Condition: Achondroplasia

Inheritance:

Autosomal dominant.

Genetic etiology:

Mutation in *FGFR3* gene encoding the fibroblast growth factor receptor type 3. Two mutations are account for the vast majority of cases of achondroplasia. Both involve the same nucleotide (1138). One is a G to A change and the other a G to C change. Both cause the same amino acid change in codon 308 and are gain of function mutations, leading to constitutive activation of the receptor.

Frequency:

1/15,000 – 1/40,000 births.

Clinical features:

Achondroplasia is associated with shortening of limbs due to premature differentiation of cartilage in the growth plate into bone. There is a characteristic facies, with frontal bossing and hypoplasia of the mid-face, lumbar lordosis, and extreme short stature. Intelligence is normal. Respiratory function may be compromised by obstructive apnea and brainstem compression. Hydrocephalus can occur due to obstruction of the sigmoid sinus.

Management:

Supportive management; monitoring for brainstem or spinal cord compression and surgery if necessary; management of sleep apnea.

Genetic counseling:

Based on autosomal dominant transmission with high rate of new mutation; genetic testing available.

Human Genetics and Genomics, Fourth Edition. Bruce R. Korf and Mira B. Irons.