



British Society for Paediatric Endocrinology and Diabetes

ACHONDROPLASIA

Achondroplasia is a genetic condition which primarily involves the skeleton and so restricts growth. It is rare, affecting about 1 in 10-30,000 people.

Cause:

Each human cell contains 46 chromosomes in 23 pairs, one of each pair inherited from the mother and one from the father. Each chromosome carries many genes like a row of pearls. Achondroplasia is caused by a fault in a single dominant gene, this implies that the disease is expressed although only one of a pair of genes is affected. Males and females are equally likely to be affected and have a 50% chance of passing the abnormal gene, and so the condition, on to children of either sex. However, in achondroplasia about three-quarters of affected people represent new mutations, a situation in which the abnormality of the gene arises spontaneously before birth and is not inherited from either parent. Unfortunately, the gene can then be passed to later generations. In 1994 it was found that the gene for achondroplasia lies on the short arm (each gene has a short and a long arm) of chromosome 4 at the site of the gene for a growth factor receptor (FGFR3), a protein in the outer wall of cells in growing bone which receive the message to divide. Nearly all affected people studied so far have had identical mutations in this gene. The mutation is easily detected so for couples at risk (because one parent is affected) prenatal diagnosis from chorionic villus sampling (removal of a sample from the placenta in early pregnancy) is now possible.

Physical features:

Affected babies are short at birth and grow slowly throughout childhood, the average final height for women is 126cm (4ft 2in) and for men is 131cm (4ft 4in). The limbs are relatively shorter than the trunk with the the upper arm and the thigh especially shortened. The head is usually large with prominence of the forehead and a flat nasal bridge. The fingers and toes are short and the hands and feet small and wide. Although the majority of affected children will be healthy, approximately 10% can develop significant complications so routine review by a paediatrician is recommended. The following list outlines the different potential problems:

- a) **Orthopaedic** - Children often show some early hypotonia (floppiness) of the limbs with delayed motor development but this usually improves and disappears in childhood. A thoracic kyphosis (curvature of the upper spine) may be present in infants which in most will gradually resolve to be replaced by a lumbar lordosis (an exaggerated lumbar curve). Approximately 10% of children have significant bowing of the tibiae (shin bones). This may require corrective surgery if there is recurrent knee or ankle pain or regular falls. Limb lengthening procedures have been used with success in children with achondroplasia with increases of 10-20 cm being possible. However this is a lengthy procedure with individuals having to wear external fixators to the leg bones for many months. It is now recommended that children are at least 10 years of age so that they can participate in the decision for surgery. Instability of the cervical spine is not a significant problem in achondroplasia.



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- b) **Neurological** – Approximately 6% of affected children will develop hydrocephalus requiring a neurosurgical procedure by the age of 5 years. The main risk of this problem is in the first two years of age so that routine measurement of head circumference and plotting on achondroplasia-specific charts is indicated. A rare complication is cervicomedullary compression (compression of the upper spinal cord at the base of the brain) which can present with episodes of apnoea (stopping breathing). This requires confirmation by a CT or MRI scan and surgical intervention. In the adolescent and adult compression of nerve roots in the spinal canal may occur with the most common symptoms being a sensation of numbness or weakness in the legs.
- c) **Respiratory/ENT and dental** – Recurrent middle ear infections is a common problem with a risk of conductive hearing loss. Therefore regular hearing assessment is recommended. Dental overcrowding may occur in older children. There may be sleep-associated breathing problems which may present with unexplained symptoms such as morning headache, poor concentration and school performance. Such problems can be identified by a sleep study which assesses breathing during sleep. This may be due to enlargement of tonsils and adenoids which will require surgical removal.

Treatment:

There is no specific treatment but it is desirable to monitor the progress of affected children to offer support and to detect early the occurrence of any complications. Most children cope remarkably well with the problems arising from their short stature and most schools are helpful. There may be a need to provide appropriate adaptations at home or at school to allow children to participate in all activities. Occupational therapists can be helpful in advising on such issues. There is no evidence that growth hormone treatment is of benefit in increasing adult height in achondroplasia.

Outlook:

Most people with achondroplasia cope extraordinarily well with the physical difficulties and lead successful and fulfilled lives. Many have distinguished themselves in various fields. Several organizations can provide support to individuals with achondroplasia including the Restricted Growth Association (www.restrictedgrowth.co.uk), the Dwarf Sports Association (www.dsauk.org) and the Child Growth Foundation (www.childgrowthfoundation.org).