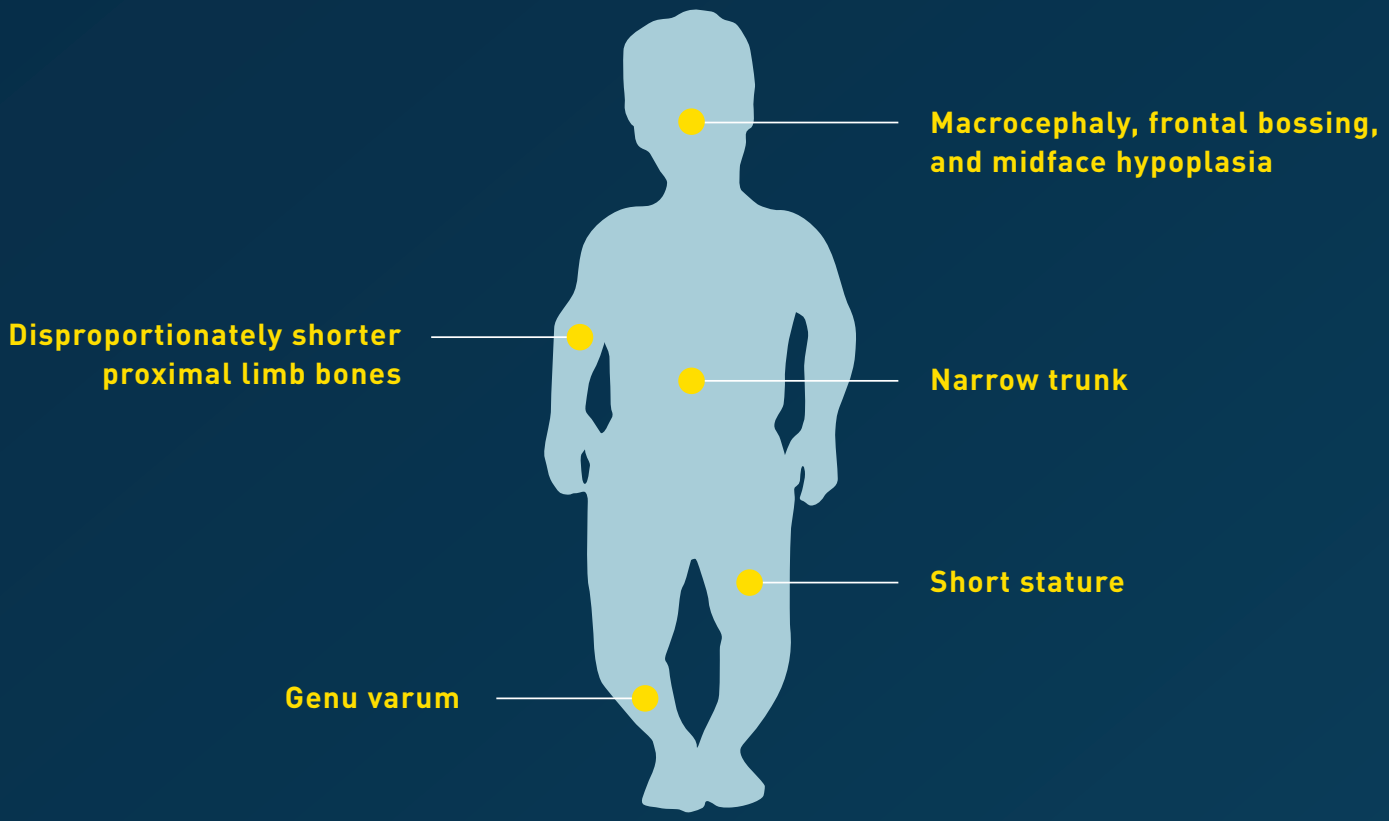

ACHONDROPLASIA
Height is a metric—health is the focus[1,2]
Find out how early and consistent growth assessments can help create a comprehensive care plan[2]
BIOMARIN®

1 IN 25,000 PEOPLE
EACH YEAR ARE BORN WITH ACHONDROPLASIA[3,4]

Achondroplasia, characterized by impaired endochondral bone growth, is the most common type of skeletal dysplasia, accounting for about 90% of disproportionate short stature.[5,6]

PHYSICAL CHARACTERISTICS[1,2,6]



ACHONDROPLASIA IS CAUSED BY A GAIN-OF-FUNCTION MUTATION IN THE FIBROBLAST GROWTH FACTOR RECEPTOR 3 *(FGFR3)* GENE AND HAS A DISTINCT PHYSICAL PRESENTATION.[6]

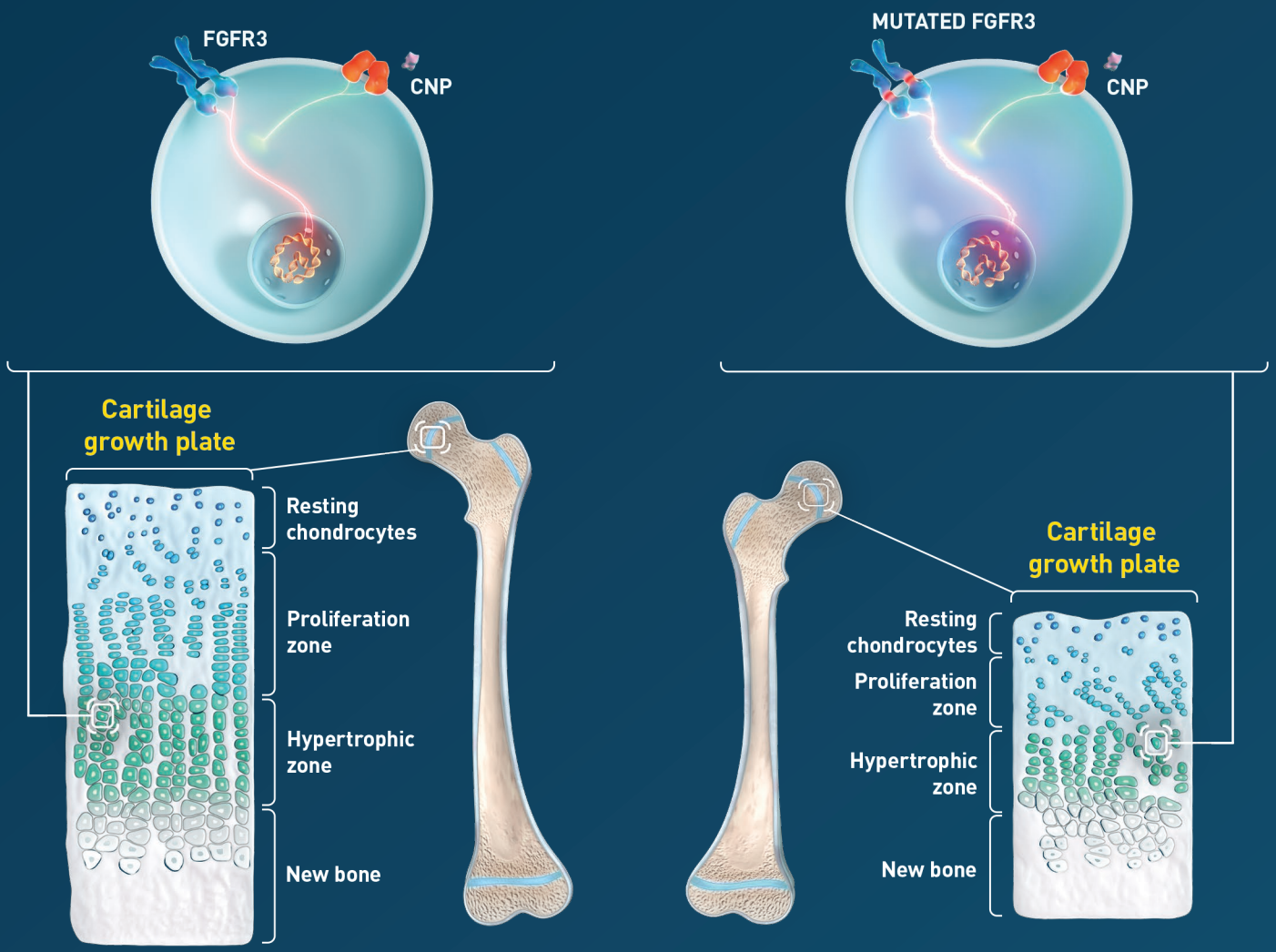
IMBALANCE BETWEEN FGFR3 AND CNP SIGNALING PATHWAYS IMPAIRS BONE GROWTH[7]

Endochondral bone growth—the replacement of cartilage by bone—is primarily regulated by 2 processes[8]:

- Signaling from **fibroblast growth factor receptor 3 (FGFR3)**, which slows linear bone growth[9]
- Counter-signaling from the **C-type natriuretic peptide (CNP) pathway**, which promotes bone growth[9]

Average Stature
The CNP pathway blocks the signal from FGFR3, resulting in typical bone growth.[9,10]

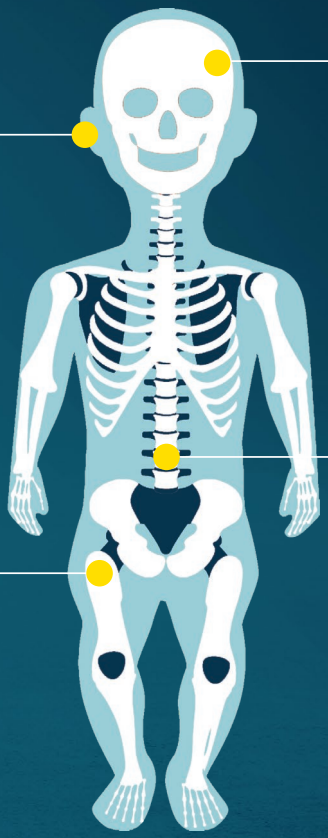
Achondroplasia
Overactive FGFR3 signaling overwhelms the CNP pathway, resulting in impaired bone growth.[9,10]



SERIOUS, MULTISYSTEMIC COMPLICATIONS CAN RESULT FROM IMPAIRED BONE GROWTH IN ACHONDROPLASIA[1]

Impaired endochondral bone growth leads to more than just short stature—progressive neurologic, orthopedic, respiratory, and physical development complications can have long-term health implications for people who have achondroplasia.[1,2]

POTENTIALLY AFFECTED SYSTEMS ACROSS LIFESPAN[10,11]



NEUROLOGIC
- Hydrocephalus
- Foramen magnum stenosis
- Cervicomedullary compression
- Central sleep apnea
- Speech delay
- Delayed motor skill development
- Delayed self-care

OTOLARYNGOLOGIC
- Middle ear infections
- Hearing loss
- Orthodontic problems
- Obstructive sleep apnea

SPINAL
- Kyphosis
- Symptomatic spinal stenosis

MUSCULOSKELETAL
- Chronic pain
- Obesity
- Limited elbow extension
- Hip flexion contractures
- Genu varum

10 X HIGHER rate of deaths expected from heart disease (ages 25-35) than the general population[3]

10 YR REDUCTION in median life expectancy compared with general population[3]

A COMPREHENSIVE CARE PLAN BEGINS WITH REGULAR GROWTH MONITORING[9]

Because achondroplasia is often diagnosed during infancy and can lead to progressive complications, early intervention can play an important role in managing its long-term impact. Achondroplasia-specific assessment of key growth measurements, which can include growth velocity, body segment proportions, weight, and occipital-frontal circumference, can enable timely intervention.[1,6,9,12]

Examples of growth measurements that can help include[12,13]:

Growth velocity

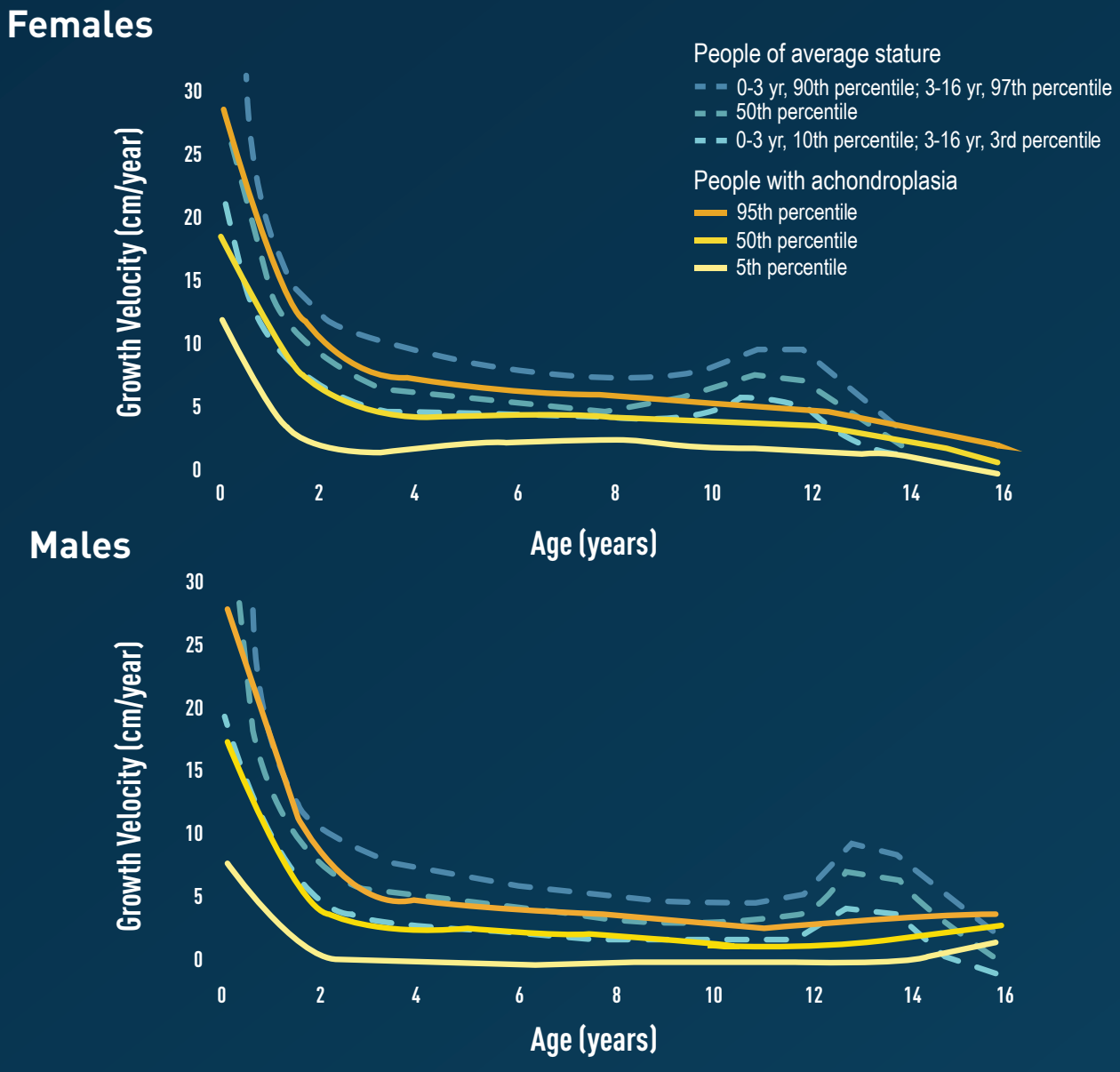
Upper to lower body proportion

Occipital-frontal circumference

Height is a metric—health is the focus[1,2]

ANNUALIZED GROWTH VELOCITY
IS A PROXY FOR ENDOCHONDRAL BONE GROWTH[13]

Children with achondroplasia have significantly reduced growth velocity—they experience slower linear growth from infancy and may not have a pubertal linear growth spurt.[13]

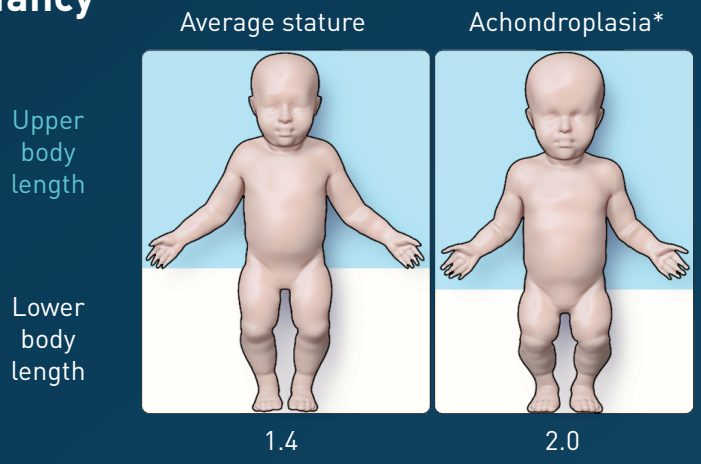


PEOPLE WITH ACHONDROPLASIA HAVE FINAL ADULT HEIGHTS THAT ARE 6-7 STANDARD DEVIATIONS BELOW THE GENERAL POPULATION MEAN.[6]

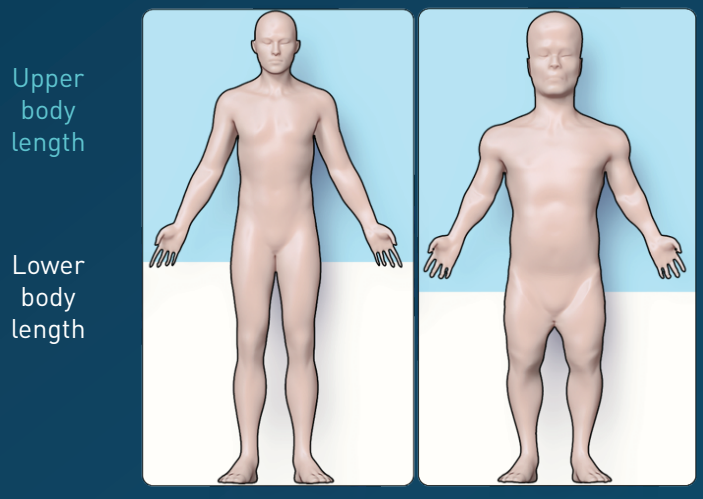
BODY SEGMENT DISPROPORTIONALITY IS AN IMPORTANT PHYSICAL MARKER OF ACHONDROPLASIA[13]

As average stature children grow into adulthood, their upper and lower body lengths become proportional. However, children with achondroplasia have a higher upper to lower body segment ratio at infancy, which continues into adulthood.[13,14]

Infancy



From 10 years old to adulthood



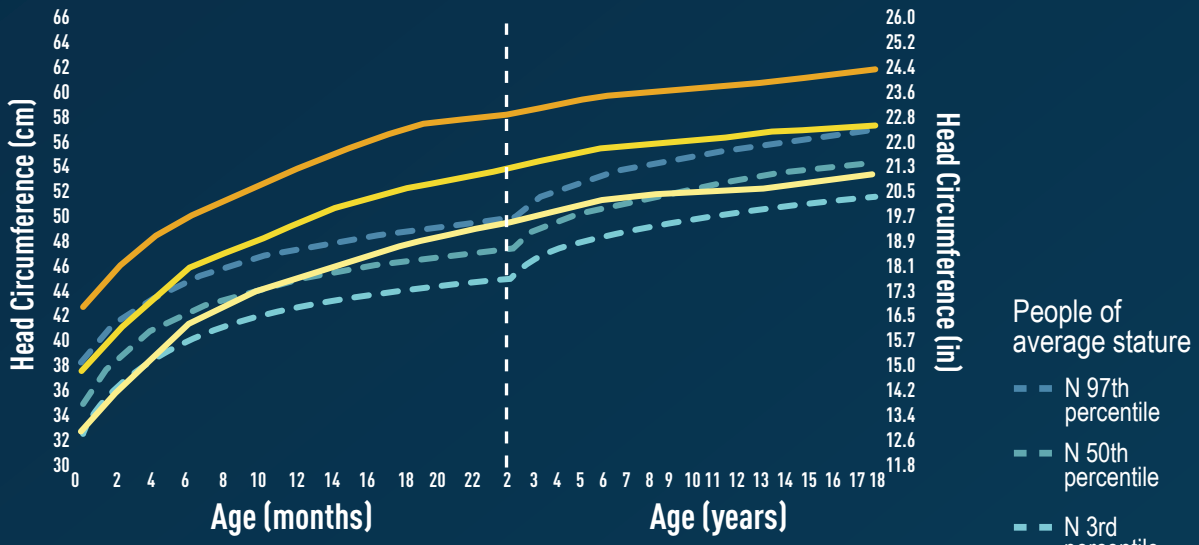
PEOPLE WITH ACHONDROPLASIA HAVE A 1.7:1 RATIO OF UPPER TO LOWER BODY LENGTH AT SKELETAL MATURITY.[14]

*These ratios represent the 50th percentile of children with achondroplasia.

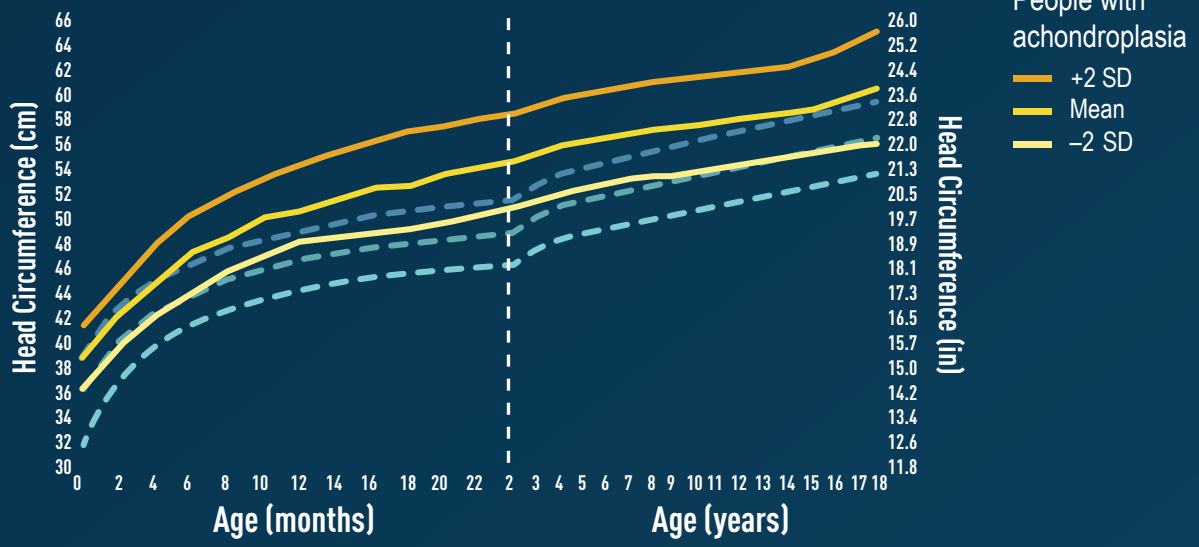
OCCIPITAL-FRONTAL CIRCUMFERENCE CAN HELP IDENTIFY POTENTIAL NEUROLOGIC COMPLICATIONS[1]

Close monitoring of the occipital-frontal circumference (OFC) using achondroplasia-specific growth charts can help identify potential neurologic complications.[1,2]

Females



Males



People of average stature
- N 97th percentile
- N 50th percentile
- N 3rd percentile

People with achondroplasia
- +2 SD
- Mean
- –2 SD

CHILDREN WITH ACHONDROPLASIA WHO EXPERIENCE A RAPID INCREASE IN HEAD SIZE OR SYMPTOMS OF INCREASED INTRACRANIAL PRESSURE MAY NEED TO BE REFERRED TO A PEDIATRIC NEUROLOGIST.[1]

CAREGIVERS CAN HELP IDENTIFY COMPLICATIONS EARLY

Discussing the signs of potential complications with parents and caregivers of people with achondroplasia can help ensure timely identification and management.

Sleep disordered breathing
Affects >50% of people with achondroplasia[12]

Genu varum (tibial bowing)
Bowing of legs can affect walking and running[15]

Symptomatic spinal stenosis
Can lead to leg weakness, incontinence, and chronic pain, especially in the back[16,17]

Pain
Especially back pain, which can result in loss of mobility[17]

Recurrent otitis media
Ear infections can affect up to 70% of people with achondroplasia[6]

Dental issues
Including misaligned teeth, a narrow palate, open bite, or underbite[17]

Obesity
Can lead to heart disease[18,19]

Functional challenges
Associated with the complications caused by achondroplasia can affect mobility, independence, and daily activities[19,20]

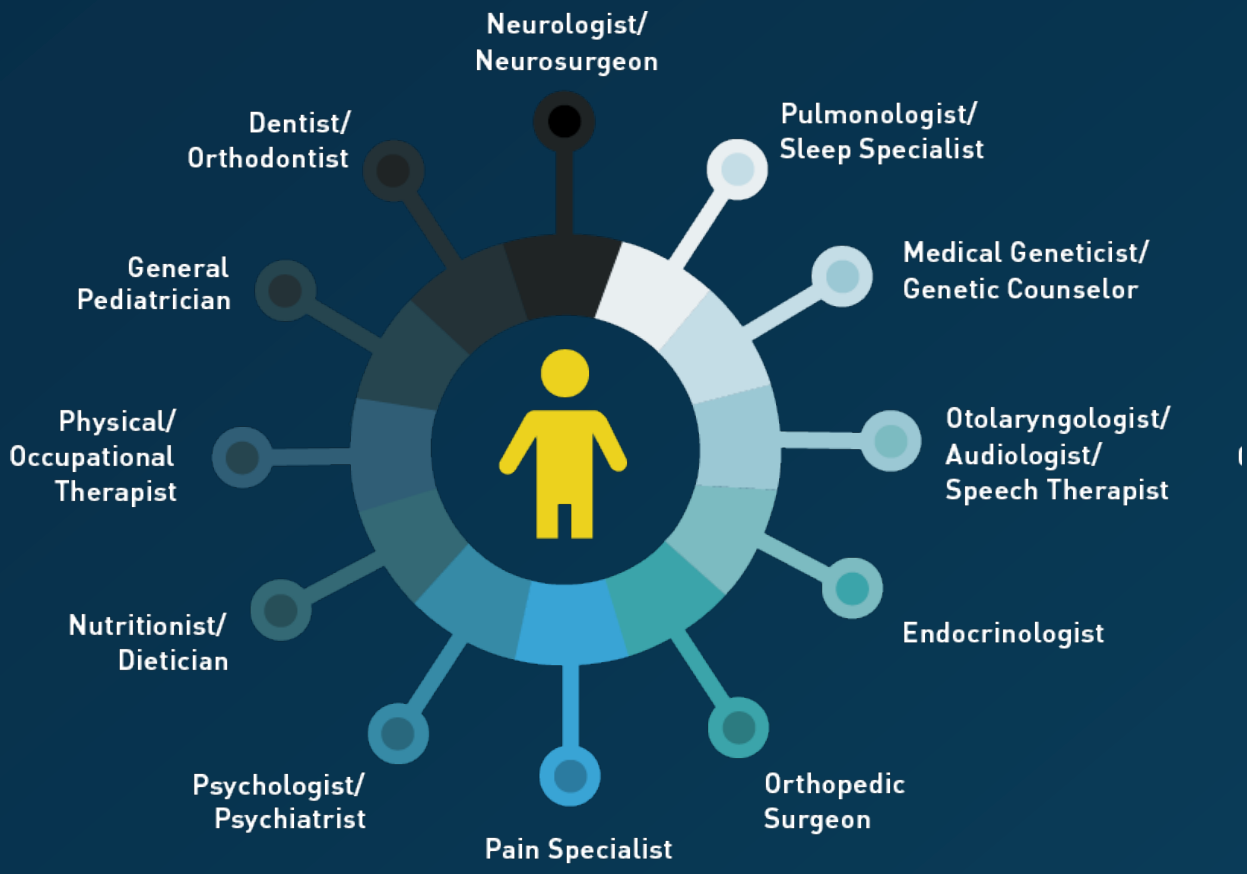
Foramen magnum stenosis
May be associated with compression of the lower brain stem and higher mortality[21-23]

Psychosocial impact
Negative appraisal of one's own stature could lead to poor self-esteem[24]

CAREGIVERS CAN VISIT ACHONDROPLASIA.COM TO LEARN MORE ABOUT THE SIGNS OF COMPLICATIONS RELATED TO ACHONDROPLASIA.

A COMMUNITY OF HEALTHCARE PROVIDERS SUPPORT PARENTS AND CAREGIVERS[2]

The multisystemic challenges of achondroplasia require a multidisciplinary team. Coordinated care is needed to provide optimal results for patients and to support their parents and caregivers.[2,6,12,17,25]

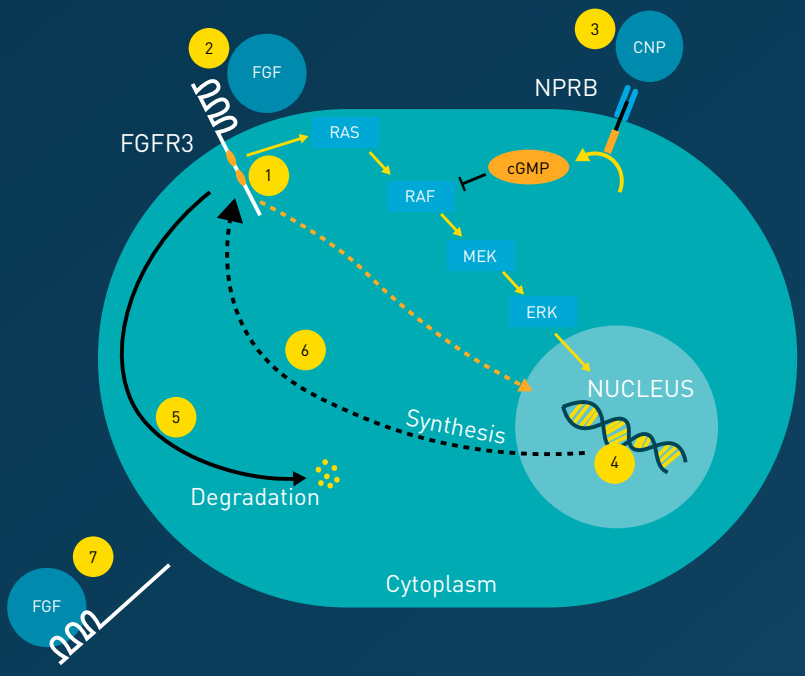


VISIT **HCP.ACHONDROPLASIA.COM** TO STAY IN THE KNOW ABOUT NEW DEVELOPMENTS.

VIEW IN 3D
Hold the camera app on your phone over the QR code.

RESEARCH INTO ACHONDROPLASIA IS ONGOING[26]

Current treatments do not address the underlying cause of achondroplasia and is limited to the management of complications. Different approaches targeting FGFR3 overactivity and the CNP pathway are under investigation. However, none of these approaches have been determined to be safe or effective or approved for use.[9,10,25-27]



1. Chemical inhibitors to reduce FGFR3 tyrosine kinase activity
2. Antibodies to block FGFR3 activation
3. Exogenous CNP to enhance CNP-mediated antagonism of downstream signals
4. RNA interference (RNAi) to reduce FGFR3 production
5. Heat shock protein 90 (Hsp90) inhibitors to induce degradation of activated FGFR3
6. Agents to disrupt direct nuclear signaling of FGFR3
7. Soluble FGFR3 decoys to prevent cellular FGF binding

NO THERAPIES FOR ACHONDROPLASIA HAVE BEEN APPROVED FOR USE OR DETERMINED TO BE SAFE OR EFFECTIVE.

HEIGHT IS A METRIC—HEALTH IS THE FOCUS[1,2]

1 in 25,000 people
each year are born with achondroplasia, which is characterized by impaired endochondral bone growth[3,6]

Regular growth assessments
using achondroplasia-specific growth charts can help identify potential complications[11,12]

Serious complications
that affect multiple physiological systems can result from impaired bone growth in achondroplasia[1,2]

Research on targeted pharmacologic approaches
to achondroplasia is ongoing[25,26]

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