



## osteogenesis imperfecta

Osteogenesis imperfecta (OI) is a group of genetic disorders that mainly affect the bones. The term "osteogenesis imperfecta" means imperfect bone formation. People with this condition have bones that break easily, often from mild trauma or with no apparent cause. Multiple fractures are common, and in severe cases, can occur even before birth. Milder cases may involve only a few fractures over a person's lifetime.

There are at least eight recognized forms of osteogenesis imperfecta, designated type I through type VIII. The types can be distinguished by their signs and symptoms, although their characteristic features overlap. Type I is the mildest form of osteogenesis imperfecta and type II is the most severe; other types of this condition have signs and symptoms that fall somewhere between these two extremes. Increasingly, genetic factors are used to define the different forms of osteogenesis imperfecta.

The milder forms of osteogenesis imperfecta, including type I, are characterized by bone fractures during childhood and adolescence that often result from minor trauma. Fractures occur less frequently in adulthood. People with mild forms of the condition typically have a blue or grey tint to the part of the eye that is usually white (the sclera), and may develop hearing loss in adulthood. Affected individuals are usually of normal or near normal height.

Other types of osteogenesis imperfecta are more severe, causing frequent bone fractures that may begin before birth and result from little or no trauma. Additional features of these conditions can include blue sclerae, short stature, hearing loss, respiratory problems, and a disorder of tooth development called dentinogenesis imperfecta. The most severe forms of osteogenesis imperfecta, particularly type II, can include an abnormally small, fragile rib cage and underdeveloped lungs. Infants with these abnormalities have life-threatening problems with breathing and often die shortly after birth.

### Frequency

This condition affects an estimated 6 to 7 per 100,000 people worldwide. Types I and IV are the most common forms of osteogenesis imperfecta, affecting 4 to 5 per 100,000 people.

### Genetic Changes

Mutations in the *COL1A1*, *COL1A2*, *CRTAP*, and *P3H1* genes cause osteogenesis imperfecta.

Mutations in the *COL1A1* and *COL1A2* genes are responsible for more than 90 percent of all cases of osteogenesis imperfecta. These genes provide instructions for making proteins that are used to assemble type I collagen. This type of collagen is the most abundant protein in bone, skin, and other connective tissues that provide structure and strength to the body.

Most of the mutations that cause osteogenesis imperfecta type I occur in the *COL1A1* gene. These genetic changes reduce the amount of type I collagen produced in the body, which causes bones to be brittle and to fracture easily. The mutations responsible for most cases of osteogenesis imperfecta types II, III, and IV occur in either the *COL1A1* or *COL1A2* gene. These mutations typically alter the structure of type I collagen molecules. A defect in the structure of type I collagen weakens connective tissues, particularly bone, resulting in the characteristic features of osteogenesis imperfecta.

Mutations in the *CRTAP* and *P3H1* genes are responsible for rare, often severe cases of osteogenesis imperfecta. Cases caused by *CRTAP* mutations are usually classified as type VII; when *P3H1* mutations underlie the condition, it is classified as type VIII. The proteins produced from these genes work together to process collagen into its mature form. Mutations in either gene disrupt the normal folding, assembly, and secretion of collagen molecules. These defects weaken connective tissues, leading to severe bone abnormalities and problems with growth.

In cases of osteogenesis imperfecta without identified mutations in one of the genes described above, the cause of the disorder is unknown. These cases include osteogenesis imperfecta types V and VI. Researchers are working to identify additional genes that may be responsible for these conditions.

## **Inheritance Pattern**

Most cases of osteogenesis imperfecta have an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell is sufficient to cause the condition. Many people with type I or type IV osteogenesis imperfecta inherit a mutation from a parent who has the disorder. Most infants with more severe forms of osteogenesis imperfecta (such as type II and type III) have no history of the condition in their family. In these infants, the condition is caused by new (sporadic) mutations in the *COL1A1* or *COL1A2* gene.

Less commonly, osteogenesis imperfecta has an autosomal recessive pattern of inheritance. Autosomal recessive inheritance means two copies of the gene in each cell are altered. The parents of a child with an autosomal recessive disorder typically are not affected, but each carry one copy of the altered gene. Some cases of osteogenesis imperfecta type III are autosomal recessive; these cases usually result from mutations in genes other than *COL1A1* and *COL1A2*. When osteogenesis imperfecta is caused by mutations in the *CRTAP* or *P3H1* gene, the condition also has an autosomal recessive pattern of inheritance.

## Other Names for This Condition

- Brittle bone disease
- Fragilitas ossium
- OI
- Vrolik disease

## Diagnosis & Management

### Genetic Testing

- Genetic Testing Registry: Osteogenesis imperfecta  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0029434/>
- Genetic Testing Registry: Osteogenesis imperfecta type 5  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1970414/>
- Genetic Testing Registry: Osteogenesis imperfecta type 7  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1853162/>
- Genetic Testing Registry: Osteogenesis imperfecta type 8  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1970458/>
- Genetic Testing Registry: Osteogenesis imperfecta type 9  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1850169/>
- Genetic Testing Registry: Osteogenesis imperfecta type 10  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3151211/>
- Genetic Testing Registry: Osteogenesis imperfecta type 12  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3151433/>
- Genetic Testing Registry: Osteogenesis imperfecta type I  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0023931/>
- Genetic Testing Registry: Osteogenesis imperfecta type III  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268362/>
- Genetic Testing Registry: Osteogenesis imperfecta with normal sclerae, dominant form  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268363/>
- Genetic Testing Registry: Osteogenesis imperfecta, recessive perinatal lethal  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268360/>
- Genetic Testing Registry: Osteogenesis imperfecta, type XI  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3151218/>

### Other Diagnosis and Management Resources

- GeneReview: COL1A1/2-Related Osteogenesis Imperfecta  
<https://www.ncbi.nlm.nih.gov/books/NBK1295>
- MedlinePlus Encyclopedia: Osteogenesis Imperfecta  
<https://medlineplus.gov/ency/article/001573.htm>

### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

### **Additional Information & Resources**

#### MedlinePlus

- Encyclopedia: Osteogenesis Imperfecta  
<https://medlineplus.gov/ency/article/001573.htm>
- Health Topic: Osteogenesis Imperfecta  
<https://medlineplus.gov/osteogenesisimperfecta.html>

#### Genetic and Rare Diseases Information Center

- Dentinogenesis imperfecta  
<https://rarediseases.info.nih.gov/diseases/6258/dentinogenesis-imperfecta>
- Osteogenesis imperfecta  
<https://rarediseases.info.nih.gov/diseases/1017/osteogenesis-imperfecta>
- Osteogenesis imperfecta type VI  
<https://rarediseases.info.nih.gov/diseases/8700/osteogenesis-imperfecta-type-vi>

### Additional NIH Resources

- National Institute of Arthritis and Musculoskeletal and Skin Diseases: Osteogenesis Imperfecta Overview  
[https://www.niams.nih.gov/Health\\_Info/Bone/Osteogenesis\\_Imperfecta/](https://www.niams.nih.gov/Health_Info/Bone/Osteogenesis_Imperfecta/)
- National Institute of Arthritis and Musculoskeletal and Skin Diseases: Questions and Answers about Heritable Disorders of Connective Tissue  
[https://www.niams.nih.gov/Health\\_Info/Connective\\_Tissue/](https://www.niams.nih.gov/Health_Info/Connective_Tissue/)

### Educational Resources

- Boston Children's Hospital  
<http://www.childrenshospital.org/conditions-and-treatments/conditions/osteogenesis-imperfecta>
- Disease InfoSearch: Osteogenesis imperfecta  
<http://www.diseaseinfosearch.org/Osteogenesis+imperfecta/5451>
- Howard Hughes Medical Institute: Genetic Mutation Explains Form of Brittle Bone Disease (October 20, 2006)  
<http://www.hhmi.org/news/genetic-mutation-explains-form-brittle-bone-disease>
- Kennedy Krieger Institute  
<https://www.kennedykrieger.org/patient-care/diagnoses-disorders/osteogenesis-imperfecta-oi>
- Lucile Packard Children's Hospital at Stanford  
<http://www.stanfordchildrens.org/en/topic/default?id=osteogenesis-imperfecta-in-children-90-P02773>
- MalaCards: osteogenesis imperfecta  
[http://www.malacards.org/card/osteogenesis\\_imperfecta](http://www.malacards.org/card/osteogenesis_imperfecta)
- Merck Manual Consumer Version  
<http://www.merckmanuals.com/home/children-s-health-issues/hereditary-connective-tissue-disorders/osteogenesis-imperfecta>
- Orphanet: Osteogenesis imperfecta  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=666](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=666)

### Patient Support and Advocacy Resources

- Little People of America (LPA)  
<http://www.lpaonline.org/>
- Little People UK  
<http://littlepeopleuk.org/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/osteogenesis-imperfecta/>

- Osteogenesis Imperfecta Foundation  
<http://www.oif.org/site/PageServer?pagename=DescOI>
- Resource list from the University of Kansas Medical Center  
<http://www.kumc.edu/gec/support/osteogen.html>

#### GeneReviews

- COL1A1/2-Related Osteogenesis Imperfecta  
<https://www.ncbi.nlm.nih.gov/books/NBK1295>

#### ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22osteogenesis+imperfecta%22>

#### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Osteogenesis+Imperfecta%5BMAJR%5D%29+AND+%28osteogenesis+imperfecta%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

#### OMIM

- OSTEOGENESIS IMPERFECTA, TYPE I  
<http://omim.org/entry/166200>
- OSTEOGENESIS IMPERFECTA, TYPE II  
<http://omim.org/entry/166210>
- OSTEOGENESIS IMPERFECTA, TYPE III  
<http://omim.org/entry/259420>
- OSTEOGENESIS IMPERFECTA, TYPE IV  
<http://omim.org/entry/166220>
- OSTEOGENESIS IMPERFECTA, TYPE V  
<http://omim.org/entry/610967>
- OSTEOGENESIS IMPERFECTA, TYPE VII  
<http://omim.org/entry/610682>
- OSTEOGENESIS IMPERFECTA, TYPE VIII  
<http://omim.org/entry/610915>
- OSTEOGENESIS IMPERFECTA, TYPE XI  
<http://omim.org/entry/610968>

## Sources for This Summary

- Byers PH. Osteogenesis imperfecta: perspectives and opportunities. *Curr Opin Pediatr*. 2000 Dec; 12(6):603-9. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/11106283>
- Cabral WA, Chang W, Barnes AM, Weis M, Scott MA, Leikin S, Makareeva E, Kuznetsova NV, Rosenbaum KN, Tiffit CJ, Bulas DI, Kozma C, Smith PA, Eyre DR, Marini JC. Prolyl 3-hydroxylase 1 deficiency causes a recessive metabolic bone disorder resembling lethal/severe osteogenesis imperfecta. *Nat Genet*. 2007 Mar;39(3):359-65. Epub 2007 Feb 4. Erratum in: *Nat Genet*. 2008 Jul; 40(7):927.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17277775>
- Cole WG. Advances in osteogenesis imperfecta. *Clin Orthop Relat Res*. 2002 Aug;(401):6-16. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12151877>
- GeneReview: COL1A1/2-Related Osteogenesis Imperfecta  
<https://www.ncbi.nlm.nih.gov/books/NBK1295>
- Morello R, Bertin TK, Chen Y, Hicks J, Tonachini L, Monticone M, Castagnola P, Rauch F, Glorieux FH, Vranka J, Bächinger HP, Pace JM, Schwarze U, Byers PH, Weis M, Fernandes RJ, Eyre DR, Yao Z, Boyce BF, Lee B. CRTAP is required for prolyl 3- hydroxylation and mutations cause recessive osteogenesis imperfecta. *Cell*. 2006 Oct 20;127(2):291-304.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17055431>
- Rauch F, Glorieux FH. Osteogenesis imperfecta. *Lancet*. 2004 Apr 24;363(9418):1377-85. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/15110498>
- Roughley PJ, Rauch F, Glorieux FH. Osteogenesis imperfecta--clinical and molecular diversity. *Eur Cell Mater*. 2003 Jun 30;5:41-7; discussion 47. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/14562271>
- Venturi G, Tedeschi E, Mottes M, Valli M, Camilot M, Viglio S, Antoniazzi F, Tatò L. Osteogenesis imperfecta: clinical, biochemical and molecular findings. *Clin Genet*. 2006 Aug;70(2):131-9. Erratum in: *Clin Genet*. 2006 Nov;70(5):455.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16879195>

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