ACHONDROPLASIA COMPLICATIONS BY AGE GROUP

Infants (birth–less than 2 years)

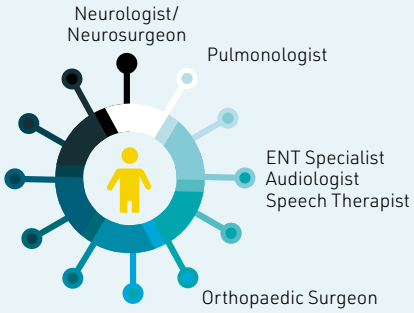
Knowing what to look for is key to proactive management, which helps mitigate complications and sets proper expectations. Complications in infants require specialised medical management, so it's important that paediatricians partner with a physician with expertise in skeletal dysplasia, and provide referrals to the necessary specialists.[1]

Adapted from Hoover-Fong J, Scott CI, Jones MC, 2020; Wright MJ, Irving MD, 2012; Ireland PJ *et al.*, 2014; and Ireland PJ *et al.*, 2011.[1-4]
These are potential complications – individual experience will vary. For diagnosis and management, please follow clinical judgement.

Potential Complication	Proactive Monitoring	Referral Specialist
Cervicomedullary compression[2]	Clinical assessment and monitoring of growth and development assessed against condition-specific charts and schedules; cranial imaging[2]	Neuroradiologist/ Neurosurgeon[2]
Sleep apnoea[1,2]	Polysomnography[1,2]	Neurosurgeon if central apnoea[2], Paediatric Pulmonologist[1], ENT Specialist if obstructive apnoea[2]
Hydrocephalus[2]	Regular monitoring of occipital-frontal circumference charts[2]	Neurosurgeon[2]
Hypotonia[1]	Assess for "floppiness," weakness, sustained lower extremity clonus, asymmetric reflexes, or choking or gagging with eating[1]	Neurosurgeon[1]
Otitis media (OM)[2]	Annual hearing assessment[1] Recurrent OM may require adenotonsillectomy and insertion of ventilation tubes[3]	ENT Specialist[2], Audiologist[1], Speech Therapist[4]
Kyphosis[2]	Clinical monitoring and counsel against unsupported sitting[2]	Orthopaedic Surgeon[1]

2% to 7.5% **Risk of sudden death** due to cervicomedullary compression[5-7]

<10% of children may require **surgical enlargement of foramen magnum**[8]



References: 1. Hoover-Fong J, Scott CI, Jones MC; Committee on Genetics. Health supervision for people with achondroplasia. *Pediatrics*. 2020;145(6):e20201010. **2.** Wright MJ, Irving MD. Clinical management of achondroplasia. *Arch Dis Child*. 2012;97(2):129-134. **3.** Ireland PJ, Pacey V, Zankl A, Edwards P, Johnston LM, Savarirayan R. Optimal management of complications associated with achondroplasia. *Appl Clin Genet*. 2014;7:117-125. **4.** Ireland PJ, McGill J, Zankl A *et al*. Functional performance in young Australian children with achondroplasia. *Dev Med Child Neurol*. 2011;(10):944-950. **5.** Ednick M, Tinkle BT, Phromchairak J, Egelhoff J, Amin R, Simakajornboon N. Sleep-related respiratory abnormalities and arousal pattern in achondroplasia during early infancy. *J Pediatr*. 2009;155(4):510-515. **6.** Pauli RM. Achondroplasia: a comprehensive clinical review. *Orphanet J Rare Dis*. 2019;14(1):1. **7.** Hecht JT, Francomano CA, Horton WA, Annegers JF. Mortality in achondroplasia. *Am J Hum Genet*. 1987;41(3):454-464. **8.** Matsushita T, Wilcox WR, Chan YY, *et al*. FGFR3 promotes synchondrosis closure and fusion of ossification centers through the MAPK pathway. *Hum Mol Genet*. 2009;18(2):227-240.

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ACHONDROPLASIA COMPLICATIONS BY AGE GROUP

Toddlers (2-4 years)

As toddlers begin to speak and stand, additional complications may become more apparent. Knowing what to look for is key to proactive management, which helps mitigate complications and sets proper expectations.

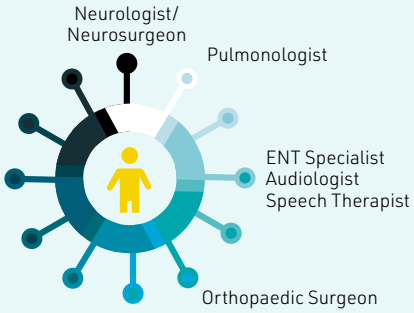
Adapted from Wright MJ, Irving MD, 2012; Hoover-Fong J, Scott CI, Jones MC, 2020; Ireland PJ *et al.*, 2014; and Ireland PJ *et al.*, 2011.[1-4] These are potential complications – individual experience will vary. For diagnosis and management, please follow clinical judgement.

Potential Complication	Proactive Monitoring	Referral Specialist
Cervicomedullary compression[1]	Repeat cranial imaging if clinical signs of cervical myelopathy, central apnoea or developmental delay[1]	Neuroradiologist/Neurosurgeon[1]
Sleep apnoea[1]	Repeat polysomnography if worsening snoring, abnormal daytime tiredness, or slow developmental progress[1]	ENT Specialist[1], Paediatric Pulmonologist[2], Neurosurgeon[1]
Otitis media (OM) Hearing impairments[2]	Annual hearing assessment[2] Recurrent OM may require adenotonsilectomy and insertion of ventilation tubes[3]	ENT Specialist[2], Audiologist[2]
Speech difficulties[2]	Perform a speech evaluation at no later than 2 years of age[2]	Speech Therapist[4]
Kyphosis[1]	Monitor for correction to hyperlordosis with walking[1]	Orthopaedic Surgeon[1]
Genu varum[2]	Consider correction if persistent pain, disturbed gait or lateral thrust[1,2]	Paediatric Orthopaedic Surgeon[1,2]

2.5% risk

While the risk of **sudden death** decreases compared with infancy, it is still a significant concern (2.5% risk for ages 1 to 4 years)[5]

Conductive hearing loss may contribute to speech delays.[2] Concerns of **delayed speech** have been reported in ~20% of children with achondroplasia[1]



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ACHONDROPLASIA COMPLICATIONS BY AGE GROUP

Children (5-14 years)

Throughout childhood, it's important to keep an eye out for otolaryngological, respiratory and orthopaedic issues as they can delay developmental milestones, such as speech and mobility, if left untreated.[1]

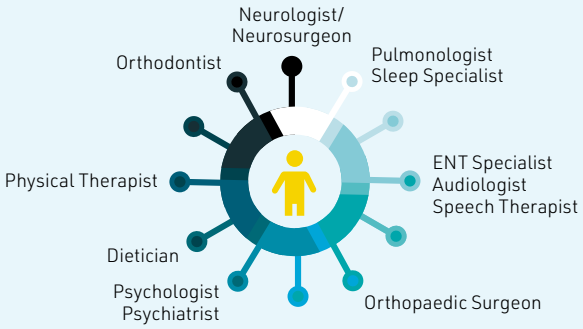
Adapted from Hoover-Fong J, Scott CI, Jones MC, 2020; Wright MJ, Irving MD, 2012; Ireland PJ *et al.*, 2011; Hunter AGW *et al.*, 1998; and Unger S *et al.*, 2017.[1-5] These are potential complications – individual experience will vary. For diagnosis and management, please follow clinical judgement.

Potential Complication	Proactive Monitoring	Referral Specialist
Sleep apnoea[2]	Consider repeat polysomnography if worsening snoring, abnormal daytime tiredness or slow developmental progress[2]	Pulmonologist[1], ENT Specialist[2], Neurosurgeon[2]
Otitis media[2]	Annual hearing assessment[1] Consider repeat assessment if concerns about speech development[2]	ENT Specialist[1], Audiologist[1], Speech Therapist[3]
Orthodontic issues[1]	Evaluate for malocclusion, crowded teeth, narrow upper jaw and crossbite[4]	Orthodontist[1]
Lumbar spinal stenosis (10 to 14 years)[2]	Check deep tendon reflexes yearly for asymmetry or increased reflexes[1]	Neurosurgeon[2], Orthopaedic Surgeon[2]
Lumbar hyperlordosis[1]	Assess for hip flexion contractures[1]	Physical Therapist or Paediatric Orthopaedic Surgeon[1]
Genu varum[2]	Assess every 1 to 2 years or sooner if problems occur[1] Consider correction if persistent pain, disturbed gait or lateral thrust[2]	Orthopaedic Surgeon[2]
Obesity[1]	Review weight control and eating habits[1]	Dietician[2]
Psychosocial impact[2]	Review socialisation and foster independence[1]	Psychologist[5], Psychiatrist[5]

20% to 54%[6,7]

Apnoeas (central or obstructive) are some of the most common respiratory problems in people with achondroplasia[7]

One study found that 10% of children with achondroplasia were **obese**[8]



References: 1. Hoover-Fong J, Scott CI, Jones MC; Committee on Genetics. Health supervision for people with achondroplasia. *Pediatrics*. 2020;145(6):e20201010. **2.** Wright MJ, Irving MD. Clinical management of achondroplasia. *Arch Dis Child*. 2012;97(2):129-134. **3.** Ireland PJ, McGill J, Zankl A *et al*. Functional performance in young Australian children with achondroplasia. *Dev Med Child Neurol*. 2011;(10):944-950. **4.** Hunter AG, Bankier A, Rogers JG, Sillence D, Scott CI Jr. Medical complications of achondroplasia: a multicentre patient review. *J Med Genet*. 1998;35(9):705-712. **5.** Unger S, Bonafé L, Gouze E. Current care and investigational therapies in achondroplasia. *Curr Osteoporos Rep*. 2017;15(2):53-60. **6.** Onodera K, Sakata H, Niikuni N, Nonaka T, Kobayashi K, Nakajima I. Survey of the present status of sleep-disordered breathing in children with achondroplasia Part I. A questionnaire survey. *Int J Pediatr Otorhinolaryngol*. 2005;69(4):457-461. **7.** Afsharpaiman S, Sillence DO, Sheikhvatan M, Ault JE, Waters K. Respiratory events and obstructive sleep apnea in children with achondroplasia: investigation and treatment outcomes. *Sleep Breath*. 2011;15(4):755-761. **8.** Hecht JT, Hood OJ, Schwartz RJ, Hennessey JC, Bernhardt BA, Horton WA. Obesity in achondroplasia. *Am J Med Genet*. 1988;31(3):597-602.

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ACHONDROPLASIA COMPLICATIONS BY AGE GROUP

Teenagers (15-18 years)

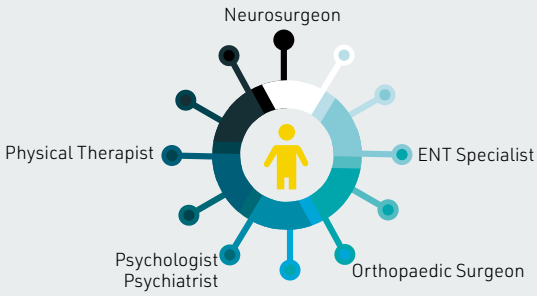
The focus of concern may change during adolescence and adulthood, when certain complications and psychosocial challenges may become more prominent.[1] Knowing what to look for is key to proactive management.

Adapted from Wright MJ, Irving MD, 2012; Hoover-Fong J, Scott CI, Jones MC, 2020; Ain MC *et al.*, 2010; and Unger S *et al.*, 2017.[1-4]
These are potential complications – individual experience will vary. For diagnosis and management, please follow clinical judgement.

Potential Complication	Proactive Monitoring	Referral Specialist
Hearing impairments[2]	Annual hearing assessment[2]	Audiologist[2]
Spinal stenosis[1]	Complete a general and neurologically oriented physical examination. Monitor for any signs or symptoms of nerve compression and check deep tendon reflexes, tone, and sensory findings[2]	Orthopaedic Surgeon[1], Neurosurgeon[1]
Chronic pain[2]	Evaluate for pain and its effect on daily life and physical activity[2]	Orthopaedic Surgeon[3], Physical Therapist[3]
Psychosocial impact[1]	Check in on social adaptation[2]	Psychologist[4], Psychiatrist[4]

32% of patients in one study experienced onset of **symptomatic spinal stenosis** by 18 years of age[5]

~16% of individuals between ages 10 and 20 **develop back pain**[6]



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ACHONDROPLASIA COMPLICATIONS BY AGE GROUP

Adults (18 years and older)

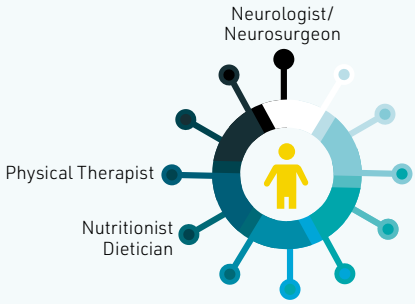
As a person with achondroplasia reaches adulthood, some medical complications may progress without intervention. Health supervision for adults includes surveillance and anticipatory guidance based on the patient and their symptoms.[1]

Adapted from Hoover-Fong J, Scott CI, Jones MC, 2020; Ain MC *et al.*, 2010; Taşoğlu Ö *et al.*, 2014; Fredwall SO *et al.*, 2020; Hecht JT *et al.*, 1988; Pauli RM, 2019; and Vivanti AJ *et al.*, 2016.[1-7] These are potential complications – individual experience will vary. For diagnosis and management, please follow clinical judgement.

Potential Complication	Proactive Monitoring	Referral Specialist
Spinal stenosis[2]	Evaluate for claudication, bladder dysfunction, leg and lower back pain, and leg weakness[2]	Physical Therapist[2], Neurosurgeon[2]
Chronic pain[1]	Evaluate for pain and its effect on daily life and physical activity[1]	Physical Therapist[2]
Osteoporosis[3,4]	Monitor for low bone density[3]	As part of routine medical care Orthopaedic Surgeon[4]
Obesity[1]	Review weight control and diet[1]	Nutritionist[5], Dietician[5]
Cardiovascular complications Hypertension[6]	Monitor weight.[1] Measure blood pressure as part of routine medical care and use forearm for blood pressure quantification if necessary[6]	As part of routine medical care
Obstetric care[7]	Management of specific risks associated with pregnancy and delivery[7]	Obstetrician[7]

40% to 70% may experience **chronic back pain**[4]

20% to 30% may have **spinal stenosis**.[4] Additionally, **genu varum** can cause joint stress and pain in knees and ankles[8]



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