Introduction
Osteogenesis imperfecta (OI) is a genetic disorder characterized by bones that break easily. OI is highly variable. Its signs and symptoms range from mild to severe. In addition to fractures, people with OI sometimes have muscle weakness, joint laxity, scoliosis, Dentinogenesis Imperfecta (DI) and hearing loss. A classification system dividing OI into several types is commonly used to help describe how severely a person is affected. Type I osteogenesis imperfecta is the mildest form of OI. It is also the most common form of OI. It is believed that 50-60 percent of people with OI have Type I OI. Type I OI can have the characteristics of an “invisible disorder.” Often it is not apparent to the casual observer.

What is Type I OI?
Nearly all cases of OI, mild or severe, are caused by a dominant genetic mutation that affects the body’s production of type 1 collagen. While there are several types of collagen in the body, only type 1 collagen has been associated with OI. Type 1 collagen is the main protein building block in bone, and is important in other connective tissues such as tendons and ligaments. When there is a problem with the body’s production of type 1 collagen, the bones are brittle and break more easily than normal. Type I OI is different from all other types of OI in an important way. A person with Type I OI has generally normal type 1 collagen but approximately half the normal amount. A person with Type II, Type III, or Type IV OI (the moderate to severe types of OI) has low levels of abnormal type 1 collagen.

Signs and Symptoms of Type I OI
OI affects people in several ways and this may vary from person to person. Even among people with Type I OI in the same family, there may be differences. The following is a list of signs and symptoms common among people with Type I OI. Many people with Type I OI have only some—not all—of these signs and symptoms:

• Bones predisposed to fracture. Most fractures occur before puberty and again in later years.
• Somewhat predisposed to other connective tissue injuries, such as dislocations.
• Skin may bruise easily.
• Height is variable and generally is below average for age. Adult height may be similar or slightly shorter when compared with unaffected family members.
• Loose joints, some muscle weakness, and lax ligaments.
• Spinal curvature (scoliosis) is frequently seen, but tends to be mild.
• Sclera (whites of the eyes) usually have a distinctly blue, or gray tint.
• Somewhat triangular face shape.
• Bone deformity absent or minimal and occurs after fractures have occurred.
• Brittle teeth (DI) possible.
• Hearing loss possible, often beginning during teen or young adult life, but may occur sooner.

Some people with Type I OI are very mildly affected. They may have only a few fractures. They are average or even above-average height, are able to walk and run, and have barely noticeable signs of OI, such as blue sclera or loose joints. In fact, some people are so mildly affected that they are not diagnosed until their teen or adult years and in some cases only after they have a child diagnosed with Type I OI. Other people with Type I OI have more distinct symptoms. They may have several dozen or more fractures; sometimes use a wheelchair, walker, braces, or crutches for mobility; be somewhat smaller than the rest of their family; and/or require treatments such as rodding surgery (see below).

In most cases, people with Type I OI seem to experience fewer fractures after puberty, when the bones are no longer growing as quickly. Even so, the genetic defect still exists, and adults with Type I OI need to be aware of
how the disorder may affect them throughout their life. This is especially important for women when they go through menopause and men over age 50. Bone density will be lower throughout life than in healthy peers.

Diagnosis
Babies with Type I OI may or may not be born with fractures. A baby may have other outward signs of OI, such as blue sclera or loose joints, but these signs may go unnoticed in a family with no history or knowledge of OI. Furthermore, blue sclera can be seen even in healthy infants until about 18 months of age. A child with Type I OI may sustain his or her first fracture during some ordinary activity, such as when a caregiver pulls on the ankles while changing a diaper, a doctor does a physical exam, or a toddler falls while learning to walk. Other children with OI may not experience fractures until the school years, when they begin participating in physical education, sports, and recreational activities.

The occurrence of a fracture after little or no injury is often the first clue that a child may have OI. To diagnose the disorder, a physician can look for other clinical features of OI including standard x-rays which may show evidence of “thin bones”, and obtain a family history to determine if other family members have a history of fractures or other OI symptoms. Diagnosis for OI is based primarily on clinical signs. Collagen testing of a skin biopsy sample and/or DNA testing of a blood sample can help confirm a diagnosis of OI in most situations. Some individuals test negative for OI despite having the disorder. It should be noted that some especially rare forms of OI do not have a collagen defect. A negative OI test does not necessarily rule out an OI diagnosis.

Families in which one parent has OI may be able to arrange for prenatal testing through chorionic villus sampling or amniocentesis. In most cases of Type I OI, this type of prenatal diagnosis requires knowledge of the affected parent’s genetic mutation. Ultrasound may not detect Type I OI in a fetus, because the child is unlikely to have fractures or bone deformity before birth. When prenatal diagnosis is not possible, or not desired, a sample of blood from the child’s umbilical cord can be taken at birth and sent for DNA analysis. When a parent has OI, it is recommended that the newborn be tested and examined by a knowledgeable clinician as soon as possible. The information will help parents make decisions about their baby’s care, and help protect the family from unwarranted child abuse allegations.

Managing and Treating Type I OI in Children
The cornerstones of treatment for a child with Type I OI are fracture management, healthy diet, therapy to regain strength and mobility after fractures or surgery, and an ongoing program of safe exercise and activity to develop muscle control and build strength. Recognizing that prolonged immobilization can weaken muscles and bones, many orthopedists prefer short-term casting of fractures, followed as soon as possible by a splint or brace that can be removed for appropriate exercise. Physical therapy for all children after a fracture, including water exercise, will reduce the effects of immobilization. This is recommended for even the mildest children. Inactivity and inappropriate diet should not be permitted to cause obesity, because excess weight adds stress on the bones and tends to further limit activity. Developing healthy life-style habits is an important part of managing OI.

Roddling surgery (in which metal rods are inserted into the long bones) is a standard treatment for children with OI in two situations: 1) to set a particularly bad fracture, or 2) to straighten and strengthen a bone that is bowed (curved) to the extent that it is breaking repeatedly. Many children with Type I OI have minimal bone deformity, and do not require roddling surgery unless they have a particularly bad fracture. Some children with Type I OI, however, do have problems with repeated fractures and increasing deformity of a long bone and in such cases roddling surgery may be appropriate.

Some infants with mild OI have delays in gross motor skills, such as pulling to a stand, crawling, or walking. These delays may be due to fractures, low muscle strength, loose joints, and/or a child’s fear of movement due to previous fractures. Physical and occupational therapy are recommended as soon as such delays are noticed. Therapists can instruct parents in the best ways to hold, position, and encourage their child to learn new skills. Most infants with OI will qualify for their state’s Early Intervention Program, which provides therapy and other services free of charge.

Older children with Type I OI will also benefit from physical and occupational therapy to maximize strength and function. Outside of therapy, regular exercise geared toward the child’s interests helps children socialize with peers, develop bone and muscle strength and maintain a healthy weight. Water therapy and swimming are particularly good exercises for children with OI, as the gravity-free environment reduces fracture risk.
Children with Type I OI may demonstrate feeding problems including difficulty chewing and swallowing foods of different textures. Adults may experience gastric reflux. Nutrition counseling can help resolve both types of problems as well as design a diet that is rich in nutrients but will not cause obesity.

The bisphosphonate medications (such as pamidronate, risedronate, alendronate and zoledronic acid) are currently being studied in clinical trials as a treatment for OI. Most clinical trials initially accepted only severely affected children. Over the years some trials have since expanded to include children who are moderately and mildly affected and who have 3 or more major fractures in a year. To date, there is not enough evidence that bisphosphonates are helpful for children with mild OI to recommend this treatment for all children. However, the individual child’s bone density and fracture history may warrant treatment with bisphosphonates. Physicians must use their clinical judgment before prescribing bisphosphonates “off label” for OI. Research into this question continues.

Managing and Treating Type I OI in Adults

Osteoporosis (low bone density) is an almost universal consequence of having OI. It is therefore vital for teens and adults with OI (both male and female) to build bone density and prevent bone loss through safe exercise, diet, and in some cases, medication. It is recommended that adults with OI have a bone density test to establish a baseline, which will allow their physician to monitor whether their bone density is changing over time. Commitment to a healthy life-style and maintaining a healthy weight are key parts of managing OI as an adult.

In addition to its importance for bone density, exercise is also important for maintaining strength, function, and general health. Swimming and water exercise provide excellent, safe exercise for people with OI. Walking (with or without aids), safe weight training, and non-contact recreational sports can also be appropriate for some people with Type I OI. It continues to be important to protect the spine and joints. Learning to stand correctly, lift objects safely and avoid twisting motions will reduce the chance of injury. Adults with OI are encouraged to consult their orthopedist, physical therapist, or other professionals knowledgeable about OI to determine the most appropriate fitness program.

Bone density can also be maintained by eating appropriate but not excessive amounts of calcium-rich food. Dairy products are the richest source of calcium, but some vegetables, some nuts, tofu, and calcium-fortified products such as orange juice and cereal are also sources. Adults with OI have the same needs for calcium as other adults; excessive consumption of calcium or use of supplements is neither necessary nor recommended, as it can lead to other health problems. Caffeine and alcohol should be consumed in moderation, as excessive intake can lead to bone loss if adequate calcium is not present. Some medications, such as steroids (for example, prednisone) and corticosteroids, also contribute significantly to bone loss. The Surgeon General’s 2004 Report on Bone Health and Osteoporosis states that smoking and exposure to second hand smoke not only causes respiratory problems, but also bone loss.

Many adults with OI take bisphosphonate medications (such as alendronate, risedronate or in some instances intravenous pamidronate). These medications are FDA-approved for preventing and treating osteoporosis in adults. The goal is to prevent additional loss of bone density. Several researchers are conducting clinical trials of bisphosphonates specifically for treating adults with OI. Other drugs, such as the parathyroid hormone-like protein in Forteo® are also being studied as treatments for adults with OI.
Many women with Type I OI are concerned about menopause and the possibility of more frequent fractures. The experience of postmenopausal women with OI varies greatly; some experience an increase in fractures, while others do not. The strategies mentioned above to maintain bone density and general health will help each woman maximize her chances to stay active and healthy as she ages. It is important to continue exercising throughout life. Bone density measurements and medicines or hormones to prevent bone loss should be discussed with the physician.

Adults with Type I OI seem to have the same risks as the general population for common health problems such as diabetes, heart disease, and cancer. Maintaining a healthy weight, exercising regularly, eating a nutritious diet, and avoiding risky behaviors such as smoking and excessive alcohol consumption are vital not only for bone health, but also for general health and well-being. In addition those with short stature, scoliosis or barrel shaped chests are advised to pay particular attention to respiratory health by having their pulmonary function tested. This test should be repeated about every 2-3 years depending on the extent of scoliosis or chest deformity. All people with OI are urged to promptly seek treatment for all respiratory infections. Flu shots and pneumonia vaccines are often recommended.

Social, Emotional and Family Issues

Many people with OI Type I do not appear disabled, so there is potential for others to misunderstand or underestimate the disorder. Parents may provide information about preventing fractures to teachers, babysitters, or other caregivers, only to have the caregivers dismiss them as being “overprotective.” Meeting with teachers and other school staff and providing written information—such as materials from the OI Foundation and a letter from the child’s doctor briefly explaining the OI diagnosis and the recommended precautions—can help reinforce the information provided by parents. It is important to set up a system to ensure that substitute teachers are aware that a child with Type I OI is in the class.

Likewise, it is important for a child’s siblings and peers to receive age-appropriate information about OI. It is common for peers to wonder why their classmate does adapted activities during physical education, or can’t participate in contact sports. Some children with mild OI are accused of being “clumsy,” “lazy,” or “faking it” when they have yet another injury. In most cases, such teasing comes out of ignorance, not malice. Many children with OI or their parents give a brief presentation to the class at the beginning of each school year to explain OI. Visual aids and props (such as the child’s braces, or a cast or splint) are particularly well-received by young children. Materials about OI for school personnel are also available from the OI Foundation.

Some families with mildly affected children have been accused of child abuse when their child goes to the emergency room with unexplained fractures. Once an OI diagnosis is made, families should ask for a letter on medical letterhead confirming the diagnosis, and explaining what it means. Copies of the letter should be kept in the diaper bag, the car, with the child’s medical and school records, and anywhere else it might be useful, particularly when the family is traveling or visiting the emergency room.

Adults with Type I OI will typically know about their diagnosis when deciding whether to have children. There is a 50 percent chance that a person with Type I OI will pass the disorder on to their child. The risk remains the same for each child. A child will usually inherit the same type of OI as his or her parent; however, it is possible that the child’s signs and symptoms will be different than the parent’s – either milder or in some cases more severe. Adults with Type I OI who are considering having children may wish to consult a genetic counselor to obtain information about their options including preimplantation genetic diagnosis (PGD). It is worthwhile to obtain a skin biopsy or DNA analysis to confirm their own OI diagnosis, before conceiving a child. Having this information on file expedites testing a newborn for OI, if the parents desire. Type I OI does not appear to affect fertility or predispose women to particular pregnancy complications. Research suggests that pregnancy and breastfeeding may affect a woman’s bone density, and may increase the risk of fracture. It is therefore particularly important that women with OI eat a calcium-rich diet and exercise appropriately while pregnant and breastfeeding.

People with Type I OI often have to deal with the conflict between their outwardly normal appearance and their underlying fragility. Deciding who to tell about their condition in social or employment situations can be difficult. Concern about strength, stamina and changes as a person ages can also affect decisions about family life, housing and careers. Adults with Type I OI recommend developing an effective personal support network.