Wolf-Hirschhorn Syndrome (4p-, Monosomy 4p)

Genetics

-4p deletion, critical region with two genes: WHSC1 and WHSC2 of unknown significance

Clinical findings/Dysmorphic features

-“Greek warrior helmet" appearance of nose (wide bridge continuing to forehead)

-Microcephaly, facial asymmetry, ptosis, structural brain anomalies, CL/P; high forehead with prominent glabella; ocular hypertelorism; epicanthus; highly arched eyebrows; short philtrum; downturned mouth; micrognathia; poorly formed ears with pits/tags

-CHD (ASD>PVS>VSD>PDA>AI>TOF)

-Intrauterine/postnatal growth retardation, hypotonia; ID of variable degree, seizures

-IgA deficiency

Etiology

-50%-60% have a de novo pure deletion of 4p16; 40%-45% have an unbalanced translocation with both a deletion of 4p and a partial trisomy of a different chromosome arm

-Approximately 1:50,000 births

-2:1 female/male ratio

Pathogenesis

-WHS is true contiguous gene syndrome with contribution of genes within a 1.6-Mb region

Genetic testing/diagnosis

-Heterozygous deletion of WHSCR on chromosome 4p16.3 by CMA, conventional G-banded cytogenetic analysis or FISH