

# KNIEST DYSPLASIA

## DESCRIPTION:

Kniest dysplasia is a constitutional bone diagnosis due to mutations in the COL2A1 gene involved in the production of type 2 collagen. Changes in the composition of this collagen leads to atypical skeletal growth, which is why affected individuals remain short in stature. In adulthood, the average height varies between 100 cm (3'3") and 140 cm (4'7").

Kniest dysplasia is autosomal dominant trait (the child of an affected parent has a one in two chance of being impacted). However, in most cases, it is a genetic mutation/variation, meaning that the child is born to parents of average height [see "Genetics"]. The prevalence of the condition is unknown.

## CHARACTERISTICS AND DIAGNOSIS:

Kniest dysplasia results in proportionate dwarfism displaying a short trunk and limbs. The physical characteristics of the diagnosis are as follows:

- Micromelia (short limbs);
- Round face with a flattened nasal root;
- Cleft palate (opening of the palate);
- Prominent joints;
- Scoliosis and/or kyphosis (humpback);
- Valgus or varus (limbs bowed inward or outward);
- Long thin fingers.

The condition is visible from birth or even before, due to the small size and peculiarities of the head and face. Radiological examination reveals thickened and atypical epiphyses (bone heads), an uncalcified femoral head, enlarged upper femoral metaphyses (growth plates under the bone head), platyspondyly (flattening and/or thickening of the vertebrae) and other vertebral malformations.

## MAIN POSSIBLE COMPLICATIONS:

**Cleft palate** (opening of the palate): This characteristic can lead to difficulties in swallowing and speaking. It may also be associated with middle ear issues, so the ears and eardrums of infants with this diagnosis should be monitored.

Surgery is possible to correct a cleft palate.



**Hearing issues:** People with Kniest dysplasia often develop hearing loss that can lead to deafness. For this reason, audiometric tests should be done at 12, 18 and 24 months of age as well as once a year thereafter. Ear infections should also be closely monitored. If necessary, a myringotomy (insertion of a ventilation tube into the eardrum) may be performed.

**Ocular issues:** Most patients present with strong myopia. There is also a significant risk of retinal detachment. Glaucoma and cataracts can also occur in 5-29% of cases.

Because of these risks, an ophthalmologic evaluation should be performed during the first six months of life and then every 6 to 12 months thereafter.

If retinal detachment or glaucoma is suspected, a specialist should be consulted without delay, as this can have serious consequences with the person's vision. Signs of retinal detachment include the appearance or sudden increase of floating bodies (filaments in the field of vision), visual disturbances like flashes of lightning, blurred vision, or even a sudden loss of vision.

Glaucoma is characterized by sudden blurry or blurred peripheral vision, eye pain, headaches, extreme sensitivity to light, red eyes, dilated pupils, as well as nausea and vomiting.

**Leg misalignment:** A varus (outward) or valgus (inward) deviation can be present.

Leg alignment, chronic knee pain and any trouble walking should be clinically monitored.

Surgery should be reserved for patients with severe and symptomatic misalignment.

**Hip degeneration:** The vast majority of people affected by Kniest dysplasia have early osteoarthritis of the hip. A coxa vara (deformity of the femur) is also common.

Radiological monitoring should be initiated beginning at the age of about 4 years, or even earlier if an abnormality is suspected. An osteotomy (surgery to repair bone and joint problems) may be performed if necessary; total hip replacement (surgery to restore a damaged joint) may be required in adults.

**Scoliosis, kyphosis or kyphoscoliosis** (combination of kyphosis and scoliosis): Because of the high risk of early development of spinal curvatures, the spine should be examined clinically every 6 months and x-rays should be taken if there is any doubt.

It is important to seek medical advice as soon as the first manifestations of issues appear. A brace or corset can correct spinal curvatures, but in some cases, especially in the presence of kyphoscoliosis, a surgical fusion may be necessary.

**Neck** (cervical spine): Cervical instability (hypermobility of the neck vertebrae) may be present. If this is the case, there is a risk of spinal cord compression, a problem that can lead to slow, gradual myelopathy (spinal cord injury) or sudden paralysis.

The first signs of myelopathy are decreased muscle endurance and tone, hyperreflexia (exaggerated reflexes) and clonus (rapid contractions and reflexes of the limbs), especially in the legs, and problems with bowel and/or bladder control (incontinence, etc.).

Because of these risks, radiographic and MRI (magnetic resonance imaging) examinations of the cervical region must be performed as soon as the diagnosis of Kniest dysplasia is made,



and then at regular intervals. In case of problems, a surgeon specialized in spinal disorders should be consulted. If the instability is severe, a cervical decompression with fusion will have to be performed.

**Respiratory system:** Respiratory problems, such as tracheomalacia or bronchomalacia, may occur due to micrognathia (insufficient development of the jaw bones), cleft palate and decreased airway size. Tracheomalacia and bronchomalacia affect the expiratory phase of breathing. Breathing is then wheezy or noisy and the person quickly becomes short of breath. Infants may have episodes of cyanosis (blue discoloration of the skin). The resulting respiratory failure can be fatal and should be closely monitored.

Assessment of respiratory status should be done at birth. If wheezing increases and the child is experiencing respiratory distress, a pediatric respirologist should be consulted.

**Anesthesia:** There are risks, especially those associated with cervical instability and respiratory problems [see "anesthesia" section].

It is therefore necessary to evaluate the stability of the cervical spine before any anesthesia. If instability is detected, an intubation with external stabilization of the neck should be performed. It will also be necessary to adapt the endotracheal tubes to the size of the patient (e.g. size of premature babies for young children and pediatric size for adults).

### TREATMENT:

The management of Kniest's dysplasia is multidisciplinary (surgery, occupational therapy, orthopedics, physiotherapy, pneumology, etc.) and preventive, and is essentially aimed at detecting complications and enabling those affected to live better and more actively.

No known treatment is effective. Growth hormone is not likely to produce favourable results, since Kniest dysplasia is secondary to an intrinsic abnormality of bone growth.

Limb lengthening, a controversial practice, is not recommended at all. Indeed, in addition to the complications and pain it can generate, this technique would create a body imbalance in people with this diagnosis.

**List of the main elements to be monitored and managed** [see the sheet "frequent interventions for people of short stature"] :

- Correction of cleft palate;
- Hearing and eye problems;
- Leg issues and hip degeneration;
- Scoliosis, kyphosis or kyphoscoliosis;
- Cervical instability with risk of spinal cord compression;
- Breathing problems.



## RESOURCES:

Association québécoise des personnes de petite taille

<https://www.aqppt.org/>

Little People of Ontario

<https://littlepeopleofontario.com/>

Regroupement québécois des maladies orphelines - Centre iRARE

<https://rqmo.org/centre-dinformation-et-de-ressources-en-maladies-rares/>

Orphanet – fact sheet on Kniest dysplasia

[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?lng=en&Expert=485](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=en&Expert=485)

Little people of America – fact sheet on Kniest dysplasia

<https://www.lpaonline.org/assets/documents/NH%20Kniest%20dysplasia1.pdf>

National Organisation for Rare Disorders

<https://rarediseases.org/rare-diseases/kniest-dysplasia/>

Genetic and Rare Diseases Information Center

<https://rarediseases.info.nih.gov/diseases/6841/kniest-dysplasia>



### Please contact us for more information

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