
osteogenesis imperfecta

Caring for children and adolescents

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Preface (Second Edition)

This second edition of the Osteogenesis Imperfecta - Handbook on Care for Children and Young People with OI is provided free as an internet book. Its publication is supported by OI Australia Inc and ConnecteD Inc. The aims are to support families and parents of young people with OI, provide updated information and stimulate research into the various facets of Osteogenesis Imperfecta. We wrote the book to help parents with the day to day care of their child with (OI), and to minimise disability in adult life. Living with a “fragile” infant or child can be a frightening experience at first.

It is very reassuring to know that there are thousands of adults with OI in the world who are living very normal lives. There are rapid advances in treatment which reduce fracture frequency and improve walking and opportunities for sport. A multidisciplinary program for young people with OI was started in Sydney at the Camperdown Children’s Hospital in 1987. While there are many types of OI, multidisciplinary management, including use of the new bisphosphonate therapies, has dramatically changed the lives of young people with OI. At this time, Cyclic Intravenous Pamidronate is still the “Gold Standard” bisphosphonate regimen for treating children with OI.

This volume is dedicated to the many children and adults with OI around the world, whose courage and ingenuity have triumphed over the challenges from their particular type of OI.

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How fragile is my child with Osteogenesis Imperfecta (OI)?

Finding out that your child or new baby has OI is alarming and confusing. 'Fragile' bones as seen in OI result in a tendency to fracture. A fracture is a broken or cracked bone. This tendency is usually mild but occasionally may be very severe. It is not always possible to tell at birth or at first diagnosis how severe it may be.

The number of fractures at birth is not always a helpful indicator. The absence of fractures before 1 year of age is similarly not always predictive. Doctors are helped by X-rays of the skeleton in determining the potential strength of bones and in assessing bone density. More accurate assessment can be made by performing total and regional bone density using Dual Energy X-ray Absorbtiometry (DEXA). This is usually performed by centres with special expertise in measuring bone density in children.

Fractures result from the combination of the inherent fragility of bone and the additional fragility which results from osteoporosis. The other factors are external forces such as trauma. In general, the frequency of fractures per year of life increases in the 2nd to 4th years (when the child becomes mobile) and then decreases between 5 – 12 years of age. Fractures are much less common during adolescence and, barring major trauma, in adult life. Each child needs to be assessed individually. The tendency to fracture varies from one type of OI to another, within each group and within each family.

In some babies with OI, the skull may be poorly formed, so the top of the head feels soft and unprotected but this becomes normal with time. Sometimes the infant is born with, or rapidly develops, deformity of the legs, arms or spine but this deformity can be prevented or reduced by current treatments. Some children with OI never have a fracture. However their gross motor development may be delayed, they may have a large head or may be just short for their age. Some children without fractures may be identified simply because of a family history of OI.

Whatever the case, certain decisions will have to be made. You will learn as parents to protect your child against fracturing. You will also have to accept that no matter how careful you are, fractures will occur and that no-one is to 'blame' when this happens, although people normally feel very sorry, guilty, or even angry.

How will I know when my child has had a fracture?

Fractures in unaffected children are usually of the 'greenstick' type where the bone is bent or broken but not snapped totally through. Greenstick fractures can occur without any deformity of the bone in question. In later life, when fractures occur, the bone usually snaps right through producing obvious deformity in the limb until set back into place by a doctor. In infants and young children with OI the majority of fractures are greenstick.

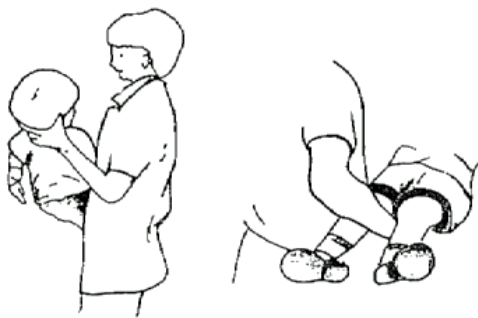
In the baby and infant in the first year, the signs and symptoms of fracture include pain, swelling and/or refusal to use a limb. Fractures may occur quite suddenly. They may occur spontaneously or they may occur associated with slight trauma (e.g. when the child is being dressed). Sometimes, you may have heard the bone snap. As the baby or infant cannot tell you exactly where it is sore and painful, you will have to look quite carefully with the child undressed for the signs. Start with the fingers or toes of the limb least likely to be affected.

In infants and toddlers, there is often a clear association with trauma. The infant will cry, be unwilling to walk or to use the limb in question and there may be deformity if there has been bending of the bone or a clean break and swelling. The crying of a baby in pain can usually be distinguished from the crying for food or whimpering for attention.

The school age child will tell you that he or she has pain and point to a particular site. Swelling and tenderness may be caused by either fractures or sprains. Sprains also occur easily in children with OI.

What can I do to prevent fractures?

Special attention should be given to lifting and carrying the child with OI. With an infant, the head, body and limbs should be well supported. With an older infant and toddler, lifting with support under the buttocks avoids stressing wrists and elbows. Lifting an infant or a toddler by the wrists may lead to fractures or sprains in the forearm or elbows.



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Sometimes fractures will occur spontaneously. There is little that can be done to prevent these. However fractures can occur when the child becomes twisted or tangled up in bedclothes or toys. Think ahead and prevent accidents, especially when away from the home 'toddler proofed' environment.

It is important that you and any other adult who looks after the child understand the first aid treatment and management of fractures. The immediate care should be to comfort the child, put the child to rest, identify the site of the fracture and splint the fracture. Once a broken bone is splinted and the child is comforted and at rest, it is often not necessary to give the child pain relieving medicine.

Pain perception is a complicated response which is enhanced by fear and anxiety. If the child learns early that relief from the pain of the fracture is provided by splinting and that firm and caring comfort is available from parents and health professionals, then a lifelong positive attitude will develop. Children sense panic, anger or parental fear.

Comprehensive care for OI

At various ages there are health checks which are important in monitoring growth, preventing disability and planning the next phase of care between parent, child and health professionals.

At present the class of medicines called bisphosphonates have been shown to be successful in medical treatment. Bisphosphonates strengthen bone, increase a sense of well-being, reduce pain and may reduce fractures. (See Medical Management)

Heredity and OI

What causes OI?

All forms of OI are able to be inherited (genetic). Each person has approximately 30,000 pairs of genes (units of inheritance). One gene of each pair comes from each parent. The causes of OI are all defects in the genes which lead to either deficiency or weakness of the supporting framework of bone. This supporting substance known as 'connective tissue' is mostly made up of type I collagen, a protein with high tensile strength. The collagen of bone is impregnated with calcium and phosphate, which is responsible for the rigidity of bone.

There are several types of OI, with various inheritance patterns. Some are dominant (if you have one copy of the gene, you show the trait) and some are recessive (you need two copies of the gene – one from each parent – to show the trait). The inheritance of these characteristics follows certain laws.

In many instances there is no family history of bone fragility, although most individuals with OI have some other members of their family with OI.

Dominant inheritance

A dominantly inherited characteristic is one for which the gene concerned dominates in its effect over that of the other gene of a pair. Where one parent carries a dominant characteristic, the characteristic will be handed down on average to half of the children. Within any one family there is a considerable variability in the effect of a disordered gene, and this variability is called expressivity.

Dominantly inherited varieties of OI

The commonest varieties of OI are inherited in an autosomal (not related to the sex of the person) dominant manner (AD). Both men and women are affected and may transmit OI to their children of either sex on average 50% of the time.

The fracture rate in the dominant forms of OI slows down at or following puberty but bone fragility persists. Fractures can recur and are more likely to commence again in the 4th – 5th decade. Some single (sporadic) cases of OI are caused by a newly occurring, autosomal dominant mutation.

Autosomal recessive (AR) inheritance

A recessive disorder is one which results when both genes of a pair are required to produce the disorder. This means that parents or other individuals carrying a single gene whose effect is recessive, do not express that effect in the presence of the other normally paired gene. It can be shown that, on average, a quarter of the children of two carrier parents will manifest the disorder, and three quarters will not. Of the normal children, two out of three, on average, will be carriers like their parents. At present there is no way of detecting carriers of recessive forms of OI.

It is only possible to tell if a family's OI is due to recessive inheritance when two normal parents have more than one affected child, or where the normal parents have an affected child and are blood relatives e.g. cousins.

Recessively inherited types of OI

Recessively inherited forms of OI are extremely rare in European populations. OI type III is the commonest type of OI in the Black populations of Southern Africa, and in the Middle East and South Asia. Recessively inherited types are often more severe than dominantly inherited types. The Bruck type, also known as OI with Congenital Joint Contractures, is inherited in an autosomal recessive fashion. It is possible that there are people with OI whose disorder is relatively mild but who in the future will be shown to have a recessively inherited form of OI.

Single cases in families

There may be a single ('sporadic') case in a family for a number of reasons. Firstly, there are some individuals whose disorder results from a fresh mutation. In other cases where there is no family history, it may result from autosomal recessive inheritance, with both parents being carriers. We cannot be sure without molecular genetic testing.

Mosaicism

In some families where the parents are not affected, but there are several affected children, the pattern of OI or DNA testing confirms that the disorder is inherited in an autosomal dominant manner. In these families some of the cells in one parent that make egg or sperm cells i.e. germinal cells in the ovaries or testes may already have the mutation. Usually no other body cells are found to have the mutation. This means that a parent will not have any indication that they have the mutation in an ovary or testis, but can have more than one child affected. While this is a rare situation, the affected children in these families have a high chance (50%) of having affected children themselves.

The types of OI

The considerable variability in OI is best accounted for by there being different types of OI (see table on page 26). Old terms such as 'Congenita' and 'Tarda' simply mean "present at birth" or "first fracture occurring later", respectively. The current classification and naming of the OI syndromes is based upon the observation of thousands of families worldwide, the pattern of inheritance in different families and the associated features.

Revisions in the past 30 years have seen the numbers being increased up to OI type XII, but at the 2009 meeting of the International Nomenclature group for Constitutional Disorders of the Skeleton, a decision was made to group the known OI syndromes into 5 groups i.e. preserving the primary four groups and adding OI type V. The newer disorders and all the known molecular defects are included as subtypes of OI types I – V.

The International OI Nomenclature 2010

Syndrome Names	Equivalent Numerical Type	Sub Types
Classic Non-deforming OI with Blue Sclerae	I	2
Common Variable OI with Normal Sclerae	IV	2
OI with Calcification in Interosseous Membranes	V	1
Progressively Deforming OI with Normal Sclerae	III	9
Perinatally lethal OI	II	8
Bruck Syndromes		2
Cole-Carpenter syndrome		1

Osteogenesis Imperfecta of the Non-deforming type (I), Common Variable type with normal sclerae (IV) and the type with fusion of the bones in the forearms (V) are all dominantly inherited and not usually diagnosed at birth. However, people with these types of OI may have hundreds of fractures in a lifetime and this may lead to short stature, spine and long bone deformity. On the other hand they may never have a fracture. They usually have normal or only mild short stature.

Osteogenesis Imperfecta of the Non-deforming type (I) is distinguished by the finding of distinctly blue-grey sclerae (the whites of the eyes) which sets it apart from most other OI syndromes. Individuals with OI type I also have an increasing frequency of hearing loss after the age of 20 years. They have easy bruising and sometimes quite marked joint hypermobility. There are many families in the world and in some parts of the world it is the most prevalent type of OI.

Common Variable type with normal sclerae (IV) is much more difficult to diagnose and requires a detailed family history, complete X-ray investigation and bone densitometry of family members. While 2 separate genes are known in which mutations may cause this type of OI, there are many other causes of osteoporosis and some are familial e.g. rheumatic or neuromuscular disorders of childhood. We have called it "common" because in a centre of expertise where nearly everyone from a defined population is assessed, it turns out to be a common disorder. Its impact is variable and like other forms of OI, early referral for treatment to prevent fractures, markedly reduces the severity and any tendency to bone deformity.

Some people with OI type I and some people with type IV also have opalescent dentine i.e. translucent teeth. These people are more likely to have a higher fracture frequency, short stature and scoliosis.

OI with calcification between the bones in the forearms (type V) is characterised by a tendency for dislocation of the elbows. People with this type of OI (type V) may have a characteristic X-ray appearance in their forearms where there is calcification in the ligament between the two forearm bones. A bone biopsy will show changes in bone which distinguish OI type V from Common Variable OI (type IV).

Progressively Deforming OI (type III) was originally characterised by progressive deformity of limbs and spine. Usually fractures occurred at birth or soon after and these people were much shorter than people with OI type IV. The sclerae which may be bluish at birth are pale bluish or normal in older children and adults. There is rarely a family history. There are many different genetic causes. In some families it results from mutations in genes which are dominantly heritable but in most parts of the world, it results from autosomal inheritance of the 9 known subtypes. In this type of OI, progressive deformity and the short stature results from the worsening osteoporosis. In Centres of Expertise, we have been able to treat severely affected children under 3 years of age, with Cyclic Intravenous Pamidronate and these children, who have Bisphosphonate modified OI, have fewer fractures, far less deformity and almost normal growth.

Some people with Progressively Deforming OI (III) have normal teeth and some have opalescent dentine. When inherited as an autosomal recessive disorder it is very common in black children from Africa and common throughout the Middle East.

Some children with OI are born with fixed joints, usually elbows and knees but sometimes more extensive fixation of their joints. OI with Congenital Joint Contractures is known as Bruck syndrome and there appear to be at least two different types distinguished by genetic and biochemical testing.

Cole-Carpenter type is usually evident by 6 months of age. These children have fractures at the ends of their bones, a feature which is also characteristic of children who have had non-accidental injury to their skeleton. Children with Cole Carpenter Syndrome also have premature fusion of the bony joints (sutures) in the skull and characteristically have prominent eyes.

Osteoporosis contributes to the increased tendency to fractures in all groups and contributes to the short stature. Just as osteoporosis results in progressive loss of height in older women, osteoporosis in some young people with OI is so rapidly progressive that there is either loss of height or stationary growth during childhood.

Are we likely to discover other types of OI?

The answer is 'yes', there are a number of minor types of OI which so far have been described in only one family. There have been other children whose OI has been difficult to classify and in the future we may be able to recognise hallmark features which characterises them as having distinctly different types of OI.

How do faulty genes result in OI?

By definition all types of OI are able to be inherited i.e. result from faults in genes which ultimately result in the disorder. There are a number of different types of OI and therefore a number of genes which can be at fault. In 2010, mutations in at least 12 genes are known and different mutations in those genes may result in different patterns of OI. Because genes operate in pairs, we expect that people with OI which results from

an alteration (spelling mistake) in just one gene of the pair might produce half normal quantities of bone matrix at the cellular level or if it is autosomal recessive, very little bone at all. Bone in all animals is not static, but is continually being turned over and remodelled. The human skeleton has a considerable capacity to compensate and bone turnover is increased in most people with OI.

The great surprise of the past few years is that most OI children are quite good at making bone. For example in OI type I, tests of bone turnover suggest that there are increased numbers of bone forming cells which means that there is 140% of normal bone production. However, bone breakdown is also increased and as a result there is an overall loss of bone each year. Research in the past decade has recognised that bone formation and bone resorption (breakdown) are coupled. Bone is formed by cells known as osteoblasts. On the other hand bone is remodelled through resorption by cells known as osteoclasts. Reduction in bone density (osteoporosis) results from:

- More bone resorption than formation
- Immobilisation
- Inadequate daily musculo-skeletal activity. This in turn may result from weakness, pain or deformity.

In different forms of OI, there are different defects, but there appear to be compensatory mechanisms and it is this overshoot in compensatory pathways that leads to all the problems.

It seems as though the bone pain, and even tiredness, result from the increased resorption of bone. This symptom is rapidly abolished when people are treated with Bisphosphonates (see Medical management). With abolition of bone pain there is a rapid reduction in the amount of sweating (hyperhidrosis) which also is such a common feature among children with 'severe' OI.

How is OI diagnosed?

When there is a family history of OI, we are able to look at the children quite early to see if they have any of the features characteristic for the type of OI in their family. When there is no family history of OI, we rely on the child having a number of fractures, or on measurement demonstrating a low bone density which might point towards a diagnosis of OI.

Clinical features

Blue Sclerae

The distinctly blue-grey colouration of the sclerae is a very characteristic feature in OI type I. However bluish sclerae are found in normal little children and one must be very careful not to over diagnose blue-grey sclerae. In OI type IV the sclerae may be bluish to grey when the children are young but the bluish tint of the sclerae fades with time. Similarly children with OI type III may have bluish sclerae and the depth of the blue-grey hue always remains intermediate between normal and OI type I.

Dentine

Opalescent dentine which results in premature wearing of the teeth and a honey brown or greyish colouration, is seen both in OI and also in the genetic disorder Dentinogenesis Imperfecta. In OI, opalescent dentine is sometimes a transient feature i.e. is present in the deciduous (baby) teeth but is not so noticeable in the permanent teeth.

Taking a family history

When OI is suggested, it is necessary to take a family history. This is most likely to be taken or analysed by a Genetic Counsellor or Clinical Geneticist. It may be very time consuming as an enquiry must be made about relatives and sometimes information must be sought from other people. It is always additional to the other findings but may be the most important factor in arriving at a diagnosis of OI.

Blood tests

The measurement of calcium, phosphorus and an enzyme called serum alkaline phosphatase (SAP) is routine. These tests are done to exclude other causes of osteoporosis. A bone protein known as osteocalcin is also used to measure the amount of bone being synthesized.

Radiographs

X-rays are best used to demonstrate fractures. There are sometimes features such as extra bones within the skull known as Wormian Bones (named after Dr. Worm so the spelling is with a capital W). If osteoporosis can be seen on the X-rays, then an accurate estimation of bone density can be obtained by bone densitometry, inevitably showing low bone density. There are an increasing number of centres with normal ranges for children at different ages which will allow an interpretation of bone density measurements.

To obtain these measurements, the child lies on the densitometer while the sweep arm moves overhead. The radiation dose is very small and about 1/10th of the radiation exposure from a single chest X-ray.

Urine tests

There are number of tests of urine markers of bone breakdown, such as urinary deoxypyridinoline. The urine has to be collected as the second urine of the day and stored frozen in the dark, wrapped in aluminium foil. Serial measurements collected under these conditions are valuable to assess bone turnover and response to treatment.

Collagen biochemistry

It is possible to take a small piece of skin and grow the cells. From these cells it is possible to derive sheets of cells which can make bone collagens. This type of test may confirm a decreased production of collagen by OI cells in some types of OI. However, the situation in the child's bones is often very different as there are mechanisms which compensate in some types of OI and bone production is increased in those children. Today, collagen biochemistry is usually undertaken for research. It takes months to get results and many children with OI will have normal studies.

Gene Analysis

There are a number of different techniques which scientists can use to do molecular genetic analysis of particular genes which cause OI. This is called gene testing. However this is very time consuming and very expensive, so that the user of these services, either the patient or the hospital, needs to pay. There are at least 12 genes to be tested. Then the result needs to be interpreted as some differences in spelling in genes (the individual's genetic code) are just family variations, known as polymorphisms. In some individuals with OI it may be possible to define the exact spelling mistake in a gene responsible for the OI in that child and family. This then allows rapid diagnosis or investigation of carrier status in other family members. Before gene testing is considered, a detailed family history must be taken and this sometime results in an important clue which will direct which gene to test. In some types of OI, for example Non-Deforming OI with Distinctly Blue Sclerae (OI type I), it is not necessary to undertake gene testing to say who is or who is not affected because the blue sclerae are always associated with the OI. Similarly in OI with Calcification in the membranes between the forearm bones (OI type V), the diagnostic test is an X-ray for the forearm or legs. When a diagnosis of OI type I or type V is made it is not necessary to pay such a large sum of money to analyse the other 10 genes. In type I or type V, gene testing is usually reserved for those families who need the information to make reproduction decisions. This is particularly true where resources for Pre-implantation genetic diagnosis are available.

Can brittle bones result from anything else?

There are several dozen rare disorders which share features in common with OI but in which there are other distinguishing characteristics. There are two alternative diagnoses to OI which result in some concern:

- Non accidental injury (child abuse)
- Juvenile Idiopathic Osteoporosis

Non Accidental Injury is an unfortunately common community problem. Sometimes the pattern of fractures is indistinguishable from the pattern seen in different types of OI. When there is a family history of OI, the suspicion that fractures result from OI should be very high. However where there is no family history of OI, it is often difficult to establish a diagnosis of OI when parents cannot explain how fractures occurred in a baby

or small child. In this situation parents may be falsely accused of non-accidental injury. It is of concern that collagen biochemistry is abnormal in just under 1 in 10 children with a provisional diagnosis of non-accidental injury suggesting they have forms of OI.

The word 'idiopathic' means that we do not know the cause. There is a very rare disorder which comes on at puberty, known as Juvenile Idiopathic Osteoporosis. It is usually self-limiting and requires only bone and mineral support and protection from injury. In a proportion of children with this, specific genetic causes can be found. In those cases of course the term "idiopathic" is inappropriate, as they have a known cause. Furthermore, this term is used inappropriately where young children have osteoporosis which cannot be explained. If one takes a careful history the children have often had symptoms for many years. Sometimes bone densitometry will reveal that one parent has osteoporosis. Sometimes bone densitometry in siblings within a family will show that other children in the family have osteoporosis i.e. the disorder is familial. In these instances we are talking of one of the types of OI.

Living with OI

At birth

Usually the birth of a baby with OI is unexpected. However, OI can sometimes be detected by ultrasound screening during pregnancy. If one of the parents has OI, there is a 50% chance that baby also has OI.

When a baby with OI lies in the womb in a normal way, delivery is not particularly hazardous. There is a risk of fractures of the arms as they lifted out. Studies have shown that normal vaginal delivery is safer than Caesarean section. The midwife or obstetrician should be informed so that they avoid holding the baby by the ankles when being measured at birth. Also, in any newborn baby at risk for OI we need to avoid testing for hip dislocation in the usual manner, or do so with extreme caution. The first fractures often occur at the time of neonatal hip examination within a few days of birth.

The first year or so

If your baby has been diagnosed at birth as having OI, you may understandably be nervous about handling when you get home. However, if you make all your movements slow, methodical and gentle, you will soon learn how much handling your infant can tolerate. When lifting and holding the baby, try to evenly support the whole body so that undue pressure is not placed on any particular part. This is achieved by holding the head and back with one hand and the buttocks with the other. Try to avoid grasping the ribs when picking up the baby as this could cause a fracture.



With permission from Association de l'Ostéogénèse Imparfaitte, France

Transporting

All members of the family can enjoy the new arrival if they are taught how to handle him or her. To move the baby from room to room, lay the baby on a pillow or use a baby carrier or Frazer chair with extra padding. A playpen (mesh sided) allows the baby to be part of the family scene and yet be protected. Many parents have found laying the baby on a sheepskin helpful. Your baby with OI may be slow to sit and crawl. When interest is shown in sitting, always make sure there is adequate support. Surround the baby with cushions and pillows to soften any falls. If a fracture occurs while the baby is trying to crawl, progress may be halted until confidence builds up again.

Feeding

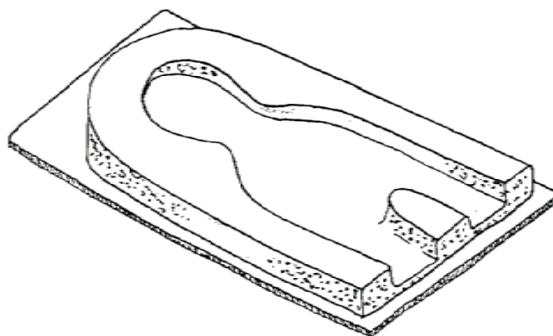
When breastfeeding or using a bottle, support the baby with a pillow so that even support is given to the whole body. The time of introduction of other foods and juices parallels that of unaffected children. Often

children with OI prefer small meals and finger foods. Some difficulties may be encountered in chewing if children have opalescent dentin and therefore a blender is useful in food preparation to avoid chipping the teeth on the food.

Bathing

A soapy, slippery baby can make even experienced parents of OI children nervous! For the newborn, first make sure everything you need is in reach before you start. An inflatable plastic canoe placed on 50 mm thick foam makes a soft-sided bath and is useful when travelling. Place the bath or basin on a counter top or table so that there is enough room to lather the baby on either a towel or sponge pad and then be rinsed off in the bath.

Alternatively cut a foam insert of 10 cm depth or greater to fill the bottom of the bath. The water can be brought to just a centimetre or so above the foam. Remember to have the water warm or baby may get a fright. The baby should be lifted – supporting the head, back and buttocks – into the bath and then eased onto the buttocks, giving you a free hand to rinse off the lather. When washing the hair, have a jug or spray attachment close by to use in rinsing. Older babies and children may enjoy bath time sitting in an open-mesh plastic laundry basket inside the bath tub. The basket provides added safety and security and is easily lifted out of the tub.



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Nappy changing

When changing your child's nappy, place your hand under the buttocks, lift the baby by the buttocks supporting the legs by your upper arm and place the nappy under the child with the other hand. Remember that lifting your child by the ankles to change the nappy could put undue pressure on the lower limbs and cause a fracture. Pilchers with side fastenings avoid pulling up over the legs, and the fabric outer layer is not as slippery as plastic alone.

Dressing

All clothing should be easy to put on and take off in order to lessen handling. Clothing should be lightweight, absorbent and non-constricting. For the newborn, the clothing ideally should be able to lie flat with either Velcro or press studs at the shoulders and front or back. This may require you to undo seams in clothes. Always press on your hand and not on the baby's body when closing the fastenings. A sleeping bag with hood is useful.

The toddler

It is essential that your child be allowed to explore the environment. There are many aids to help attain mobility which can help your toddler to explore his surroundings.

The pre-schooler

The chance to experience the stimulation of a preschool is important for both the child and the family, but presents extra risks of fracture. While your child may not be able to do as many physical activities as his/her peers, swimming should be encouraged. Swimming is excellent both as physical therapy as the buoyancy of the water enables movement otherwise not possible and is also important in building confidence in physical activities.

School

Children and adults with OI generally have normal intelligence. They may have a higher verbal intelligence than normal and advanced social maturity for their age. They may have difficulty with mathematics and space-form perception due to a lack of experience of the physical world around them. Early education should be directed at normalising early infant experience.

You will need to identify your child's special needs then ask for assistance with an evaluation to see whether a special needs teacher will be necessary at preschool and school. For the severely affected child, you will want to explore all the possibilities with an emphasis on integration.

Teachers need to know what to do if your child has a fracture at school. All schools in NSW have a book entitled 'Physical as Anything' in which there is a chapter on OI. Although the fractures are less frequent at or near puberty, children and teenagers with OI should avoid body contact sports and others such as horse-riding and trampolining which can cause crush fractures of the vertebrae. Short stature which is associated with OI is often a source of concern after the fractures have ceased, and emphasis should be placed on developing interests which will increase self-esteem. Clothes are important as a sign of belonging so try to allow your child to choose his/her own modern clothes.

Orthopaedic care

Your orthopaedic surgeon will play a central role in the long term management of your child. Specific areas you will need to address include fracture care, prevention of deformity, percutaneous intramedullary rodding, scoliosis prevention and treatment.

Preventing scoliosis

Those children who have had early physiotherapy, supported seating and regular swimming while their spine is still growing, have less curvature.

Preventing skull base deformity

The bottom of the skull which is usually convex gradually flattens out and then becomes concave in some people with OI. This is known as Basilar Impression. It is found in about one quarter of people with Common Variable OI with normal sclerae and is five times more common in people with opalescent dentine. The skull base can press upwards on the bottom of the brain, producing a particular type of headache which is worse on coughing, flickering of the eyes (nystagmus), or episodes of dizziness. Delaying upright posture by reclining infants until they are ready to sit upright by themselves, may help. In our centre all babies with OI are reclined until they are able to hold their head up independently. We recommend X-ray screening of the lateral skull in all children with Common Variable OI at 4 years and then review every 3 years.

The management of fractures

Sometimes a fracture is obvious, but children rarely remember accurately some specific episode of trauma or swelling. They may not complain of pain for some hours after the injury. Undisplaced fractures frequently occur in OI, but should be treated as if they were complete.

Fractures will account for most of the painful episodes in the life of a child or adult with OI. It is therefore useful to have a fracture treatment plan. A useful pain prevention program might include:

- (a) Practice visualisation and relaxation.
- (b) Preparedness for fracture i.e. have splints and bandages on hand.
- (c) Confident, calm, matter-of-fact handling of the fracture when it occurs.
- (d) Offer first aid through splinting or other means.
- (e) Decide on urgency of medical assessment, X-ray and treatment and means of getting there.
- (f) Add psychological support.

Should I call the doctor for every fracture?

YES. Whether or not deformity is evident, fractures may be displaced and lead to limb shortening. When deformity is present, it is important that this is corrected. Those children who have had careful professional evaluation and setting of fractures have less disability in adult life.

Medical advice and treatment (splinting) should be sought even when fractures are not obvious and when it would be reassuring to know definitely or not. A fracture may be missed if it is looked for too early, especially in the OI patient where the bone density is low and X-Rays have poor contrast.

Guidelines for X-rays

Since the bone density is low in patients with OI, it is important that the radiographer recognises this and reduces the intensity of the X-rays to allow adequate visualisation, and reduce the need to redo exposures.

First aid

Types of fractures

An open fracture is one where the skin is broken as well as the bone, but this occurs very rarely in OI. Open fractures are serious because they can result in severe blood loss and internal infection. A closed fracture is one where the skin surface around the damaged bone is not broken.

Upper arm fractures

1. Support the injured arm across the chest with the finger tips close to the opposite shoulder.
2. Apply a collar and cuff sling and secure the arm to the chest with a broad or narrow-fold triangular bandage but avoid pressure on the fracture site. Allow the elbow to hang freely.

Forearm fractures

1. Make a splint with a rolled-up newspaper, magazine or card that is long enough to support the arm from the elbow to the fingers. Roll it around the arm so that it fits closely at the elbow and over the hand or use it as a gutter-splint. Secure it with one or two bandages or with adhesive tape.
2. Apply an arm sling. Check that the pulse at the wrist is present to ensure that the bandages are not too tight.
3. If the elbow cannot be bent, lie the child down and place the injured arm beside the trunk. Do not attempt to bend the elbow forcibly. Ask the child or another adult to support the arm with the other hand if possible and place soft padding between the injured arm and the body.
4. Secure the injured arm to the body with several broad bandages around the wrist and thigh, the upper arm and trunk and the forearm and the trunk.

Leg fractures

1. Lay child down and place padding between legs.
2. Gently bring uninjured limb to the injured limb.
3. Apply a figure-of-eight bandage around the ankles and feet.
4. Apply a broad bandage around the knees and tie on the uninjured side.
5. Check the circulation of both limbs (colour and temperature of feet).

Pain management

Pain may result from fractures, treatment of fractures, muscular spasm, sprains and following surgery.

Psychological preparation for pain

While children with OI come to expect pain, its timing is rarely of their choosing. It is best if they and the care-givers are prepared and can deal with it immediately. Preparedness for pain should reduce its intensity and duration. Pain is often talked about in terms of intensity (how bad it feels) and the duration (how long it lasts). The intensity of pain can be lessened and in older children there are a number of approaches which can be used.

Mental/physical states which make pain feel worse include: anxiety, panic, cold, tiredness, hunger, depression.

Approaches which may lessen pain duration or intensity include: splinting, analgesia, relaxation, distraction techniques, e.g. visualisation and autogenic training, transcutaneous electrical nerve stimulation (TENS).

Postoperative pain

This is ideally prevented by appropriate post-operative pain relieving medication usually morphine or pethidine by injection or infusion.

Pain from injections

Many children have a phobia about injections despite the fact that a successful intravenous needle causes only fleeting pain. For children who are requiring repeated injections, e.g. Pamidronate therapy, the local anaesthetic EMLA (lignocaine; prilocaine) cream can be particularly valuable. It can be applied to the injection site under a dressing two hours before the injection. EMLA patches are available and allow easy application.

Medical management of OI

Calcium and minerals

The skeleton needs new calcium every day. Good sources are low fat milk, low fat cheese and low fat yoghurt. Low fat dairy products are preferred as there is more calcium per portion with low fat products.

Bisphosphonates

The bisphosphonates are a class of medicines which increase bone density by reducing the rate of bone resorption. They do this by a direct effect on the bone resorbing cells called osteoclasts. There is also evidence that they stimulate osteoblasts to form bone, so they are less likely to break.

There are a number of bisphosphonates which can be used in the treatment of OI. The bisphosphonates are poorly absorbed by mouth. Two bisphosphonates are being trialled in OI as oral medicines. Alendronate (Fosmax®) is being trialled in North America. Risedronate (Actonel®) is trialled in the United Kingdom and Australia. With oral bisphosphonates there is a potential risk of causing burning and scars to the swallowing passage known as the oesophagus. Thus Alendronate is not being used in children under the age of 6 years. Etidronate (Bonefos®) has not been trialled in children.

Two bisphosphonates are being trialled in an intravenous form. Zoledronate is a very potent bisphosphonate and is still too early to say how it will be best used in OI. Pamidronate (Aredia®) has been extensively used worldwide without major side effects. At present it is the drug of choice for treatment of OI.

Cyclic Intravenous Pamidronate can:

- reduce bone pain
- increase bone density
- improve the child's feeling of wellbeing and increase mobility
- decrease the rate of fractures
- reduce deformity

There are several regimens which are being employed but in Australia and Europe the regimen preferred for use of Cyclic Intravenous Pamidronate is a monthly or second monthly intravenous infusion. These infusions are given over 1 or 2 hours in hospital under supervision. Treatment needs to be monitored at six monthly intervals. After the initial phase of several years of treatment, less frequent monitoring is possible.

The major side effect of Cyclic Intravenous Pamidronate is a febrile 'flu-like' illness which follows about 20 hours after the first dose. This occasionally recurs with subsequent doses but is usually a response to the first dose only.

Dental management

Opalescent dentine is encountered in less than 20% of individuals with OI type I, type III and type IV. It most commonly affects both primary and secondary teeth, but it may be more marked in the primary dentition. There is premature wear of the teeth and chipping of the enamel from the defective dentine.

Early regular dental care is essential in all forms of OI. The need to extract teeth due to dental decay or periodontal disease has complications, e.g. bone fracture and prolonged bleeding. Fortunately complications are rare in children.

When opalescent dentine is present, the back teeth can be protected by stainless steel crowns to prevent the marked wearing down which would otherwise occur. The other teeth can be covered with composite or ionoglass strip crowns to protect them from wear and enhance their appearance.

For the older patient, in whom the teeth have worn away, overlay dentures may be provided. No extractions are necessary, and an acceptable appearance can be restored, chewing is efficient and retention is good. However, there has been a trend towards fixed prosthetic replacement.

Rehabilitation

The goal of rehabilitation in OI is to achieve community mobility with or without aids. Now with Cyclic Intravenous Pamidronate treatment it is conceivable that even patients with OI type III will be able to walk in time. Previously these people required a wheelchair or sticks for mobility.

In childhood, gait and footwear advice should be sought. Because of the laxity of ligaments in the feet there is a tendency to flat feet (fallen arches). Early treatment prevents deformity and improves comfort and endurance. A physiotherapy program aimed at strengthening the small muscles of the feet can be helpful, as can walking on sand.

The small joints of the hands are also hypermobile. An Occupational Therapist can assist with analysis of hand function and therapy. This includes prescription of aids for writing and notetaking, especially during the school years.

Teenage years

Friends and the peer group

Children with OI should be encouraged to care for themselves as much as possible. Their mobility is limited and so their chance to establish social and subsequently sexual relationships is restricted. They need to have as much contact as possible with able bodied young people to enable them to mature emotionally, intellectually and sexually.

Adolescence

Adolescents with OI undergo the normal changes of puberty. Skeletal deformity may make the practical management of menstruation difficult and the use of the contraceptive pill has some advantages. Opportunity should be given to adolescents to discuss the fantasies and realities of their future with their peers and their parents, and premarital and genetic counselling made available. Services exist for counselling parents of OI children, people with OI and couples where one or both have OI. The difficulties likely to be experienced in sexual activity are those imposed by skeletal deformities and the possibility of fractures. These will be different in each case and each couple can be creative to arrive at their own solution.

Noise and hearing

There is evidence that repeated microfractures in the 3 tiny bones in the ear cause deformity which interferes with the normal mobility of these bones. While stapedectomy (removal of the stapes bone in the ear) and implantation of a piston may give improvement, the improvement is not always sustained. Surgical treatment may not be an option for severe hearing impairment and hearing aids may be recommended.

As a consequence, every effort should be made to preserve hearing by

- (a) Avoidance of sound trauma at home and in the work place. In this regard portable sound systems should have a decibel-minimisation/AVLS switch to limit sound trauma to the ear.
- (b) Regular hearing assessment and correction of correctable impairment such as glue ear in childhood.

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Books for parents

Chiasson R-M, Munns C, Zeitlin L. Interdisciplinary Treatment Approach for Children with Osteogenesis Imperfecta. Montreal, Shriners' Hospital for Children (Canada) 2004.

Prepared by the staff of the Shriners' Hospital (for Crippled Children) Montreal and reflecting their approach to the Multidisciplinary care of children with OI of which they are the Centre of Expertise in the Shriners' Hospitals network of North America. The chapter by Dr Fassier is a nice approach for parents and professionals new to the field. The bisphosphonate regimens are different from those used in Australia and most parts of Europe.

Cintas Holly Lea, Gerber Lynn H (eds). Children with Osteogenesis Imperfecta; Strategies to Enhance Performance. Gaitersburg, Osteogenesis Imperfecta Foundation 2005.

A comprehensive and extremely valuable text for your therapists.

Glauser HG. Living with Osteogenesis Imperfecta. A Guidebook for Families. Osteogenesis Imperfecta Foundation, Inc.

An account of the care of children and adults with OI written from a North American perspective. Published before the major advances in care of children with OI resulting from treatment with bisphosphonates. (See OIF website). As the author is the mother of an OI child it has a personal touch which means that it is valuable and speaks to parents.

Wacaster P. Managing Osteogenesis Imperfecta. Osteogenesis Imperfecta Foundation 1996.

An extremely interesting account written and edited by Patricia, a medical practitioner and parent herself but written before the major advances resulting from treatment with bisphosphonates. (See OIF website). It attests to the period of very active physical and surgical approaches for OI. It also brings a personal account to the text.

Web resources

OI Resources

OI Australia: <http://www.oiaustralia.org.au/>

OI Federation of Europe: <http://www.oife.org/>

This site is about OI and the OI Societies of Belgium, Britain, Czechoslovakia, Denmark, France, Germany, Finland, Norway, Sweden, and The Netherlands.

OI Foundation Inc – United States <http://www.oif.org/>

A useful site for parents and people with OI.

Centre for Genetic education: <http://www.genetics.com.au>

The fact sheets on this site are available to parents and are used by genetic counsellors in counselling parents. They summarize the patterns of inheritance, details about genetic testing and outline the approaches such as prenatal diagnosis about which families may need information

Articles for health professionals

Individual types of OI

Non-Deforming OI with Distinctly Blue Sclerae – OI type I

Paterson CR, McAllion S, Miller R. Heterogeneity of Osteogenesis Imperfecta type I. *Journal of Medical Genetics* 1983; 20:203-205.

Common Variable OI with Normal Sclerae – OI type IV

Paterson CR, McAllion S, Shaw JW. Clinical and radiographical features of Osteogenesis Imperfecta type IV. *Acta Paediat Scand* 1987; 76:548-552.

Progressively Deforming OI – OI type III – autosomal recessive

Forlino A, Cabral WA, Barnes A, Marini JC. New perspectives on Osteogenesis Imperfecta. *Nature Reviews Endocrinology* 2011; 7:540-557.

Sillence DO, Barlow KK, Cole WG, Dietrich S, Garber AP, Rimoin DL. Osteogenesis Imperfecta type III. Delineation of the phenotype with reference to genetic heterogeneity. *American Journal of Medical Genetics* 1986; 23:821-832.

Progressively Deforming OI – OI type III – autosomal dominant

Lund AM, Nicholls AC, Schwartz M, Skovby F (1997). Parental mosaicism and autosomal dominant mutations causing structural abnormalities of collagen I are frequent in families with Osteogenesis Imperfecta type III/IV. *Acta Paediatrica* 86(7):711-718.

OI with calcification in Interosseous membrane – OI type V

Glorieux FH, Rauch F, Plotkin H, Ward L, Travers R, Roughley P, Lalic L, Glorieux D, Fassier F, Bishop N (2000). Type V Osteogenesis Imperfecta: A new form of brittle bone disease. *Journal of Bone and Mineral Research* 15(9):1650-1658.

Fleming F, Woodhead H, Briody JN, Hall J, Cowell CT, Ault J, Kozlowski K, Sillence DO. Cyclic Bisphosphonate Therapy in Osteogenesis Imperfecta type V. Case Report and Review of the Literature. *Journal of Paediatrics and Child Health* 2005; 41:147-151.

Cole-Carpenter syndrome

Cole DEC, Carpenter T (1987). Bone fragility, craniosynostosis, ocular proptosis, hydrocephalus, and distinctive facial features: a newly recognised type of osteogenesis imperfecta. *J Pediatr* 110:76-80.

Bruck syndrome

Breslau-Siderius EJ, Engelbert RHB, Pals G, vander Sluijs JA. Bruck syndrome: a rare combination of bone fragility and multiple joint contractures. *Journal of Pediatric Orthopaedics* 1998; 7:35-38.

Perinatally Lethal OI – OI type II

Sillence DO, Barlow KK, Garber AP, Hall JG, Rimoin DL. Osteogenesis Imperfecta type II. Delineation of the phenotype with reference to genetic heterogeneity. *American Journal of Medical Genetics* 1984; 17:407-423.

Subsequent to the publication of this paper it was shown that many cases in North American and European populations arise as a result of fresh dominant mutation. Recurrence in sibs in those families is due to germinal cell mosaicism. However in the last 5 years many different genetic forms of perinatally lethal OI have been discovered and the majority result from autosomal recessive inheritance with a 25 % recurrence risk for future children.

Rehabilitation and therapy

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The Classification of Osteogenesis Imperfecta 2010

AD = autosomal dominant, AR = autosomal recessive

OI Type	Inheritance	Scleral Colour	Teeth	Clinical Features
I (2 subtypes)	AD	Very blue	Normal or Opalescent Dentine	Bone fragility varies from mild to severe; hearing loss
II (2 subtypes A and B)	AD	Bluish to white	Variable Dentine anomaly	Extremely severe bone fragility with crumpled long bones but normal ribs
II - 6 Subtypes	AR	Bluish to white	Usually normal	Extremely severe bone fragility with crumpled long bones but normal ribs
III - 2 subtypes	AD	Bluish to white	Variable Dentine anomaly	Variable but often severe bone fragility in infancy; progressive skeletal deformity
III - 8 Subtypes	AR	Bluish to white	Usually normal	Variable but often severe bone fragility in infancy progressive skeletal deformity includes former types VI, VII, VIII
IV (2 subtypes)	AD	Bluish fading to white	Normal or Opalescent Dentine	Bone fragility mild to severe; deformity mild to severe
V	AD	White	Normal	Calcification in interosseous membranes tendency to hyperplastic callus
Bruck 1	AR	White	Normal	Joint contractures at birth
Bruck 2	AR	White	Normal	Joint contractures at birth
Cole-Carpenter	?	White	Normal	Craniosynostosis. Moderate to severe bone fragility
Osteoporosis-eye disease (several different types)	AR	White	Normal	Retinal blindness or cataracts Intellectual disability