Ksenia Zukowsky, PhD, APRN, NNP-BC ❍ Section Editor

CE 3.0 HOURS Continuing Education

Osteogenesis Imperfecta Types I-XI

Implications for the Neonatal Nurse

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ABSTRACT

Osteogenesis imperfecta (OI), also called "brittle bone disease," is a rare heterozygous connective tissue disorder that is caused by mutations of genes that affect collagen. Osteogenesis imperfecta is characterized by decreased bone mass, bone fragility, and skin hyperlaxity. The phenotype present is determined according to the mutation on the affected gene as well as the type and location of the mutation. Osteogenesis imperfecta is neither preventable nor treatable. Osteogenesis imperfecta is classified into 11 types to date, on the basis of their clinical symptoms and genetic components. This article discusses the definition of the disease, the classifications on the basis of its clinical features, incidence, etiology, and pathogenesis. In addition, phenotype, natural history, diagnosis and management of this disease, recurrence risk, and, most importantly, the implications for the neonatal nurse and management for the family are discussed.

Key Words: brittle bone disease, COL1A1, COL1A2, collagen disorders, osteogenesis imperfecta

Osteogenesis imperfecta (OI) is a rare connective tissue disorder that is caused by mutations of genes that affect collagen.[1-4] Collagen is the major protein of connective tissues, which is the framework of bones. When collagen is not functioning properly or there is lack of collagen in the tissue, bones break easily. Characteristics of OI are the following: decreased bone mass, easy fracturing of bones, and skin hyperlaxity. Osteogenesis imperfecta is neither preventable nor curable. The focus of management in OI patients is to reduce fractures, increase function, and reduce disability. Some treatment options are surgery, pharmacological and pain management, and physical therapy. Bedside nurses must be knowledgeable about OI to provide the best care possible; however, a multidisciplinary team approach is imperative to help the patient and the parents caring for infants born with OI.

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The author declares no conflict of interst.

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DOI: 10.1097/ANC.0000000000000094

REVIEW OF LITERATURE

Osteogenesis imperfecta was thought to have affected Ivar the Boneless, who lived in Denmark in the ninth century, who reportedly was unable to walk on his "soft legs" and was, therefore, carried into battle on a shield.[5] Reported cases of OI were found in the medical literature sometime during the 1600s.[2,5] In 1849, W. Vrolick coined the term "osteogenesis imperfect," and, in 1906, E. Looser divided the disorder into the following 2 forms: congenital, which occurred when fractures were found in utero, and tarda, when fractures presented at birth.[5] However, this "system" did not differentiate the phenotypical and molecular presentations that OI possesses. Over the next 70 years, many medical professionals attempted to differentiate the types of OI such as OI letalis, OI tarda levis, OI tarda type II, and OI with mild long bone disease on the basis of the physical characteristics of OI alone.[6] In 1979, Sillence et al conducted an epidemiological and genetical study of OI in Victoria, Australia.[6] On the basis of their findings, they classified OI into "4 distinct syndromes" based on radiographic findings, clinical characteristics, and mode of inheritance,

calling this the "Sillence Classification of Osteogenesis Imperfecta."[2,3,6,7] This classification has become the gold standard for classifying OI (Table).

In 2004, Rauch and Glorieux[8] expanded the classification by adding 3 additional groups, types V, VI, and VII, which had the clinical symptoms of OI, but had defective genes other than *COL1A1* or *COL1A2* described in detail in the following sections. In 2007, type VIII was added by Cabral et al, who classified this OI because of a leucine proline-enriched proteoglycan (leprecan) 1 (*LEPRE1*) mutation. The mutated *LEPRE1* gene causes a severe deficiency or absence of polyl 3-hydroxylase (P3H1*)*.[5,7,9,10] A *LEPRE1* mutation is caused by autosomal recessive inheritance.[7] Since then, types IX, X, and XI have been described in the latest literature.[9,10] However, there is much debate in the literature about how to classify these new additions and those that may be discovered in the future.

Incidence

The incidence of all forms of OI worldwide varies in the literature ranging from 1 in 5000[2] to 1 in 20,000,[1,3,8,9,11,12] occurring equally in females and males, as well as race and ethnicity.[3,6,8,9] In the United States alone, an estimated 20,000 to 50,000 people have OI.[5,13] The most common forms of OI are types I and IV.[14] Types I through IV are thought to be transmitted mostly by autosomal dominant inheritance, which occurs when an individual with OI has a 50% chance of passing it on to his or her offspring.[2,4] Recently, autosomal-recessive patterns of inheritance have been identified, accounting for 10% of all OI types VI through XI.[14] This occurs when 2 parents do not have the phenotypical features of OI, but each carries 1 copy of the affected gene. With this form of inheritance, there is a 25% chance that their children will not be affected nor carry the gene, 25% chance that their children will be affected and have OI, and 50% chance that their children will carry the affected gene but will not be affected. However, approximately 35% of OI cases are caused by a new mutation at the time of conception for those without a family history of OI.[5,12]

Etiology and Pathogenesis

To understand the process of OI, the normal structure of collagen and bone must be explained. The major structural protein of bone is type I collagen, which also makes up skin and connective tissue to provide structure and strength for the body. Osteogenesis imperfecta is caused by mutations of genes that affect the body's production of collagen.

COLA1A and *COL1A2* are genes that encode the α-chains, α_1(I) and α_2(I) of type I collagen.[9] The normal process of collagen formation is that type I collagen is made up of 2 proα_1(I) chains, found on chromosome 17, and 1 proα_2 (I) chain, found on chromosome 7.[2,4,9,10,11,15-17] Collagen is a triple helix made up of glycine-X-Y repeats, with glycine being the most crucial amino acid holding the helix together.[4] If another amino acid takes its place, a quantitative or qualitative defect occurs. Mutations of *COL1A1* are more likely to be lethal, whereas mutations of *COL1A2* are nonlethal 80% of the time.[9,10] Dominantly inherited OI is caused by mutations of these 2 genes, *COL1A1* and *COL1A2*, in 90% of OI cases.[2,5,10,11] Mutations in these genes are also associated with the classic forms of types I to IV OI.

Type I OI occurs because of a mutation defect that impairs the production of 1 of the 2 proα_1(I) collagen; the collagen is normal but insufficient.[4] There is a premature termination codon affecting the *COL1A1* gene, termed a "nonsense-mediated decay."[10,16]

Type II OI occurs because of mutations/substitutions within the glycine codons of genes for the α_1 or α_2 collagen chain disrupting the helical structure, thus producing abnormal collagen molecules.[4] Mutations of *COL1A1* resulted in the lethal form, whereas *COL1A2* mutations were nonlethal in 80% of mutations.[10] In types III and IV, mutations/substitutions occur on the glycine codons of the α_1 or α_2 collagen chain disrupting the helical structure, thus producing abnormal collagen molecules.[4]

The other 10% of OI cases are caused by mutations of other genes that encode the proteins involved in the synthesis of type I collagen. Mutations that affect the structure, synthesis, folding, secretion, and matrix organization of type I collagen cause recessive OI that includes types V through XI.[9] Type V is "histologically distinct," but there is no abnormal type I collagen or collagen-associated proteins; however, the exact cause remains elusive.[9,10] Type VI is caused by mutations in the *SERPINF1* gene that is responsible for coding proteins involved in collagen posttranslational modifications, folding, and secretion.[18] *SERPINF1* is responsible for coding pigment epithelium-derived factor.[9] The *SERPINF1* gene is thought to be a key factor in bone deposition and remodeling; however, the synthesis and secretion of type I collagen are normal.[18]

Types VII through IX are based on the gene, where the mutation occurs during the collagen 3-hydroxylation complex.[9] There are genes that encode the protein complex responsible for prolyl-3-hydroxylation, a process that interacts with type I collagen.[9] Mutations of the 3 proteins in this complex are cartilage-associated protein (*CRTAP*), *P3H1* (or *LEPRE1*), and peptidyl-prolyl cis-trans isomerase B (*PPIB*).[9,10] These types affect the recessive types VII, VIII, and IX, respectively.[9]

Recently, "collagen chaperone defects" have been identified. *SERPINH1* and *FKBP10* are genes that encode HSP47 and FKBP65, respectively.[9,10] These genes assist with the folding of the polypeptides of collagen.

TABLE. Expanded Sillence Classification of Osteogenesis Imperfecta (OI)

Type	Severity	Clinical Features	Inheritance/Gene Affected
I	Mild to moderate	Blue sclera, hypermobility of the joints, thin, loose skin, and fractures of the extremities Type A: no DI Type B: with DI	AD or spontaneous mutations affecting *COL1A1* (null alleles)
II	Lethal	Short limbs, small chests (causing underdeveloped lungs), soft skulls, intrauterine fractures, and blue sclera	Dominant mutation or parental mosaicism affecting *COL1A1* or *COL1A2*
III	Severe	Frequent fractures, markedly short stature, spine curvatures, compression fractures of the vertebrae, scoliosis, and triangular face	AD affecting *COL1A1* or *COL1A2*
IV	Moderate to severe	Moderate to severe growth retardation, bowing of the femurs, and long bone fractures	AD affecting *COL1A1* or *COL1A2*
V	Moderate	Moderate to severe growth retardation, long bone fractures with the characteristic feature of hypertrophic calluses at fracture sites, dislocation of the radial head secondary to calcification of the interosseous membrane	AD, do *not* involve deficits of type I collagen but still not known which gene is affected
VI	Moderately severe	Moderate to severe growth retardation, scoliosis, "codfish vertebrae," and mineralization of bone	AR, affecting *SERPINF1* gene
VII	Moderate to severe	Partial expression of *CRTAP* leads to moderate bone dysplasia resembling type IV; complete absence of *CRTAP* leads to severe bone dysplasia resembling type II OI	AR, affecting *CRTAP* gene
VIII	Severe to lethal	Severe growth deficiency, severe under mineralization of the bones, white sclera, severe osteoporosis, and "popcorn" calcifications	AR, mutations of the *LEPRE1* gene
IX	Severe to lethal	Severe growth deficiency and shortened bowed limbs	AR, affecting *PPIB* gene
X	Severe to lethal	Multiple bone deformities and fractures, osteopenia, DI, blue sclera, and severe bone dysplasia	AR, affecting *SERPINH1* gene
XI	Severe	Short bowed limbs, joint contractures, platyspondyly, and scoliosis	AR, affecting *FKBP10* gene

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; DI, dentinogenesis imperfecta.
Data from Hackley.[2] Bishop,[10] Glorieux.[16]

SERPINH1 missense mutations are associated with type X OI, and *FKBP10* mutations with type XI OI.

Phenotype and Natural History

Depending on the type of OI, the clinical signs may not surface for years. The phenotype present can be determined according to the affected chain of type I procollagen as well as the type and location of the mutation.[4] However, most infants with OI present with fractures, fragile bones, bone deformities, blue sclera, and laxity of joints and ligaments.[1,3,16] Other characteristics of OI are muscle weakness, respiratory complications such as pneumonia, dentinogenesis imperfecta (DI) (dentin deficiency in either the primary or secondary teeth, in which the affected teeth may easily chip or break, and the teeth are discolored and misshapen), bleeding, neurologic manifestations such as basilar invagination of the skull (upward protrusion of the top of the spine into the base of the skull), hydrocephalus, and syringohydromyelia of the spinal cord (dense tissue on the spinal cord that causes pain and paresthesia followed by

muscular atrophy of the upper extremities).[12] Although there may be motor delays, individuals with the nonlethal types of OI are not intellectually and cognitively affected. The severity of OI is dependent on the following 3 things: "the affected alpha chain, the position of the mutation, the substituting amino acid, or the combination of these three variables."[18(p2)] Some characteristics do not appear until later in age such as hearing loss, blue sclera, or dentition abnormalities.

Type I affects 45% to 50% of the OI population, and its clinical severity is mild to moderate.[1] The collagen is normal but produced an insufficient amount.[1,2,4] This type may be missed in infancy but presents later because most of the fractures occur when ambulation begins and then later in their life.[3] These patients have mild nondeforming skeletal deformities. They are further classified into the following 2 types: type A, which is without DI, and type B, which is with DI.[1-3,15] At birth, phenotypic features include blue sclera; hypermobility of the joints; thin, loose skin; and fractures of the extremities or a broken clavicle during delivery.[1] One characteristic commonly found in OI is a triangular face that is caused by frontal bossing or prominent frontal bones and a narrow jawbone.[1] Approximately 50% patients have hearing loss and mild scoliosis as they age.[5] Life expectancy for this type is normal.[5]

Type II occurs in 10% of the OI population and is lethal, with infants dying within the first month of life.[1,15] The mutation involves substitutions of glycine in the *COL1A1* and *COL1A2* genes, rendering the genes defective.[1-3,5-7,8,11,12,15] Type II can be found during routine ultrasounds between 15 and 20 weeks' gestation because of multiple fractures; bowing of the femurs; short, deformed extremities; and "thin and porous" bones.[2,3] Most infants with this type of OI die at birth or within the first few weeks of life because of respiratory failure secondary to rib fractures causing rib cage distortion. These babies present with multiple healing fractures and fractures that occur with the birthing process.[1]

Type III, known as "severely deforming OI," occurs in 20% of cases and is apparent at birth.[1-3,5,7] These patients are small for gestational age in both height and weight, have a triangular face, and have fractures at birth.[1-3,5,7] They are at increased risk for DI, hearing loss, severe scoliosis, and very short stature.[2,7] Radiographic images show kyphoscoliosis (curvature of the spine either lateral or posterior), compression fractures or the vertebrae, Wormian bones in the skull (extra bone pieces in the cranial sutures), and fractures that heal deformed.[1] Many also have platybasia or basilar invagination (infolding of the skull base that affects the brainstem).[9] Life expectancy is decreased in this population, with mortality caused by pulmonary complications because of their severe thoracic malformation.[3,9]

Type IV is "moderately severe" affecting 20% of OI cases.[1] These patients have less severe skeletal deformities of the spine, extremities, and thorax than type III but more severe than type I.[1] Kyphoscoliosis and osteopenia are more common, whereas DI, basilar invagination, short stature, and hearing loss may occur but are less common.[2,9] Dozens of fractures of the long bones occur, but ambulation is achieved and life expectancy is not affected.[12]

Type V is "moderately severe" affecting 5% of OI cases. It is similar to type IV in the frequency of fractures and the magnitude of deformity within the skeletal structure.[5] The main characteristic of type V OI is large hypertrophic calluses at fractures sites on the largest bones.[5] In addition, dislocation of the radial head occurs as a result of calcification in the interosseous membrane between the ulna and the radius.[5,15]

Type VI is "moderately severe" and is based on a higher amount of osteoid and fish-scale pattern when histology of the bone is done.[8] This type is extremely rare and is identified by mineralization in biopsied bone.[5]

Type VII is also "moderately severe" with symptoms similar to type IV.[5,8] This type has been reported only in a Native American community in northern Quebec, Canada.[8] The main characteristics that distinguish this type from the other types are rhizomelia, which is shortened limbs, and coxa vara, which is a deformity of the hip where the angle between the head and the shaft of the femur is reduced by 120°, resulting in a shortened leg on the affected side.[8,10,17]

Type VIII is moderate to lethal in severity. Type VIII OI is similar to types II and III in that it is distinguished by severe growth deficiency and severe undermineralization of the bones,[5] platyspondyly, and scoliosis.[15] Additional characteristics include white sclera, soft skull with wide open fontanel, and a round face instead of the triangular face.[17]

Type IX is a severe form of OI that includes progressive deformity, severe growth delay, and radiological features similar to types II and III.

Type X possesses characteristics similar to type I OI, multiple bone fractures, osteopenia, DI, and blue sclera.[17]

Type XI OI has been found in Turkish and Mexican patients and have moderate to severe OI.[9] In addition to long bone fractures and laxity of the ligaments, scoliosis and platyspondyly, or flattened vertebral bodies throughout the axial skeleton, can occur.[9] Some may have joint contractures.[17]

Diagnosis

When an infant or child presents with multiple unexplained fractures, many skeletal disorders such as juvenile idiopathic osteoporosis, Bruck syndrome, Cole–Carpenter syndrome, hypophosphatasia, juvenile Paget disease, panostotic fibrous dysplasia, osteoporosis pseudoglioma syndrome, and even

child abuse should be considered in the differential diagnosis.[15,16] Diagnosis of OI is made by looking at family history, medical history, findings from physical examination, and x-rays.

Family history may or may not include a family history of OI as subtle signs such as short stature or bruising. Physical examination would include inspecting the head and face. Oftentimes, an infant with OI has what seems to be macrocephaly secondary to their disproportionately small body. Notable may be a triangular face caused by frontal bossing and small chin and blue to blue-gray sclerae. The skull may be soft, with fontanels larger than normal.[12] The chest wall is short and narrow on inspection, and callus formation on the ribs may be palpated.[12]

The next most obvious physical signs of OI are the short and bowed limbs and "frog-like" position of the lower extremities. X-rays should be obtained to look at fractures in the stages of healing as well as osteopenia; spinal x-rays to determine if there are vertebral compressions or "codfish vertebrae," which are bones in the spine; and skull x-rays may reveal wormian bones, which are small irregular bones found along the suture lines.[12] In addition, bone mineral density examinations and dual-energy x-ray absorptiometry may help in the diagnosis.[8] The dual-energy x-ray absorptiometry scan can determine the severity of the OI and the response to treatment.[15] Confirmation of OI is made by biochemical testing, which involves taking a small skin biopsy to study the collagen makeup of type I collagen with results available in 6 weeks to 3 months.[12] Eighty-five percent of OI cases are confirmed and have a positive abnormal skin biopsy result, confirming the molecular analysis of mutations of the encoding genes, *COL1A1* and *COL1A2*, of type I collagen. However, 15% cases are negative and need additional blood to look at DNA-based sequencing to determine which molecular and biochemical defects and gene mutation are responsible for OI.[12] However, there is not 1 genetic or protein analyses test that can diagnose OI alone; therefore, testing is both time and money intensive.[15]

Management

At present, there is no medical or surgical treatment to cure OI. The focus in managing OI patients is to reduce fractures, increase function, and reduce disability. Some treatment options include medical, surgical, pharmacological, and physical therapies. Understandably, trying to prevent fractures is the upmost priority. However, even nonaccidental trauma can cause fractures because of the brittleness of bones in individuals affected with OI.

Medical treatment involves splinting to immobilizing fractures, instead of casting, so that movement is allowed to decrease osteopenia[1-3] Rehabilitative therapy is instituted at birth in infants and should continue throughout the life span of those affected with OI to help maintain bone mass, increase function, and muscle strength.[19] Swimming and water exercises are a good modality to help improve muscle strength, balance, and range of motion. The number of fractures and the age at which fractures occur influence the patient's ability to walk and their long-term prognosis. External orthotic immobilization can help arrest the progression of basilar invagination.[11]

Dental care is important during the first years of life including orthodontic assessments. Capping teeth with hard polymers helps prevent fractures by coating and shaping the teeth.[11] Hearing aids and/or cochlear implantation can help hearing loss, which is a very common complication in adulthood.[11]

Surgical treatment includes "intramedullary rodding" the femur, tibia, or humerus bones.[1] Rodding surgery is for those with type III moderate to severe OI to improve weight bearing in the lower extremities.[19] It involves inserting a titanium or stainless steel rod into the medullary canal, which is the internal cavity of the bone. This procedure is used to minimize repeat fractures and decrease bone deformities, which interfere with function.[1] Individuals with kyphoscoliosis may undergo spinal fusion, in which vertebrae are fused together with metal rods or bone grafts.[1]

Pharmacological treatment involves acute or chronic pain management. This includes prescription and over-the-counter pain relievers personalized to the individual patient's needs. Pharmacological administration of calcium and vitamin D through diet or supplements should be considered.[11] However, controlled trials of pharmacological administration of calcium, fluoride, steroids, and vitamins C and D were found to be ineffective.[1,11]

Growth hormones and bisphosphonates are other pharmacological modalities that should be evaluated for each individual case and type of OI. Growth hormones have been found to stimulate osteoblasts and collagen synthesis, which stimulate bone growth.[11] The use of growth hormones seems to be more beneficial for the moderate types of OI, specifically type I and some with type IV OI.[11] However, long-term effects are not known, and informed consent should be obtained before its use.[11] Bisphosphonates, which include pamidronate and alendronate, are synthetic agents that are showing promising results in decreasing bone resorption and increasing bone density.[2,4,11] Giving pamidronate intravenously every 1 to 4 months was found to decrease bone pain and increase bone mass and density.[16] Although pamidronate seems to be promising for moderate to severe OI, it is most beneficial if given early and in conjunction with surgery[1,16] Downfalls include that it must be given intravenously and needs to be administered every few months, and the long-term effects are not known.[1,19]

Alendronate is given orally and has been found to increase bone mineral density, but again long-term effects are unknown.[11]

Ultimately, the only "cure" for this disease is by eliminating the mutated genes that cause OI. One modality being investigated is bone marrow transplant. This is replacing the mutant cells with normal cells to normalize tissue function.[11] In addition, antisense suppression therapy, which decreases or silences the mutant allele without interfering with the normal allele, has been researched. However, there are many technical difficulties with both modalities to biochemically transform OI, and further investigation of both of these therapies is needed.[11]

Recurrence Risk and Genetic Counseling

Having an infant born with OI unexpectedly raises some questions about how and why this happened. A genetics consult helps the family decide whether they want to pursue antenatal and/or prenatal diagnosis for future pregnancies because most types are an autosomal dominant inheritance.

There are 4 ways to occur OI.[12] The most common method of inheritance is autosomal dominant. A parent with OI has the faulty gene and has a 50% chance of passing it on to all pregnancies.[12] The second method of inheritance, which occurs in 85-90% of OI is autosomal dominant. In about 90% of families whose parents do not have symptoms of OI, it is thought to be caused by a new mutation that occurred in either the egg or the sperm at the time of conception.[12] The recurrent risks for subsequent pregnancies are less than 5%, which is the same risk of OI in the general population.[12] The third cause is mosaicism, which is thought to occur in 10% of those who do not have symptoms of OI in 1 parent.[12] The mutation occurs in some of the cells in their body and is passed on to their offspring. The subsequent risk of OI in future pregnancies can range between 10% and 50%.[12] Finally, autosomal recessive carriers cause very unusual forms of OI.[12] This is when each parent contributes 1 faulty gene, and the child is affected with OI.

Before getting pregnant, antenatal biochemical testing of both parents can be done to determine if either parent is a carrier of OI. In addition, RNA and DNA testing of both parents can identify the specific collagen mutation that causes OI.[12] Prenatal testing may also detect OI. These tests include an ultrasound, amniocentesis, and chorionic villus sampling. An ultrasound can be done around 16 to 20 weeks to detect bone abnormalities. Type I may not be detected on ultrasound; type II can be detected between 14 and 16 weeks; and types III and IV can be detected at 18 to 20 weeks.[1] Amniocentesis can be done between 14 and 16 weeks to look at the cells in the amniotic fluid, and chorionic villus sampling can be perfumed to look for abnormal collagen and genetic mutations on DNA.[1]

Implications for Nurses and the Family

Implications for the medical team when an infant has OI begin in the delivery room. If it is a known OI, resuscitation should be instituted gently. If the infant is not breathing and/or mask ventilation is needed, stimulation and application of the mask should be performed delicately. If intubation is needed, being very judicious with positioning is appropriate because a neck fracture could occur while trying to intubate. Once the infant is stable, care must be taken to minimize fractures in the NICU. Education for the nurses caring for the baby should be provided by looking up OI: A guide for nurses is found on the US Department of Health and Human Services and the National Institutes of Health. A sign for all who come in contact with the infant should be placed on the bed on how to change the diaper, change clothes, feed, hold, and position the infant. All movements should be gentle, slow, and well-thought-out. When changing the diaper, lift under the buttocks not by the ankles.[12] When changing clothes, do not pull or twist extremities.[12] When holding or positioning the babies for feedings, watch the extremities to avoid abnormal positioning because their joints are so hyperlax.[12] Intravenous lines must be placed without pulling or bending the extremity.[2] Good physical examinations and x-rays can determine what fractures have healed and new fractures that have occurred. Pain management is also an essential element for an infant with OI who has fractures.[2] Referrals should be made to a pediatric orthopedist, physical therapist, and OI support group to help both the parents and the infant when discharged.[12]

Offering support and education for the family should start when diagnosis of OI is suspected. Supporting their feelings and allowing them to grieve are imperative, especially when it is an unknown case of OI. Encouraging the parents to participate in the cares and demonstrating how to handle, feed, dress, and diaper their baby will foster confidence to care for their child. Teaching them how to care for casts and perform exercises helps them learn to manage their child.[2] Clothes with wide openings and a special car seat with extra padding or car bed may be needed.[12] Signs and symptoms of fractures and protecting the injured body part need to be taught because new fractures will occur.[2,12] Parents should also be advised to carry a letter on hospital letterhead stating that the child has OI as to facilitate appropriate care.[2,12]

Discharge planning should include a multidisciplinary approach with referrals to a pediatrician who feels comfortable caring for an infant with OI, physical and occupational therapy, and a pediatric orthopedist. Support groups and voluntary organizations

that provide community resources for the parents can help with supporting emotional and educational needs as well as to improve their quality of life. Such resources include Osteogenesis Imperfecta Foundation, the Brittle Bone Society, OI Village, and Children's Brittle Bone Foundation.[2] There may be some cases where an infant with OI is so critically ill that they may not go home. In such cases, referrals to a palliative care team, hospice, and/or ethical team to help support the family may be needed.[2]

CONCLUSIONS

Osteogenesis imperfecta is the most common connective tissue disorder. It is typically characterized by bone fragility, encompasses a wide range of phenotypes, and continues to evolve. Management of infants with OI has shown that growth hormones and pamidronate coupled with surgical treatment are the most promising way to care for these individuals. Even though there are many identified mutations that cause OI, treatment of the patient to improve their quality of life should be taken precedence over identifying the specific mutation. The focus of treatment must involve a multidisciplinary approach, which includes physical and occupational therapies.

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