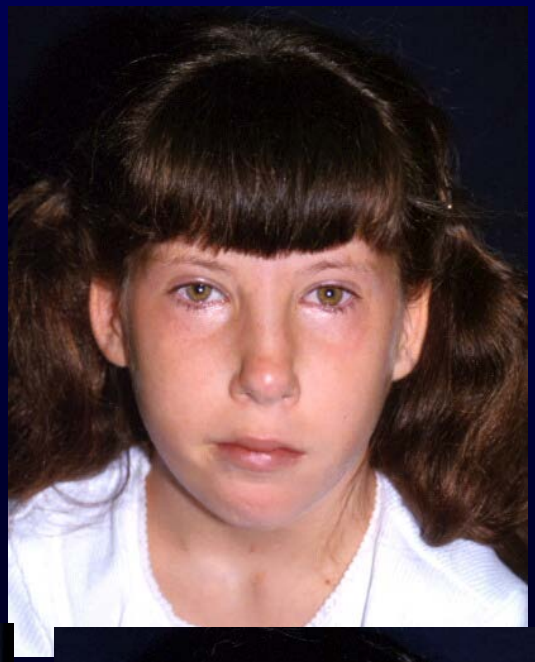
B

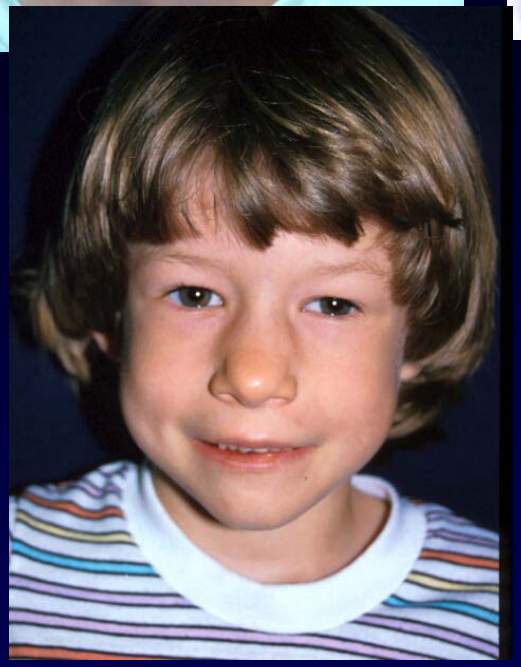
Both have FISH positive 22q11.2 deletions and both had DiGeorge sequence (note cardiac scars too). Baby A has normal face, baby B is dysmorphic with prominent forehead, blunted nasal tip and tented shape to mouth.

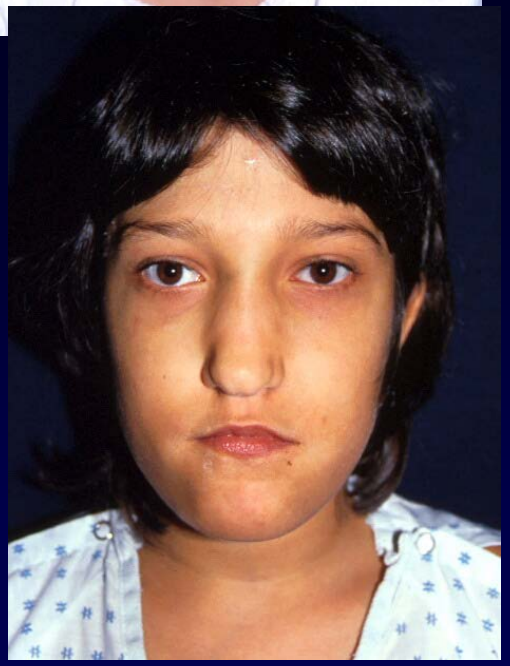
Velo-cardio-facial Syndrome (Shprintzen)

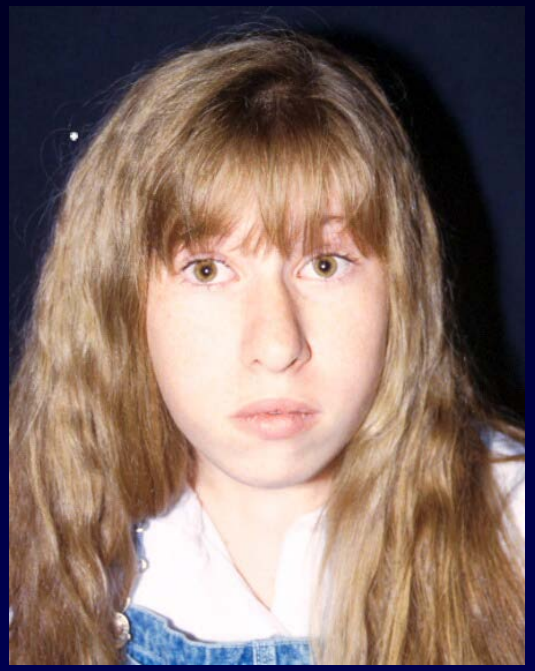
- Cleft palate, velo-pharyngeal incompetence
- Slender fingers
- Cardiovascular defects (VSD)
- Microcephaly
- Prominent nose with square root
- Learning delay with psychological disorders

- Etiology: 22q11.2 microdeletion, detectable chromosome microarray or by FISH analysis





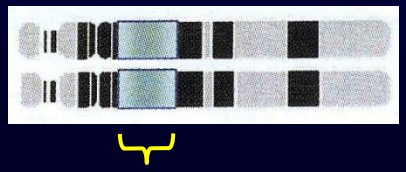


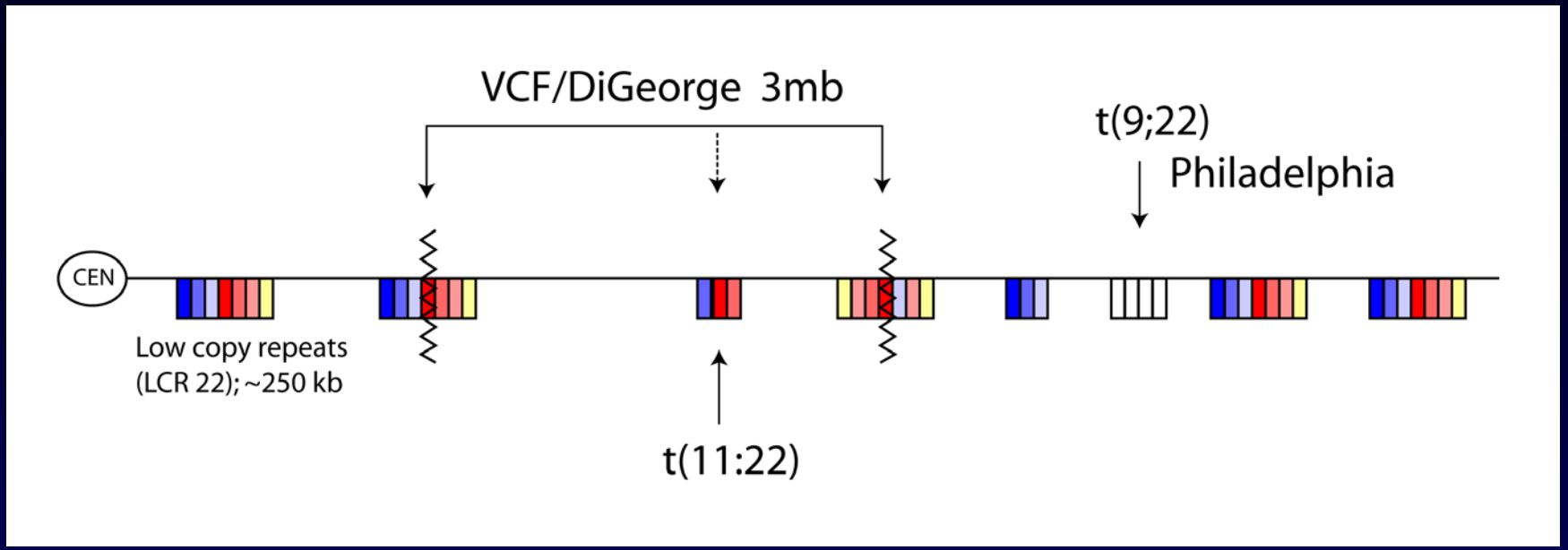


Diagnostic Clues

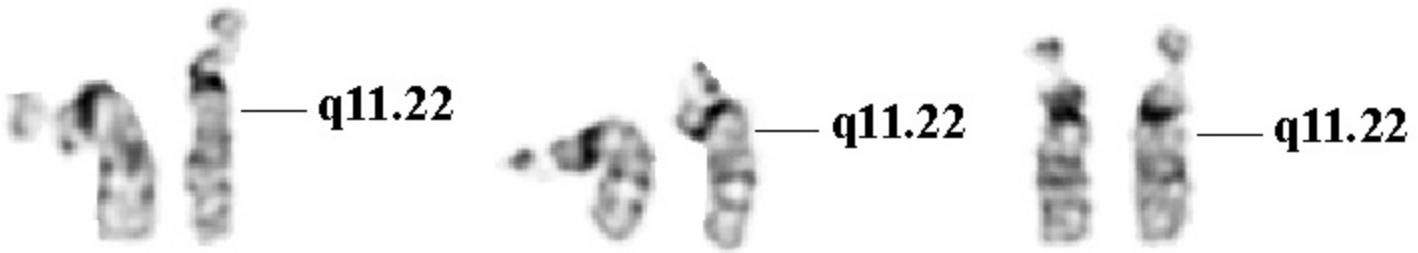
Slender hands
Cardiac defects
Cleft palate
Hypernasal speech

Gene map of 22q11.2 showing repetitive gene cassettes, with the two most common breakpoints of the deletion indicated by the jagged lines.





The 22q11.2 microdeletion cannot be seen by routine chromosome study. These are normal #22's, but if they had the deletion, it would not be visible by this method but would be detected by chromosome microarray study.



Chromosome 22 pairs by GTG-banding

550-850 band levels (ISCN 1995)