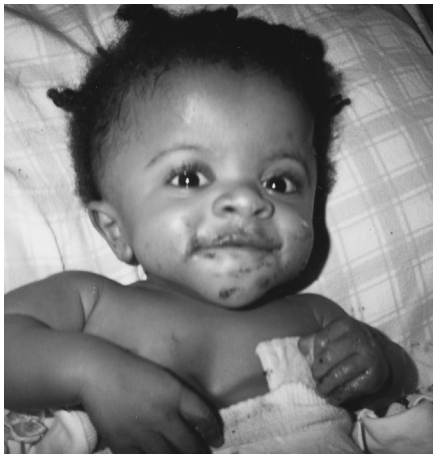
Osteogenesis Imperfecta



A Guide for Nurses

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Osteogenesis Imperfecta: A Guide for Nurses

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Introduction

For people with osteogenesis imperfecta (OI), interacting with the health care system can be complicated and time consuming. Frequently, people with OI require the services of several health care providers in settings that include the physician's office, an outpatient clinic, the emergency department or hospital, and/or a medical research facility. At each location, the nurse plays an important role in caring directly for the patient and providing patient and family education about OI. Because optimum management of OI is achieved through a multi-disciplinary team approach, it often becomes the nurse's role to facilitate care coordination and transitioning needs.

In recent years, a great deal of new knowledge has been derived from worldwide interest in bone and genetic research. This progress is changing many aspects of our understanding of OI and expanding treatment options. Because OI is a rare disorder, many nurses may not have cared for an affected child or adult and are only familiar with textbook descriptions. This booklet provides an introduction to OI and serves as a reference tool for nurses.

Basic Facts

Osteogenesis imperfecta, also known as brittle bone disease, is a genetic disorder of connective tissue characterized by bones that fracture easily, often from little or no apparent trauma. It is highly variable in severity from patient to patient, ranging from very mild to lethal. In addition to having fractures, people with OI often have muscle weakness, joint laxity, skeletal malformations, and other connective tissue problems.

The prevalence of OI is approximately 1 in 20,000, including patients diagnosed after birth. OI occurs with equal frequency among males and females and among all racial and ethnic groups. Patients with OI have the full range of intellectual capabilities as seen in the general population. There is nothing inherent in the disorder that affects cognitive abilities. Life expectancy varies according to the underlying severity of the disorder and ranges from very brief (Type II OI) to average. Medical treatment for OI is increasingly understood.

Patients with osteogenesis imperfecta usually have a faulty gene that instructs their bodies to make too little type I collagen or poor quality type I collagen. Type I collagen is the protein "scaffolding" of bone and other connective tissues. Inheritance, in nearly all cases, follows an autosomal dominant pattern, although sporadic cases are common. When there is no family history of OI, the disease is caused by new dominant mutations.

Patients are often knowledgeable about their health status and the problems associated with OI. Accordingly, the opinions, requests, and instructions of adult patients and parents of children with OI should be respected.

Depending on the severity of OI, the following characteristics may be seen:

- skeletal malformation
- short stature – Growth impairment is severe in all those individuals with Type II and Type III OI, moderate in those with Type IV, and relatively less in those with Type I.

- muscle weakness
- ligamentous laxity
- smooth, thin skin
- triangular face
- dental manifestations – Dentinogenesis imperfecta is present in about 50 percent of patients with OI. Deciduous teeth are usually more severely affected than permanent teeth.
- blue sclerae – Approximately 50 percent of people with OI have blue, purple, or gray-tinted sclerae.
- respiratory complications – Lung complications, such as pneumonia, represent a significant cause of death for those with Type II and III OI. Pneumonias are seen in children and adults, and cor pulmonale, a type of heart failure, is seen in adults.
- cardiac complications – Mitral valve prolapse (laxity) is seen but is not as common as in some other connective tissue disorders.
- hearing loss – In those with OI, hearing loss is frequent.
- thermal instability – Those with OI experience slightly higher than normal body temperature, sensitivity to heat and cold, excessive sweating, pseudomalignant hyperthermia after anesthesia.
- blood vessel fragility – Patients may exhibit easy bruising, frequent nosebleeds, and, in a small number of patients, profuse bleeding when injured.
- neurologic manifestations – Basilar invagination of the skull, hydrocephalus, and syringohydromyelia of the spinal cord may be seen in patients with the more severe forms of OI.

Types of OI

In 1979, Sillence and others devised a classification scheme that divides OI into four types based on clinical, radiographic, and genetic distinctions. Features of OI vary not only between types but within each type as well. Patients with OI may present with some but not all of the clinical features. Children and adults with milder OI may have few obvious signs. Some patients appear to have characteristics of several types. Patients may walk unassisted; require the assistance of walkers, crutches, or braces; or be wheelchair-dependent. All types of OI may include dentinogenesis imperfecta and varying degrees of blue sclera. The frequency of fractures may decrease after puberty. An increase in fractures may be seen in women following menopause and in men in later life.

While the Sillence classification is part of the commonly accepted language of OI, nurses are urged to look beyond type alone. The key to optimal care is to be aware of the patient's specific symptoms and capabilities and to treat each patient individually. See **Appendix 2: Sillence Classifications of OI** (page 30) for a summary of information about the types of OI.

- **Type I** – Mildest form of the disorder. Manifests with relatively few fractures, minimal limb deformities, blue sclera, and high incidence of hearing loss. Stature may be average or slightly shorter than average for the unaffected family members. Hearing loss onset is primarily in young adulthood but may occur in early childhood. Some patients have few fractures or obvious signs of OI. Some patients experience multiple fractures of the long bones, compression fractures of the

vertebrae, and have chronic pain. Dentinogenesis imperfecta may or may not be present. Life expectancy seems to be normal.

- **Type II** – Most severe form; features severe osteoporosis. Infants are frequently premature or stillborn and are small for gestational age. Multiple fractures in the womb lead to bowing and shortening of the long bones at birth. The head is large for body size, with severe undermineralization. The rib cage is small and narrow, and palpation of the rib cage reveals "beading" from calluses due to rib fractures *in utero.* The sclerae are almost uniformly dark blue/gray. In the newborn period, it can be difficult to distinguish between Type II and severe Type III OI. Infants with Type II usually die in the immediate postnatal period from respiratory and cardiac complications. Rare cases of infants surviving into childhood have been reported.

- **Type III** – Most severe type for those patients who survive the perinatal period. Multiple long bone fractures may be present at birth but without the severe thoracic malformation seen in Type II OI. Frequent fractures of the long bones, tension of muscle on soft bone, and disruption of the growth plates lead to bowing and progressive malformation with short stature. Marked short stature, kyphoscoliosis, compression fractures of the vertebrae, and pectus carinatum or pectus excavatum occur frequently. The head is large for body size. Sclera may be white or tinted blue, purple, or grey, and dentinogenesis imperfecta may be present or absent. Patients with Type III are generally diagnosed at birth due to multiple fractures. Many patients with Type III use wheelchairs or other mobility aids. Some are independent ambulators within the home. Use of assistive devices to independently perform activities of daily living is common. Surgery may be required to support and straighten bowed limbs. Life span may be somewhat reduced. While some individuals are living into their sixties and seventies, there appear to be clusters of mortality due to pulmonary complications in early childhood, teens, and thirties to forties.

- **Type IV** – Moderately affected, with the diagnosis possibly made at birth but more frequently later, because the child may not fracture until he or she is ambulatory. Bowing of the long bones is present to a lesser extent than in Type III. Patients have moderate-to-severe growth retardation, which is one factor that distinguishes them clinically from Type I OI. Scoliosis and ligamentous laxity may also be present. Dentinogenesis imperfecta may be present or absent. Although the Sillence classification indicates that patients have white sclera, blue sclera have also been seen. Type IV OI can range in severity from similar to Type I to resembling Type III. Life span is not affected.

Recently, researchers have reported additional types that do not involve a defect of type I collagen. Clinically, these patients are similar to Type IV OI. Additional radiographic or histologic data are required to diagnose Types V and VI.

- **Type V** – Moderate in severity and similar to Type IV but also characterized by large hypertrophic calluses that develop at sites of fractures or surgical procedures. Calcification of the membrane between the radius and ulna restricts forearm rotation.

- **Type VI** – Extremely rare, moderate in severity, and only identified through bone biopsy.

Diagnosis

The **diagnostic process** may include:

- physical exam
- medical history, including pregnancy and childbirth information
- family history
- bone density testing
- x rays
- collagen (protein) testing using a skin biopsy
- molecular testing
- blood and urine tests to rule out conditions other than OI.

The **physical exam** includes assessment for abnormalities in:

- skull formation
- fontanel closure
- head circumference
- facial shape
- scleral hue
- dentition
- hearing
- chest shape
- shape of spine, presence/degree of scoliosis, and kyphosis
- shape of long bones
- segment measurements (upper and lower extremities)
- height/length (compared to unaffected children)
- body proportions
- bruising/scarring
- joint mobility
- development (physical and cognitive).

Some characteristics are age-dependent. Hearing loss may not be apparent in infancy or childhood. Bone malformation may not be present in an infant or young child with mild disorder. Pale blue sclerae are normal up to 18 months of age. Intense scleral hue and its presence past 2 years of age can suggest the need for further evaluation for OI. While tinted sclerae are a characteristic of OI, it is important to note that only some patients exhibit blue sclera. See **Appendix 2: Sillence Classifications of OI** (page 30) for additional information.

Testing is likely to include these components: (For a more detailed explanation, see the section **Genetic Basis and Diagnostic Testing for OI** (page 19)).

- **Blood and Urine Tests** – Used to rule out other diagnoses, such as rickets or hypophosphatasia. Blood tests other than DNA analysis are not conclusive or diagnostic for OI.

- **Radiography** – Typically reveals osteopenia (low bone density), fractures (new, subclinical, or old healing), bowing of long bones, vertebral compressions, and wormian bones of the skull. In some children and adults with mild forms, these alterations may be difficult to identify.

- **Dual Energy X-ray Absorptiometry (DXA)** – A type of bone mineral density test. This is an adjunct test useful when compared to age- and sex-matched peers using Z-scores for children and T-scores for adults. Some machines require special software to test children. Short statured individuals can give deceptively low values. Scores obtained from different machines usually cannot be statistically compared.

- **Collagen Testing (Skin Biopsy)** – Requires a small skin sample taken from the arm, leg, or foreskin (during circumcision). Cells are grown in a culture medium and analyzed for defects in quantity or quality of collagen protein that they synthesize. Approximately 85 percent of people with OI will have a positive (abnormal) skin biopsy result. Fifteen percent of cases diagnosed clinically and radiographically as having OI will have a negative skin biopsy result (typically in milder cases). Results are usually available in 6 weeks to 3 months.

- **DNA Analysis** – Allows identification of a specific mutation in a person's type I collagen genes that causes OI. Blood or a skin sample can be used for this analysis. Cord blood obtained at delivery can also be saved for testing. The precise proportion of people with OI who have abnormalities detected is not certain but is probably similar to that for protein (collagen) testing. Results may take longer than 3 months.

- **Prenatal Testing** – Often requested when OI is present in one of the parents or in a sibling. If the mutation in DNA is known, DNA from the fetus can be obtained by chorionic villus sampling (CVS) or by amniocentesis. Protein studies can be done using cultured chorionic villus cells but not amniocytes.

- **Ultrasound** – Ultrasound examination of the fetus can detect Type II OI at about 14 to16 weeks gestation and Type III OI at about 18 to 20 weeks. Other forms of OI may be detectable if there are intrauterine fractures.

- **Testing for Recurrence Risk** – Families with one affected child are often concerned about the possibility of recurrence and should be referred for genetic counseling. Once a specific OI-causing mutation is identified, further genetic testing becomes increasingly possible. With one affected parent, the risk of having an affected child is generally about 50 percent with each pregnancy. After one affected child born to unaffected parents, the recurrence risk is 2 to 5 percent.

Standard Treatments

Because there is no cure for OI, its management or treatment currently focuses on minimizing fractures and maximizing mobility and independent function. Aggressive rehabilitation is an important part of treatment for most types of OI. Prolonged immobilization can further weaken

bones and lead to muscle loss, weakness, and fracture cycles. Many orthopaedists prefer to treat fractures with short-term immobilization in lightweight casts, splints, or braces to allow some movement as soon as possible after a fracture.

When managing OI in children and adults, rehabilitative treatment – including physical therapy and exercise – is increasingly emphasized. Goals include improving cardiovascular function; prevention or reduction of problems associated with misalignment of hips, knees, and ankles; and development of optimal peak bone mass. The need for exercise starts in infancy and continues throughout life. Various orthotics to support ankles, knees, and wrists are often necessary. Braces may also be part of a treatment program.

Swimming and water therapy have been shown to be not only enjoyable but of benefit to children and adults with OI.

Orthopaedic surgical treatments may include inserting rods in the long bones of the arms and/or legs to control fractures and improve malformations that interfere with function. See **Rodding** (page 19) for additional information. Spinal surgery is sometimes necessary to correct scoliosis or prevent it from worsening.

Treatment with fluoride, calcitonin, vitamin D, and high doses of calcium has generally been judged as ineffective for osteogenesis imperfecta. Increasingly, bisphosphonates are being administered "off label" (i.e., for a use not approved by the U.S. Food and Drug Administration) to adults and children with OI. Both positive and negative aspects of treatment have been reported. See the section **Research: Experimental Treatments** (page 23) for additional information. Persons with OI should only consider taking bisphosphonates in a clinical research protocol or under the care of a physician experienced in their use.

Educating the Family of a Newly Diagnosed Patient

Most parents of a child with osteogenesis imperfecta can report exactly where and when they first learned about their child's diagnosis. The quality and quantity of information and the manner in which it was given profoundly affect the parents, the child, and the whole family for years to come. Often this task becomes a nurse's responsibility. A sensitive, accurate, and hopeful presentation of information can help foster a sense of partnership between the health care providers and the family and avoid misunderstandings. Ongoing communication with families will be necessary due to the large amount of information. Learning that one's child has a genetic disorder can be shocking and confusing for the parents and extended family.

Parents need to be reassured that nothing they did prior to or during pregnancy caused OI. They need to be reassured that OI does not affect a child's ability to think and learn. With some adaptations in the physical environment, children who have OI go to school, make friends, grow up, and have families and careers of their own.

If the person receiving an initial diagnosis is an older child, teenager, or young adult, counseling about lifestyle changes and precautions for avoiding fractures may be necessary. Teens and adults also will benefit from information about the genetics of OI or a referral to a genetic counselor.

In addition to the need for information, there is an ongoing need for emotional support for patients of every age and their families. Teens and the newly diagnosed young adult may be in particular need of this support.

Nurses need to reassure parents and patients with OI that although this is a rare disorder, there are physicians and therapists in many parts of the country who are experienced in the care of people with it. Also, progress is being made with surgical, medical, and rehabilitative treatment. Nurses can reassure those who are new to OI that most families quickly develop a broad understanding about the disorder and become experts in caring for their affected family member.

Coping with and adjusting to having a child diagnosed with OI can be stressful for families. It is normal for families to go through the stages of grief (i.e. denial, anger or resentment, bargaining, depression, and finally acceptance). Families will continue to experience these feelings at different stages during their child's life. Nurses can encourage families to express their thoughts and assure them that their feelings of disappointment, anger, and sadness are normal. It is also important to help families find support for coping with their feelings. A referral to family social services may be helpful.

Accurate information about osteogenesis imperfecta is important. The Osteogenesis Imperfecta Foundation's Information on Request service, by telephone (1-800-981-2663) or e-mail (bonelink@oif.org), is available to provide information to physicians, nurses, other health care providers, and family members. Books, brochures, videos, and other resources are also available. Health care professionals should not hesitate to contact the OI Foundation and should encourage parents and adults with OI to do so as well.

While the Internet can be a convenient resource, some Web sites and "chat rooms" contain inaccurate information. Health care professionals working with families should guide them to Internet sites that provide reliable information. Information on the Osteogenesis Imperfecta Foundation Web site at www.oif.org is reviewed by its medical advisory council. This Web site also provides information about support groups and chat rooms. Networking with other families who are struggling with similar issues can be a source of support.

Nurses should encourage parents to seek professional help if they seem to be overwhelmed or excessively sad or angry.

Neonatal and Nursery Care

Although nurses who work in neonatal intensive care units and nursery departments have experience caring for very small and fragile infants, there are certain medical concerns to consider when caring for an infant with OI. The infant may have an unusually soft skull, startle very easily, and have malformation and fractures in various stages of healing.

Handling Suggestions:

- All movements should be slow, methodical, and gentle.
- Never push, pull, twist, bend, apply pressure, or try to straighten arms or legs.
- Infants with OI should not be picked up under the axillae or around the rib cage because this can cause rib fractures.
- The head and trunk should be supported with one hand while the other hand supports the buttocks.
- Keep fingers spread apart to provide a wider base of support and an even distribution of support pressure.
- When lifting or turning the baby for feeding, dressing, or diapering, apply support to the broadest possible area. One safe and effective way is to slide one hand underneath the child's buttocks to the back with some support under the head. Place the other hand on the chest and abdomen, "sandwiching" the baby between the two hands.
- When diapering the baby, do not lift the baby by the ankles as this could result in a fracture. Slide your hand under the buttocks to lift the baby, then remove and replace the diaper.
- Infants with fractures may be immobilized with a cast or splint to reduce motion and provide stabilization. Such infants must not be placed prone on their stomachs because suffocation can occur.
- Care should be taken when changing dressings and bedding to protect the infant's arms, wrists, and fingers.
- When dressing the infant, bring garments over the limbs; do not pull a limb through a sleeve or pants leg. Pulling, twisting, or getting caught in clothing can cause fractures.
- It is important that babies with OI receive affection and are held and touched by parents and other caregivers.

See **Appendix 1: Quick Tips: Caring for the Patient with Osteogenesis Imperfecta** (page 28) for additional information.

Feeding: Infants with OI can be poor feeders. Some babies display a weak sucking reflex and may require small, frequent feedings. The combination of small stature, feeding problems, and slow growth may be mistaken for failure to thrive.

Breast milk is an excellent source of calories for virtually all infants, including those with OI. Breastfeeding can create a special bond between the mother and child. Babies with all but the most severe forms of OI should be capable of being breastfed. However, those with the most severe forms of OI may have breathing difficulties that interfere with the ability to suck. Rapid respirations can predispose to aspiration. If the baby is not able to breastfeed, the mother may opt to pump breast milk and feed the child breast milk from a bottle.

To avoid fracture, the same care taken for other activities should be taken when holding and positioning the infant. When feeding the infant, the mother should be especially careful to avoid having the baby positioned with an arm behind the back or a leg pressed against the mother's body in such a way as to put pressure on an arm or leg at an abnormal angle.

Burping should be done very gently to reduce the chance of fractures, especially of the ribs. Soft taps, possibly with padding over the hand, are recommended. Gently rubbing the baby's back while taking gentle bouncing steps may also be beneficial. When picking up the infant for burping, it is important to provide both front and back support. The caregiver should lay the baby on his or her back and bend over to pick up the baby. The caregiver's hands should be positioned under the infant, as described under **Handling Suggestions** (page 8), while the caregiver's shoulder should very gently touch the baby. At this point, the baby is supported under the back and positioned on the shoulder as the caregiver moves up and backward.

Bedding: A standard crib mattress is most suitable for the baby with OI. Waterbeds and soft bedding should never be used.

Positioning: Infants who spend an extended period of time in the nursery should be repositioned regularly. The unusually soft skull can be flattened from prolonged time in any one position. Occasionally a gel pad is necessary to protect the back of the skull. Rolled blankets or sheets or soft foam wedges can support sidelying. Rib fractures, a malformed chest, etc., will preclude placing the baby in the prone position (i.e., on the stomach).

Preparing for Discharge from the Hospital: Parent education should include explanation and demonstration of the procedures for holding, lifting, diapering, and general infant care. The return demonstration will ensure that the parents are comfortable with each skill. If possible, these skills also should be demonstrated to other family members and friends who will be assisting in caring for the child at home. Reading material such as the brochure *Caring for Infants and Children with OI* is available free of charge from the OI Foundation and can be given to the family.

Because new fractures are to be expected, parents should also receive training in conjunction with the orthopaedic surgeon on how to recognize a fracture and protect the injured body part while traveling to the hospital or clinic. A letter on hospital letterhead stating that the child has been diagnosed with osteogenesis imperfecta can facilitate obtaining appropriate care if the family arrives at the Emergency Department or needs to seek treatment at a different facility.

Parents will need to acquire a car seat that, in some cases, will also be used as a baby carrier. A contoured foam insert may be needed to provide a good fit. See **Car Seats** (page 25) for details regarding car seats.

Parents should be advised to choose clothing with wide openings that allows them to slide the garment over the baby's arms or legs without pulling the limbs. Clothing without ribbons, buttons, pockets, and ruffles is also safer for the baby.

Discharge planning should include referral to a local OI support group or contact with another family of a child with OI (with their approval). Referrals also should be provided to a pediatrician, pediatric orthopaedist, physical therapist, and other services in the community that offer treatment and support for children with OI.

Primary Care

Children and Teens: In addition to care provided by orthopaedic surgeons, pulmonologists, and endocrinologists who specialize in pediatric patients, children with OI must receive primary pediatric services to maintain health and prevent illness. The primary care provider is an important resource for healthy living and preventive care as well as for common acute illnesses not directly related to the child's OI, such as otitis media, strep throat, etc.

The primary care staff needs to work closely not only with the child and family but also with the orthopaedic surgeon, physical and occupational therapists, and OI clinic or research facility, as appropriate. Multidisciplinary care is paramount for optimal outcomes. The primary care provider may be asked to provide referrals and recommendations to specialists and may also need to make recommendations for the patient's physical limitations in activities at school and in other settings. It should be recognized that parents and older children with OI become knowledgeable about both the disease and the special accommodations or limitations that may be needed.

Patients with OI should be seen by a primary care provider regularly, just like any other patient of the same age. Health care providers caring for infants and children in the primary care setting should be aware that osteogenesis imperfecta is a highly variable disorder, ranging from very mild to very severe. The OI Foundation can provide considerable reference material to caregivers (www.oif.org). Some children with the mild form of the disorder may have few fractures, whereas those with a more severe form fracture frequently. Some children are not able to stand independently for measurements of stature and may need to be measured lying down. Pressure should not be applied to bowed legs in an attempt to straighten limbs for measurement. The child may lag behind his or her peers in physical development and may not crawl or walk independently without intervention from physical therapy. See the **Physical and Occupational Therapy** section (page 14) for additional information. The patient may instinctively develop alternate methods of locomotion, such as commando crawling or scooting.

Hearing may be impaired. The patient may wear hearing aids and require more structured communication.

Referral to a pediatric dentist is especially important for patients with OI, who may also have manifestations of dentinogenesis imperfecta.

Despite the wide-ranging effects of OI on multiple body systems, parents and children still need information on normal child health and safety issues. Information should be tailored to the patient and family's specific situation. Always consider the patient's age and level of function, not size, when providing information or guidance. Occupational and physical therapists can be quite helpful with providing suggestions for adaptations and accommodations for patients with OI.

Transition to Adult Care: Transition to adult medical care may be difficult for patients who have received frequent, highly specialized care from pediatric specialists and children's hospitals. Families often have developed strong bonds with nurses, assistants, physicians, therapists, and other health care providers. Patients may have concerns about insurability, future

care with new health care providers, etc. However, transition to adult care can occur successfully for patients with OI if the process is carefully coordinated and initiated well before the patient outgrows a system or provider. It is helpful to:

- encourage the older child to be his or her own advocate, by speaking to health care providers directly and providing accurate information about his or her own medical history.
- provide the family with a referral list of physicians in the community who are familiar with OI.
- obtain signed "authorization to release information" forms so complete medical records can be sent to new health care providers.
- be aware of insurance requirements and work with the family to facilitate any transition between insurance carriers.

Adults: Ongoing primary care is essential for the adult. Presence of a chronic disorder does not preclude the patient from experiencing unrelated health problems. Patients with OI should receive care that follows the same guidelines for routine assessments as other patients. The health care provider needs to address childbearing and sexuality issues – just as he or she would with any other adult patient – while also considering the diagnosis of OI. Women with OI should receive the full spectrum of well-woman care.

The health care provider should understand that no two individuals with OI are exactly alike, and not all patients will have the same complications or secondary signs of the disorder. In adults after puberty, the fracture rate usually decreases as a consequence of hormonal and other metabolic changes affecting collagen and bone. Other medical problems related to the basic collagen defect, such as tendon, muscle, and joint problems, may assume more importance. Later in life, fractures may become more frequent, especially in women after menopause. Maintaining bone density is a primary concern for men and women. Recurrent dismissal of symptoms as simply an aspect of OI may lead to diagnostic errors.

All patients should be counseled to maintain a healthy lifestyle, which would include not smoking or quitting if they currently smoke, exercising safely within the spectrum of their abilities, and eating a healthy, well-balanced diet. Swimming and other low-impact recreational activities, performed with appropriate cautions, are often ideal for the patient with OI. Physical therapy may be ordered to assist in developing a targeted exercise program.

Nutrition

Children and adults with OI should be advised to eat a balanced diet, which includes a variety of vitamins and minerals and is low in fat and added sugar. Excessive weight gain should be avoided to reduce stress on compromised bones, lungs, and heart. Extra calcium does not reverse the collagen defect that causes OI and could lead to an increased risk of kidney stones. However, adequate calcium and vitamin D are necessary to optimize bone mass and prevent bone loss. Patients taking bone-altering medications may need supplemental calcium if dietary intake is insufficient, but a calcium supplement should be used only under the advice of a clinician. Because RDA guidelines were developed for people of average height and weight, the required amounts of nutrients may vary for people with OI.

Constipation is a problem for some patients. Eating a high-fiber diet, drinking plenty of water and other fluids (particularly for those patients prone to excessive perspiration), and being physically active may help reduce constipation. Medications may also be ordered to alleviate the symptom.

Some infants may show slow weight gain. Some toddlers and children with OI who are short in stature may eat very little at any one time, which could be mistaken for failure to thrive.

Medical Procedures

Previous experience can help dictate the best way to perform medical procedures for a patient. Parents, older children and adults with OI, and the primary care nurse are all resources for this information. The diversity of patients with OI makes it difficult to generalize and requires multiple options for procedures.

Assessing the Patient with OI: In addition to the information required in a medical history, the following information should be considered during the nurse's assessment:

- **Age** – Many individuals with OI are markedly short in stature and can be mistaken for someone who is chronologically and intellectually much younger.
- **Head Size** – Head size tends to be appropriate for age in persons with short stature so that there is the appearance of macrocephaly.
- **Eyes** – Assess for evidence of tinted sclera.
- **Hearing** – Assess for impairment that compromises conversations, safety, etc.
- **Teeth** – Assess for evidence of dentinogenesis imperfecta.
- **Drugs and Supplements** – Inquire about prescription medications as well as any herbs or dietary supplements. Some individuals receive drugs as participants in a research protocol.
- **Rods** – Since rodding surgery is a common treatment for people with OI, it is important to document the presence and location of rods. In some cases, rods may interfere with MRI, DXA, or CT studies or other radiology procedures.
- **Bleeding** – Some individuals with OI have a history of excessive bleeding. This is related to capillary fragility and may manifest itself in frequent nosebleeds, bruising, and greater than normal bleeding during surgery. Drugs such as aspirin may contribute to prolonged bleeding time.
- **Respiratory Function** – Many individuals with the more severe forms of OI have a compromised respiratory system due to scoliosis, chest malformation, or short stature. The compromise can be serious enough to impact activities of daily living and lower resistance to infection. Nurses are advised to be alert to the early stages of respiratory distress or respiratory failure to prevent a crisis from developing.

Immunizations: Patients with OI can and should receive all immunizations listed by the CDC immunization guidelines. "Chronic illness" is not a contraindication to immunization. However, logical precautions related to the patient's physical condition should be considered. It is important for the health care provider to keep in mind that patients with OI bruise easily, have fragile skin, and may fracture. Parents can help hold their child when the health care provider administers immunizations. The patient should never be held in a position where a twist or

sudden movement could fracture a limb. If possible, EMLA[1] cream or other topical anesthetic should be applied prior to the immunizations. The use of combined vaccines greatly reduces the number of injections for the child. Children who have developed a severe fear of needles or medical procedures may require slight sedation prior to receiving an immunization to reduce the chance of fractures.

Patients with OI may have higher baseline temperatures and can develop a fever indicating a reaction to immunization. If ordered by the clinician, parents may be counseled to use acetaminophen or ibuprofen as necessary to control the child's fever. Body size as well as age should be considered in choosing dosages.

Respiratory function may be compromised, and both adults and children are more susceptible to respiratory infection if there is thoracic malformation. Adults and older children with OI may be especially good candidates for the pneumonia vaccine. Flu shots also represent an option. Patients with OI should be encouraged to discuss these preventive measures with their primary care doctor.

Using Caution When Obtaining Blood Pressure:

- Guard against inflating the blood pressure cuff too tightly, because this could lead to bruising or fractures in patients with severe OI. An automatic BP cuff with the pressure preset cannot be controlled and should not be used.
- Avoid obtaining a blood pressure in an arm that has repeatedly fractured and/or has a bowing malformation, as the bone may be especially predisposed to fracture. The blood pressure may be obtained in the thigh for those patients with bilateral arm malformations.
- The blood pressure cuff size should be appropriate for the patient. Small-stature adults may need pediatric-sized equipment.
- Young patients may tolerate the procedure best if a parent holds the child on his or her lap. This will also assist in keeping the child still. To reduce the child's anxiety, demonstrate the procedure on a stuffed animal or doll and explain to the child that you are going to give the arm a gentle "hug."

Performing Venipuncture and Inserting IVs: There are special considerations when performing venipuncture or inserting an IV in children and adults with OI. Veins may be small and fragile. Patients, particularly those with Type I OI, may bruise easily. The skin is soft and thin due to poor quality collagen, and there is the risk of causing a fracture. It is beneficial to listen to information provided by parents and older children and adults with OI who can identify sites of previously successful venipunctures.

[1] Brand names included in this publication are provided as examples only, and their inclusion does not mean that these products are endorsed by the National Institutes of Health or any other Government agency. Also, if a particular brand name is not mentioned, this does not mean or imply that the product is unsatisfactory.

Parents should be asked if they would like to be involved in immobilizing their child. If they decline, they may help distract and comfort the child. Warming blankets, if available, may help in locating the small veins of infants and toddlers. On active infants and toddlers, use a blanket (papoose technique) to immobilize the child. Utilize neonatal or pediatric nursing staff assistance for difficult venipunctures. In addition:

- It is helpful to ensure that the patient is well hydrated the day before performing the venipuncture. Allow the patient to drink water the night before the test unless a scheduled test or surgery prohibits oral fluid intake.
- Reduce anxiety by offering a topical anesthetic, such as EMLA or Ela-MAX cream, to minimize discomfort.
- Tourniquets should be used with caution. Do not use a tourniquet if the patient has a current humeral fracture. Tourniquets may be used over either the sleeve of the shirt or a wrap of kerlex or coban. A manual blood pressure cuff could be used as a tourniquet on the patient with severe OI because it exerts a wider dispersal of pressure on the bone. The cuff should not be inflated over 80 mm Hg.
- Minimize the length of time the tourniquet is in place.
- Do not pull on the extremity or bend it in an unnatural position. Any twisting motion or pressure can cause a fracture.
- The limb should be supported on a flat surface. The arm board should support the entire forearm so there is no pressure on the shaft of the ulna and radius. An arm board can be used to perform a venipuncture using a hand or foot vein. An arm board should not be used on a bowed extremity.
- To accommodate small veins, use the smallest needle size feasible to obtain samples for lab tests.

CPR: Nurses should be aware of a patient's DNR status or "No CPR" order and should adhere to the rules of the institution when caring for any patient. As a lifesaving measure, CPR can be performed on patients with OI, despite the possibility of higher risk of rib fractures. In one report, manual chest compressions (two-finger method) on an infant with Type II OI with multiple pre- and postnatal fractures did not result in new rib fractures as evidenced by serial chest radiographs (Sewell & Steinberg, 2000). The force used for the compressions can be adjusted to achieve the desired depth in each situation. Children with OI will likely require less force than healthy children to achieve the proper compression depth.

When performing CPR on an adult patient with OI, the patient's chronological age should be used as a reference for the proper ratio of compressions to breaths, keeping in mind the size of the patient. Less force may be required to achieve desired compression depth.

Physical and Occupational Therapy

Children with all types of OI often have motor delay and can be assisted by developmental assessment through referral to rehabilitation professionals, such as physical therapists, occupational therapists, and physiatrists. The increased risk of gross motor delay – caused by skeletal malformation and decreased strength and endurance – warrants early referral. Children

with mild OI may only require occasional services. Children with Types III and IV OI will require more extensive assistance. Every effort must be made to provide the child with a means of independent mobility. Equipment recommendations may consist of bracing, walkers, or crutches for ambulation and ADL (aids to daily living) adaptive equipment. In the case of non-ambulatory patients, consideration will be made for manual or power wheelchair mobility. As the child enters school, mobility is particularly important because it facilitates age-appropriate social interaction.

The need for strength and endurance training, postfracture rehabilitation, and continued rehabilitative treatment frequently persists later in life. Adults may need to work with a rehabilitation professional to develop an appropriate program that can be performed at home or at the local gym. Maintaining bone density, developing strength, expanding cardiorespiratory function, and remaining mobile are important goals for the therapy program for adults as well as children with OI.

The therapist must partner with parents and patients to set feasible and appropriate goals for formal physical therapy and/or for exercise and recreational activities at home. Programs based on the individual's interests – which include activities that are enjoyable as well as beneficial – are more likely to be successful.

Emergency Department Care

Patients with OI may have substantial experience with fracture management and orthopaedic procedures due to ongoing medical and surgical needs. They are often very knowledgeable about their health status and problems associated with OI. Accordingly, the opinions, requests, and instructions of adult patients and parents of children with OI should be respected.

Children and adults with OI may also present to the Emergency Department with problems unrelated to OI that are seen in the general population and need to be evaluated as such.

General Guidelines: A fall, head injury, accident, nontraumatic fracture, or respiratory compromise may bring the OI patient to the Emergency Department. In these situations, the degree of injury may be more severe than typical for the degree of trauma. When informed that a patient has been diagnosed with OI, medical personnel should record this information prominently in the hospital chart.

The nurse should also inquire if the patient has had rodding surgery. See **Rodding** (page 19) for detailed information on rodding. Nurses need to take extra care when handling the patient's limbs or removing clothing from a limb that has been rodded. Some rods interfere with radiology studies, such as MRI, CT, and dual energy x-ray absorptiometry (DXA).

Caution should be taken when transferring a patient. Sudden pulling of limbs, neck, or spine should be avoided. Never twist, bend, apply pressure, or try to straighten a limb, since some limbs cannot be straightened due to an existing malformation of the bone or contractures. Many patients have scoliosis, which affects positioning. Parents, family members, and older patients can provide guidance about appropriate alignment for the patient.

Parents should be allowed to stay with their child at all times in the Emergency Department to comfort their child and help with transferring or positioning the child. This should include accompanying the child into the examining room and Radiology Department.

Side rails of stretchers should be padded to prevent the child or small adult from slipping through an opening and to protect against injury. Always make sure the side rails of the hospital bed are secure. Use caution when tightening straps on a stretcher, applying splints, or using restraints so as to avoid fracture. Blankets and sheets should be kept loose, and care should be taken when removing them to prevent catching the patient's fingers or toes in a fold of the blanket or sheet.

Medical equipment sized by age of the patient may not be appropriate for the patient with OI. Small adult or pediatric-sized equipment may be needed for some adult patients. Equipment for the head or face, such as an oxygen mask, is usually determined by age.

Acute Fracture Care: Bones affected by OI fracture easily, and therefore, the severity of a fracture is not always related to the level of trauma. No external sign of injury may be apparent. Soft tissue injury around a fracture is less likely because the bone usually cracks before the ligaments and tendons tear. The patient may experience a serious fall or accident with no fractures or may unexpectedly fracture performing normal daily activities.

Patients frequently experience microfractures that are not visible on x ray immediately following the injury. Due to low bone density, possible nondisplaced fracture, decreased soft tissue reaction, and bone malformation in some patients, the fracture may not be discernible. Followup x rays 1 to 2 weeks after the event may reveal the fracture due to the formation of callus. If a fracture is suspected due to pain, swelling, the patient's inability to use the limb (especially in a child), or the patient's or family's insistence of likely fracture, the limb should be treated as if it is fractured until followup x rays are obtained. If the bone is indeed fractured, the patient will be much more comfortable with the limb immobilized. If a fracture is not diagnosed, a few days of immobilization should not cause permanent damage.

If an orthopaedist is not immediately available, appropriate splinting techniques should be used to immobilize the affected limb until there is definitive orthopaedic treatment. If the patient uses an orthotic device, it can often serve as an effective splint. Bone malformations require added consideration when immobilizing a fracture.

Pain: It is a myth that patients with osteogenesis imperfecta feel less pain than patients without OI. If possible, the staff should minimize handling until after pain relief is administered. Do not hesitate to use splints and wraps to reduce motion of a painful limb and to minimize spasm. Adequate pain relief is paramount prior to any procedure, assessment, or x ray.

Other Conditions Secondary to OI Seen in the Emergency Department: Staff in the Emergency Department may also see patients with OI for respiratory and cardiac problems. Any adult with OI, but particularly those with Type III OI or those with short stature, may have compromised cardiorespiratory functions due to malformation of the rib cage, scoliosis and kyphosis, rib fractures, pneumonia, etc. Patients may have heart valve problems, including aortic valve insufficiency, aortic aneurysm, mitral valve regurgitation, and mitral valve prolapse. Medical therapy for mitral valve prolapse may include antibiotics to prevent rhythm abnormalities and valve infections.

Patients should be instructed to seek prompt treatment for respiratory infections and difficulty breathing. Due to the decreased chest volume, restrictive pulmonary disorder is commonly seen in severe cases of OI. Pulmonary complications can occur due to rib fractures, muscle weakness of the chest wall, heart valve disorders, chronic bronchitis, or asthma. Respiratory complications including pneumonia represent a significant cause of death for those with Type II and III OI.

In adults with basilar invagination of the skull base, complications may occur with central (brain stem) respiratory control. Headache upon coughing may be an important clinical symptom.

Medical bracing of the ribs will not improve pulmonary function in adults. However, controlled oxygen therapy, BiPAP, inhaled bronchodilators for asthma, inhaled glucocorticoids, and antibiotic use for chronic bronchitis may be indicated.

Some patients have hyperhydrosis and may need significant fluid replacement. Otherwise, metabolic chemistries should be unremarkable if there is no dehydration.

Medication dosages may need to be adjusted for patients with OI. Medicines should be titrated to body weight, not age, even in the case of the adult patient with OI.

Kidney stones are sometimes associated with OI and can cause hematuria and flank pain. OI is not related to a lack of calcium. High urine calcium levels are observed in some patients.

Child Abuse Allegations: The child with OI may present to the Emergency Department with a fracture that is more severe than the reported trauma. Thorough examination may reveal multiple fractures in various stages of healing. These signs are commonly taken as evidence of non-accidental injury or child abuse. Health care providers unfamiliar with OI may not recognize an undiagnosed case of OI. Medical professionals need to be aware that no particular type of fracture is typical or indicative of OI (Marlowe et al, 2002). Clinical features vary widely. Children with mild OI may have few obvious clinical features.

It has been estimated that seven percent of children who have unexplained fractures have an underlying medical condition (Wardinsky et al, 1995). Other disorders that may include unexplained fractures are Ehlers-Danlos Syndrome, hypophosphatasia, and disorders of vitamin D metabolism. The physician and nurse should consider these uncommon conditions when a patient presents to the Emergency Department with fractures of uncertain cause.

Parents are advised to carry a letter from the child's primary care physician stating the OI diagnosis and provide hospital staff with this information. Such documentation should be prominently displayed on the patient's chart.

Surgical Services

The surgical nurse should be aware of the special needs of patients with OI to ensure safe and effective care. This care begins in the preoperative setting by providing clear communication and reassurance to the patient and his or her family. The nurse should carefully listen to and address all concerns to optimize communication and the patient's clinical outcome. Signage indicating

the diagnosis of OI should be placed on the patient's hospital chart, bed, wheelchair, etc. The surgical and post surgical needs of the patient with a hearing impairment must also be taken into consideration.

Anesthesia: Some anesthesia risks are associated with patients with OI that distinguish them from the general population. Anesthesia personnel need to be aware of the susceptibility of fracture from movement, impact, or stress. Alternative procedures for intubation, such as fiber optics inserted nasally, may be necessary when treating some patients. Dosage may also be affected by the patient's smaller body size.

Chest and rib malformations and scoliosis may compromise breathing. Other risks include fragile dentition, joint stiffness, or heart valve disease.

The small stature of a person with moderate to severe OI often determines the choice of equipment. The endotracheal tube size used should be determined by the size of the head instead of the size of the body.

Patients with OI can exhibit increased body temperature during anesthesia and after surgery. The reason for this is unclear but may be related to an increased metabolic rate. The increased temperature is most often not associated with malignant hyperthermia. Precautions, such as avoiding the use of warming blankets or heavy drapes, are often effective and sufficient. Occasionally, ice packs or other cooling measures may be needed.

Some anesthetic agents such as atropine should be avoided because they may exacerbate increased body temperature. In general, anesthesia is safe and well tolerated in children and adults with OI.

Transferring the Patient: In the operating room, the patient may feel apprehensive about transferring from the stretcher to the operating table. Explaining your intended actions and then moving the patient slowly may alleviate anxiety. It may be helpful to use a roller when transferring the patient to eliminate undue stress on any limbs.

Positioning the Patient: Positioning the patient for surgery requires awareness of specific needs for the patient by the surgical nurse, anesthesiologist, and surgeon. Skeletal malformations necessitate extra planning and attention. All limbs should be supported and well padded. Soft padding may be needed to prop up bowed legs or to support the patient's curved spine. Keep in mind that the patient's skin is thinner and more prone to bruising than that of a patient without OI. Restraints should be applied after the patient is relaxed.

Intubation: Intubation can be challenging due to fragile teeth, scoliosis, neck malformation, and joint laxity. Care should be taken to avoid hyperextending the neck when inserting an endotracheal tube. Alternative procedures for intubation, such as fiber optics inserted nasally, may be necessary when treating some OI patients. The endotracheal tube size used should be determined by the size of the head instead of the size of the body. Spinal malformation, such as scoliosis or kyphosis, may impair pulmonary function. The occurrence of restrictive lung disease and cardiac problems is increased (Herring, 2002).

Rodding: Rod insertion is a common surgical procedure performed on patients with OI. Rodding is most often used to treat children with moderate to severe OI. In teens and adults, rodding and other surgery is usually reserved for difficult fractures that are not healing well or for alignment problems. Rodding is performed to correct long bone malformation or decrease fracture recurrence at a particular site. It is performed more commonly in the lower limbs than upper limbs. The style of rod and the purpose of the surgery will determine the specific procedure. Osteotomies may be performed and wedges cut from the bone to correct malformation. An intramedullary rod is then inserted. Reaming of the medullary cavity may be required. The limb is immobilized in a cast until union of the bone is achieved. Depending on the style of rod chosen, the rod may need to be replaced as the child grows.

Specific Recommendations for the Recovery Period: Based on the diagnosis of OI, the following procedures and precautions are typically followed:

- Obtain only one blood pressure upon arrival at postanesthesia care unit, unless clinical condition requires more frequent monitoring. Use a manual BP cuff. Automatic cuffs can cause fractures.
- Closely monitor airway patency with careful head positioning, due to limited range of motion of the head.
- Avoid hyperextension of the neck.
- Administer appropriate fluid hydration according to weight, due to tendency for dehydration.
- Closely monitor IV patency to reduce the need to reinsert an IV.
- Monitor pulmonary function closely.
- Support extremities at all times without twisting or hyperextension.
- Use pillows and pads when positioning the patient for comfort.
- Move the patient's body as a whole unit.
- A child in diapers should never be held up by the legs for diaper changes. Two persons should be available to change diapers. If only one person is available for the diaper change, one hand should be placed under the buttocks with the child's legs supported with the forearm while the diaper is positioned with the other hand.

Genetic Basis and Diagnostic Testing for OI

Genetics: With rare exceptions, OI results from mutations in the type I collagen genes and is considered to be a dominantly inherited disorder. On the basis of a limited number of population surveys, the overall frequency of OI in the general population is about 1 in 20,000. Because some infants die at birth and would not be included in these surveys, the birth incidence is slightly higher, perhaps 1 in 15,000 -18,000 births. In families in which OI occurs in more than one generation with clearly dominant inheritance, the risk of recurrence of OI is 50 percent for each pregnancy.

When parents who have no symptoms of OI have a child with OI, they will inquire about how this occurred in their family and about the risk of recurrence. For the great majority of these families (about 90 percent), their child's OI was caused by a new mutation that took place in the egg or sperm near the time of conception. Their risk of recurrence in subsequent pregnancies is

approximately equal to the risk of OI in the general population. In the remainder of these families (about 10 percent), the child's OI results from mosaicism for the mutation in one parent. A mosaic parent has the mutation in some of the cells of his or her body, including some of the egg or sperm cells. The mosaic parent usually appears to be unaffected or only mildly affected. Parental mosaicism can be determined by genetic testing. For these parents, the risk of subsequent affected children is between 10 and 50 percent per pregnancy.

There are very unusual forms of OI that seem to be inherited in a recessive fashion, which means that each parent is a carrier and contributes one altered gene each to their child, who is then affected with OI.

Another aspect of OI genetics is its prevalence in the general population, that is, its occurrence among all living individuals. Individuals with OI will have children of their own. In general, this occurs more frequently at the milder end of the OI spectrum. When prevalence is considered, children with OI who are born into families with OI will constitute a larger proportion of cases with OI. In a recent survey in Finland (Kuurila et al, 2000), about 65 percent of individuals with OI were in families where a prior generation was affected, and the remaining 35 percent were isolated cases without a family history.

Osteogenesis imperfecta is a disorder of connective tissue. Defects in the structure or quantity of type I collagen cause most cases of OI. Type I collagen is the primary structural protein of bone and skin. It is composed of three chains that are twisted together to form a triple helix. Two of the chains are identical. These are called the alpha 1, or α1, chains. The third chain is similar to the first two but not identical to it. This is called the alpha 2, or α2, chain.

Each of the three chains is made up of uninterrupted repetitions of the amino acid triplet Gly-X-Y, where Gly is glycine, X is often proline, and Y is frequently hydroxyproline. The presence of a glycine at every third position along the chains is crucial for proper folding of the collagen helix inside the cells where it is produced. Glycine is the smallest amino acid and the only amino acid that can fit in the internal space of the triple helix. Bonds formed between glycine residues on one chain and X-position residues on an adjacent chain are important for the stability of the helix. After the collagen helix is formed in the cells, it is secreted into the matrix and processed into its mature form. The mature collagen helices then spontaneously assemble into bundles of collagen, called fibrils, in the extracellular matrix of bone and skin.

OI is usually caused by a mutation in one of the two genes, either COL1A1 or COL1A2, that code for the α1 and α2 chains of type I collagen, respectively. Patients with Types V and VI OI do not have mutations in type I collagen; the gene(s) involved in these conditions is not known. For mutations in type I collagen, there is a general correlation between the type of collagen mutation and the Sillence types.

Type I OI is usually caused by a quantitative defect of the α1 chain. One copy of the gene does not produce collagen chains so that patients make only half the proper amount of type I collagen. All of the collagen made by these patients is of normal structure; it is simply the amount that is reduced.

Types II, III, and IV OI are caused by structural mutations in one of the collagen genes. About 85 percent of these mutations are changes that result in the substitution of a larger amino acid for one of the glycine residues that should occur in every third position along the chains. The term used by geneticists for these mutations is "missense mutations." Subsequently, folding of the collagen helix inside the cell is delayed at the substituting amino acid, allowing time for extra sugar groups to be added to the collagen alpha chains. The remaining 15 percent of collagen structural mutations are more unusual rearrangements.

Identifying the OI-causing mutation contributes to genetic counseling for the family and to OI research, but the mutation is not the only factor that determines the severity of OI in an individual patient. In some cases, patients with an identical collagen mutation may have phenotypes (i.e., clinical features) that differ enough that they are classified into different Sillence types. For optimal clinical care, the key is to treat each patient individually rather than by the "label" of his or her Sillence type or specific mutation.

Diagnostic Testing for OI: As with all genes in the body, DNA is the basis for inheritance. DNA contains sections that are expressed (exons) and sections that are not expressed (introns). DNA is translated into RNA, which contains only those sections that are expressed. The RNA is then used to make proteins, which are the building blocks for the human body. The protein, RNA, and DNA can all be tested to diagnose OI.

- **Biochemical Testing of Collagen Protein** – Biochemical (protein) testing allows researchers to learn about the structure and amount of the collagen protein that the cells of the body are producing. About 85 percent of people with OI will have a positive collagen protein biochemical test abnormality. Fifteen percent of cases diagnosed clinically and radiographically as OI will have a negative collagen protein biochemical test. This test requires a skin biopsy to obtain living cells that produce collagen. The punch biopsy, about 1/16 inch diameter, is taken from the arm or leg under idocaine anesthetic. Foreskin taken during circumcision can also be used. The skin cells are grown in a culture medium. The collagen produced by the cells is isolated from both the culture medium in which the cells are growing (secreted collagen) and the inside of the cell (intracellular collagen). Collagen chains are compared by gel electrophoresis to the collagen chains of control subjects without OI. Patients with OI who have structural defects of collagen often show two populations of chains, one with normal gel migration and one with delayed migration. This results in protein gel bands that appear wider in OI than in controls or that may even migrate as two distinctly separate bands on the gel. Diagnosis of the collagen quantitative defect of Type I OI is also apparent on gel electrophoresis.

- **Sequencing RNA or DNA to Identify the Specific Collagen Mutation** – RNA or DNA sequencing allows researchers to determine the specific change in a person's genes for type I collagen that causes OI. Either RNA or DNA testing can locate the mutation that causes OI if it results in changes in the amino acid sequence of the protein. For many mutations, both methods are equally sensitive, but the RNA-based testing will not identify a mutation if the mutation results in an unstable RNA (i.e., premature termination codons). Such mutations are only detectable in the DNA.

- **RNA (cDNA)-based Testing** – This approach uses the RNA (complementary DNA) made by the COL1A1 and COL1A2 genes. RNA-based testing usually requires a skin biopsy, although in some instances enough collagen RNA can be isolated from white cells. The RNA is then copied to make a DNA copy, which is then sequenced in its entirety.

- **DNA-based Testing** – DNA sequencing can be performed using a routine blood sample or skin biopsy. Because the collagen genes are moderately large, laboratories do not sequence entire genes. Instead, the genes are tested exon by exon (i.e., the expressed portions of genes). In this strategy, regions are amplified using the polymerase chain reaction and then either sequenced directly or tested by a technique such as conformation sensitive gel electrophosesis (CSGE) to detect differences between the two copies of the gene. Only exons that have abnormal CSGE findings are sequenced. This method detects most structural defects of collagen protein (those that cause Types II, III, and IV OI) and also detects chain termination mutations that cause Type I OI. The DNA-based testing is more likely than the RNA-based testing to detect mutations at exon boundaries. However, some mutations are overlooked because not all mutations cause abnormal CSGE. No functional correlation between mutation and biochemistry is determined in this testing.

- **Radiography** – X rays should be obtained on any child in whom OI is suspected. X rays can usually confirm the diagnosis and may reveal osteoporosis, bowing of long bones, and vertebral compressions, depending on the severity of the condition. In some children and adults with mild forms, these alterations may be difficult to identify. In addition, x rays can help identify subclinical or old healing fractures. Lateral x rays of the skull in infants may show wormian bones, which can be a component of OI. Wormian bones are not seen in all patients with OI and are not unique to OI.

- **Dual Energy X-ray Absorptiometry (DXA)** – DXA (bone density testing) can be a useful adjunct to clinical examination and diagnosis. However, the bone density must be compared to age- and sex-matched peers. Z-scores *(not* the T-scores routinely used for adult patients) are essential for analyzing bone densities in children. Generally, a Z-score of -1 to +1 standard deviation (SD) is considered within normal range, with 0 being the mean for healthy children of the same age and sex.

- **Urine and Blood Tests** – Urine and blood tests, other than DNA analysis, are not conclusive or diagnostic for OI. They may, however, be used to rule out other conditions, such as hypophosphatasia.

Testing for Risk of Recurrence: Most patients with OI have unique collagen mutations. Approximately 300 OI-causing mutations in type I collagen are currently recorded in the international Database of Human Type I and Type III Collagen Mutations. Families with one affected child are often concerned about the possibility of recurrence and should be referred for genetic counseling. Once a specific OI-causing mutation is identified through collagen biopsy or DNA analysis of the affected family member, further tests become possible. The child's biological parents can have DNA testing performed on a blood sample to determine whether one of them is a mosaic carrier for OI. Mosaic carriers may have no symptoms of OI but carry the mutation in a percentage of their cells.

Prenatal Testing: When OI is present in one of the parents or in a previous child in the family, prenatal testing is often requested. Ultrasound of the fetal skeleton or amniocentesis or chorionic villus sampling to obtain cells and DNA are the available tests.

- **Ultrasound** may detect bone malformation as early as 16 to 20 weeks gestation. It is extremely difficult to differentiate between Types II and III OI based on ultrasound.
- **Amniocentesis** is useful for molecular detection of previously known mutations but not for biochemical tests of collagen protein.
- **Chorionic villus sampling (CVS)** can be performed between 10 and 13 weeks of pregnancy. The cultured chorionic villi cells can be used for molecular detection of a previously known mutation or to detect the protein abnormalities previously identified.

Research: Experimental Treatments

Bisphosphonates: Experimental drugs for OI, including bisphosphonates, are being investigated at multiple centers in the United States and in other countries, either in clinic or clinical research settings. As significant numbers of patients are currently receiving bisphosphonates, the primary care nurse should be aware of the potential benefits and drawbacks.

Bisphosphonates are potent inhibitors of bone resorption (breakdown) and were originally developed as treatment for postmenopausal osteoporosis and hypercalcemia. They are currently approved by the U.S. Food and Drug Administration (FDA) for the prevention or treatment of osteoporosis and the treatment of Paget's disease of bone in women and men. They are frequently prescribed "off label" for adults who have OI with symptoms of osteoporosis. In adults, bisphosphonates can stabilize bone density. And in many cases of bone density loss due to osteoporosis, bisphosphonates can increase bone density.

In the early 1990s, some investigators began treating children with OI with intravenous pamidronate, a second-generation bisphosphonate (Glorieux et al, 1998). Reports appeared that pamidronate decreased pain and fracture rate as well as improved mobility and bone density in affected children. Research continues with this drug and the newer IV and oral bisphosphonates. Questions that remain to be answered include long-term side effects as well as impact on bone quality and bone health, the dosing schedule that maximizes benefits and minimizes detrimental effects, and the time to end or cut back therapy as well as the benefit to patients with milder OI. Potential drawbacks of bisphosphonate administration seem to be emerging from wider studies. Surgeons have reported delayed healing of osteotomies in some cases. There are anecdotal reports of increased bone brittleness and fracture rate after prolonged treatment with bisphosphonates.

Bone Marrow Transplant: A highly experimental and unproven treatment for OI is bone marrow transplantation. Although articles published from this research suggest a positive effect on growth and fracture rate, there is little data to support these claims. At this time, bone marrow transplantation is not a recommended treatment for OI.

Gene Therapy: While gene therapy holds promise in theory, the actual application of such therapies is not imminent.

Growth Hormone (rGH) Therapy: Short stature is a significant feature of osteogenesis imperfecta. Studies of growth hormone administration reported that some children with Type I or Type IV OI responded to the treatment with increased linear growth. A few children with Type IV OI attained normal height curves. Responders to rGH also experienced positive changes in bone histology and small increases in bone density. Combining growth hormone therapy with bisphosphonates is being investigated.

Social Services

The services that social workers provide can be very valuable for patients with OI and their families. There are many issues involved in caring for a person with OI, such as education, funding for specialized equipment and medical services, and coping with and adjusting to this life-long disorder. Knowledge of the resources available to deal with these issues will greatly benefit families and individuals coping with OI.

Social services can assist with identifying the following resources:

- Hospital and community-funded programs for counseling, support, and information
- Early intervention programs for infants and toddlers
- Public education services for eligible preschool children
- The Federal law, *Individuals with Disabilities Education Act* (IDEA)
- The National Dissemination Center for Children with Disabilities (NICHCY), at 1-800-695-0285, and each State's office of special education, which is within its department of education
- Each State's Children with Special Health Care Needs Program. This program provides health and support services to children with special needs (from birth to age 21) and their families. Eligibility and services vary from State to State. The *Directory of State Title V CSHCN Programs: Eligibility Criteria and Scope of Services* can be accessed at http://cshcnleaders.ichp.edu/TitleVDirectory/directory.htm.
- Each State's departments of social services and public health (which may administer some of the programs)
- Osteogenesis Imperfecta Foundation
- Easter Seals
- Family Voices
- Each State's vocational rehabilitation program
- Mental health services
- Independent living centers
- Nutrition counseling
- Medicare, Medicaid, and Social Security information
- Mercy Medical Airlift program

Transportation

Parents will often ask the nurse about the best way to transport their child in different situations. Equipment for infants and children should meet local requirements for safety, provide head support, be easy to use, and be appropriate for the child's size and weight. Commercially

available equipment may need to be modified to meet the needs of a smaller than average infant or young child. Because of the child's slow growth, the patient will most likely need to remain in a car seat or booster seat much longer than his or her friends. Therefore, it is important to be sensitive to the child's feelings.

Some adults with OI also require special accommodations for travel. The use of booster seats, harness style seat belts, and professionally installed tie-downs for wheelchairs may be necessary. Consultation with an experienced occupational therapist may help to determine the best fit and most appropriate equipment.

Car Seats: Car seats are geared to the child's weight and ability to sit up. All car seats should be approved for safety and anchored correctly in the vehicle. It is not safe to place foam padding between the plastic shell and the padded cover. This will compress in the event of a car accident. If a softer surface is required, it is better to use a folded, thin baby blanket. Removable cotton slipcovers are suggested because they are cooler, and children with OI often perspire excessively. It is always best to place a car seat in the back seat of the vehicle. Many parents place a label on the top edge of the car seat stating the diagnosis, physician name and phone number, emergency contact phone number, and HANDLE WITH CARE instructions in the event of a car accident.

- **Infant Car Seats** are designed for children who weigh less than 20 pounds. Features to look for include a well-padded harness and a head hugger support pillow. This commercially available U-shaped pillow is used to position the baby's head at midline. Small rolls of towels, baby blankets or other padding can be added to hold the child's hips in line. Some infant car seats can be fitted with a contoured foam insert.

- **Full Size Car Seats** are designed for children who weigh more than 20 pounds. Additional features to those already listed include low sides, a 5-point harness, and no flip-down bar. Such seats are more easily adapted to children in different types of casts. Examples of infant seats and full-size car seats suitable for children with OI include the Snug Seat (www.snugseat.com) and the Britax Roundabout (www.britax.com).

- **Booster Seat** laws vary from State to State. Some States have adopted laws requiring booster seats for children age 8 to 12 who are shorter than 4 feet 9 inches or weigh less than 60 pounds. Some States are also advising adults of short stature to consider using a booster seat in private vehicles. Booster seats offer significant protection to the passenger, and their use is recommended. There are two types of booster seats: high backs and backless. Both can be used in any vehicle equipped with lap-shoulder belts if the passenger weighs more than 40 pounds. If a backless seat places the head above the top of the car seat, a high-back booster is recommended to safely support the head.

Transporting a Child in a Cast: Parents should discuss different cast options with their physician prior to surgery to allow adequate preparation to bring the child home from the hospital. Any time a child is in a spica cast or long leg cast, especially after a rodding surgery, special car seat arrangements may be needed. A standard car seat may be used if it can be set in a reclining position that still allows for easy entry and exit. If that is not possible, several

manufacturers make child-size car seats that are especially adapted to accommodate spica casts or braces. In many communities, the Easter Seals organization or children's hospital has programs to rent or loan these seats to families. The seats can also be purchased or rented from a local durable medical equipment company, but they may need to be ordered in advance. A prescription from the physician is usually required for a spica car seat. Some insurance companies provide coverage of at least part of the purchase or rental cost. Older children who are too large for a car seat may require the use of a vest-type restraint that allows them to safely recline on the back seat. The E-Z-On Vest Company (800-323-6598 or www.ezonpro.com) sells commercially available vests that meet this need.

Parents should become familiar with the mechanics of the car seat before discharge day. A child in a cast is awkward and heavy to handle. By using good body mechanics, the parents will avoid injury to themselves or additional injury to their child.

Pain management options should be discussed with the physician during the discharge planning period. Administering a dose of pain medication prior to the trip home may allow maximal comfort for the child while riding in the car. Additional support and comfort can be added to the seat by using soft padding around the child.

Other Equipment: A stroller is an important piece of equipment for any child. For the child with OI, the following features should be considered when purchasing a stroller: light weight; sturdy; easy to fold; adjustable seat positions allowing reclining, semireclining, and upright sitting; support for the spine and head; and easy entry and exit (i.e., no leg holes or fixed bar across the front). It can be very helpful if the stroller is wide enough to accommodate casts. Strollers that have a good suspension and swivel wheels provide a smoother ride than other models.

Travel by Airplane: If it is necessary to travel by air to receive medical treatment in another city, families and adult patients should be informed about the various Mercy Medical Airlift programs that function in each state to provide air transportation. If the patient/family is using a commercial airline, they should inform the airline prior to the departure date about any special needs and become knowledgeable about rules related to traveling with oxygen, wheelchairs, or walkers.

Public Transportation: Children and adults with OI who use public transportation, such as city buses, school buses, and taxi cabs, should be made aware of some safety concerns. The patient/parent should look for appropriate use of wheelchair tie-downs, avoid riding in the back of a bus, choose to ride in the back seat of a taxi or other passenger vehicle, and wear seat belts. Harness-style seat belts are available for installation in some school buses. The child with OI should be seated in a middle seat of the school bus to reduce "bouncing" when the bus travels on rough surfaces. These concerns should be discussed with the health care provider. Some communities require referral from the physician to gain access to paratransit programs.

Air Bags: Air bags in automobiles may present a risk of injury to drivers and passengers who have OI. If the driver must sit closer than 10 inches from the steering wheel, an on-off switch can be installed that allows the air bag to be manually disabled. Any decision to disconnect an air bag needs to be discussed by the person with OI and his or her physician. It is advisable to disconnect

the air bag only when the physician feels that injury from the air bag is a greater risk than injury from hitting the steering wheel, dashboard, or windshield in the event of an accident. Injury from hitting these areas can occur even with the use of seat belts. Newer car models have air bags that deploy with less force than older models. The National Highway Traffic Safety Administration (NHTSA) provides the form "Request for an Air Bag On-Off Switch" and the accompanying brochure, *Air Bags & On-Off Switches: Information for an Informed Decision.* This form and brochure are available at the NHTSA Web site www.safercar.gov/airbags, NHTSA hotline 1-800-424-9393, AAA Clubs, and State motor vehicle departments.

Legal Responsibility

The nurse who is new to caring for a patient with OI may have concerns about legal liability if the patient is injured while in the nurse's care. As in any similar situation, it is important for the nurse to be fully informed about the hospital or employer's guidelines. It is always advisable to cultivate a positive relationship with the patient and the patient's family by making a good faith effort to understand the special needs of the OI patient and to be attentive to information provided by the patient, parent, or spouse.

Appendix 1

Quick Tips:
Caring for the Patient with Osteogenesis Imperfecta

General:

- Enlist parent or adult patient support when caring for a person with OI.
- Use pediatric-sized equipment as indicated for adolescents and adults with OI who are short statured.
- It is preferable to use manual BP cuffs. Use caution if the arm has repeatedly fractured or has a bowing malformation. Bowing of a limb may result in a higher than expected BP.
- Insertion of IVs may require additional stabilization of the skin over the insertion site. Be aware that the patient's skin may be more thin and fragile than that of patients without OI.
- Short stature may affect the appropriate dosage of medication. Weight, more than age, should be taken into consideration.
- Do not rely on the patient's appearance to indicate his or her physical or intellectual age.
- Patients may have a higher baseline temperature, perspire more, and be more sensitive to warm temperatures than other patients. Fever, however, should not be dismissed.
- If a patient is self-splinting a limb, it may indicate a fracture. However, the patient may not show outward signs of pain at the time a fracture occurs.
- Fractures may not be immediately evident on x ray.
- Measure lengths instead of heights for patients who cannot stand. Leg lengths may differ. Length should be measured on both sides of the body.
- Late fontanel closure is seen in some patients. The fontanels may remain open until age 3 or 4.
- Fractures can occur with a remarkable lack of force. Patients may fracture due to a sneeze, standing on tiptoes, or even by turning a page in a book.
- Address the patient at his or her height by crouching, kneeling, or sitting.

Handling:

- Do not underestimate the fragility of patients with OI. Patients with mild OI may have few visible signs of their fragility.
- Never twist, jerk, or bend a limb.
- Evenly support the head, trunk, and buttocks when lifting a baby.
- When handling a patient with OI, regardless of age, move in a slow, methodical, and gentle manner.
- Listen to the patient or parent for assistance with safe handling.
- Do not grab the ankles when changing a diaper. Lift with one hand under the child's bottom.
- Do not attempt to straighten a bowed limb or try to force a contracted joint to straighten.
- Parents may prefer to wrap or splint the fracture themselves instead of having the fractured bone casted. However, parents must have good judgment and be able to splint or wrap the fracture properly.
- Place signage indicating the diagnosis of OI and "fragile bones" on the child's bed, wheelchair, and hospital chart.
- Delayed development of head control may be complicated by a relative macrocephaly. Care and caution are advised when supporting the child's head.
- Avoid bouncing or sudden movements when handling the patient.

Appendix 2

Sillence Classifications of OI

Type	Features	Inheritance
I	Stature is normal or slightly shorter than average compared to unaffected members of the family. Little or no malformation of extremities, blue sclera, hearing loss in 50% of patients. Further subdivided into Types I-A & I-B based on absence (A) or presence (B) of dentinogenesis imperfecta. Dentinogenesis imperfecta is rare.	Autosomal dominant
II	Lethal in the perinatal period. Minimal cranial mineralization, beaded ribs, compressed femurs, marked long bone malformation, platyspondyly (vertebral compressions). Sclera dark blue/gray.	Autosomal dominant (new mutations) Parental mosaicism
III	Very short stature. Progressive malformation of long bones, usually with moderate malformation present at birth. Scleral hue varies, often lightening with age. Potential for hearing loss. Dentinogenesis imperfecta common but not present in all patients.	Autosomal dominant Autosomal recessive (extremely rare) Parental mosaicism
IV	Variable short stature and mild to moderate bone malformation. White or blue sclera. Hearing loss occurs in some patients. Further subdivided into Types IV-A and IV-B based on absence (A) or presence (B) of dentinogenesis imperfecta. Dentinogenesis imperfecta common.	Autosomal dominant Parental mosaicism

Appendix 3

Glossary

Allele: One of the two copies of each gene containing specific inheritable characteristics.

Autosomal: The gene for this disorder is not on a sex chromosome (X or Y), which indicates that the abnormal gene can affect males or females equally.

Basilar invagination: Also referred to as Basilar Impression (BI). It features upward protrusion of the top of the spine into the base of a soft skull. It can result in neurological complications that are potentially very serious. Symptoms can include headache, double vision, imbalance, and arm or leg weakness. About 50 percent of people with Type III OI or Type IV OI have moderate or severe BI.

Chorionic villus sampling (CVS): Technique used in prenatal diagnosis. Chorion cells, which are found on the wall of the uterus, are collected from the pregnant mother. These cells have the same origin as the fetal cells and can be analyzed to detect certain fetal abnormalities including OI.

Collagen: A fibrous insoluble protein found in the connective tissue, including skin, bone, ligaments, and cartilage. Collagen represents about 30 percent of the total body protein. There are many types of collagen. Defects of type I collagen are known to cause OI.

Cor pulmonale: Hypertrophy or failure of the right ventricle resulting from disorders of the lungs, pulmonary vessels, or chest wall.

Dentinogenesis imperfecta: Hereditary aplasia or hypoplasia of the enamel and dentin of a tooth. Characterized by translucent gray to yellow brown teeth involving both deciduous and permanent teeth. The enamel fractures easily, leaving exposed dentin that undergoes rapid attrition. Dentinogenesis imperfecta can be seen in patients with osteogenesis imperfecta or can be caused by a separate, inherited autosomal dominant trait.

Dominant: Term used to describe a genetic disorder, such as OI, that is caused by a single abnormal gene. This gene can be inherited from the mother or the father or be the result of a spontaneous mutation.

Genotype: The genetic constitution of an individual.

Heterogeneous: Composed of dissimilar or unlike parts.

Histologic: Study of the microscopic structure of tissue.

Hydrocephalus: Having an increased accumulation of cerebrospinal fluid within the cerebral ventricles, which results from interference with normal circulation and absorption of the fluid.

Hypertrophic: Having an abnormal increase in bulk of a body part; not related to tumor formation.

Kyphoscoliosis: Kyphosis – a curving forward or hump-backed or bent malformation of the spine, combined with scoliosis – a lateral curvature of the spine. Congestive heart failure is sometimes an eventual complication of severe malformation.

Mosaicism: A rare genetic situation when one parent has an OI mutation in a percentage of the cells in his or her body, including the reproductive cells that give rise to his or her sperm or eggs. In these cases, there is a possibility that the parents will have more than one child with OI. The mosaic parent may be totally unaffected or have only mild symptoms.

Osteopenia: Reduced bone mass as well as decreased calcification or bone density. It does not imply a cause or specific diagnosis.

Osteopetrosis: Hereditary condition characterized by excessive calcification of bones causing spontaneous fractures and marble-like appearance. Also called marble bone disease.

Osteoporosis: Condition of diminished amount of bone tissue, without respect to cause.

Osteotomy: Surgically cutting through a bone.

Pectus carinatum: The flattening of the chest on either side with forward projection of the sternum resembling the keel of a boat.

Pectus excavatum: A hollow at the lower part of the chest caused by a backward displacement of the xiphoid cartilage.

Phenotype: The physical appearance of an individual.

Recessive: An individual carries an altered gene that will not affect him or her. However, when two carriers of the same altered gene have children, each pregnancy carries a 25 percent chance of an affected child who has inherited two altered genes.

Sillence: Dr. David Sillence, a physician and researcher based in Australia, developed the Type I, Type II, Type III, and Type IV system of categorization currently in use. These four classifications combine clinical symptoms with genetic components. The Sillence classification system has been generally accepted since 1979.

Syringohydromyelia: The presence in the spinal cord of longitudinal cavities lined by dense tissue that are not caused by vascular insufficiency. Clinically, pain and paresthesia are followed by muscular atrophy of the hands and arms, but tactile sensation is preserved. Later, spastic paralysis of the lower extremities and scoliosis of the lumbar spine may occur.

Type I collagen: The major structural protein that functions as a significant part of the underlying structure of bone, ligaments, skin, and other connective tissue.

Wormian bones: Small, irregular bones in the cranial structure that are apparent on x ray. They resemble the appearance of a cracked, dried-up lake bed. Wormian bones are not considered a "symptom" of OI, since they cause no difficulty, but are a common finding in people with OI. Wormian bones also occur in other disorders.

Appendix 4

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Diagnosis:
Contact the Osteogenesis Imperfecta Foundation to obtain contact information for centers that perform **Collagen Biopsy** or **DNA Analysis.** Testing is available on a fee-for-service basis but also may be provided to participants in clinical research trials.

Primary Care / Nutrition / Medical Procedures:
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Social Services:

Family Voices at www.familyvoices.org
Easter Seals at www.Easter-Seals.org
Osteogenesis Imperfecta Foundation at www.oif.org
NICHCY (National Dissemination Center for Children with Disabilities) at www.nichcy.org

Transportation:

National Patient Travel Center/Mercy Medical Airlift at www.patienttravel.org, or telephone 1-800-296-1217

Health Information:

NIH Osteoporosis and Related Bone Diseases ~ National Resource Center at www.niams.nih.gov/bone

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