RESEARCH ARTICLE

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Nosology and Classification of Genetic Skeletal Disorders: 2015 Revision

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The purpose of the nosology is to serve as a "master" list of the genetic disorders of the skeleton to facilitate diagnosis and to help delineate variant or newly recognized conditions. This is the 9th edition of the nosology and in comparison with its predecessor there are fewer conditions but many new genes. In previous editions, diagnoses that were phenotypically indistinguishable but genetically heterogenous were listed separately but we felt this was an unnecessary distinction. Thus the overall number of disorders has decreased from 456 to 436 but the number of groups has increased to 42 and the number of genes to 364. The nosology may become increasingly important today and tomorrow in the era of big data when the question for the geneticist is often whether a mutation identified by next generation sequencing technology in a particular gene can explain the clinical and radiological phenotype of their patient. This can be particularly difficult to answer conclusively in the prenatal setting. Personalized medicine emphasizes the importance of tailoring diagnosis and therapy to the individual but for our patients with rare skeletal disorders, the importance of tapping into a resource where genetic data can be centralized and made

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available should not be forgotten or underestimated. The nosology can also serve as a reference for the creation of locus-specific databases that are expected to help in delineating genotype–phenotype correlations and to harbor the information that will be gained by combining clinical observations and next generation sequencing results.

Key words: skeletal dysplasias; nosology; molecular basis of disease; dwarfism

INTRODUCTION

The publication of a nosology of skeletal dysplasias started 45 years ago in Paris and has seen multiple revisions [1970, 1971a,b, 1979, 1983, 1998; Hall, 2002; Lachman, 1998; McKusick and Scoot, 1971; Rimoin, 1979; Spranger, 1992; Superti-Furga and Unger, 2007; Warman et al., 2011] The current nosology revision took place in Bologna, Italy just prior to the 11th International Skeletal Dysplasia Society meeting organized by Professor Luca Sangiorgi. In the 2015 version of the nosology, the number of conditions has decreased while the number of genes has increased dramatically. This is a reflection of consolidation of repeat entries into a single one when there is no discernible phenotypic difference while at the same time acknowledging the discovery of new genes. The inclusion of MIM numbers is maintained as this invaluable database is often a first reference for clinicians. There is not a complete concordance between MIM and the nosology because of different inclusion and review criteria and thus MIM retains some obsolete diagnoses and duplicates others (under differing names or eponyms).

This version of the nosology is the 9th edition and while it contains several new disorders, it is not radically different from its predecessor [Warman et al., 2011]. The groups of disorders remain a hybrid mix as they are defined either by a single gene or group of related genes (e.g., FGFR3 chondrodysplasia group and sulphation disorders group), or by a particular phenotypic feature (e.g., dysplasias with multiple joint dislocations), or by some radiological finding (e.g., metaphyseal dysplasia group and slender bone dysplasia group).

When the concept of the skeletal dysplasia families was first elaborated, it was hoped that there would be a limited number of molecular based groups with each group containing multiple allelic disorders [Spranger, 1985]. However, the biology of the skeletal dysplasias has turned out to be much richer, and more complex than anticipated. So while it makes sense to have a type 2 collagen disorder group where there is some similarity between conditions but enough phenotypic difference to warrant separate diagnoses (e.g., Stickler syndrome versus achondrogenesis type 2), there are many other genes that, to the best of our knowledge, are not associated with a "skeletal dysplasia family," those with no wide spectrum (e.g., *SEDL* (Spondyloepiphyseal dysplasia tarda) or Spondyloepimetaphyseal dysplasia with joint laxity-leptodactylic type). For these genes and conditions, it still makes sense to group them with clinically or radiographically similar disorders.

Table I has been simplified with the columns "locus" and "gene" merged into one. For some disorders, the etiology is a copy number disturbance and thus they are not single gene disorders in the classic sense. For those disorders with a known causative gene, the chromosomal location of that gene is often not important (especially if it is an autosome), and when necessary, the information can be readily retrieved from public databases.

The criteria used for inclusion of disorders are unchanged from the previous revision [Warman et al., 2011]. They are:

1) Significant skeletal involvement, corresponding to the definition of skeletal dysplasias, metabolic bone disorders, dysostoses, and skeletal malformation and/or reduction syndromes.
2) Publication and/or listing in MIM (observations, even those by experts in the field should not find their way into the nosology before they have achieved peer-reviewed status).
3) Genetic basis proven by pedigree or very likely based on homogeneity of phenotype in unrelated families.
4) Nosologic autonomy confirmed by experimental analysis.

We have included conditions in which only one family has been described but for which the gene has been identified. For e.g., the heterozygous mutations in *FZD2* in dominant omodysplasia [Saal, et al., 2015].

The total number of diseases has gone down (from 456 to 436) thanks to grouping of phenotypically indistinguishable entities and despite the appearance of several new conditions (e.g., MAGMAS related skeletal dysplasia) [Mehawej et al., 2014].

A few groups have changed names in this edition and the overall number has increased from 40 to 42. The short-rib dysplasia (with or without polydactyly) group has become the ciliopathies with major skeletal involvement group. Due to the increasing number and complexity of the brachydactylies, the group has now been made into two separate categories: brachydactylies without extraskeletal manifestations and brachydactylies with extraskeletal manifestations. The ectrodactylies have been given their own group.

The field of osteogenesis imperfecta (OI) continues to expand with multiple new genes. We have chosen to stick with the Sillence classification that was phenotypically and not molecularly based [Sillence and Rimoin, 1978; Sillence et al., 1979]. For this reason, OI type 5 is included as it is radiologically distinguishable from types 1 through 4. OI is the archetype of a skeletal dysplasia for which molecular diagnosis relies on next generation sequencing but prognosis is based on the careful phenotypic observations collected over the last four decades [Van Dijk and Sillence, 2014]. Examples are also available from other domains of medical genetics (spino–cerebellar ataxia or Meckel–Gruber syndrome).

DISCUSSION

The pace of disease related gene discovery has accelerated phenomenally in recent years thanks to the development of next-generation sequencing technologies and increasing availability of whole exome sequencing. This has led to both expansion and contraction of the nosology. It has expanded to incorporate new genes and new conditions but also contracted as we recognize our limits in differentiating by phenotype. While each patient may be unique, there are clear advantages both medical and human to belonging to a group of similar individuals [Superti-Furga, 2014]. It is truly an exciting time as we struggle to correctly interpret the

TABLE I.

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
1. FGFR3 chondrodysplasia group					
Thanatophoric dysplasia type 1 (TD1)	AD	187600	*FGFR3*	FGFR3	Includes previous San Diego type
Thanatophoric dysplasia type 2 (TD2)	AD	187601	*FGFR3*	FGFR3	
Severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN)	AD	187600	*FGFR3*	FGFR3	
Achondroplasia	AD	100800	*FGFR3*	FGFR3	
Hypochondroplasia	AD	146000	*FGFR3*	FGFR3	
Camptodactyly, tall stature and hearing loss syndrome (CATSHL)	AD	610474	*FGFR3*	FGFR3	Inactivating mutation
Hypochondroplasia–like dysplasia(s)	AD, SP				Similar to hypochondroplasia but unlinked to FGFR3, probably heterogeneous; uncertain diagnostic criteria
See also group 33 for craniosynostoses syndromes linked to *FGFR3* mutations, as well as LADD syndrome in group 41 for another *FGFR3*-related phenotype					
2. Type 2 collagen group					
Achondrogenesis type 2 (ACG2; Langer-Saldino)	AD	200610	*COL2A1*	Type 2 collagen	
Platyspondylic dysplasia, Torrance type	AD	151210	*COL2A1*	Type 2 collagen	See also Severe Spondylodysplastic dysplasias (group 14)
Hypochondrogenesis	AD	200610	*COL2A1*	Type 2 collagen	
Spondyloepiphyseal dysplasia congenital (SEDC)	AD	183900	*COL2A1*	Type 2 collagen	
Spondyloepimetaphyseal dysplasia (SEMD) Strudwick type	AD	184250	*COL2A1*	Type 2 collagen	Includes previous SMD Algerian type, Dysspondyloenchondromatosis and former SMD with severe genu valgum
Kniest dysplasia	AD	156550	*COL2A1*	Type 2 collagen	
Spondyloperipheral dysplasia	AD	271700	*COL2A1*	Type 2 collagen	
Mild SED with premature onset arthrosis	AD		*COL2A1*	Type 2 collagen	
SED with metatarsal shortening (formerly Czech dysplasia)	AD	609162	*COL2A1*	Type 2 collagen	
Stickler syndrome type 1	AD	108300	*COL2A1*	Type 2 collagen	See also COL11A1, COL11A2, and COL9A1
3. Type 11 collagen group					
Stickler syndrome type 2	AD	604841	*COL11A1*	Type 11 collagen alpha-1 chain	
Marshall syndrome	AD	154780	*COL11A1*	Type 11 collagen alpha-1 chain	
Stickler syndrome type 3 (non-ocular)	AD	184840	*COL11A2*	Type 11 collagen alpha-2 chain	
Fibrochondrogenesis	AR	228520	*COL11A1,*	Type 11 collagen alpha-1 chain,	
	AR, AD	614524	*COL11A2*	Type 11 collagen alpha-2 chain	
Oto-spondylo-mega-epiphyseal dysplasia (OSMED), recessive type	AR	215150	*COL11A2*	Type 11 collagen alpha-2 chain	
Oto-spondylo-mega-epiphyseal dysplasia (OSMED), dominant type (Weissenbacher–Zweymüller syndrome, Stickler syndrome type 3)	AD	277610	*COL11A2*	Type 11 collagen alpha-2 chain	
See also Stickler syndrome type 1 in group 2					
4. Sulphation disorders group					

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
Achondrogenesis type 1B (ACG1B)	AR	600972	*DTDST*	SLC26A2 sulfate transporter	Formerly known as Fraccaro type achondrogenesis
Atelosteogenesis type 2 (AO2)	AR	256050	*DTDST*	SLC26A2 sulfate transporter	Includes de la Chapelle dysplasia, McAlister dysplasia, and "neonatal osseous dysplasia"
Diastrophic dysplasia (DTD)	AR	222600	*DTDST*	SLC26A2 sulfate transporter	
MED, autosomal recessive type (rMED; EDM4)	AR	226900	*DTDST*	SLC26A2 sulfate transporter	See also multiple epiphyseal dysplasias and pseudoachondroplasia group (group 9)
SEMD, PAPSS2 type	AR	612847	*PAPSS2*	PAPS-Synthetase 2	Formerly "Pakistani type". See also SEMD group (group 13)
Brachyolmia, recessive type	AR	612847	*PAPSS2*	PAPS-Synthetase 2	Probably includes Toledo and Hobaek types of brachyolmia
Chondrodysplasia gPAPP type (includes Catel–Manzke-like syndrome	AR	614078	*IMPAD1*	Golgi 3-prime phosphoadenosine 5-prime phosphate 3-prime phosphatase	
Chondrodysplasia with congenital joint dislocations, CHST3 type (recessive Larsen syndrome)	AR	608637	*CHST3*	Carbohydrate sulfotransferase 3; chondroitin 6-sulfotransferase	Includes recessive Larsen syndrome, Humero–Spinal Dysostosis, and SED Omani type
Ehlers–Danlos syndrome, CHST14 type ("musculo-skeletal variant") See also group 7 and group 20 for other conditions with multiple dislocations.	AR	601776	*CHST14*	Carbohydrate sulfotransferase 14; dermatan 4-sulfotransferase	Includes Adducted Thumb–Clubfoot syndrome
5. Perlecan group					
Dyssegmental dysplasia, Silverman–Handmaker type	AR	224410	*PLC (HSPG2)*	Perlecan	
Dyssegmental dysplasia, Rolland–Desbuquois type	AR	224400	*PLC (HSPG2)*	Perlecan	
Schwartz–Jampel syndrome (myotonic chondrodystrophy)	AR	255800	*PLC (HSPG2)*	Perlecan	Mild and severe forms; includes previous Burton dysplasia
6. Aggrecan group					
SED, Kimberley type	AD	608361	*AGC1*	Aggrecan	
SEMD, Aggrecan type	AR	612813	*AGC1*	Aggrecan	
Familial osteochondritis dissecans	AD	165800	*AGC1*	Aggrecan	
7. Filamin group and related disorders					
Frontometaphyseal dysplasia	XLD	305620	*FLNA*	Filamin A	Some cases apparently lack FLNA mutations
Osteodysplasty Melnick–Needles	XLD	309350	*FLNA*	Filamin A	
Otopalatodigital syndrome type 1 (OPD1)	XLD	311300	*FLNA*	Filamin A	
Otopalatodigital syndrome type 2 (OPD2)	XLD	304120	*FLNA*	Filamin A	
Terminal osseous dysplasia with pigmentary defects (TODPD)	XLD	300244	*FLNA*	Filamin A	
Atelosteogenesis type 1 (AO1)	AD	108720	*FLNB*	Filamin B	Includes Boomerang dysplasia, Piepkorn dysplasia, and spondylohumerofemoral (giant cell) dysplasia
Atelosteogenesis type 3 (AO3)	AD	108721	*FLNB*	Filamin B	

Larsen syndrome (dominant)	AD	150250	*FLNB*	Filamin B	
Spondylo-carpal-tarsal dysplasia	AR	272460	*FLNB*	Filamin B	Some cases unlinked to FLNB
Frank-ter Haar syndrome	AR	249420	*SH3PXD2B*	TKS4	
(see also group 4 for recessive Larsen syndrome and group 20 for conditions with multiple dislocations)					
8. TRPV4 group					
Metatropic dysplasia	AD	156530	*TRPV4*	Transient receptor potential cation channel, subfamily V, member 4	Includes "hyperplastic", lethal and non-lethal forms
Spondyloepimetaphyseal dysplasia, Maroteaux type (Pseudo-Morquio syndrome type 2)	AD	184095	*TRPV4*	Transient receptor potential cation channel, subfamily V, member 4	Includes Parastremmatic (MIM 168400)
Spondylometaphyseal dysplasia, Kozlowski type	AD	184252	*TRPV4*	Transient receptor potential cation channel, subfamily V, member 4	
Brachyolmia, autosomal dominant type	AD	113500	*TRPV4*	Transient receptor potential cation channel, subfamily V, member 4	
Familial digital arthropathy with brachydactyly	AD	606835	*TRPV4*	Transient receptor potential cation channel, subfamily V, member 4	
9. Ciliopathies with major skeletal involvement					
Chondroectodermal dysplasia (Ellis-van Creveld)	AR	225500	*EVC1*	EvC gene 1	See also Weyers acrofacial (acrodental) dysostosis in group 34
			EVC2	EvC gene 2	
Short rib–polydactyly syndrome (SRPS) type 1/3 (Saldino–Noonan/Verma–Naumoff)	AR	208500	*DYNC2H1*	Dynein, cytoplasmic 2, heavy chain1	There is significant clinical and radiological overlap between SRP1/3 and ATD. Some forms of both remain unlinked to the known genes.
		613091	*IFT80*	Intraflagellar transport 80 (homolog of)	
			WDR34	WD repeat-containing protein 34	
Asphyxiating thoracic dysplasia (ATD; Jeune)	AR	263510	*DYNC2H1*	Dynein, cytoplasmic 2, heavy chain1	
			IFT80	Intraflagellar transport 80 (homolog of)	
			WDR34	WD repeat-containing protein 34	
			TTC21B	Tetratricopeptide repeat domain-containing protein 21B	
			WDR19	WD repeat-containing protein 19	
			IFT172	Intraflagellar transport 172	
			IFT140	Intraflagellar transport 140	
SRPS type 2 (Majewski)	AR	263520	*DYNC2H1*	Dynein, cytoplasmic 2, heavy chain1	
			NEK1	Never in mitosis gene a-related kinase 1	
SRPS type 4 (Beemer)	AR	269860			Not yet proven ciliopathy
SRPS type 5	AR	614091	*WDR35*	WD repeat-containing protein 19	
Oral-facial-digital syndrome type 4 (Mohr–Majewski)	AR	258860	*TCTN3*	Tectonic family, member 3	
Cranioectodermal dysplasia (Levin-Sensenbrenner) type 1, 2	AR	218330	*IFT122*	Intraflagellar transport 122	

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
		613610	*WDR35*	WD repeat-containing protein 35	
		614099	*WDR19*	WD repeat-containing protein 19	
			IFT43	Intraflagellar transport 43	
Thoracolaryngopelvic dysplasia (Barnes)	AD	187760			
See also paternal UPD14 and cerebro-costo-mandibular syndrome					
10. Multiple epiphyseal dysplasia and pseudoachondroplasia group					
Pseudoachondroplasia (PSACH)	AD	177170	*COMP*	COMP	
Multiple epiphyseal dysplasia (MED) type 1 (EDM1)	AD	132400	*COMP*	COMP	
Multiple epiphyseal dysplasia (MED) type 2 (EDM2)	AD	600204	*COL9A2*	Collagen 9 alpha-2 chain	
Multiple epiphyseal dysplasia (MED) type 3 (EDM3)	AD	600969	*COL9A3*	Collagen 9 alpha-3 chain	
Multiple epiphyseal dysplasia (MED) type 5 (EDM5)	AD	607078	*MATN3*	Matrilin 3	
Multiple epiphyseal dysplasia (MED) type 6 (EDM6)	AD	120210	*COL9A1*	Collagen 9 alpha-1 chain	
Multiple epiphyseal dysplasia (MED), other types					Some MED-like cases unlinked to known genes
Stickler syndrome, recessive type	AR	120210	*COL9A1*	Collagen 9 alpha-1 chain	See also groups 2 and 3
Familial hip dysplasia (Beukes)	AD	142669	4q35		
Multiple epiphyseal dysplasia with microcephaly and nystagmus (Lowry–Wood)	AR	226960			
See also Multiple Epiphyseal Dysplasia, recessive type (rMED; EDM4) in sulphation disorders (group 4), Familial osteochondritis dissecans in the Aggrecan group, as well as ASPED in the Acromelic group					
11. Metaphyseal dysplasias					
Metaphyseal dysplasia, Schmid type (MCS)	AD	156500	*COL10A1*	Collagen 10 alpha-1 chain	
Cartilage-hair hypoplasia (CHH; metaphyseal dysplasia, McKusick type)	AR	250250	*RMRP*	RNA component of RNAse H	Includes anauxetic dysplasia
Metaphyseal dysplasia, CHH-like, POP1 type	AR		*POP1*	Processing of precursor RNA	
Metaphyseal dysplasia, Jansen type	AD	156400	*PTHR1*	PTH/PTHrP receptor 1	Activating mutations-see also Blomstrand dysplasia (group 23)
Eiken dysplasia	AR	600002	*PTHR1*	PTH/PTHrP receptor 1	Activating mutations-see also Blomstrand dysplasia (group 23)
Metaphyseal dysplasia with pancreatic insufficiency and cyclic neutropenia (Shwachman–Bodian–Diamond syndrome, SBDS)	AR	260400	*SBDS*	SBDS protein	
Metaphyseal anadysplasia type 1	AD, AR	602111	*MMP13*	Matrix metalloproteinase 13	Includes SEMD Missouri type.
Metaphyseal anadysplasia type 2	AR	613073	*MMP9*	Matrix metalloproteinase 9	
Metaphyseal dysplasia, Spahr type	AR	250400	*MMP13*	Matrix metalloproteinase 13	Includes autosomal recessive anadysplasia
Metaphyseal dysplasia with maxillary hypoplasia	AD	156510	*RUNX2*	Runt-related transcription factor 2	
12. Spondylometaphyseal dysplasias (SMD)					
Spondyloenchondrodysplasia (SPENCD)	AR	271550	*ACP5*	Tartrate-resistant acid phosphatase (TRAP)	Includes combined immunodeficiency with autoimmunity and

					spondylometaphyseal dysplasia (MIM 607944)
Odontochondrodysplasia (ODCD)	AR	184260			
SMD, Sutcliffe type or corner fractures type	AD	184255			Some cases are linked to COL2A1 but not the original family
SMD with cone-rod dystrophy	AR	608940	*PCYT1A*	Phosphate cytidylyltransferase 1	
SMD with retinal degeneration, axial type	AR	602271			
See also SMD Kozlowski (group TRPV4) as well as SMD Sedaghatian type in group 14; there are many individual reports of SMD variants.					
13. Spondylo-epi-(meta)-physeal dysplasias (SE(M)D)					
Dyggve–Melchior–Clausen dysplasia (DMC)	AR	223800	*DYM*	Dymeclin	Includes Smith–McCort dysplasia (MIM 607326)
		615222	*RAB33B*	RAS-associated protein rab33b	
Immuno-osseous dysplasia (Schimke)	AR	242900	*SMARCAL1*	SWI/SNF-related regulator of chromatin subfamily A-like protein 1	
SED, Wolcott–Rallison type	AR	226980	*EIF2AK3*	Translation initiation factor 2-alpha kinase-3	
SEMD, Matrilin type	AR	608728	*MATN3*	Matrilin 3	See also matrilin-related MED in group 10
SEMD, short limb–abnormal calcification type	AR	271665	*DDR2*	Discoidin domain receptor family, member 2	See also other dysplasias with stippling in group 21
SED tarda, X-linked (SED-XL)	XLR	313400	*SEDL*	Sedlin	
Spondylodysplastic Ehlers–Danlos syndrome	AR	612350	*SLC39A13*	Zinc transporter ZIP13	
SPONASTRIME dysplasia	AR	271510			
Platyspondyly (brachyolmia) with amelogenesis imperfecta	AR	601216			
CODAS syndrome	AR	600373	*LONP1*	LON peptidase 1	
See also: Opsismodysplasia (group 14), mucopolysaccharidosis type 4 (Morquio syndrome) and other conditions in group 27, as well as PPRD (SED with progressive arthropathy) in group 31					
14. Severe spondylodysplastic dysplasias					
Achondrogenesis type 1A (ACG1A)	AR	200600	*TRIP11*	Golgi-microtubule-associated protein, 210-KD; GMAP210	
Schneckenbecken dysplasia	AR	269250	*SLC35D1*	solute carrier family 35 member D1; UDP-glucuronic acid/UDP-N-acetylgalactosamine dual transporter	
Spondylometaphyseal dysplasia, Sedaghatian type	AR	250220	*GPX4*	Glutathione peroxidase 4	
Severe spondylometaphyseal dysplasia (SMD Sedaghatian-like)	AR		*SBDS*	SBDS gene, function still unclear	
Opsismodysplasia	AR	258480	*INPPL1*	Inositol polyphosphate phosphatase-like 1	Includes lethal and milder cases
MAGMAS related skeletal dysplasia	AR		*MAGMAS*	Presequence translocase-associated motor 16	
See also: Thanatophoric dysplasia, types 1 and 2 (group 1); ACG2 and Torrance dysplasia (group 2);					

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
Fibrochondrogenesis (group 3); Achondrogenesis type 1B (group 4); and Metatropic Dysplasia (group 8)					
15. Acromelic dysplasias					
Tricho-rhino-phalangeal dysplasia types 1/3	AD	190350	*TRPS1*	Zinc finger transcription factor	
Tricho-rhino-phalangeal dysplasia type 2 (Langer–Giedion)	AD	150230	*TRPS1 and EXT1*	Zinc finger transcription factor and Exostosin 1	Microdeletion syndrome; see also Multiple Cartilagineous Exostoses in group 28
Acrocapitofemoral dysplasia	AR	607778	*IHH*	Indian hedgehog	
Geleophysic dysplasia	AR	231050	*ADAMTSL2*	ADAMTS-like protein 2	Some forms unlinked to either gene
	AD	614185	*FBN1*	Fibrillin 1	
Acromicric dysplasia	AD	102370	*FBN1*	Fibrillin 1	Includes acrolaryngeal dysplasia, previously known as Fantasy Island dysplasia or Tattoo dysplasia
Weill–Marchesani	AD		*FBN1*	Fibrillin 1	
	AR		*ADAMTS10*	A disintegrin-like and metalloproteinase with *thrombospondin type 1 motif, 10,17*	
	AR		*ADAMTS17*		
			LTBP2	Latent transforming growth factor-beta-binding protein 2	
Myhre dysplasia	AD	139210	*SMAD4*	Mothers against decapentaplegic, drosophila, homolog of, 4	
Acrodysostosis	AD	101800	*PDE4D*	Phosphodiesterase 4D, camp-specific	Includes some cases of acroscyphodysostosis
			PRKAR1A	Protein kinase, camp-dependent, regulatory, type 1, alpha	
Angel-shaped phalango-epiphyseal dysplasia (ASPED)	AD	105835			Possibly related or allelic to Brachydactyly type C
Albright hereditary osteodystrophy	AD	103580	*GNAS*	Guanine nucleotide-binding protein, alpha-stimulating activity polypeptide 1	Includes some cases of acroscyphodysostosis
See also brachydactyly group (group 37)					
16. Acromesomelic dysplasias					
Acromesomelic dysplasia type Maroteaux (AMDM)	AR	602875	*NPR2*	Natriuretic peptide receptor 2	
Grebe dysplasia	AR	200700	*GDF5*	Growth and Differentiation Factor 5	Includes acromesomelic dysplasia Hunter–Thompson type; see also Brachydactylies (group 34)
Fibular hypoplasia and complex brachydactyly (Du Pan)	AR	228900	*GDF5*	Growth and Differentiation Factor 5	See also Brachydactylies (group 34)
Acromesomelic dysplasia with genital anomalies	AR	609441	*BMPR1B*	Bone morphogenetic protein receptor 1B	
Acromesomelic dysplasia, Osebold-Remondini type	AD	112910			
17. Mesomelic and rhizo-mesomelic dysplasias					
Dyschondrosteosis (Leri–Weill)	Pseudo-AD	127300	*SHOX*	Short stature–homeobox gene	Includes Reinhardt–Pfeiffer dysplasia,

					MIM 191400
Langer type (homozygous dyschondrosteosis)	Pseudo-AR	249700	*SHOX*	Short stature–homeobox gene	
Omodysplasia	AR	258315	*GPC6*	Glypican 6	
Omodysplasia, dominant	AD	164745	*FZD2*	Frizzled 2	
Robinow syndrome, recessive type	AR	268310	*ROR2*	Receptor tyrosine kinase-like orphan receptor 2	Includes previous COVESDEM (costo–vertebral segmentation defect with mesomelia); see also brachydactyly type B
Robinow syndrome, dominant type	AD	180700	*WNT5A*	Wingless-type mmtv integration site family, member 5a	
		601365	*DVL1*	Dishevelled 1	
Mesomelic dysplasia, Kantaputra type	AD	156232		Duplications in HOXD gene cluster	Includes Mesomelic dysplasia, Korean type
Mesomelic dysplasia, Nievergelt type	AD	163400			
Mesomelic dysplasia, Kozlowski–Reardon type	AR	249710			
Mesomelic dysplasia with acral synostoses (Verloes–David –Pfeiffer type)	AD	600383	*SULF1 and SLCO5A1*	Heparan sulfate 6-O-endosulfatase 1 and solute carrier organic anion transporter family member 5A1	Microdeletion syndrome involving two adjacent genes
Mesomelic dysplasia, Savarirayan type (Triangular Tibia–Fibular Aplasia)	SP	605274	6p22.3 deletions		Possibly related to Nievergelt dysplasia.
18. Campomelic dysplasia and related disorders					
Campomelic dysplasia (CD)	AD	114290	*SOX9*	SRY-box 9	Includes acampomelic campomelic dysplasia (ACD), mild campomelic dysplasia (MIM 602196) and isolated Pierre–Robin
Stüve–Wiedemann dysplasia	AR	601559	*LIFR*	Leukemia Inhibitory Factor Receptor	Includes former neonatal Schwartz–Jampel syndrome or SJS type 2
Kyphomelic dysplasia, several forms		211350			Probably heterogeneous
See also group 33 for craniosynostoses syndromes linked to FGFR2					
19. Slender bone dysplasia group					
3-M syndrome	AR	273750	*CUL7*	Cullin 7	Includes dolichospondylic dysplasia and Yakut short stature syndrome
		612921	*OBSL1*	Obscurin-like 1	
		614205	*CCDC8*	Coiled-coil domain-containing protein 8	
Kenny–Caffey dysplasia	AR	244460	*TBCE*	Tubulin-specific chaperone E	Referred to in OMIM as type 1 but does not correspond to disorder described by Kenny and Caffey which is the dominant form
Kenny–Caffey dysplasia	AD	127000	*FAM111A*	Family with sequence similarity 111, member A	
Osteocraniostenosis	AD	602361	*FAM111A*	Family with sequence similarity 111, member A	
Microcephalic osteodysplastic primordial dwarfism type 1/3 (MOPD1)	AR	210710	*RNU4ATAC*	RNA, U4ATAC small nuclear	Includes Taybi–Linder cephaloskeletal dysplasia
Microcephalic osteodysplastic primordial dwarfism type 2	AR	210720	*PCNT2*	Pericentrin 2	

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
(MOPD2; Majewski type)					
IMAGE syndrome (intrauterine growth retardation, metaphyseal dysplasia, adrenal hypoplasia, and genital anomalies)	AD	614732	*CDKN1C*	Cyclin-dependent kinase inhibitor 1C	Possibly heterogeneous
Hallermann-Streiff syndrome	AR	234100			Mutations in *GJA1* reported in one case only
See also Cerebro-arthro-digital dysplasia					
20. Dysplasias with multiple joint dislocations					
Desbuquois dysplasia (with accessory ossification centre in digit 2)	AR	251450	*CANT1*	Calcium-activated nucleotidase 1	Other variants with or without accessory ossification centres unlinked to *CANT1*
Desbuquois dysplasia with short metacarpals and elongated phalanges (Kim type)	AR	251450	*CANT1*	Calcium-activated nucleotidase 1	
Desbuquois dysplasia type 2	AR	615777	*XYLT1*	Xylosyltransferase 1	
Pseudodiastrophic dysplasia	AR	264180			
SEMD with joint laxity (SEMD-JL) leptodactylic or Hall type	AD	603546	*KIF22*	Kinesin family member 22	
SEMD with joint laxity (SEMD-JL) Beighton type	AR	271640	*B3GALT6*	Beta-1,3-galactosyltransferase polypeptide 6	
See also: SED with congenital dislocations, CHST3 type (group 4); Atelosteogenesis type 3 and Larsen syndrome (group 7)					
21. Chondrodysplasia punctata (CDP) group					
CDP, X-linked dominant, Conradi-Hünermann type (CDPX2)	XLD	302960	*EBP*	Emopamil-binding protein	
CDP, X-linked recessive, brachytelephalangic type (CDPX1)	XLR	302950	*ARSE*	Arylsulfatase E	
CHILD (congenital hemidysplasia, ichthyosis, limb defects)	XLD	308050	*NSDHL*	NAD(P)H steroid dehydrogenase-like protein	
Keutel syndrome	AR	245150	*MGP*	Matrix gamma-carboxyglutamic acid	
Greenberg dysplasia	AR	215140	*LBR*	Lamin B receptor, 3-beta-hydroxysterol delta (14)-reductase	Includes hydrops-ectopic calcification-moth-eaten appearance dysplasia (HEM) and dappled diaphyseal dysplasia
Rhizomelic CDP type 1	AR	215100	*PEX7*	Peroxisomal PTS2 receptor	
Rhizomelic CDP type 2	AR	222765	*DHPAT*	Dihydroxyacetonephosphate acyltransferase (DHAPAT)	
Rhizomelic CDP type 3	AR	600121	*AGPS*	Alkylglycerone-phosphate synthase (AGPS)	
CDP tibial-metacarpal type	AD/AR	118651			Nosologic status uncertain
Astley–Kendall dysplasia	AR?				Relationship to OI and to Greenberg dysplasia unclear
Note that stippling can occur in maternal auto-immune disease and several syndromes such as Zellweger, Smith–Lemli–Opitz and others. See also desmosterolosis as well as SEMD short limb-abnormal calcification type in group 13.					

22. Neonatal osteosclerotic dysplasias					
Blomstrand dysplasia	AR	215045	*PTHR1*	PTH/PTHrP receptor 1	Caused by recessive inactivating mutations; see also Eiken dysplasia and Jansen dysplasia
Desmosterolosis	AR	602398	*DHCR24*	3-beta-hydroxysterol delta-24-reductase	See also other sterol-metabolism related conditions
Caffey disease (including prenatal, infantile and attenuated forms)	AD	114000	*COL1A1*	Collagen 1, alpha-1 chain	See also osteogenesis imperfecta related to collagen 1 genes (group 24)
Caffey dysplasia (severe variants with prenatal onset)	AR	114000			
Raine dysplasia (lethal and non-lethal forms)	AR	259775	*FAM20C*	Dentin matrix protein 4	Includes lethal and non-lethal cases
See also Astley–Kendall dysplasia and CDPs in group 21					
23. Osteopetrosis and related disorders					
Osteopetrosis, severe neonatal or infantile forms (OPTB1)	AR	259700	*TCIRG1*	Subunit of ATPase proton pump	
Osteopetrosis, severe neonatal or infantile forms (OPTB4)	AR	611490	*CLCN7*	Chloride channel 7	
Osteopetrosis, severe neonatal or infantile forms (OPTB8)	AR	615085	*SNX10*	Sorting Nexin 10	
Osteopetrosis, infantile form, with nervous system involvement (OPTB5)	AR	259720	*OSTM1*	Grey lethal/Osteopetrosis associated transmembrane protein	Includes former osteopetrosis with infantile neuraxonal dysplasia
Osteopetrosis, intermediate form, osteoclast-poor (OPTB2)	AR	259710	*RANKL (TNFSF11)*	Receptor activator of NF-kappa-B ligand (Tumor necrosis factor ligand superfamily, member 11)	
Osteopetrosis, infantile form, osteoclast- poor with immunoglobulin deficiency (OPTB7)	AR	612302	*RANK (TNFRSF11A)*	Receptor activator of NF-kappa-B	*See also* Familial expansile osteolysis in Osteolysis group (group 28)
Osteopetrosis, intermediate form (OPTB6)	AR	611497	*PLEKHM1*	Pleckstrin homology domain-containing protein, family M, member 1	
Osteopetrosis, intermediate form (OPTA2)	AR	259710	*CLCN7*	Chloride channel pump	
Osteopetrosis with renal tubular acidosis (OPTB3)	AR	259730	*CA2*	Carbonic anhydrase 2	
Osteopetrosis, late-onset form type 1 (OPTA1)	AD	607634	*LRP5*	Low density lipoprotein receptor-related protein 5	Includes Worth type osteosclerosis (MIM 144750)
Osteopetrosis, late-onset form type 2 (OPTA2)	AD	166600	*CLCN7*	Chloride channel 7	
Osteopetrosis with ectodermal dysplasia and immune defect (OLEDAID)	XL	300301	*IKBKG (NEMO)*	Inhibitor of kappa light polypeptide gene enhancer, kinase of	
Osteopetrosis, moderate form with defective leucocyte adhesion (LAD3)	AR	612840	*FERMT3 (KIND3)*	Fermitin 3 (Kindlin 3)	
Osteopetrosis, moderate form with defective leucocyte adhesion	AR	612840	*RASGRP2 (CalDAG-GEF1)*	Ras guanyl nucleotide-releasing protein 2	
Pyknodysostosis	AR	265800	*CTSK*	Cathepsin K	
Osteopoikilosis	AD	155950	*LEMD3*	LEM domain-containing 3	Includes Buschke–Ollendorff syndrome (MIM 166700)
Melorheostosis with osteopoikilosis	AD	155950	*LEMD3*	LEM domain-containing 3	Includes mixed sclerosing bone dysplasia
Osteopathia striata with cranial sclerosis (OSCS)	XLD	300373	*WTX*	FAM123B	
Melorheostosis	SP				No germ line LEMD3 mutations identified so far

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
Dysosteosclerosis	AR	224300	*SLC29A3*	Solute carrier family 29 (nucleoside transporter)	
Note: osteomesopyknosis may represent a form of osteopetrosis					
24. Other sclerosing bone disorders					
Craniometaphyseal dysplasia, autosomal dominant type	AD	123000	*ANKH*	Homolog of mouse ANK (ankylosis) gene	Gain of function mutations
Diaphyseal dysplasia Camurati–Engelmann	AD	131300	*TGFB1*	Transforming growth factor beta 1	
Hematodiaphyseal dysplasia Ghosal	AR	231095	*TBXAS1*	Thromboxane A synthase 1	
Hypertrophic osteoarthropathy	AR	259100	*HPGD*	15-alpha-hydroxyprostaglandin dehydrogenase	Includes cranio-osteoarthropathy and cases of recessive pachydermoperiostosis
Pachydermoperiostosis (hypertrophic osteoarthropathy, primary, autosomal dominant)	AD	167100			Relationship to recessive form (MIM 259100, HPGD deficiency) unclear
Oculo-dento-osseous dysplasia (ODOD) mild type	AD	164200	*GJA1*	Gap junction protein alpha-1	
Oculo-dento-osseous dysplasia (ODOD) severe type	AR	257850	*GJA1*	Gap junction protein alpha-1	Possibly homozygous form of mild ODOD
Osteoectasia with hyperphosphatasia (juvenile Paget disease)	AR	239000	*OPG*	Osteoprotegerin	
Sclerosteosis	AR,AD	269500, 614305	*SOST,* *LRP4*	Sclerostin, Low density lipoprotein receptor-related protein 4	
Endosteal hyperostosis, van Buchem type	AR	239100	*SOST*	Sclerostin	Specific 52 kb deletion downstream of *SOST*
Trichodentoosseous dysplasia	AD	190320	*DLX3*	Distal-less homeobox 3	
Craniometaphyseal dysplasia, autosomal recessive type	AR	218400	*GJA1*	Gap junction protein alph-1	
Diaphyseal medullary stenosis with malignant fibrous histiocytoma	AD	112250			Also known as Hardcastle
Craniodiaphyseal dysplasia	AD	122860	*SOST*	Sclerostin	Dominant negative
Craniometadiaphyseal dysplasia, Wormian bone type	AR	615118			Also known as Schwartz–Lelek dysplasia
Endosteal sclerosis with cerebellar hypoplasia	AR	213002			
Lenz-Majewski hyperostotic dysplasia	SP	151050	*PTDSS1*	Phosphatidylserine synthase 1	
Metaphyseal dysplasia, Braun–Tinschert type	AD	605946			
Pyle disease	AR	265900			
25. Osteogenesis imperfecta and decreased bone density group					
For comments the classification of Osteogenesis imperfecta, please refer to the text					
Osteogenesis imperfecta, non-deforming form (OI type 1)	AD		*COL1A1*	Collagen 1 alpha-1 chain,	Form with persistently blue sclerae
			COL1A2	Collagen 1 alpha-2 chain,	
Osteogenesis imperfecta, perinatal lethal form (OI type 2)	AD, AR		*COL1A1*		
			COL1A2		
			CRTAP	Cartilage-associated Protein	See also Bruck syndrome (below)
			LEPRE1	Leucine proline-enriched proteoglycan (leprecan) 1	

			PPIB	Peptidylprolyl isomerase B (cyclophilin B)	
Osteogenesis imperfecta, progressively deforming type (OI type 3)	AD, AR		*COL1A1* *COL1A2,* *CRTAP* *LEPRE1* *PPIB*		
			SERPINH1	Serpin peptidase inhibitor, clade H, member 1	
			BMP1	Bone morphogenetic protein 1	
			FKBP10	FK506 binding protein 10	
			PLOD2	Procollagen lysyl hydroxylase 2	
			SERPINF1	Serpin peptidase inhibitor, clade F, member 1	
			SP7	SP7 transcription factor (Osterix)	
			WNT1	Wingless-type MMTV integration site family, member	
			TMEM38B	Transmemebrane protein 38B	
			CREB3L1	OASIS	
			SEC24D	SEC24-related gene family, member D	
Osteogenesis imperfecta, moderate form (OI type 4)	AD, AR		*COL1A1* *COL1A2,* *CRTAP* *PPIB* *FKBP10* *SERPINF1* *WNT1* *SP7*		Sclerae generally normal
Osteogenesis imperfecta with calcification of the interosseous membranes and/or hypertrophic callus (OI type 5)	AD	610967	*IFITM5*	Interferon-Induced Transmembrane Protein 5	
X-linked osteoporosis	XL	300910	*PLS3*	Plastin 3	May be the same as Juvenile idiopathic osteoporosis (MIM259750)
Bruck syndrome type 1 (BS1)	AR	259450	*FKBP10*	FK506 binding protein 10	See autosomal recessive OI, above; intrafamilial variability between OI3 and BS1 documented
Bruck syndrome type 2 (BS2)	AR	609220	*PLOD2*	Procollagen lysyl hydroxylase 2	
Osteoporosis-pseudoglioma syndrome	AR	259770	*LRP5*	LDL-receptor related protein 5	May mimic OI types 3 and 4
LRP5 primary osteoporosis	AD		*LRP5*		
Calvarial doughnut lesions with bone fragility	AD	126550			
Idiopathic juvenile osteoporosis	SP	259750			Some patients reported with heterozygous mutations in the *LRP5* gene and perhaps X-linked osteoporosis
Cole-Carpenter dysplasia (bone fragility with	AD	112240	*P4HB*	Prolyl 4-hydroxylase, beta-subunit	See also craniosynostosis syndromes in

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
craniosynostosis)					group 30
Spondylo-ocular dysplasia	AR	605822	*XYLT2*	Xylosyltransferase 2	Probably heterogeneous
Osteopenia with radiolucent lesions of the mandible	AD	166260			
Ehlers-Danlos syndrome, progeroid form	AR	130070	*B4GALT7*	Xylosylprotein 4-beta-galactosyltransferase deficiency	
Geroderma osteodysplasticum	AR	231070	*GORAB*	SCYL1-binding protein 1	
Cutis laxa, autosomal recessive form, type 2B (ARCL2B)	AR	612940	*PYCR1*	Pyrroline-5-carboxylate reductase 1	Skeletal features overlapping with progeroid EDS and geroderma osteodysplasticum
Cutis laxa, autosomal recessive form, type 2A (ARCL2A) (Wrinkly skin syndrome)	AR	278250, 219200	*ATP6V0A2*	ATPase, H+ transporting, lysosomal, V0 subunit A2	Skeletal features overlapping with progeroid EDS and geroderma osteodysplasticum
Singleton–Merten dysplasia	AD	182250			
26. Abnormal mineralization group					
Hypophosphatasia, perinatal lethal, infantile and juvenile forms	AR	241500	*ALPL*	Alkaline phosphatase, tissue non-specific (TNSALP)	Intrafamilial variability
Hypophosphatasia, juvenile and adult forms	AD	146300	*ALPL*	Alkaline phosphatase, tissue non-specific (TNSALP)	Includes odontohypophosphatasia
Hypophosphatemic rickets, X-linked dominant	XLD	307800	*PHEX*	X-linked hypophosphatemia membrane protease	
Hypophosphatemic rickets, autosomal dominant	AD	193100	*FGF23*	Fibroblast growth factor 23	
Hypophosphatemic rickets, autosomal recessive, type 1 (ARHR1)	AR	241520	*DMP1*	Dentin matrix acidic phosphoprotein 1	
Hypophosphatemic rickets, autosomal recessive, type 2 (ARHR2)	AR	613312	*ENPP1*	Ectonucleotide pyrophosphatase/phosphodiesterase 1	
Hypophosphatemic rickets with hypercalciuria, X-linked recessive	XLR	300554	*CICN5*	Chloride channel 5	Part of Dent's disease complex
Hypophosphatemic rickets with hypercalciuria, autosomal recessive (HHRH)	AR	241530	*SLC34A3*	Sodium-phosphate cotransporter	
Neonatal hyperparathyroidism, severe form	AR	239200	*CASR*	Calcium-sensing receptor	
Familial hypocalciuric hypercalcemia with transient neonatal hyperparathyroidism	AD	145980	*CASR*	Calcium-sensing receptor	
Calcium pyrophosphate deposition disease (familial chondrocalcisnosis) type 2	AD	118600	*ANKH*	Homolog of mouse ANK (ankylosis) gene	Loss of function mutations (see craniometaphyseal dysplasia in group 24)
See also Jansen dysplasia and Eiken dysplasia					
27. Lysosomal Storage Diseases with Skeletal Involvement (Dysostosis Multiplex group)					
Mucopolysaccharidosis type 1H/1S (Hurler, Hurler–Scheie, Scheie)	AR	607014	*IDA*	Alpha-1-Iduronidase	
Mucopolysaccharidosis type 2 (Hunter)	XLR	309900	*IDS*	Iduronate-2-sulfatase	
Mucopolysaccharidosis type 3A (Sanfilippo A)	AR	252900	*HSS*	Heparan sulfate sulfatase	
Mucopolysaccharidosis type 3B (Sanfilippo B)	AR	252920	*NAGLU*	N-Ac-beta-D-glucosaminidase	

Mucopolysaccharidosis type 3C (Sanfilippo C)	AR	252930	*HSGNAT*	Ac-CoA: alpha-glucosaminide N-acetyltransferase	
Mucopolysaccharidosis type 3D (Sanfilippo D)	AR	252940	*GNS*	N-Acetylglucosamine 6-sulfatase	
Mucopolysaccharidosis type 4A (Morquio A)	AR	253000	*GALNS*	Galactosamine-6-sulfate sulfatase	
Mucopolysaccharidosis type 4B (Morquio B)	AR	253010	*GLBI*	Beta-Galactosidase	
Mucopolysaccharidosis type 6 (Maroteaux-Lamy)	AR	253200	*ARSB*	Arylsulfatase B	
Mucopolysaccharidosis type 7 (Sly)	AR	253220	*GUSB*	Beta-Glucuronidase	
Fucosidosis	AR	230000	*FUCA*	Alpha-Fucosidase	
Alpha-Mannosidosis	AR	248500	*MANA*	Alpha-Mannosidase	
Beta-Mannosidosis	AR	248510	*MANB*	Beta-Mannosidase	
Aspartylglucosaminuria	AR	208400	*AGA*	Aspartyl-glucosaminidase	
GMI Gangliosidosis, several forms	AR	230500	*GLB1*	beta-Galactosidase	
Sialidosis, several forms	AR	256550	*NEU1*	Neuraminidase (sialidase)	
Sialic acid storage disease (SIASD)	AR	269920	*SLC17A5*	Sialin (sialic acid transporter)	
Galactosialidosis, several forms	AR	256540	*PPGB*	Beta-Galactosidase protective protein	
Multiple sulfatase deficiency	AR	272200	*SUMF1*	Sulfatase-modifying factor-1	
Mucolipidosis II (I-cell disease), alpha/beta type	AR	252500	*GNPTAB*	N-Acetylglucosamine 1-phosphotransferase, alpha/beta subunits	
Mucolipidosis III (Pseudo–Hurler polydystrophy), alpha/beta type	AR	252600	*GNPTAB*	N-Acetylglucosamine 1-phosphotransferase, alpha/beta subunits	
Mucolipidosis III (Pseudo–Hurler polydystrophy), gamma type	AR	252605	*GNPTG*	N-Acetylglucosamine 1-phosphotransferase, gamma subunit	
Other conditions resembling storage diseases: congenital disorders of glycosylation and geleophysic					
28. Osteolysis group					
Familial expansile osteolysis	AD	174810	*RANK (TNFRSF11A)*		Includes expansile skeletal hyperphosphatasia (MIM 602080)
Mandibuloacral dysplasia type A	AD	248370	*LMNA*	Lamin A/C	
Mandibuloacral dysplasia type B	AR	608612	*ZMPSTE24*	Zinc metalloproteinase	
Progeria, Hutchinson–Gilford type	AD	176670	*LMNA*	Lamin A/C	
Torg–Winchester syndrome	AR	259600	*MMP2*	Matrix metalloproteinase 2	Includes Nodulosis–Arthropathy–Osteolysis syndrome (MIM 605156)
Hajdu–Cheney syndrome	AD	102500	*NOTCH2*	NOTCH2	Includes serpentine fibula-polycystic kidney syndrome
Multicentric carpal-tarsal osteolysis with and without nephropathy	AD	166300	*MAFB*	V-maf musculoaponeurotic fibrosarcoma oncogene family, protein b	
See also Pycnodysostosis, cleidocranial dysplasia, Keutel and Singleton–Merten syndrome. Note: several neurologic conditions may cause acroosteolysis					
29. Disorganized development of skeletal components group					
Multiple cartilaginous exostoses 1	AD	133700	*EXT1*	Exostosin-1	

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
Multiple cartilaginous exostoses 2	AD	133701	*EXT2*	Exostosin-2	
Multiple cartilaginous exostoses 3	AD	600209			Unclear if other genes/loci
Cherubism	AD	118400	*SH3BP2*	SH3 domain-binding protein 2	
Fibrous dysplasia, polyostotic form (McCune–Albright)	SP	174800	*GNAS*	Guanine nucleotide-binding protein, alpha-stimulating activity subunit 1	Somatic mosaicism and imprinting phenomena
Progressive osseous heteroplasia	AD	166350	*GNAS*	Guanine nucleotide-binding protein, alpha-stimulating activity subunit 1	Gene subject to imprinting
Gnathodiaphyseal dysplasia	AD	166260	*TMEM16E*	Transmembrane protein 16E	
Metachondromatosis	AD	156250	*PTPN11*	Protein-tyrosine phosphatase nonreceptor-type 11	
Osteoglophonic dysplasia	AD	166250	*FGFR1*	Fibroblast growth factor receptor 1	See also Craniosynostosis syndromes in group 30
Fibrodysplasia ossificans progressiva (FOP)	AD, SP	135100	*ACVR1*	Activin A (BMP type 1) receptor	
Neurofibromatosis type 1 (NF1)	AD	162200	*NF1*	Neurofibromin	
Carpotarsal osteochondromatosis	AD	127820			
Cherubism with gingival fibromatosis (Ramon syndrome)	AR	266270			
Dysplasia epiphysealis hemimelica (Trevor)	SP	127800			
Lipomembraneous osteodystrophy with leukoencephalopathy (presenile dementia with bone cysts; Nasu–Hakola)	AR	221770	*TREM2, TYROBP*	Triggering receptor expressed on myeloid cells 2, Tyro protein tyrosine kinase-binding protein	
Enchondromatosis (Ollier) and Enchondromatosis with hemangiomata (Maffucci)	SP	166000	*IDH1, IDH2*	Isocitrate dehydrogenase 1, 2	Role of *PTHR1* mutations found in a few cases only, role still unclear
Metaphyseal chondromatosis with D-2-hydroxyglutaric aciduria	SP	614875	*IDH1, IDH2*	Isocitrate dehydrogenase 1, 2	
Genochondromatosis	SP/AD	137360			
Gorham-Stout					
See also: Proteus syndrome in group 30; Spondyloenchondrodysplasia in group 12;					
30. Overgrowth (tall stature) syndromes with skeletal involvement					
Weaver syndrome	SP/AD	277590	*EZH2*	Enhancer of zeste, drosophila, homolog 2	Some cases reported with *NSD1* mutations (see Sotos syndrome)
Sotos syndrome	AD	117550	*NSD1*	Nuclear receptor-binding su-var, enhancer of zeste, and trithorax domain protein 1	Some cases may have *NFIX* mutations (see Marshall–Smith syndrome)
Sotos-like syndrome	AD		*SETD2*	Set domain containing protein2	
Marshall–Smith syndrome	SP	602535	*NFIX*	nuclear factor I/X	Some clinical overlap with Sotos syndrome (see above)
Proteus syndrome	SP	176920	*AKT1*	v-akt murine thymoma viral oncogene homolog 1	Some Proteus-like cases have mutations in the *PTEN* gene
CLOVES	SP	612918	*PIK3CA*	Phosphatidylinositol 3-kinase, catalytic, alpha	

Marfan syndrome	AD	154700	*FBN1*	Fibrillin 1	
Congenital contractural arachnodactyly	AD	121050	*FBN2*	Fibrillin 2	
Loeys–Dietz syndrome types 1A,1B, 2A, 2B, 3, 4	AD	609192, 610168, 608967, 610380, 613795, 614816	*TGFBR1* *TGFBR2,* *SMAD3* *TGFB2*	TGFbeta receptor subunit 1 TGFbeta receptor subunit 2 SMA related protein3 TGFbeta 2	
Overgrowth syndrome with 2q37 translocations	SP	--	*NPPC*	Natriuretic peptide precursor C	Overgrowth probably caused by overexpression of *NPPC*
Overgrowth with macrodactyly and NPR2 gain of function	AD	---	*NPR2*	Natriuretic peptide receptor 2	
Overgrowth syndrome with skeletal dysplasia (Nishimura–Schmidt, endochondral gigantism)	SP?				Nosologic status unclear but conspicuous skeletal phenotype(s)
See also: Shprintzen–Goldberg syndrome in Craniosynostosis group					
31. Genetic inflammatory/rheumatoid-like osteoarthropathies					
Progressive pseudorheumatoid dysplasia (PPRD; SED with progressive arthropathy)	AR	208230	*WISP3*	WNT1-inducible signaling pathway protein 3	
Chronic infantile neurologic cutaneous articular syndrome (CINCA)/neonatal onset multisystem inflammatory disease (NOMID)	AD	607115	*CIAS1*	Cryopyrin	
Sterile multifocal osteomyelitis, periostitis, and pustulosis (CINCA/NOMID-like)	AR	147679	*IL1RN*	Interleukin 1 receptor antagonist	
Chronic recurrent multifocal osteomyelitis with congenital dyserythropoietic anemia (CRMO with CDA; Majeed syndrome)	AR	609628	*LPIN2*	Lipin 2	
Hyperostosis/hyperphosphatemia syndrome	AR	610233	*GALNT3*	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 3	
Hyaline fibromatosis syndrome	AR	236490	*ANTXR2*	Anthrax toxin receptor 2	Previously known as Infantile systemic hyalinosis, Juvenile Hyaline Fibromatosis (JHF, 228600) and Puretic syndrome
32. Cleidocranial dysplasia and related disorders					
Cleidocranial dysplasia	AD	119600	*RUNX2*	Runt related transcription factor 2	
CDAGS syndrome (craniosynostosis, delayed fontanel closure, parietal foramina, imperforate anus, genital anomalies, skin eruption)	AR	603116			
Yunis–Varon dysplasia	AR	216340	*FIG4*		
Parietal foramina (isolated)	AD	168500	*ALX4* *MSX2*	Aristaless-like 4 Muscle segment homeobox 2	See also Frontonasal dysplasia type 1 (group 34)
See also: pycnodysostosis, wrinkly skin syndrome, and several others. See also metaphyseal dysplasia with maxillary hypoplasia in Group 11					

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
33. Craniosynostosis syndromes					
Pfeiffer syndrome (FGFR1-related)	AD	101600	*FGFR1, FGFR2*	Fibroblast growth factor receptor 1 and 2	Most have *FGFR1* P252R mutation Includes Jackson–Weiss syndrome (MIM 123150) and Antley–Bixler variants caused by *FGFR2* mutations (see below)
Apert syndrome	AD	101200	*FGFR2*	Fibroblast growth factor receptor 2	
Craniosynostosis with cutis gyrata (Beare–Stevenson)	AD	123790	*FGFR2*	Fibroblast growth factor receptor 2	
Crouzon syndrome	AD	123500	*FGFR2*	Fibroblast growth factor receptor 2	
Bent bone dysplasia	AD	614592	*FGFR2*	Fibroblast growth factor receptor 2	
Crouzon-like craniosynostosis with acanthosis nigricans (Crouzonodermoskeletal syndrome)	AD	612247	*FGFR3*	Fibroblast growth factor receptor 3	Defined by specific *FGFR3* A391E mutation
Craniosynostosis, Muenke type	AD	602849	*FGFR3*	Fibroblast growth factor receptor 3	Defined by specific *FGFR3* P250R mutation
Antley–Bixler syndrome	AR	201750	*POR*	Cytochrome P450 oxidoreductase	Similar cases with F*GFR2* mutations classified by MIM as Antley–Bixler without genital anomalies may be variants of Pfeiffer syndrome
Craniosynostosis Boston type	AD	604757	*MSX2*	MSX2	Heterozygous P148H mutation in a two families
Saethre–Chotzen syndrome	AD	101400	*TWIST1*	TWIST	
Shprintzen–Goldberg syndrome	AD	182212	*SKI*	SKI	
Baller–Gerold syndrome	AR	218600	*RECQL4*	RECQ Protein-like 4	*RECQL4* might not account for all cases of Baller–Gerold
Carpenter syndrome	AR	201000 614976	*RAB23* *MEGF8*		
Coronal craniosynostosis	AD	615314	*TCF12*	Transcription factor 12	
Complex craniosynostosis	AD	600775	*ERF*	ETS2 repressor factor	
See also Cole-Carpenter syndrome in group 24, CDAGS syndrome in group 29, and Craniofrontonasal syndrome in group 34, Philadelphia type craniosynostosis (IHH duplication) in group 39					
34. Dysostoses with predominant craniofacial involvement					
Mandibulo-facial dysostosis (Treacher Collins, Franceschetti–Klein)	AD, AD, AR	154500	*TCOF1, POLR1D, POLR1C*	Treacher Collins-Franceschetti syndrome 1, Polymerase (RNA) I polypeptide D, Polymerase (RNA) I polypeptide C	
Oral-facial-digital syndrome type I (OFD1)	XLR	311200	*CXORF5*	chr. X open reading frame 5	
Weyers acrofacial (acrodental) dysostosis	AD	193530	*EVC1 EVC2*	Ellis-van Creveld 1 protein	See also ciliopathy group
Endocrine-cerebro-osteodysplasia (ECO)	AR	612651	*ICK*	Intestinal cell kinase	

Craniofrontonasal syndrome	XLD	304110	*EFNB1*	Ephrin B1	
Frontonasal dysplasia, type 1	AR	136760	*ALX3*	Aristaless-like-3	
Frontonasal dysplasia, type 2	AR	613451	*ALX4*	Aristaless-like-4	
Frontonasal dysplasia, type 3	AR	613456	*ALX1*	Aristaless-like 1	
Hemifacial microsomia	SP/AD	164210			Includes Goldenhar syndrome and Oculo–Auriculo–Vertebral spectrum; probably genetically heterogeneous
Miller syndrome (postaxial acrofacial dysostosis)	AR	263750	*DHODH*	Dihydroorotate dehydrogenase	
Acrofacial dysostosis, Nager type	AD/AR	154400	*SF3B4*	Splicing factor 3, subunit 4	
Acrofacial dysostosis, Rodriguez type	AR	201170			
Mandibulofacial dysostosis with microcephaly	AD	610536	*EFTUD2*	Elongation factor tu gtp-binding domain-containing 2	
See also Oral-facial-digital syndrome type IV in the Ciliopathies with major skeletal involvement group					
35. Dysostoses with predominant vertebral with and without costal involvement					
Currarino triad	AD	176450	*HLXB9*	Homeobox gene HB9	
Spondylocostal dysostosis type 1 (SCD01), type 2 (SCD02), type 3(SCD03), type 4 (SCD04),	AR	277300	*DLL3*	Delta-like 3	
		608681	*MESP2*	Mesoderm posterior 2	
		609813	*LFNG*	Lunatic fringe	
		613686	*HES7*	Hairy-and-enhancer-of-split-7	
type 5 (SCD05)	AD	122600	*TBX6*	T box 6	
Spondylothoracic Dyostosis (STD)	AR		*MESP2*	Mesoderm posterior 2	
Vertebral segmentation defect (congenital scoliosis) with variable penetrance	AD		*MESP2*	Mesoderm posterior 2	
			HES7	Hairy-and-enhancer-of-split-7	
Klippel–Feil anomaly with laryngeal malformation	AD	148900	*GDF6*	Growth and differentiation factor 6 and 3	Role of *GDF6* mutations in dominant spondylothoracic dysostosis unclear
		613702	*GDF3*		
	AR	214300	*MEOX1*	Mesenchyme homeobox 1	
Cerebro-costo-mandibular syndrome (rib gap syndrome)	AD	117650	*SNRPB*	Small Nuclear Ribonucleoprotein polypeptide B and B-prime	
Cerebro-costo-mandibular-like syndrome with vertebral defects	AR	611209	*COG1*	Component of oligomeric Golgi complex 1	Also classified as CDG type IIg
Diaphanospondylodysostosis	AR	608022	*BMPER*	Bone morphogenetic protein-binding endothelial cell precursor-derived regulator	Possibly overlaps with ischiospinal dysostosis
Spondylo-megaepiphyseal-metaphyseal dysplasia (SMMD)	AR	613330	*NKX3-2*	NK3 Homeobox 2	
See also Spondylocarpotarsal dysplasia in group 7					
36. Patellar dysostoses					
Ischiopatellar dysplasia (small patella syndrome)	AD	147891	*TBX4*	T-box gene 4	
Nail-patella syndrome	AD	161200	*LMX1B*	LIM homeobox transcription factor 1	
Genitopatellar syndrome	AR?	606170	*KAT6B*		
Ear-patella-short stature syndrome (Meier–Gorlin)	AR	224690	*ORC1*	Origin recognition complex	
		613800	*ORC4*		
		613803	*ORC6*		
		613804	*CDT1*		
		613805	*CDC6*		

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
See also MED group for conditions with patellar changes as well as ischio-pubic-patellar dysplasia as mild expression of campomelic dysplasia					
37. Brachydactylies (without extraskeletal manifestations)					
Brachydactyly type A1	AD	112500	*IHH*	Indian Hedgehog	
Brachydactyly type A1	AD				
Brachydactyly type A2	AD	112600	*BMPR1B*	Bone Morphogenetic Protein Receptor, 1B	
Brachydactyly type A2	AD	112600	*BMP2*	Bone Morphogenetic Protein Type 2	Regulatory mutations
Brachydactyly type A2	AD	112600	*GDF5*	Growth and Differentiation Factor 5	
Brachydactyly type B	AD	113000	*ROR2*	Receptor Tyrosine Kinase-like Orphan Receptor 2	See also Robinow syndrome/COVESDEM
Brachydactyly type B2	AD	611377	*NOG*	Noggin	
Brachydactyly type C	AD, AR	113100	*GDF5*	Growth and Differentiation Factor 5	See also ASPED (group 14) and other *GDF5* disorders
Brachydactyly type D	AD	113200	*HOXD13*	Homeobox D13	
Brachydactyly type E	AD	113300	*PTHLH*	Parathyroid hormone-like hormone (Parathyroid hormone related peptide, PTHRP)	
Brachydactyly type E	AD	113300	*HOXD13*	Homeobox D13	
Brachydactyly with anonychia (Cooks syndrome)	AD	106995	*SOX9*		Regulatory mutations
38. Brachydactylies (with extraskeletal manifestations)					
Brachydactyly-mental retardation syndrome	AD	600430	*HDAC4*	Histone deacetylase 4	Some patients have microdeletions involving contiguous genes (chr. 2q37 deletion syndrome)
Hyperphosphatasia with mental retardation, brachytelephalangy, and distinct face	AR		*PIGV*	Phosphatidylinositol-glycan biosynthesis class V protein (GPI mannosyltransferase 2)	
Brachydactyly-hypertension syndrome (Bilginturan)	AD	112410	*PDE3A*	Phosphodiesterase 3A	
Microcephaly-oculo-digito-esophageal-duodenal syndrome (Feingold syndrome)	AD	164280	*MYCN*	nMYC oncogene	
Hand-foot-genital syndrome	AD	140000	*HOXA13*	Homeobox A13	
Rubinstein–Taybi syndrome	AD	180849	*CREBBP*	CREB-Binding Protein	
Rubinstein–Taybi syndrome	AD	180849	*EP300*	E1A-Binding Protein, 300-KD	
Brachydactyly, Temtamy type	AR	605282	*CHSY1*	Chondroitin sulfate synthase 1	
Christian type brachydactyly	AD	112450			
Coffin–Siris syndrome1	AR	135900			Mutations in various components of the SWI/SNF complex have been reported in patients with a diagnosis of Coffin-Siris syndrome
Adams–Oliver	AD	100300	*ARHGAP31*		

	AR	614219	*DOCK6*		
	AD	614814	*RBPJ*		
	AR	615297	*EOGT*		
Catel–Manzke syndrome	AR	616145	*TGDS*	TDP-Glucose 4,6 Dehydratase	See also Chondrodysplasia gPAPP type in Group 4
See also group 20 for other conditions with brachydactyly as well as brachytelephalangic CDP.					
39. Limb hypoplasia–reduction defects group					
Ulnar-mammary syndrome	AD	181450	*TBX3*	T-box gene 3	
de Lange syndrome	AD	122470	*NIPBL*	Nipped-B-like	
	XL	300590	*SMC1A*		
	AD	619759	*SMC3*		
	AD	614701	*RAD21*		
	XL	300882	*HDAC8*		
Fanconi anemia *(see note below)*	AR	227650	*(several)*		Several complementation groups and genes
Thrombocytopenia-absent radius (TAR)	AR	274000	*RBM8A*		
Thrombocythemia with distal limb defects	AD		*THPO*	Thrombopoietin	Distal limb defects postulated as consequence of vascular occlusions
Holt-Oram syndrome	AD	142900	*TBX5*	T-box gene 5	
Okihiro syndrome (Duane–radial ray anomaly)	AD	607323	*SALL4*	SAL-like 4	
Cousin syndrome	AR	260660	*TBX15*	T-box gene 15	
Roberts syndrome	AR	268300	*ESCO2*	Homolog of Establishment of Cohesion - 2	
Split-hand-foot malformation with long bone deficiency (SHFLD3)	AD	612576	*BHLHA9*		Duplications
Tibial hemimelia	?	275220			
Tibial hemimelia-polysyndactyly-triphalangeal thumb	AD	188740	*SHH-ZRS*		Also mesomelic dysplasia Werner type
Acheiropodia	AR	200500	*LMBR1*	Putative receptor protein	Partial LMBR1 deletion affecting expression of Sonic Hedgehog (SHH) gene
Tetra-amelia	AR	273395	*WNT3*	Wingless-type MMTV integration site family, member 3	
Terminal transverse defect	?	102650			
Al-Awadi Raas-Rothschild limb-pelvis hypoplasia-aplasia	AR	276820	*WNT7A*	Wingless-type MMTV integration site family, member 7A	
Fuhrmann syndrome	AR	228930	*WNT7A*	Wingless-type MMTV integration site family, member 7A	
RAPADILINO syndrome	AR	266280	*RECQL4*	RECQ Protein-like 4	
Poland					
Femoral hypoplasia-unusual face syndrome (FHUFS)	SP/AD?	134780			Some phenotypic overlap with FFU syndrome (below)
Femur-fibula-ulna syndrome (FFU)	SP?	228200			
Hanhart syndrome (Hypoglossia-hypodactylia)	AD	103300			
Gollop-Wolfgang	AD	228250	*BHLHA9*		Triplications
Scapulo-iliac dysplasia (Kosenow)	AD	169550			
Note: the particularly complex genetic basis of Fanconi					

(*Continued*)

TABLE I. (*Continued*)

Group/Name of Disorder	Inheritance	MIM No.	Locus or Gene	Protein	Notes
anemia and its complementation groups is acknowledged but not further listed in this Nosology. The Reader is referred to MIM or to specialized reviews. - *See also* CHILD in group 20 and the mesomelic and acromesomelic dysplasias.					
40. Ectrodactyly with and without other manifestations					
Ankyloblepharon-ectodermal dysplasia-cleft lip/palate (AEC)	AD	106260	*P63 (TP63)*	Tumor Protein p63	
Ectrodactyly-ectodermal dysplasia cleft-palate syndrome Type 3 (EEC3)	AD	604292	*P63 (TP63)*	Tumor Protein p63	
Ectrodactyly-ectodermal dysplasia cleft-palate syndrome type 1 (EEC1)	AD	129900			
Ectrodactyly-ectodermal dysplasia-macular dystrophy syndrome (EEM)	AR	225280	*CDH3*	Cadherin 3	
Limb-mammary syndrome (including ADULT syndrome)	AD	603273	*P63 (TP63)*	Tumor Protein p63	
Split hand-foot malformation, isolated form, type 4 (SHFM4)	AD	605289	*P63 (TP63)*	Tumor Protein p63	
Split hand-foot malformation, isolated form, type 1 (SHFM1)	AD	183600	*DLX5 DLX6*	Distal-less Homeobox 5 Distal-less Homeobox 6	
Split hand-foot malformation, isolated form, type 3 (SHFM3)	AD	246560	10q		Duplications
Split hand-foot malformation, isolated form, type 5 (SHFM5)	AD AR	606708	*WNT10B*	Wingless-type MMTV integration site family, member 7A	
Hartsfield syndrome	AD	615465	*FGFR1*	Fibroblast growth factor receptor 1	
41. Polydactyly-Syndactyly-Triphalangism group					
Preaxial polydactyly type 1 (PPD1)	AD	174400	*SHH-ZRS*	Sonic Hedgehog	Regulatory mutation
Postaxial polydactyly type A	AD	174200	*GLI3*	Gli-Kruppel Family Member 3	Most cases are not *GLI3* related
Postaxial polydactyly type B	Complex				
Triphalangeal thumb (TPT)-polydactyly syndrome	AD	174500	*SHH-ZRS*	Sonic Hedgehog	Regulatory mutation
Preaxial polydactyly type 3 (PPD3)	AD	174600			
Preaxial polydactyly type 4 (PPD4)	AD	174700	*GLI3*	Gli-Kruppel Family Member 3	
Greig cephalopolysyndactyly syndrome	AD	175700	*GLI3*	Gli-Kruppel Family Member 3	
Pallister–Hall syndrome	AD	146510	*GLI3*	Gli-Kruppel Family Member 3	
Synpolydactyly (complex, fibulin1-associated)	AD	608180	*FBLN1*	Fibulin 1	
Synpolydactyly	AD	186000	*HOXD13*	Homeobox D13	
Townes–Brocks syndrome (renal-ear-anal-radial syndrome)	AD	107480	*SALL1*	SAL-like 1	
Lacrimo-auriculo-dento-digital syndrome (LADD)	AD	149730	*FGFR2*	Fibroblast growth factor receptor 2	
Lacrimo-auriculo-dento-digital syndrome (LADD)	AD	149730	*FGFR3*	Fibroblast growth factor receptor 3	
Lacrimo-auriculo-dento-digital syndrome (LADD)	AD	149730	*FGF10*	Fibroblast growth factor 10	
Acrocallosal syndrome	AR	200990	*KIF7*	Kinesin family member 7	

Acro-pectoral syndrome	AD	605967			
Acro-pectoro-vertebral dysplasia (F-syndrome)	AD	102510	*WNT6*	Wingless-type mmtv integration site family, member 6	Regulatory mutations
Mirror-image polydactyly of hands and feet (Laurin–Sandrow syndrome)	AD	135750	*SHH-ZRS*	Sonic Hedgehog	Regulatory mutations; some cases unlinked
Cenani–Lenz syndactyly	AR	212780	*LRP4*	Low density lipoprotein receptor-related protein 4	
Cenani–Lenz like syndactyly	SP (AD?)		*GREM1, FMN1*	Gremlin 1, Formin 1	Monoallelic duplication of both loci (observed in one case only so far)
Syndactyly, Malik–Percin type	AD	609432	*BHLHA9*		
STAR syndrome (syndactyly of toes, telecanthus, ano- and renal malformations)	XL	300707	*FAM58A*		
Syndactyly type Lueken	AD	185900	*IHH*	Indian Hedgehog	Regulatory mutations
Oculodentodigital dysplasia, Syndactyly type 3 (IV-V)	AD	185900	*GJA1*	Gap junction protein alpha-1	
Syndactyly Haas type	AD	186200	*SHH-ZRS*	Sonic Hedgehog	Regulatory mutations
Syndactyly with metacarpal and metatarsal fusion	AD	186300	*HOXD13*		
Metacarpal 4-5 fusion syndrome	XL	309630	*FGF16*	Fibroblast growth factor 16	
Syndactyly with craniosynostosis (Philadelphia type)	AD	185900	*IHH*	Indian Hedgehog	Regulatory mutations
Syndactyly with microcephaly and mental retardation (Filippi syndrome)	AR	272440	*CKAP2L*	Cytoskeleton associated protein 2-like	
Meckel syndrome type 1,2,3,4,5,6	AR	249000	*MKS1*		
		603194	*TMEM216*		
		607361	*TMEM67*		
		611134	*CEP290*		
		611561	*RPGRIP1L*		
		612284	*CC2D2A*		
Note: the Smith–Lemli–Opitz syndrome can present with polydactyly and/or syndactyly. See also the SRPS group.					
42. Defects in joint formation and synostoses					
Multiple synostoses syndrome type 3	AD	612961	*FGF9*	FGF9	
Proximal symphalangism type 1	AD	185800	*NOG*	Noggin	
Proximal symphalangism type 2	AD	185800	*GDF5*	Growth and Differentiation Factor 5	
Radio-ulnar synostosis with amegakaryocytic thrombocytopenia	AD	605432	*HOXA11*	Homeobox A11	
Liebenberg syndrome	AD	186550	*PITX1*	Paired-like homeodomain transcription factor 1	Regulatory mutations
Congenital club foot	AD	119800	*PITX1*	Paired-like homeodomain transcription factor 1	Includes forms with polydactyly/limb malformations
See also Spondylo-carpal-tarsal dysplasia; mesomelic dysplasia with Acral Synostoses; and others.					

mountains of genetic information and look forward with curiosity to the tenth edition of the nosology.

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