

OSTEOGENESIS IMPERFECTA (OI)

DESCRIPTION :

Osteogenesis imperfecta (OI) is a group of constitutional bone conditions caused primarily by a type I collagen defect. They primarily affect the COL1A1 gene or the COL1A2 gene, which encodes type I collagen. OI is characterized by bone fragility causing multiple spontaneous fractures. The adult height of people with this disease varies according to the type of the diagnosis. Type I has little or no effect on height. Type III, IV, V and VI patients have varying degrees of short stature (more in type III).

Two other types, VII and VIII, affect the CRTAP and LEPRE1 genes respectively. In these, short stature is common.

OI affects approximately 1 in 15-20,000 births. The condition is an autosomal dominant trait [see "Genetics"].

CHARACTERISTICS AND DIAGNOSIS :

OI-associated fractures can cause issues that can lead to a severe debilitating condition. The physical features of osteogenesis imperfecta vary greatly depending on the diagnosed type. Here are some of the specifics:

- Small size;
- Triangular facies;
- Bone irregularities;
- Issues of the rib cage and spine;
- Loose joints, ligament laxity and muscle weakness;
- Imperfect dentinogenesis (tooth formation);
- Blue or grey sclera;
- Heart valve disorders.

The diagnosis, essentially clinical, is based on the observation of a multiplication of fractures, following minimal trauma, or even in the absence of trauma. Babies with moderate to severe forms of OI are often born with one or more fractures. In addition, infants with moderate forms of OI will have fractures as a result of their parents' daily handling, or when they begin to stand and walk. Some very mild cases of OI are diagnosed later (in adolescence or adulthood).

Specifically, the diagnosis is based on bony and extraosseous signs. X-rays reveal osteoporosis and the presence of wormian-type bones. Bone densitometry (examination of bone density) confirms low bone mass.

DNA tests are also performed to confirm the diagnosis. However, since not all the genetic causes of OI have been identified yet, a negative test is not enough to invalidate the diagnosis.



PRIMARY POSSIBLE COMPLICATIONS :

Fragility of the skin and blood vessels: May cause hematomas and nosebleeds, especially in children.

Hearing loss: Usually occurs in the early 20s. More than 50% of people with OI have a hearing loss.

Treatment for hearing loss varies. It involves delicate surgery due to the brittleness of the bones, or the usage of a hearing aid.

Dental issues: Are related to dentinogenesis imperfecta and must be treated early. The use of fluoride, both orally and locally (toothpastes), is recommended.

The treatment most often involves placing crowns on milk teeth. Implants may also be necessary in adulthood.

Visual issues: Myopia and the risk of retinal detachment.

Retinal detachment causes a visual loss that can be severe and permanent. Symptoms to watch for are decreased vision and visualizations such as flashing lights or floating dots.

Breathing issues: When breathing issues occur, they are aggravated by irregularities of the chest wall, spine, and lung collagen. The main problem affecting people with OI is the loss of lung capacity. As a result, a respiratory infection, insufficient oxygen supply or other breathing problems can lead to respiratory failure that could cause death. Respiratory failure is the leading cause of death for people with OI.

Symptoms to watch for include wheezing or noisy breathing, shortness of breath, fatigue, insomnia, headaches and sleep disturbances.

Because of this fragility, it is strongly recommended that people with OI do not smoke and avoid exposure to second-hand smoke. In addition, increased attention should be paid to viral (cold and flu) and bacterial (bronchitis and pneumonia) infections, as well as allergies and asthma (if present). Although these problems are not directly caused by OI, they can lead to respiratory complications. It is therefore recommended that all respiratory infections be treated promptly and that vaccinations be given against influenza and pneumonia. If necessary, a sleep study may also be useful to diagnose a possible nocturnal respiratory issue (sleep apnea). Some upper body exercises can increase breathing capacity. Finally, care should be taken to regularly monitor lung function and the amount of oxygen in the blood (oxygenation).

Heart issues:

- **Valvulopathy (heart valve dysfunction):** Can progress slowly over years with no apparent clinical manifestation. If the problem worsens, it may be necessary to replace the damaged valves through surgery (valvuloplasty).

The most common symptoms of valve disease are discomfort, chest tightness or



pressure, palpitations, shortness of breath, fatigue, weakness and dizziness.

- **Aortic aneurysm (localized dilation of the aorta):** The majority of small and medium-sized aneurysms do not cause symptoms. As the aneurysm grows, the affected person may feel a "second heart" beating in the abdomen. When an aneurysm ruptures, it is a life-threatening emergency. People will experience sudden onset pain in the abdomen and/or back, dizziness or loss of consciousness.
- **Ruptured cerebral blood vessels (cervical aneurysm):** Signs to watch for are the sudden onset of a severe headache, sometimes accompanied by nausea and vomiting. Loss of consciousness may occur. If such symptoms appear, it is necessary to contact the emergency room immediately.

Because of these risks, people with OI should have their blood pressure monitored. Exercise resistance and endurance tests are also recommended.

Basilar impression: Cranial issues characterized by an upward displacement of the occipital hole (an opening at the base of the skull that allows the spinal cord to pass through) with the first vertebrae appearing to be embedded in the cranial cavity. This diagnosis may be the cause of neurological complications.

Signs of complications to watch for are headaches, sharp reflexes with weakness of the lower limbs, or damage to cranial nerves such as the trigeminal nerve. A nuclear magnetic resonance imaging (MRI) examination should be performed if these symptoms are present.

Anaesthesia: The risk of complications is increased due to skeletal (thoracic and spinal), respiratory and cardiac issues resulting from OI.

In the event of an operation, it is therefore necessary to ensure that an experienced anaesthetist is consulted and present. Finally, before implementing any invasive technique, it is necessary to have an assessment of pulmonary and cardiac function completed [see the "anaesthesia" section].

TREATMENT :

There is no curative treatment for OI. Symptomatic management is multidisciplinary. Surgery and orthopedics are essential to correct bone and spinal issues and prevent long bone fractures. Osteopathy and physiotherapy improve independence by facilitating the assessment of motor deficits, reducing the risk of falls and encouraging patients to exercise.

Drugs used in the treatment of osteoporosis, such as bisphosphonates and teriparatide, are also used to increase bone density and prevent bone loss. However, these drugs are not curative. Also, prevention of vitamin D and calcium deficiency is fundamental at any age. Finally, it is important to note that a treatment is currently undergoing clinical trials.



Among the most common surgeries are:

- Bone nailing, which consists of inserting telescopic nails into long bones to control fractures and consolidate bones. The nails lengthen with growth. This surgical operation is mostly performed on children.
- Posterior spinal arthrodesis (rods attached to the back of the spine) to stabilize the spine and allow sitting in a wheelchair.

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/>

Osteogenesis Imperfecta Foundation

<http://www.oif.org/site/PageServer>

Orphanet – fact sheet on osteogenesis imperfecta

[https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=654&Disease_Disease_Search_diseaseGroup=osteogenesis-imperfecta&Disease_Disease_Search_diseaseType=Pat&Disease\(s\)%20concerned=Osteogenesis-imperfecta&title=Osteogenesis-imperfecta&search=Disease_Search_Simple](https://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=654&Disease_Disease_Search_diseaseGroup=osteogenesis-imperfecta&Disease_Disease_Search_diseaseType=Pat&Disease(s)%20concerned=Osteogenesis-imperfecta&title=Osteogenesis-imperfecta&search=Disease_Search_Simple)

Introduction to Osteogenesis Imperfecta. A Guide for Medical, Professional, Individuals and Families Affected by OI, Osteogenesis Imperfecta Foundation, 2013

http://www.oif.org/site/DocServer/Medical_Guide_revised_2013.pdf?docID=15641

Physical and Occupational Therapist. Guide to Treating Osteogenesis Imperfecta, Osteogenesis Imperfecta Foundation [no date]

http://www.oif.org/site/DocServer/PT_guide_final.pdf?docID=201

Respiratory Issues in Osteogenesis Imperfecta, Osteogenesis Imperfecta Foundation, 2015

http://www.oif.org/site/DocServer/Respiratory_Issues.pdf?docID=7621



Nathalie Boëls, *Le nanisme. Se faire une place au soleil dans un monde de grands*, Montréal, éditions du CHU Sainte-Justine, 2008



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