

Psychosocial aspects of osteogenesis imperfecta

Glenda L. Shea-Landry, BA, MA
David E.C. Cole, MD, PhD, FCCMG

Osteogenesis imperfecta is a heterogeneous group of inherited disorders characterized by bone fragility and recurrent fractures. It is currently classified into four types on clinical grounds and appears to arise from different disorders of bone collagen synthesis. The biochemical identification of disturbances in collagen metabolism and the genetic delineation of new mutations of collagen genes have made prenatal diagnosis by molecular methods feasible in some cases. Most people with osteogenesis imperfecta suffer frequent fractures (and sometimes consequent serious disability), for which there are few effective preventive measures. This disorder may have a profound psychosocial influence on patients and their families. In this report the extent of this influence is reviewed and aspects important to the medical community are highlighted; these include the emotional burdens imposed by unfounded suspicions of child abuse, the social and financial costs of repeated hospitalization and immobility, and the frustrations generated by the lack of helpful, practical information for families and health care workers. An important social out-

come has been the rise of self-help organizations, exemplified by the Canadian Osteogenesis Imperfecta Society. For Canadian families the society has been an important vehicle for exchange of information and an active, positive response to a lifelong, often severely disabling disorder.

L'osteogenesis imperfecta, ou fragilité essentielle des os, constitue un groupe hétérogène de maladies héréditaires prédisposant la plupart des sujets atteints aux fractures répétées. On en reconnaît actuellement quatre formes cliniques dont chacune semble représenter une anomalie distincte de la synthèse du collagène osseux. La connaissance de ces anomalies et la notion de néomutations des gènes concernés en permettent dans certains cas le diagnostic biochimique prénatal. On a peu de mesures préventives à opposer aux fractures et aux graves infirmités qui en résultent parfois. Elles ont sur les malades et leurs familles de profondes incidences qui font l'objet du présent article, où l'accent est mis sur leur intérêt pour le médecin: les tensions affectives causées par d'injustes soupçons de mauvais traitements aux enfants, les conséquences sociales et pécuniaires de l'hospitalisation répétée et de l'immobilisation, la frustration engendrée chez les familles et les professionnels soignants par le manque d'information utile. Aussi doit-on considérer comme une acquisition importante la naissance des organismes d'entraide, comme la Canadian Osteogenesis Imperfecta Society, qui d'ores et déjà assiste les familles concernées par l'échange d'information et favorise un point de vue positif sur ces maladies, qui durent toute la vie et causent souvent de redoutables infirmités.

From the Department of Pediatrics, Dalhousie University, Halifax

Dr. Cole is an assistant professor of pediatrics at Dalhousie University and the recipient of a scholarship from the Canadian Life and Health Insurance Association.

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Reprint requests to: Dr. David E.C. Cole, Rm. 415, Izaak Walton Killam Hospital for Children, 5850 University Ave., Halifax, NS B3J 3G9

Osteogenesis imperfecta is a group of Mendelian genetic disorders that are defined by brittleness or fragility of the bones and impaired collagen metabolism.¹ Recent advances in diagnosis and biochemical analysis have begun to clarify the complex relation between the genetic mutations and their clinical presentations.

At present the classification of Silience and colleagues^{2,3} provides the best means of distinguishing among the various clinical entities and offering the patient or family reasonable prognostic advice.⁴ Type I, the tarda or mildest form of osteogenesis imperfecta, is distinguished by blueness of the sclera, perinatal or postnatal onset of fractures and a pattern of autosomal dominant inheritance. Type II, the lethal congenita or prenatal form, is now considered a genetically heterogeneous category of both autosomal recessive conditions and disorders due to new, spontaneously arising, dominant mutations.^{3,7} Since there is a recurrence risk for subsequently born siblings of 25% with the former and 0% with the latter, distinguishing between the two groups is important in the counselling of prospective parents. Prenatal diagnosis of this uniformly lethal condition can often be made in the second trimester by ultrasonography.^{8,9} Type III, a rarer disorder, is also genetically heterogeneous and may display either a dominant or a recessive pattern of inheritance.⁵ Its chief distinguishing features are the more severe and more frequent fractures compared with type I, the progressive limb deformities and the absence of blueness of the sclera. Type IV is uncommon and has been less well defined. Paterson and associates¹⁰ consider it to be milder than type I, the patients having normal sclera and only moderate deformities of the long bones; however, it is more likely to be associated with dentinogenesis imperfecta.

It is ironic that our knowledge of the individual molecular defects in patients with osteogenesis imperfecta is growing more rapidly than our understanding of the pathogenesis of the bony abnormalities and their relation to the natural history of the condition. Studies of collagen biosynthesis in cultured fibroblasts have shown that osteogenesis imperfecta type I cells produce the different types of collagen molecules in abnormal proportions: production of the bone form of collagen is reduced, whereas production of the skin collagen fraction is increased.¹¹ With the isolation and cloning of certain collagen genes it is now possible in some cases to identify the specific genetic defect. There are reports of at least a dozen different mutations that result in either decreased collagen synthesis or the formation of an unstable collagen molecule that does not integrate with other forms of collagen or other matrix components and ultimately undermines the mechanical strength of bone.^{7,12,13} As our understanding of these molecular events grows, our ability to make an accurate genetic diagnosis is improving. Thus, patients with osteogenesis imperfecta and their families should be

encouraged to undergo skin biopsy for fibroblast culture in an attempt to delineate the biochemical or molecular defect. This may be particularly important in calculating recurrence risks and establishing an accurate prenatal diagnosis.^{4,8}

Unfortunately, efforts to treat this condition have been frustratingly unsuccessful. Although daily intramuscular injections of calcitonin may reduce the number of fractures in some cases,¹⁴ the bone fragility is unresponsive to any form of medical intervention in most cases.¹ In infants and children with progressively deforming disease, minimizing the extent of disability is a formidable challenge; prompt and effective orthopedic care is of paramount importance. In some patients the severely deformed limb bone may be sawn into small hollow segments through which a metal rod is inserted in shish-kebab fashion, thereby straightening and lengthening the limb.¹ In others these physical measures may not be possible or may not prove sufficient to prevent disability.

Little has been written about the family setting and psychosocial consequences of osteogenesis imperfecta. This review will draw on the available literature and on the results of a study conducted by one of us.¹⁵

Psychosocial factors

Parents and family

The behaviour of the parents of a child born with osteogenesis imperfecta is strongly conditioned by their immediate reactions to the deformity and disability of their child.^{16,17} Initial shock and immobility may be followed by anger, often because there is no knowledgeable person available to counsel them about the disorder. Feelings of guilt may surface. As Schild¹⁸ put it, "a fear that one possesses a defective gene causes a momentous insult to the ego and fosters inadequate parental functioning". Further, some parents fear they will not be able to provide adequate care for the child. However, the child born into a family that already has an affected member may enter a more secure environment.

As the family begins to accept the child's disorder an imbalance may develop in which the mother becomes overinvolved in an intense relationship with the child while the father and the siblings are pushed outside the "magic circle".¹⁹ Nevertheless, the rest of the family is expected to make considerable lifestyle and financial sacrifices. Members of the extended family are sometimes seen as a hindrance to the family's interaction. Grandparents, aunts and uncles may deny the condition or even reject the child. More distant relatives may show undue concern, perhaps because they believe that the disorder reflects unfavourably on their own genetic constitutions.

Children less severely affected with osteogenesis imperfecta may suffer repeated fractures

before the diagnosis is made. The unexplained fractures may raise the suspicion of child abuse in the minds of hospital personnel and others.¹ While these suspicions linger, the parents must contend with feelings of guilt and unfocused anxiety.

Once the diagnosis is made, most parents learn to cope with new fractures, and hospital personnel may become less certain about how to handle the infant and insensitive to practical suggestions the parents offer. Use of the bed card provided by the Canadian Osteogenesis Imperfecta Society (COIS) (Fig. 1) is one way of protecting the child from improper handling.

Like all parents of the severely disabled, parents of children with osteogenesis imperfecta need an abundance of patience, courage and faith. They may find it difficult to persuade others that their child has real limitations for which specific allowances have to be made. Constant awareness of their child's fragility makes routine activities a source of crisis in everyday living. And they must help the child resist the cultural imperatives to participate in sports and to take physical risks.

Growing up

Going to school is particularly frightening for children with osteogenesis imperfecta, and for their parents, who must struggle to accept that the benefits of academic and social growth outweigh the physical risks. However, children with severe

handicaps will find it harder to realize these benefits if they are excluded from activities and interactions with their peers because of their functional restrictions and episodes of illness or because of the reactions of their peers or parents.¹⁹

Severely affected older children comment on the general immobility of being confined to a wheelchair, the social problems associated with short stature, and the pain and specific immobility due to recurrent fractures, which may be more prevalent at the time of the growth spurt in adolescence. As well, physical disability often obscures concerns over such matters as physical appearance, sexual development and peer acceptance, concerns that the handicapped child shares with other children.

Adulthood

After early childhood the problems of immobility and of social and financial dependence continue to beset the person severely affected with osteogenesis imperfecta.¹⁸ Patients come to depend heavily on family, friends and neighbours for mobility, yet many potential helpers are deterred from assisting those in greatest need by the fear that they will be "responsible" for new fractures. Lack of easy access to public transportation and buildings enhances the patients' physical and social isolation and limits their occupational and educational choices and their ability to contribute economically to increasing their own mobility. Some have experienced discrimination in the workplace, and employers rarely offer them more than a subsistence income.

Patients with milder forms of osteogenesis imperfecta have unique problems arising from the conflict between their outwardly normal appearance and their underlying fragility. As adults they face the certainty of new fractures and hospital stays. They must compete on an equal footing with their physically healthy counterparts yet often encounter difficulty in obtaining insurance or getting dispensation for legitimate absences from work. Despite their often serious medical and orthopedic problems, they may be excluded from community support or special aid programs.

The physician's role

When first confronted with a newborn who has multiple fractures and skeletal deformities the physician may feel somewhat at a loss, if only because of the very limited medical literature dealing with osteogenesis imperfecta. Initially the differentiation between a lethal (type II) and a nonlethal (type III) form of osteogenesis imperfecta will be the critical issue. Helpful in this context is a careful evaluation of respiratory and neurologic function, since patients with significant pulmonary hypoplasia or a major intracranial insult usually

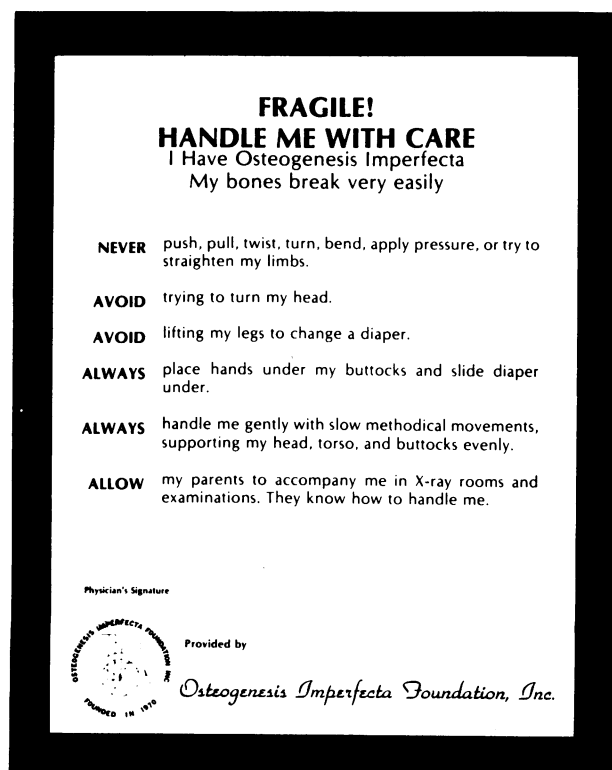


Fig. 1 — Bed card provided on request by the Osteogenesis Imperfecta Foundation, Inc., through the Canadian Osteogenesis Imperfecta Society to families with members who have osteogenesis imperfecta.

have type II osteogenesis imperfecta and, hence, a guarded prognosis. On the other hand, infants with type III osteogenesis imperfecta and adequate pulmonary reserve may thrive despite markedly deformed limbs and multiple rib or skull fractures. In either case it is important to be completely candid with the parents from the very start, emphasizing the extreme heterogeneity of these disorders and the impossibility of accurately predicting the ultimate outcome until the pattern of the fractures and bone growth is established. At the same time, one can point to the extraordinary achievements of adults with severe but nonlethal osteogenesis imperfecta and can support the parents' natural inclination to see their infant as a "terrific fighter", overcoming what seem to be considerable odds against survival.

Patients with mild osteogenesis imperfecta (type I) may not come to the physician's attention until after the first few fractures. Because of the favourable prognosis and the natural improvement that accompanies this disorder, the physician can promote a very favourable point of view, emphasizing the importance of normal peer relations, the need for exercise (swimming is an excellent form of vigorous exercise suitable for any patient with osteogenesis imperfecta who has access to a pool and adequate supervision) and the bright outlook for normal adulthood.

For any patient with osteogenesis imperfecta appropriate referrals to a skilled orthopedic team and a knowledgeable physiotherapy service will go far to obviate complications due to suboptimal setting of fractures or a poor recovery from surgical repairs. Patients with dentinogenesis imperfecta (Table I) or other dental complications should be seen by a dental team familiar with the disorder.²⁰ All patients should be seen by a cardiologist so as to identify any of the potentially troublesome cardiovascular complications of the collagen defect,

such as aortic valve incompetence accompanying aortic root dilatation.²¹ All patients should also undergo a formal hearing test as soon as practically possible, and most should probably be retested regularly to identify any hearing loss at an early stage. Perhaps the most important referral one can make is to another family with a child who has osteogenesis imperfecta. The practical information that these parents accumulate with time cannot be acquired elsewhere, and most parents of a child in whom osteogenesis imperfecta has just been diagnosed are extremely grateful for this kind of support.

The Canadian Osteogenesis Imperfecta Society

The medical response to osteogenesis imperfecta is necessarily limited, and in view of the substantial social and physical problems associated with this disorder the spontaneous development of related self-help organizations is hardly surprising.²² The establishment of COIS in 1983 followed the examples of the British Brittle Bone Society and the American Osteogenesis Imperfecta Foundation in the 1970s.

Membership in COIS is open to anyone interested in the welfare of people with osteogenesis imperfecta, including parents, friends, medical personnel and other health care professionals. For a modest annual fee, members and other interested parties receive several times a year the newsletter *Connect*. The self-professed aims of the society are as follows: to provide emotional support on a personal level for parents and people with osteogenesis imperfecta; to acquaint medical personnel, hospitals, educational institutions and social agencies with all facets of osteogenesis imperfecta; to encourage Canadian medical research into the underlying causes of osteogenesis imperfecta; to

Table I — Classification of osteogenesis imperfecta*

Type†	Inheritance	Onset of fractures	Deformities	Prognosis
I (tarda)	Autosomal dominant	Perinatal or postnatal	Limited	Good; however, later-onset problems include presenile hearing loss and severe osteoporosis ⁵
II (congenita)	Autosomal recessive or dominant‡	Prenatal	Multiple and very severe	Intrauterine death, stillbirth or limited postnatal survival
III	Autosomal recessive or dominant§	Prenatal or perinatal	Progressive and usually severe	Frequently severely disabled
IV	Autosomal dominant	Usually postnatal	Mild to moderate	Other than the deformities, good; in adults, less severe hearing loss and osteoporosis ⁵

*Adapted from Silience and colleagues.^{2,3}

†Types I and IV may occur with dentinogenesis imperfecta and are then designated IB and IVB. If dentinogenesis imperfecta is not present, the designations IA and IVA apply.

‡These forms can now be distinguished in some cases by biochemical studies or direct genetic analysis with cDNA collagen probes and DNA hybridization techniques.⁴

§While some cases represent new dominant mutations, autosomal recessive inheritance in at least one individual has been confirmed by biochemical identification of carrier status in the parents.⁵

keep an up-to-date library of literature, both medical and general, pertaining to osteogenesis imperfecta; to promote an understanding and awareness of "brittle bones" by the general public; to establish and maintain a confidential central registry of patients with osteogenesis imperfecta; and to solicit and receive funds to carry out the aims of the society.

Most families have expressed support for these goals, irrespective of their interest or direct involvement in the national organization. Local chapters of COIS have also provided families with several different kinds of informal aid, such as relief from a sense of isolation, knowledge that others have similar problems, and the opportunity to exchange helpful information on methods of home management and treatment. Thus, physicians should contact the organization for assistance in finding centres with expertise in clinical and laboratory diagnosis and for help in identifying families of patients with osteogenesis imperfecta in the same community who can help with the management of the new patient.

Readers wishing to receive a copy of the COIS newsletter or to learn more about osteogenesis imperfecta are invited to contact the society at PO Box 607, Station U, Toronto, Ont. M8Z 5Y9.

Conclusion

Osteogenesis imperfecta is an uncommon, complex genetic disorder with multiple modes of inheritance. It cannot be cured. The inherent bone fragility that characterizes the condition leads to frequent fractures and sometimes serious disabilities and thus places a considerable demand on our health care system.

Progressive deformities are among the most daunting of prospects for severely affected patients and their families. When immobility ensues, the family bears most of the enormous responsibility for making the patient's environment as normal as possible. The health care system also provides some assistance, but a common effort is needed, if only to ensure that each patient attains his or her maximum potential for social, intellectual and economic growth. COIS is a self-help organization that has arisen out of a perceived need of patients and their families to achieve this potential. Developing a better response to the social issues has been a welcome counterbalance to current scientific efforts to expand our understanding of the genetic defects and their pathophysiologic consequences.

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