TABLE 427-2 CLASSIFICATION OF OSTEOGENESIS IMPERFECTA (OI)

Phenotype	Type	Typical Features	Inheritance	Gene Defect	Protein Defect
Nondeforming OI with blue sclerae	I	Mild to moderate bone fragility, normal or near-normal stature, blue sclerae, normal dentition in most, hearing loss in ~50%	AD	***COL1A1***	Collagen I haploinsufficiency
				COL1A2	
Perinatally lethal OI	II	Extreme bone fragility, short stature, long bone bowing, blue sclerae	AD	***COL1A1***	Collagen I structural mutations
				COL1A2	
		Normal/pale blue sclerae, normal dentition and hearing	AR	*CRTAP*	Collagen posttranslational modification and folding machinery
				LEPRE1	
				PPIB	
Progressively deforming OI	III	Moderate to severe bone deformity, blue sclerae at birth, hearing loss and abnormal dentition common	AD	***COL1A1***	Collagen I structural mutations
				COL1A2	
			AR	*CRTAP*	Collagen posttranslational modification and folding machinery
				LEPRE1	
				PPIB	
				FKBP10	
				SERPINH1	
				BMP1	Proteolytic removal of procollagen N-propeptide
				WNT1	Wnt cell signaling pathway
				SERPINF1	PEDF - growth factor signaling?
				TMEM38B	Cation channel, Ca^{2+} release
Common variable OI with normal sclerae	IV	Mild to moderate, bone fragility, normal sclerae, variable dentition, hearing loss in <10%	AD	***COL1A1***	Collagen I structural mutations
				COL1A2	
				WNT1	Wnt cell signaling pathway
			AR	*CRTAP*	Collagen posttranslational modification and folding machinery
				FKBP10	
				SP7/OSX	Transcription factor, bone formation defect
OI with calcification of the interosseous membranes	V	Calcification of the interosseous membranes in forearm and legs and/or hypertrophic callus; variable bone deformity, normal sclerae and dentition	AD	*IFITM5*	Transcription factor, bone formation defect
Bruck syndrome type 1		Contractures with pterygia, fractures in infancy or early childhood, postnatal short stature, severe limb deformity, and progressive scoliosis	AR	*FKBP10*	Collagen folding machinery
Bruck syndrome type 2		As for Bruck syndrome type 1	AR	*PLOD2*	Collagen posttranslational modification of lysine

Abbreviations: AD, autosomal dominant; AR, autosomal recessive.

Note: Predominant OI gene mutations (>90%) are in *COL1A1* and *COL1A2* (in bold typeface).

pregnancy and after menopause. A few women from families with mild variants of OI do not develop fractures until after menopause, and their disease may be difficult to distinguish from postmenopausal osteoporosis.

Incidence Type I OI has a frequency of about 1 in 15,000–20,000 births. Type II OI has a reported incidence of about 1 in 60,000. Only a limited number of patients with the severe forms of OI have been reported, and the combined incidence of the severe forms that are recognizable at birth (types II, III, and IV) may be higher than 1 in 60,000.

Skeletal Effects In type I OI, the fragility of bones may be severe enough to limit physical activity or be so mild that individuals are unaware of any disability. Radiographs of the skull in patients with mild disease may show a mottled appearance because of small islands of irregular ossification. In type II OI, ossification of many bones is frequently incomplete. Continuously beaded or broken ribs and crumpled long bones (accordina femora) may be present. For reasons that are not apparent, the long bones may be either thick or thin. In types III and IV, multiple fractures from minor physical stress can produce severe deformities. Kyphoscoliosis can impair respiration, cause cor pulmonale, and predispose to pulmonary infections. The appearance of "popcorn-like" deposits of mineral in x-rays of the ends of long bones is an ominous sign. Progressive neurologic symptoms may result from basilar compression and communicating hydrocephalus. Type V OI is recognized by the presence of dislocated radial heads and hyperplastic callus formation.

In all forms of OI, bone mineral density is decreased. However, the degree of osteopenia may be difficult to evaluate because recurrent fractures limit exercise and thereby diminish bone mass. Surprisingly, fractures appear to heal normally.

Ocular Features The sclerae can be normal, gray, slightly bluish, or bright blue. The color is probably caused by a thinness of the collagen layers of the sclerae that allows the choroid layers to be seen. Blue sclerae, however, are an inherited trait in some families who do not have increased bone fragility.

Dentinogenesis The teeth may be normal, moderately discolored, or grossly abnormal. The enamel generally appears normal, but the teeth may have a characteristic amber, yellowish brown, or translucent bluish gray color because of a deficiency of dentin that is rich in type I collagen. The deciduous teeth are usually smaller than normal, whereas permanent teeth are frequently bell-shaped and restricted at the base. In some patients, the teeth readily fracture and need to be extracted. Similar tooth defects, however, can be inherited without any evidence of OI.