intheknow
ABOUT ACHONDROPLASIA

InTheKnow Patient FAQs

Achondroplasia

1. What is achondroplasia?

Achondroplasia is a rare genetic condition, occurring in about one in 25,000 live births, that affects how the majority of the bones in the body grow.[1] People living with achondroplasia have disproportionate short stature, which is apparent in the lengths of the different parts of the limbs and also in the proportion of trunk and limb length.[2]

2. Are there any medical complications associated with achondroplasia? What are the most common complications?

Besides extreme short stature, there can be impaired bone growth throughout the body which can result in serious health complications, including foramen magnum compression, sleep apnoea, bowed legs, mid-face hypoplasia, permanent sway of the lower back, spinal stenosis and recurrent ear infections.[1,3]

Complications can worsen with age, and may require surgery, such as spinal cord decompression and straightening of bowed legs.[1,3] Two thirds of people living with achondroplasia suffer with chronic pain.[4]

3. What causes achondroplasia and restricted bone growth?

The condition is caused by impaired bone growth, and effects can be seen in the long bones, spine, face and base of the skull.[1]

In someone with achondroplasia, a change in the fibroblast growth factor receptor 3 (*FGFR3*) gene is what leads to impaired bone growth.[1] The FGFR3 receptor sends more signals to slow bone growth than it should, and the body's natural C-type natriuretic peptide (CNP) is not enough to balance the increased *FGFR3* signaling. As a result, bones receive more signals to slow down and bone growth is impaired.

4. What is the impact of achondroplasia on life expectancy?

Mortality rates are increased in achondroplasia relative to the average population; overall survival and the average life expectancy for individuals with achondroplasia can be reduced by as much as 10 years.[5,6,7,8]

5. How many people live with achondroplasia in Europe?

The overall prevalence in Europe of achondroplasia is 3.5 per 100,000 individuals and the global prevalence of achondroplasia is 4.6 per 100,000 individuals.[9]

Diagnosis

1. How is achondroplasia diagnosed? When is it diagnosed?

Achondroplasia is usually diagnosed using a mixture of clinical observations, radiography, and molecular testing.[10]

A diagnosis can be made at any age, but observation during the neonatal period (the first 4 weeks of a child's life) is the most common. 4 out of 5 people receive a diagnosis at birth.[11]

2. Is achondroplasia hereditary?

Yes. If one parent has achondroplasia, the probability of passing the condition on is 50%,[12] and if both parents have achondroplasia, the probability of passing the condition on is 75%.[12,13]

However, most cases of achondroplasia are not inherited, approximately 80% of children with achondroplasia have parents of average stature and have the condition as the result of a spontaneous gene mutation.[1]

3. Will a person with achondroplasia have children with achondroplasia?

A person with achondroplasia will not always have children with the condition. If one parent has achondroplasia, the probability of passing the condition on is 50%,[12] and if both parents have achondroplasia, the probability of passing the condition on is 75%.[12,13]

4. Can average-statured parents have children with achondroplasia?

Yes. Approximately 80% of children with achondroplasia have parents of average stature and have the condition as the result of a spontaneous gene mutation.[1]

Infancy and childhood

1. What medical or mobility complications can there be for infants and children with achondroplasia?

Achondroplasia affects many different parts of the body, and the body parts affected can vary depending on the age of each individual. Changes in the proportions and development of the body may lead to various disabilities, which may in turn affect day-to-day living, social and mental factors, and quality of life (QoL).[10,14]

For example, compression of the spinal cord can lead to neurological problems and associated disability in people living with achondroplasia.[1,3,4] It may also create respiratory or nervous system symptoms, particularly in childhood, resulting in sudden death in 5%–10% of children with achondroplasia.[3]

Additionally, children compensate for their disproportionately heavy head and shortened limbs, which affects the way they crawl, transition from sitting to standing and develop various motor skills.[3,14,15]

2. What physical activities might be challenging for an infant or child with achondroplasia?

Significant short stature, as well as disproportionally short limbs, can mean that people living with achondroplasia experience mobility and accessibility issues, with the built environment not tailored for people of short stature. This can impact the ability to manage personal hygiene, make it difficult to carry out activities of daily living, take part in school, and affect overall independence and quality of life. It can also have an impact on self-confidence and self-image.[16]

3. Is cognitive function impacted or impaired for an infant or child with achondroplasia?

Infants or children with achondroplasia do not usually experience impaired cognitive functions including learning, decision making and problem solving, memory, or attention. However they may have delayed speech development milestones, which is thought to be linked to otitis media (inflammation of the ear) and hearing loss.[3,17]

4. Will infants and children with achondroplasia need to go to a specialist school?

No, as cognitive function is not impacted by achondroplasia, a child's educational needs should be assessed in the same way as any other child.

5. Does growing up with achondroplasia typically impact a child's mental health?

Studies have found that people with achondroplasia can have lower mental health scores than the general population.[4] However, children have demonstrated a strong sense of self-concept, coping strategies and psychological adaptation despite negative experiences related to their height.[1]

6. Will an infant or child with achondroplasia be able to make the same social relationships as other children?

Yes. However, infants and children living with achondroplasia can face a range of social and personal challenges throughout their lives. For example, the physical differences which arise as a result of achondroplasia can also cause unwanted attention, name-calling, or bullying.[16]

Adolescence

1. Are there any physical or medical complications from achondroplasia that can arise during the teenage years?

Achondroplasia affects many different parts of the body, and the body parts affected can vary depending on the age of each individual. Changes in the proportions and development of the body may lead to various disabilities, which may in turn affect day-to-day living, social and mental factors, and quality of life (QoL).[10,14]

Common complications that arise during the teenage years include: obesity, pain, and social adaptation challenges.

2. Does achondroplasia typically impact the mental health of teenagers?

Studies have found that people with achondroplasia can have lower mental health scores than the general population.[4]

3. Does a person develop their independence into adulthood at a similar rate to their peers who do not have achondroplasia?

Children with achondroplasia may develop their independence later than those without the condition. For example, they often require more physical assistance for everyday tasks such as hair brushing, toilet training and other aspects of self-care.[3,18] However, this is more relevant to children and infants. Access to physiotherapy, occupational therapy, and speech and language therapy may assist children and their families to gain independence, particularly around the time of starting school.[3,18]

4. Does achondroplasia impact school grades?

No, education levels can be comparable to those of the average population.[3,18,19,20] However, children may be more likely to miss school than their peers due to the volume of medical appointments or health problems associated with the condition.

Adulthood

1. Can a person with achondroplasia have children? Does achondroplasia impact fertility?

People with achondroplasia have normal sexual development and are able to have children, however certain problems such as infertility and early menopause are more common.[21]

2. Will a person with achondroplasia have children with achondroplasia?

A person with achondroplasia will not always have children with the condition. If one parent has achondroplasia, the probability of passing the condition on is 50%,[12] and it both parents have achondroplasia, the probability of passing the condition on is 75%.[12,13]

3. What might the impact of achondroplasia be on adults with the condition in the workplace? Are there types of work that people with achondroplasia are not able to do?

Navigating public spaces, reaching objects and daily activities may be more difficult for adults with achondroplasia. Work participation is reported as challenging, and employment levels as well as annual incomes are on average lower than the general population.[20]

4. What height can a fully grown adult with achondroplasia expect to grow to?

Height differences are marked by 2 years of age and deviation from average population height increases with age into adulthood.[1,22] The average height for adults with achondroplasia compared to the adult population is:

- Males: 4ft 4” (1.31 m) compared with 5ft 10” (1.8 m)
- Females: 4ft 1” (1.24 m) compared with 5ft 6” (1.67 m)[23,24]

5. Does achondroplasia typically impact the mental health of adults?

Studies have found that people with achondroplasia can have lower mental health scores than the general population.[4]

The influence of personality, family support, ethnic environment and culture can strongly influence mental health. People with achondroplasia may have higher levels of isolation, lower levels of self-esteem and a greater incidence of depression than is seen in the average population.[19]

Managing Achondroplasia

1. Which doctors will be involved in the care of someone with achondroplasia?

Achondroplasia incurs several risks that manifest at different life stages; monitoring across a number of clinical specialisms is needed to ensure potentially life-threatening or life-limiting symptoms are identified.

This can include: ENT specialists, audiologists, endocrinologists, genetic counsellors, geneticists, neurologists, paediatricians, occupational therapists and physiotherapists, orthopaedic surgeons, psychologists, and pulmonologists.

2. How frequently might a person with achondroplasia be expected to visit hospital?

Life with achondroplasia, or caring for a child with achondroplasia, can be a constant series of medical appointments, surgeries, and progressive complications with lifelong consequences. Treating the complications of achondroplasia involves symptomatic management, surgical intervention, and lifelong, specialised, follow-up care led by an expert coordinating a multidisciplinary care team.[3]

About BioMarin

1. Who is BioMarin?

Established in 1997, BioMarin is a world leader in developing and commercialising first- or best-in-class therapies for rare genetic diseases. We take pride in going where the science leads us, pioneering breakthrough treatments for debilitating and life-threatening conditions where we can significantly improve upon the current standard of care.

Our culture revolves around the ethos that no disease should go untreated, and our people are driven to discover, develop, and commercialise medicines that give patients, their families, and their caregivers hope where there was little or none. We fuel our R&D engine by looking for opportunities that align with our strengths and competencies. And we relentlessly pursue exciting, early-stage science that has the potential to change the course of disease.

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References: 1. Pauli R M 'Achondroplasia: a comprehensive clinical review' *Orphanet J Rare Dis*. 2019;14:1. **2.** Merker A *et al*. 'Development of body proportions in achondroplasia: Sitting height, leg length, arm span, and foot length' *Am J Med Genet A* 2018; 176 (9): 1819–1829. **3.** Ireland P J *et al*. 'Optimal management of complications associated with achondroplasia' *Applied Clinical Genetics*. 2014;7:117-125. **4.** Fredwall S O *et al*. 'Current knowledge of medical complications in adults with achondroplasia: A scoping review' *Clinical Genetics* 2020;97.1:179-197. **5.** Hecht J *et al*. 'Mortality in Achondroplasia' *Am. J. Hum. Genet*. 1987;41:454-464. **6.** Hashmi S S *et al*. 'Multicenter study of mortality in achondroplasia' *Am J Med Genet A*. 2018 Nov;176(11):2359-2364. **7.** Simmons K *et al*. 'Mortality in babies with achondroplasia: revisited'. *Birth Defects Res A Clin Mol Teratol*. 2014 Apr;100(4):247-9. **8.** Wynn J *et al*. 'Mortality in Achondroplasia Study: A 42-Year Follow Up' *Am J Med Genet A*. 2007;143A:2502–2511 . **9.** Foreman P K *et al*. 'Birth prevalence of achondroplasia: A systematic literature review and meta-analysis' *Am J Med Genet*. 2020;1–20. **10.** Trotter TL, Hall JG; American Academy of Pediatrics Committee on Genetics. Health supervision for children with achondroplasia. *Pediatrics* 2005; 116 (3): 771–783. **11.** Horton WA, Hall JG and Hecht JT. Achondroplasia. *Lancet* 2007; 370 (9582): 162–172. **12.** Jorde LB. Genes and genetic diseases. In: Pathophysiology: The Biologic Basis for Disease in Adults and Children. 7th ed. Elsevier Mosby; 2014. **13.** Rousseau F, Bonaventure J, Legeai-Mallet L *et al*. Mutations in the gene encoding fibroblast growth factor receptor-3 in achondroplasia. *Nature* 1994; 371 (6494): 252–254. **14.** Haga N. Management of disabilities associated with achondroplasia. *J Orthop Sci* 2004; 9 (1): 103–107. **15.** Pauli RM. Achondroplasia: A comprehensive clinical review. *Orphanet J Rare Dis* 2019; 14 (1): 1. **16.** The Experience of Living with Achondroplasia. Data on File. **17.** Galasso C, Siracusano M, El Malhany N *et al*. Cognitive phenotype and language skills in children with achondroplasia. *Minerva Pediatr* 2019; 71 (4): 343–348. **18.** Ireland PJ, McGill J, Zankl A *et al*. Functional performance in young Australian children with achondroplasia. *Dev Med Child Neurol* 2011; 53 (10): 944–950. **19.** Gollust SE, Thompson RE, Gooding HC *et al*. Living with achondroplasia in an average-sized world: An assessment of quality of life. *Am J Med Genet* 2003; 120A (4): 447–458. **20.** Fredwall SO, Steen U, de Vries O et al. High prevalence of symptomatic spinal stenosis in Norwegian adults with achondroplasia: A population-based study. *Orphanet J Rare Dis* 2020; 15 (1): 123. **21.** Ghumman S, Goel N, Rajaram S, Singh KC, Kansal B, Dewan P. Pregnancy in an achondroplastic dwarf: a case report. *J Indian Med Assoc*. 2005 Oct;103(10):536, 538. PMID: 16498757. **22.** Del Pino M *et al*. 'Height growth velocity during infancy and childhood in achondroplasia' *Am J Med Genet A* 2019 Jun;179(6):1001-1009. **23.** MedlinePlus. Achondroplasia. Available at: https://ghr.nlm.nih.gov/condition/achondroplasia. Accessed August 2021. **24.** WorldData.info. Average sizes of men and women. Available at: https://www.worlddata.info/average-bodyheight.php. Accessed August 2021.