

Introduction to
Osteogenesis
Imperfecta:

A Guide for
Medical
Professionals,
Individuals
and Families
Affected by OI

OSTEOGENESIS
IMPERFECTA

OI

FOUNDATION

Introduction to Osteogenesis Imperfecta

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Imperfecta** was reviewed by:

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A **newborn** lets out a sharp cry while he is being cleaned and weighed. He screams when he is picked up or when someone touches his leg. An x-ray reveals a fractured femur, as well as several healed rib fractures.



Parents bring their **one-year-old daughter** to the emergency room. She was pulling to a stand, when suddenly the parents heard a “pop” and the little girl fell to the floor, crying with the pain of a broken leg. This is the toddler’s third fracture since birth.



A **teenager** checks into the hospital for the second time this year. A few months ago, he had a new metal rod put into his tibia. This time, he will undergo risky surgery on his spine. Doctors hope that the surgery will halt his progressively worsening scoliosis.



At her annual check-up, a **45-year-old woman** asks her physician for a referral to a good orthopedist. The woman had several dozen bone fractures in her childhood and teen years. Although she has been fracture-free as an adult, she is concerned that menopause will weaken her already fragile bones, leading to another cycle of fractures.

The **newborn**, the **toddler**, the **teenager**, and the middle-aged **woman** all have **osteogenesis imperfecta**, or “brittle bone disorder.” Osteogenesis imperfecta (OI) is a genetic disorder that causes fragile bones and other connective tissue symptoms.

This brochure provides the latest information on osteogenesis imperfecta for health care providers and people affected by OI.

Myths and Facts about Osteogenesis Imperfecta

Due to the work of many dedicated scientists and physicians, a great deal has been learned about osteogenesis imperfecta in the last 10 years. **Today, most of the babies born with OI have a good chance of leading independent, successful, and satisfying lives.** Traditional treatments are being perfected, and new treatments for strengthening OI bone are on the horizon. Because OI is a rare disorder, the first time parents hear the words “osteogenesis imperfecta” may be when their child is diagnosed. Likewise, it is not unusual for community based health care providers to have little or no experience with OI.

Myth: A baby with osteogenesis imperfecta should always be carried on a pillow and discouraged from moving.

Fact: Although there are handling techniques and precautions that are useful when caring for an infant with OI, it is in the child’s best interest to be held and touched, and encouraged to explore independent movement to the greatest extent possible. Immobility increases bone loss and fragility, leading to more fractures.

Myth: You can easily distinguish fractures caused by osteogenesis imperfecta from those caused by child abuse.

Fact: Children with osteogenesis imperfecta can have all types of fractures including but not limited to spiral, rib, incomplete and displaced. Distinguishing OI from child abuse requires a thorough assessment by a medical professional who is familiar with the full range of OI characteristics.

Myth: OI affects only the bones.

Fact: Although fragile bones are the hallmark of OI, many parts of the body are affected by OI. Skeletal features include fragile bones, bone deformity, and short stature. Non-skeletal symptoms affect the heart, skin, blood vessels, muscles, tendons,

internal organs and eyes. In addition, breathing problems, hearing loss, loose joints, excessive perspiration and brittle teeth are common.

Myth: OI is a childhood disorder; people grow out of it by their teens.

Fact: OI is a genetic disorder that is present throughout a person's lifetime. Many people with OI have fewer fractures after puberty when growth stops, but the genetic difference remains. Fractures and other complications occur throughout the lifespan; especially after menopause in women and after age 60 in men. Non-skeletal problems can be serious.

Myth: Everyone who has OI is shorter than average, has blue sclera (whites of the eyes), and uses a wheelchair.

Fact: The appearance of people with OI varies considerably. Although many people with OI are short-statured, people with milder forms may be of near-average height and have no obvious symptoms of OI. About 50 percent of people with OI have tinted sclera that can range in color from nearly white to dark blue or gray. People with OI also have variable mobility, ranging from independent walking to full-time wheelchair use.

Myth: Everyone who has OI is diagnosed at birth.

Fact: Although present from conception, OI can be diagnosed at many different ages from birth into adulthood. The most severe forms are usually diagnosed at birth or shortly after. Other forms may not be diagnosed until the child has a series of broken bones. OI Type I, the most common and mildest form of OI, is rarely diagnosed at birth.

What is Osteogenesis Imperfecta?

OI is a complicated and variable disorder. Its major feature is a fragile skeleton, but many other body systems are also affected. An early definition of OI was bones that break easily plus hearing loss. **OI is caused by a mutation (change) in a gene that affects bone formation, bone strength and the structure of other tissues.** OI occurs equally among males and females and it occurs in all racial and ethnic groups. It is estimated that approximately 25,000 to 50,000 people in the U.S. have OI.

People with OI experience broken bones from infancy through puberty. The frequency typically decreases in the young adult years but may increase again later in life. Respiratory problems including asthma are often seen. Short stature, rib cage deformities and spine curves make breathing problems more severe. **Other medical characteristics and issues include:**

- Bone deformity, and bone pain.
- Short stature.
- Spine curves.
- Hearing loss is present in more than 50% of people with OI.
- Brittle teeth (dentinogenesis imperfecta or DI) are seen in 50% of people who have OI.
- Vision problems including myopia and risk for retinal detachment.
- Loose joints, ligament laxity, and muscle weakness are common.
- Cardiac issues.
- Basilar Invagination, a serious neurological problem, is seen in some people with the more severe forms of OI.

OI exhibits wide variation in appearance and severity. Severity is described as mild, moderate, or severe. The most severe forms lead to early death. Clinical features (observable signs) vary widely not only

between types, but within types, and even within the same family. Some features are age dependent. Children with milder OI, in particular, may have few obvious clinical features. Since the 1970's a list of numbered types has been used to describe the different forms of OI. **For a detailed list of OI Types including clinical signs, degree of severity and mutation please see the OI Foundation website.**

Below are some of the distinguishing features of the major types of OI.

Type I (Mild)

- Most common and mildest type of OI; few obvious symptoms.
- Normal or near-normal height. Stature may be average or slightly shorter than average when compared with unaffected family members, but within the normal range for age.

Type II (Most Severe)

- Infants may die within weeks from respiratory or heart complications.
- Numerous fractures and severe bone deformity are evident at birth.
- Small stature with underdeveloped lungs, and low birth weight.

Type III (Severe)

- Progressive bone deformity is often seen.
- Fractures are present at birth, and x-rays may reveal healed fractures that occurred before birth.
- Short stature.
- Barrel-shaped rib cage.
- Spinal curvature and compression fractures of vertebrae.

Type IV (Moderate)

- Between Type I and Type III in severity and height.
- Mild to moderate bone deformity.
- Spinal curvature and compression fracture of vertebrae.
- Barrel-shaped rib cage.

Type V (Moderate)

- Similar to Type IV in appearance and symptoms of OI.
- Large hypertrophic calluses form at fracture or surgical procedure sites.
- Calcification of the membrane between the radius and ulna restricts forearm rotation. Mutation is not in the collagen pathway; dominant inheritance.

Type VI (Moderate)

- Extremely rare; similar to Type IV in appearance.
- Distinguished by a characteristic mineralization defect seen in biopsied bone. Mutation is not in the collagen pathway; recessive inheritance.

Type VII (Severe)

- Recessive inheritance.

Type VIII (Very Severe)

- Similar to Type II but with recessive inheritance.
- Severe growth deficiency and under mineralization of the skeleton.

How Is OI Inherited?

Osteogenesis imperfecta (OI) is a genetic disorder. Most cases (90 percent) involve a change in type 1 collagen—the protein “scaffolding” of bone and other connective tissues. A faulty gene reduces either the amount or the quality of type 1 collagen throughout the body. These mutations are inherited in a dominant manner. **The other 10 percent of cases are caused by mutations in other genes that are inherited in either a dominant or a recessive manner.**

Children inherit two copies of each gene – one from each parent. When OI is caused by a dominant mutation only one copy of the OI gene mutation is necessary for the child to have OI. **In the majority of cases, the gene is either inherited from a parent who has OI or results from a spontaneous new mutation**

occurring at the time of conception. In rare cases dominant OI can occur when a parent is mosaic for an OI mutation. This means that an OI causing mutation is present in a percentage of one parent's cells, but does not cause any symptoms in the parent. For a child to inherit OI in a recessive manner, the gene mutation must come from both parents. In this situation, the parents do not have OI, but both carry the mutation in their genes.

When a child with OI is born into a previously unaffected family the chance of having another child with OI varies depending on whether the cause is a dominant or recessive mutation. Parents in this situation are urged to consult with a geneticist (a physician who has special training in genetics). Genetic testing can confirm whether OI was inherited in a dominant or recessive manner and the risks for mosaicism can be discussed.

A person who has dominant OI has a 50 percent chance of passing on the disorder to each of his or her children. An affected child will have the same mutation, and therefore the same type of OI, as the parent. However, the expression—the degree of severity, or number of fractures—may be different among family members. Unaffected siblings of a child with dominant OI have no greater risk of having children with OI than anyone in the general population. Unaffected siblings of a child with recessive OI have a 67 percent chance of being a carrier for the recessive gene. Genetic testing is available for siblings.

How is OI Diagnosed?

Broken bones that occur from little or no trauma are often the first indication that an infant or child may have OI. Babies with moderate or severe forms of OI are often born with broken bones. Children with milder OI (Type I) often sustain their first broken bone as a result of normal activity—during a diaper change, while being lifted

or burped, or when they begin standing and walking. Some very mild cases of OI Type I are not diagnosed until the teen or adult years.

OI remains primarily a clinical diagnosis. A physician, usually a geneticist, who is familiar with all types of OI, can often diagnose the condition based on the presence of fractures and other clinical features. A family history for the disorder can help confirm a diagnosis, although spontaneous or recessive mutations do occur in previously unaffected families.

There are three types of laboratory tests available to help confirm a diagnosis of OI. Dominant forms of OI (the types of OI caused by a dominant mutation to type I collagen genes) can be tested for via DNA-based testing using blood or saliva or protein-based testing (collagen screening) using cultured skin cells. Genetic testing is also available when a recessive form of OI is suspected. Because all genetic causes for OI have not yet been identified, a negative collagen or DNA test does not exclude an OI diagnosis. Additional blood and urine tests are often used to rule out other disorders such as Hypophosphatasia or rickets.

The more severe forms of OI can be diagnosed prenatally. Ultrasound can detect bowing, fractures, shortening or other bone abnormalities. But even when ultrasound is done by a highly qualified professional, it may not be possible to pinpoint the type of OI or differentiate between Type II or Type III. Cells obtained through amniocentesis can be used for DNA analysis. In familial OI, the affected parent's mutation must be known before chorionic villus sampling (CVS) is performed.

How is OI Treated?

There is no cure for OI, but there are ways to manage the symptoms. Despite the obstacles, many people who have OI lead productive and fulfilling lives well into their adult years. **The goal of all treatment is to minimize fractures, enhance independent function, and promote general health.** Treatment may include fracture care, physical therapy, surgical procedures, medications and mobility aides.

Fracture Care. Casting, splinting and bracing broken bones can help them heal properly. **However long periods of immobility can further weaken bones and lead to muscle loss, weakness, and more fractures.** Many orthopedists prefer to treat fractures with short term immobilization in lightweight casts, splints, or braces to allow some movement as soon as possible after the fracture.

Physical Therapy and Safe Exercise. Goals for physical therapy include expanding and maintaining function and promoting independence. A typical program includes muscle strengthening and aerobic conditioning. Physical therapy often begins in infancy to counteract the delay in motor skill development many children experience due to OI related muscle weakness. Adaptive devices may be needed. **Occupational therapy can help with fine motor skills and selection of adaptive equipment for daily living.** As a child with OI grows older and gains more independence, he or she will benefit from continued physical activity, such as adapted physical education. Adults with OI also benefit from safe, regular exercise to maintain bone and muscle mass. Swimming and water therapy are particularly well-suited for people with OI of all ages, as it allows independent movement with little fracture risk. Walking is also excellent exercise for those who are able (with or without mobility aids).

Surgery. Surgery may be needed to repair a broken bone, correct bone deformities such as bowing, stabilize the spine or repair tiny bones in the middle ear. Many children with OI undergo a surgical procedure known as rodding, in which metal rods are inserted into the long bones to control fractures and improve deformities that interfere with function. Both non-expandable and expandable rods are available.

Medications. Bisphosphonate drugs, which are currently approved by the Food and Drug Administration (FDA) to prevent and treat osteoporosis and bone complications of cancer are used off label to increase bone density in children and adults with moderate and severe OI. **These drugs do not build new bone, or improve the quality of bone, but they slow the loss of existing bone.** They have been shown to reduce fractures in children and in some people to relieve bone pain. Other treatments under study include teriparatide (a drug based on the parathyroid hormone), growth hormone, and gene therapies.

Healthy Lifestyle. People with OI benefit from a healthy lifestyle that includes safe exercise and a nutritious diet. Adequate intake of nutrients, such as Vitamin D and calcium is necessary to maintain bone health, however, extra-large doses of these nutrients are not recommended.

Maintaining a healthy weight is important since extra weight adds stress to the skeleton, heart and lungs and reduces the ability to move easily. In addition, people with OI should avoid smoking, second hand smoke, excessive alcohol or caffeine consumption and steroid medications, all of which reduce bone density.

Other treatments that focus on OI related symptoms include:

- Hearing aids
- Crowns for brittle teeth

- Supplemental oxygen for people with breathing problems
- Mobility aids such as walkers, crutches, canes and wheelchairs

Are There Precautions to Take When Caring for People with OI?

- Never pull or push a limb, or bend it into an awkward position not even to take an x-ray.
- Use caution when inserting IVs, taking blood pressure, or performing other medical procedures to avoid causing injury. Avoid use of automatic blood pressure cuffs.
- Always dose medicines to the size, NOT the age of short statured adults.
- When a fracture is suspected, minimize handling of the affected limb.
- Respect the opinions, advice, or instructions provided by parents, children, and adults with OI. Based on experience they give good directions for the safest ways to lift, carry or reposition. Having dealt with dozens of fractures and medical procedures, even children have a good sense of when a bone is broken even before x-rays are taken.

Handle babies with extra care.

- Lift a baby with OI by placing one hand under the buttocks and legs, and the other hand under the shoulders, neck and head.
- Do not lift the baby from under the armpits.
- Do not lift by the ankles to change a diaper; rather slide a hand under the buttocks.
- Babies do not need to be kept on a pillow or soft surface. Encourage babies to explore independent movement.
- Supporting infants in a variety of positions (e.g., side lying, stomach lying) develops muscles that will help with sitting and standing later on.

For more Information:
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