



# Diagnosis of Osteogenesis Imperfecta

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Osteogenesis Imperfecta (OI) is a rare genetic condition present from birth. Its most striking feature is fragile bones that may fracture easily. Therefore, it is frequently called “brittle bone disease”.

**It is important to diagnose OI as soon as possible so that treatment can start, however due to OI being a rare disease, getting a precise diagnosis may be challenging**

## Description of OI

OI is a disorder of collagen, a protein which forms the framework for the bone structure. In OI, the collagen may be of poor quality, or there may just not be enough to support the mineral structure of the bones. This makes the bones weak and fragile and results in the bones being liable to fracture at any time with minimal trauma or sometimes even without trauma. Some people with OI, however, hardly have any symptoms but in others OI may lead to physical disability requiring the use of walking sticks, walking frames or wheelchairs. As the composition of collagen in the bone is not correct, even when there are no fractures there will be other problems connected to the condition, such as the ligaments stretching more easily, allowing dislocation of joints. The joint hypermobility can significantly affect the quality of life as it results in fatigue of many muscle groups. As a result, the mobility and performance of ordinary tasks of everyday living are impaired. The majority of individuals with OI suffer from bone and muscle pain. However, there are several individuals who have very mild features of the condition as well.

\*Please read this Factsheet in conjunction with the BBS Factsheet About OI



## Diagnosis

It is important to diagnose OI as soon as possible so that treatment can start, however due to OI being a rare disease, getting a precise diagnosis may be challenging. Genetic testing is possible, but it is not undertaken routinely. OI remains a clinical diagnosis.

For individuals with a family history of OI, early detection may be easier, given that a routine prenatal screening by ultrasound may identify this in the unborn infant, whilst genetic testing can usually confirm the diagnosis. Where there is no family history of OI and if a genetic abnormality remains undetected, an OI diagnosis can be made on the basis of clinical features (such as the presence of fractures); however, this may prove more difficult. Given that the detection rate is very low with lack of family history or input from a specialist in diagnosing bone conditions, this can therefore lead to missed diagnoses and/or diagnostic errors.



## Genetics

The majority of OI cases are caused by defects in the amount or quality of Type 1 collagen, therefore initial testing for abnormalities in COL1A1 and COL1A2 (which are the two genes that encode for type 1 collagen and will account for 90% of cases) should be carried out. If the results of these are normal, consideration should then be given to testing for the rarer forms of OI. Although the results will not be available for some time they are important not only for confirmation of the diagnosis but for genetic counselling to the parents for future pregnancies.

\*You can read more about Genetics of OI in the Genetics Factsheet.



## Clinical Presentation

There are several ways in which a baby with OI may present in the neonatal period.

### Severe Forms:

Antenatal detection at the time of routine ultrasound scans is increasingly identifying severe forms in utero. Skeletal abnormalities such as bowed limbs, fractures, and small chest size may lead to a precise diagnosis of OI or a broader description as a lethal skeletal dysplasia which is only recognised as OI after birth.

If not identified in the antenatal period, some severely affected infants with small, deformed chests due to the presence of multiple rib fractures will develop respiratory insufficiency within a few days of birth requiring assistance ranging from supplemental oxygen to positive pressure ventilation. More commonly, a severely affected baby will present at birth with evidence of short stature, bowed limbs and multiple fractures. Subsequent investigation with review of skeletal surveys by experienced clinicians will usually lead to a diagnosis of OI which can be confirmed by genetic testing.

### Mild and Moderate Forms:

These may present in the neonatal period in several ways. There may be evidence of a short, bowed femur which might have been detected on an antenatal scan. It is often not apparent that this is due to OI until the child starts to fracture, which may not be for some months or years after birth. An alternative presentation is with a dislocated or unstable hip due to the ligamentous laxity known to be characteristic of OI. An occasional, but uncommon, presentation is when an affected baby presents in the neonatal period with a long bone fracture, which leads to the identification of other fractures (including rib fractures) on skeletal survey.

Symptoms of OI will vary from person to person, but may include:

- Fractures that can occur with minimal force – this varies from child to child.
- Bones may have an altered shape, for example, they may be shortened or bowed.
- The whites of the eyes may appear more blue or grey than normal.
- Joints can be hypermobile or very flexible
- Some degree of joint or bone pain may be present
- Problems with formation of teeth (dentinogenesis imperfecta, or DI)
- Children with OI may tire easier than other children
- Hearing problems are known to affect people with OI usually after puberty.
- Children with OI tend to be shorter than other children.

## Assessment

There are a number of investigations of importance when a baby presents with a suspected diagnosis of OI. No single test can identify OI. To diagnose OI, doctors will look at carrying out:

### Physical Exam:

OI is diagnosed clinically in the majority of cases, that is, the doctor will carry out a physical examination of your child and take a full medical and family history. During a physical exam, the doctor may:

- Measure the length of limbs.
- Measure the head circumference.
- Examine the eyes and teeth.
- Examine the spine and rib cage.



If you or your child has noticed any hearing problems, the doctor may refer you to a hearing specialist or paediatrician, who can perform a comprehensive hearing test.

Personal and family medical history will also be taken into consideration, which include questions about:

- Broken bones.
- Hearing loss.
- Brittle teeth.
- Adult height.
- Whether close relatives have had children together.



### Blood Tests:

Blood Tests may include bone profile & vitamin D to exclude other causes for weak bones. A blood test may also be performed to identify specific genetic mutations associated with Osteogenesis Imperfecta.

### X-rays

Imaging such as x-rays is usually suggested to check for special changes of OI in the skull as well as fractures and bone changes in other parts of the skeleton. Sometimes a full xray of the skull, chest, back, arm, legs, hands and feet is requested. An X-ray may be used to look at your child's bone structure for signs of past fractures and to assess the alignment of the bones. Additional imaging of the cervical spine and brain may be indicated in severely affected infants for the presence of cervical spine abnormalities which may compromise spinal cord function, or hind brain abnormalities such as basilar invagination.

It is important that the X-rays are reviewed by a radiologist with experience in problems of the skeleton.

Bone density scans (DEXA) can be carried out on children weighing more than 10kg, but there is not enough data available to give accurate results for children under five years old.



## Differential Diagnosis

Although both OI and child abuse are diagnostic considerations in the child with multiple fractures, other disorders that may be considered in the neonatal period include: prematurity, hypophosphatasia, mucopolipidosis type II (I-cell disease) and Menkes disease. In children and adolescents with fractures, the differential diagnosis may include idiopathic juvenile osteoporosis, hypophosphatasia and celiac disease among the more commonly encountered disorders.

## Notes

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