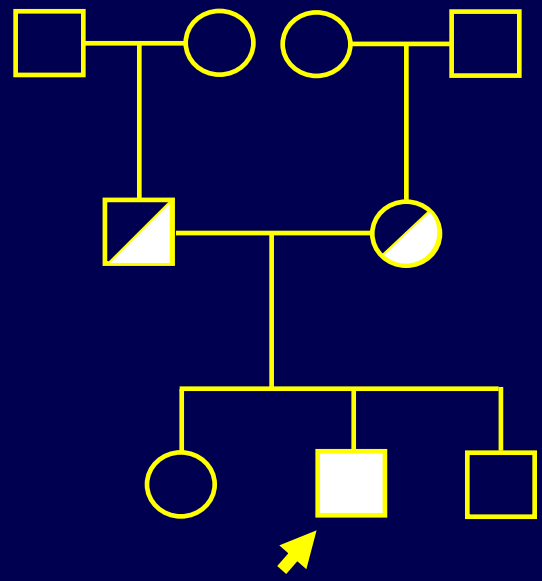
Biotinidase Deficiency

- Disorder of biotin recycling
- Biotinidase gene at 3p25
- Autosomal recessive disorder with 25% recurrence risk
- Two types:
  - Partial = 10-30%
  - Profound = <10%

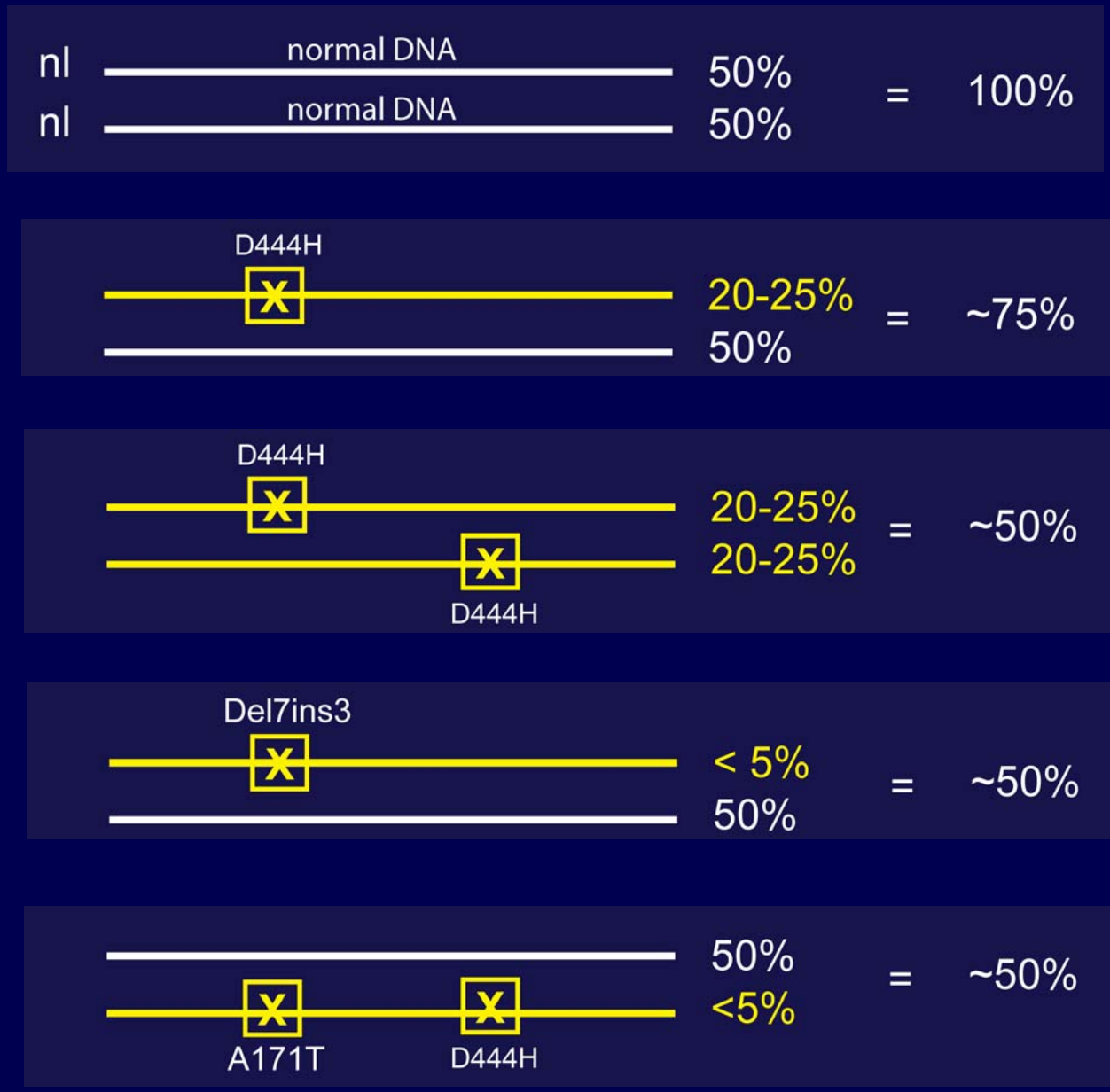


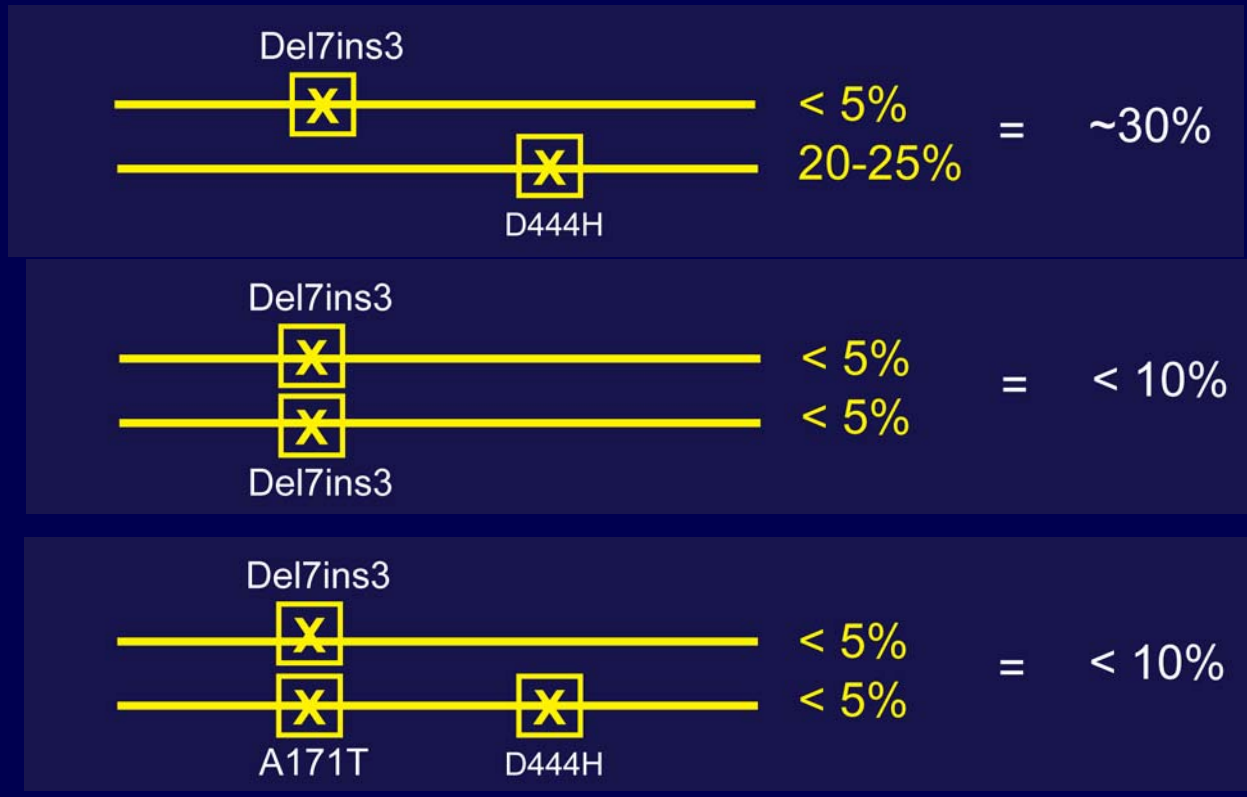
Diagnosis of Biotinidase Deficiency

- Neonatal blood spot screening
- Confirmation by blood enzyme testing with control
- DNA testing
  - Not necessary for confirmation of diagnosis
  - Rapid presumptive diagnosis is some cases
  - Valuable information for genetic counseling

Molecular Genetics of Biotinidase Deficiency

- 8 mutations: 60-70%
  - Q456H
  - R538C
  - D444H
  - A171T
  - F403V
  - R157H
  - D252G
  - G98del7ins3
- D444H is almost always seen in partial deficiency
  - except when A171T and D444H occur together


nl
normal DNA
50%
nl
normal DNA
50%
=
100%
D444H
20-25%
50%
=
~75%
D444H
20-25%
20-25%
D444H
=
~50%
Del7ins3
< 5%
50%
=
~50%
50%
<5%
A171T
D444H
=
~50%


Del7ins3
< 5%
20-25%
=
~30%
D444H
Del7ins3
< 5%
< 5%
=
< 10%
Del7ins3
Del7ins3
< 5%
< 5%
=
< 10%
A171T
D444H

Value of DNA testing

- Rapid information after newborn screening if:
  - 2 severe mutations: high likelihood of <10%
  - 1 severe mutation and D444H (without A171T): high likelihood of 10-30%
- Normal DNA test result does not exclude biotinidase deficiency
  - Blood enzyme testing: gold standard