American Journal of Medical Genetics 113:65–77 (2002)

Rapid Publication

International Nosology and Classification of Constitutional Disorders of Bone (2001)

Christine M. Hall*
Department of Radiology, Great Ormond Street Children's Hospital, London, United Kingdom

The last International Classification of Constitutional Disorders of Bone was published in 1998. Since then rapid advances have been made in identifying the molecular changes responsible for defined conditions and new disorders are constantly being delineated. For these reasons a further update on the classification is appropriate. It has been expended to not only the osteochondrodysplasias (33 groups) but also genetically determined dysostoses (3 groups).

KEY WORDS: osteochondrodysplasia; dysostosis; gene

The International Working Group on the Classification of Constitutional Disorders of Bone met in Oxford on September 4th and 5th 2001 to update the last classification which had been drawn up in Los Angeles in 1997 (Table I). While this latest classification remains a combination of morphological and molecular groupings it is anticipated that two parallel but interacting classifications will evolve: one clinical, identifying accepted terminology or nosology, and the other molecular, to help further understand the pathogenesis of individual disorders.

The major change in the classification has been the addition of genetically determined dysostoses to the skeletal dysplasias or osteochondrodysplasias. This is because in clinical practice these two groups overlap. Dysostoses may be defined as skeletal malformations occurring singly or in combination. The dysostoses are static and their malformations occur during blastogenesis (the first eight weeks of embryonic life). This is in contrast to the skeletal dysplasias which often present after this stage, have a more general skeletal involvement and continue to evolve as a result of active gene involvement throughout life. Only those dysostoses which have an identified chromosomal locus have been included. They have been divided into three groups: those with predominant cranial and facial involvement, those with predominant axial involvement, and those with predominant involvement of the extremities. The first group includes in particular the various craniosynostoses occurring as a result of FGFR mutations. The second group includes the various vertebral segmentation defect disorders, and the third, the ectrodactylys and Fanconi syndrome groups. The brachydactylys were included in the 1997 classification in Group 17, the acromelic and acromesomelic dysplasias, and now remain in the acromelic dysplasia group, although they could logically move into the dysostosis classification.

A few of the more major changes to the skeletal dysplasia classification will be identified.

1. SADDAN — *s*evere *a*chondroplasia, *d*evelopmental *d*elay and *a*canthosis *n*igricans has been included in the achondroplasia group.

2. The severe spondylodysplastic group has deleted the San Diego type of lethal platyspondylic dysplasia, which has been identified as the same as thanatophoric dysplasia type I. The group has been expanded to include opsismodysplasia and spondylo-metaphyseal dysplasia type Sedaghatian and is a collection of morphologically similar disorders.

This paper was prepared by Dr. Hall on behalf of the International Nomenclature Group. Members of the International Nomenclature Group: Peter Beighton, Cape Town, South Africa; Clair Francomano, Bethesda, USA; Andres Giedion, Zurich, Switzerland; Christine Hall, London, UK (chair); Judith Hall, Vancouver, Canada; William Horton, Portland, USA; Ilkka Kaitila, Helsinki, Finland; Debbie Krakow, Los Angeles USA; Ralph Lachman, Los Angeles, USA; Martine Le Merrier, Paris, France; Geert Mortier, Gent, Belgium; Stephan Mundlos, Berlin, Germany; Andrew Poznanski, Chicago, USA; David Rimoin, Los Angeles, USA; Ravi Savarirayan, Australia; David Sillence, Sydney, Australia; Jurgen Spranger, Mainz, Germany; Andrea Superti-Furga, Zurich, Switzerland; Sheila Unger, Canada; John Washbrook, London, UK; Matt Warman, Cleveland, USA; William Wilcox, Los Angeles, USA; Robin Winter, London, UK.

*Correspondence to: Dr. Christine M. Hall, Department of Radiology, Great Ormond Street Children's Hospital, London WC1N 3JH, UK. E-mail: hallc@gosh.nhs.uk

Received 28 May 2002; Accepted 24 June 2002
DOI 10.1002/ajmg.10828

TABLE I. Update of Classification of Constitutional Disorders of Bone*

Osteochondrodysplasia	Mode of inheritance*	OMIM syndrome	Comments	Chromosome locus	Gene	Gene product	OMIM gene/ protein
Osteochondrodysplasias							
1. *Achondroplasia group*							
Thanatophoric dysplasia, type I (includes San Diego Type)	AD	187600		4p16.3	*FGFR3*	FGFR3	134934
Thanatophoric dysplasia, type II	AD	187601		4p16.3	*FGFR3*	FGFR3	134934
Achondroplasia	AD	100800		4p16.3	*FGFR3*	FGFR3	134934
Hypochondroplasia	AD	146000		4p16.3	*FGFR3*	FGFR3	134934
Hypochondroplasia	AD	146000		other			
SADDAN (severe achondroplasia, developmental delay, acanthosis nigricans)	AD	134934		4p16.3	*FGFR3*	FGFR3	
2. *Severe spondylodysplastic dysplasias*							
Lethal platyspondylic skeletal dysplasias (Torrance type, Luton type)	SP	270230 151210					
Achondrogenesis type 1A	AR	200600					
Opsismodysplasia	AR	258480					
SMD Sedaghatian type	AR	250220	See also: thanatophoric dysplasia, types I/II achondrogenesis types IB/II and group 3.				
3. *Metatropic dysplasia group*							
Fibrochondrogenesis	AR	228520					
Schneckenbecken dysplasia	AR	269250					
Metatropic dysplasia (various forms)	AD	156530					
4. *Short-rib dysplasia (SRP) (with or without polydactyly) group*							
SRP type I/III (Saldino-Noonan/ Verma-Naumoff)	AR	263510 263510					
SRP type II (Majewski)	AR	263520					
SRP type IV (Beemer)	AR	269860					
Asphyxiating thoracic dysplasia (Jeune)	AR	208500					
Chondroectodermal dysplasia (Ellis-van Creveld dysplasia)	AR	225500		4p16			
Thoracolaryngopelvic dysplasia (Barnes)	AD	187760					
5. *Atelosteogenesis-omodysplasia group*							
Atelosteogenesis type I (includes "Boomerang dysplasia")	SP	108720					
Omodysplasia I (Maroteaux)	AD	164745					
Omodysplasia II (Borochowitz)	AR	258315					
Atelosteogenesis type III	AD	108721					
de la Chapelle dysplasia	AR	256050	See also: Group 6	5q32-q33	*DTDST*	Sulfate transp.	
6. *Diastrophic dysplasia group*							
Achondrogenesis 1B	AR	600972		5q32-q33	*DTDST*	Sulfate transp.	
Diastrophic dysplasia	AR	222600		5q32-q33	*DTDST*	Sulfate transp.	
MED Autosomal Recessive type	AR	226900	See also: Group 11	5q32-q33	*DTDST*	Sulfate transp.	
7. *Dyssegmental dysplasia group*							
Dyssegmental dysplasia, Silverman-Handmaker type	AR	224410			*PLC (HSPG2)*	Perlecan	

Dyssegmental dysplasia, Rolland-Desbuquois type	AR	224400					
8. *Type II collagenopathies*							
Achondrogenesis II (Langer-Saldino)	AD	200610		12q13.1-q13.3	*COL2A1*	Type II collagen	120140
Hypochondrogenesis	AD	200610		12q13.1-q13.3	*COL2A1*	Type II collagen	120140
Spondyloepiphyseal dysplasia (SED) congenita	AD	183900		12q13.1-q13.3	*COL2A1*	Type II collagen	120140
Spondyloepimetaphyseal dysplasia (SEMD) Strudwick type	AD	184250		12q13.1-q13.3	*COL2A1*	Type II collagen	120140
Kniest dysplasia	AD	156550		12q13.1-q13.3	*COL2A1*	Type II collagen	120140
SED Namaqualand type	AD	142670		12q13.1-q13.3	*COL2A1*	Type II collagen	120140
Spondyloperipheral dysplasia	AD	271700		12q13.1-q13.3	*COL2A1*	Type II collagen	120140
Mild SED with premature onset arthrosis	AD			12q13.1-q13.3	*COL2A1*	Type II collagen	120140
Stickler dysplasia type I	AD	108300		12q13.1-q13.3	*COL2A1*	Type II collagen	120140
9. *Type XI collagenopathies*							
Stickler dysplasia type II	AD	604841	Heterogeneous with or without ocular involvement				
Stickler dysplasia type III	AD	184840	Without ocular involvement	1p21	*COL11A1*	Type XI collagen	120280
Marshall syndrome	AD	154780		1p21	*COL11A1*	Type XI collagen	120280
Otospondylomegaepiphyseal dysplasia (OSMED)	AR	215150		6p21.3	*COL11A2*	Type XI collagen	120290
Otospondylomegaepiphyseal dysplasia (OSMED)	AD	215150		6p21.3	*COL11A2*	Type XI collagen	120290
10. *Other spondyloepi-(meta)-physeal [SE(M)D] dysplasias*							
X-linked SED tarda	XLD	313400		Xp22.2-p22.1	*SEDL*	SEDLIN	300202
SEMD Handigodu type	AD?		? the same as Mseleni joint disease				
Progressive pseudorheumatoid dysplasia	AR	208230		6q22-q23	*WISP3*		603400
Dyggve-Melchior-Clausen dysplasia	AR	223800					
Wolcott-Rallison dysplasia	AR	226980		2p12	*EIF2AK3*	Transcription factor	
Immuno-osseous dysplasia (Schimke)	AR	242900					
Schwartz-Jampel syndrome	AR	255800		1q36-34	*PLC (HSPG2)*	Perlecan	142461
SEMD with joint laxity (SEMDJL)	AR	271640					
SEMD with multiple dislocations (Hall) (leptodactylic type)							
SPONASTRIME dysplasia	AR	271510					
SEMD short limb-abnormal calcification type	AR	271665	See also: Group 12				
SEMD Pakistani type	AR	603005		10q23-24	*PAPSS2*	PAPSS2	603005
Anauxetic dysplasia	AR		See: opsismodysplasia Group 2				
11. *Multiple epiphyseal dysplasias & pseudoachondroplasia*							
Pseudoachondroplasia	AD	177170	See also: Groups 8/10	19p12-13.1	*COMP*	COMP	600310
Multiple epiphyseal dysplasia (MED)	AD	132400	See also: Group 6	19p13.1	*COMP*	COMP	600310
(Fairbanks and Ribbing types)	AD	600204		1p32.2-33	*COL9A2*	Type IX collagen	120260
	AD	600969		20q13.3	*COL9A3*	Type IX collagen	120270
	AD			2p23-24	*MATN3*	Matrilin 3	602109
Familial hip dysplasia (Beukes)	AD	142669		4q35			

TABLE I. (*Continued*)

Osteochondrodysplasia	Mode of Inheritance*	OMIM syndrome	Comments	Chromosome locus	Gene	Gene product	OMIM gene/ protein
12. *Chondrodysplasia punctata (CDP) (stippled epiphyses group)*							
Rhizomelic CDP type 1	AR	215100		6q22-q24	*PEX7*	PTS2 receptor	601757
Rhizomelic CDP type 2	AR	222765		1q42	*DHPAT*	DHAPAT	602744
Rhizomelic CDP type 3	AR	600121		2q31	*AGPS*	ADHAPS deficiency	603051
CDP Conradi-Hünermann type	XLD	302960		Xp11.23-11.22	*EBP*	EBP	300205
CDP X-linked recessive type (brachytelephalangic)	XLR	302940 302950		Xp22.3	*ARSE*	Arylsulfatase E	300180
CDP Tibia-metacarpal type	AD	118651					
CHILD (limb-reduction-icthyosis)	XLD	308050		Xp11	*NSDHL*		
CHILD (limb-reduction-icthyosis)	XLD	308050		Xq28	*NSDHL* *EBP*		300275 300205
Hydrops-ectopic calcification-moth-eaten appearance HEM (Greenberg dysplasia)	AR	215140					
Dappled diaphyseal dysplasia	AR						
13. *Metaphyseal dysplasias*							
Jansen type	AD	156400		3p22-p21.1	*PTHR*	PTHR/PTHRP	168468
Schmid type	AD	156500		6q21-q22.3	*COL10A1*	COL10 αchain	120110
Cartilage-Hair-Hypoplasia (McKusick)	AR	250250		9p13	*MRMP*		
Metaphyseal anadysplasia (various types)	AD/XLD	309645					
Metaphyseal dysplasia with pancreatic insufficiency and cyclic neutropenia (Shwachmann Diamond)	AR	260400					
Adenosine deaminase (ADA) deficiency	AR	102700		20q-13.11	*ADA*	Adenosine deaminase	102700
Metaphyseal chondrodysplasia Spahr type	AR	250400					
Acroscyphodysplasia (various types)	AR	250215					
14. *Spondylometaphyseal dysplasias (SMD)*							
Spondylometaphyseal dysplasia Kozlowski type	AD	184252					
Spondylometaphyseal dysplasia (Sutcliffe/corner fracture type)	AD	184255					
SMD with severe genu valgum (includes Schmidt and Algerian types)	AD	184253	See also: SMD Sedaghatian type (Group 2)				
15. *Brachyolmia spondylodysplasias*							
Hobaek (includes Toledo type)	AR	271530-630					
Maroteaux type	AR						
Autosomal dominant type	AD	113500					
16. *Mesomelic dysplasias*							
Dyschondrosteosis (Leri-Weill)	AD	127300		Xpter-p22.32	*SHOX*		
Langer type (homozygous dyschondrosteosis)	AR	249700		Xpter-p22.32	*SHOX*		
Nievergelt type	AD	163400					

Kozlowski-Reardon type	AR					
Reinhardt-Pfeiffer type	AD	191400				
Werner type	AD	188770				
Robinow type, dominant	AD	180700				
Robinow type, recessive	AR	268310	9q22	*ROR2*	NTRKR2	
Mesomelic dysplasia with synostoses	AD	600383				
Mesomelic dysplasia Kantaputra type	AD	156232	2q24-q32			
Mesomelic dysplasia Verloes type	AD	600383				
Mesomelic dysplasia Savarirayan type						
17. *Acromelic dysplasias*						
Acromicric dysplasia	AD	102370				
Geleophysic dysplasia	AR	231050				
Myhre dysplasia		139210				
Weill-Marchesani dysplasia	AR	277600				
Trichorhinophalangeal dysplasia types I/III	AD	190350 190351	8q24.12	*TRPS1*		
Trichorhinophalangeal dysplasia type II (Langer-Giedion)	AD	150230	8q24.11-q24.13	*TRPS1* *EXT1*		
Brachydactyly type A1	AD	112500	2q35-36	*IHH*		600726
Brachydactyly type A2	AD	112600				
Brachydactyly type A3		112700				
Brachydactyly type B	AD	113000	9q22		ROR2	602337
Brachydactyly type C	AD	113100	20q11.2	*GDF5*	Cartilage derived morphogenic protein 1	601196
Brachydactyly type D	AD	113200				
Brachydactyly type E	AD	113300	2q37			
Pseudohypoparathyroidism (Albright Hereditary Osteodystrophy)	AD	103580	20q13	*GNAS1*	Guanine nucleotide binding protein of edenylate cyclase α-subunit	139320
Acrodysostosis	SP(AD)	101800				
Saldino-Mainzer dysplasia	AR	266920				
Brachydactyly-hypertension dysplasia (Bilginturan)	AD	112410	12p12.2-p11.2	*CACP*		
Craniofacial conodysplasia	AD					
Angel-shaped phalango-epiphyseal dysplasia (ASPED)	AD	105835				
Camptodactyly arthropathy coxa vara pericarditis (CACP)	AR		1q25-31			
Christian brachydactyly	AD	112450				
18. *Acromesomelic dysplasias*						
Acromesomelic dysplasia type Maroteaux	AR	602875	9p13-p12			
Acromesomelic dysplasia type Campailla-Martinelli	AR					
Acromesomelic dysplasia type Ferraz/Ohba	AD					
Acromesomelic dysplasia type Osebold Remondini	AD	112910				
Grebe dysplasia	AR	200700	20q11.2	*CDMP1*	Cartilage derived morphogenic protein 1	601146
Cranioectodermal dysplasia	AR	218330				

TABLE I. (*Continued*)

Osteochondrodysplasia	Mode of Inheritance*	OMIM syndrome	Comments	Chromosome locus	Gene	Gene product	OMIM gene/ protein
19. *Dysplasias with predominant membranous bone involvement*							
Cleidocranial dysplasia	AD	119600		6p21	*CBFA1*	Core binding factor α1-subunit	600211
Yunis-Varon dysplasia	AR	216340					
Parietal foramina (isolated)	AD	168500		11q11.2	*ALX4*	Aristaless-like 4	605420
Parietal foramina (isolated)	AD	168500		5q34-q35	*MSX2*	Muscle segment homeobox 2	123101
20. *Bent-bone dysplasia group*							
Campomelic dysplasia	AD	114290		17q24.3-q25.1	*SOX9*	SRY-box 9	211970
Cumming syndrome	AR	211890					
Stüve-Wiedemann dysplasia (neonatal Schwartz-Jampel)	AR	601559					
			See also: Antley-Bixler syndrome				
21. *Multiple dislocations with dysplasias*							
Larsen syndrome	AD	150250		3p21.1-p14.1			
Larsen-like syndromes (including La Reunion Island)	AR	245600					
Desbuquois dysplasia	AR	251450					
Pseudodiastrophic dysplasia	AR	264180					
			See also Group 10				
22. *Dysostosis multiplex group*							
Mucopolysaccharidosis IH	AR	252800		4p16.3	*IDA*	α-1-Iduronidase	
Mucopolysaccharidosis IS	AR	252800		4p16.3	*IDA*	α-1-Iduronidase	
Mucopolysaccharidosis II	XLR	309900		Xq27.3-q28	*IDS*	Iduronate-2-sulfatase	
Mucopolysaccharidosis IIIA	AR	252900		17q25.3	*HSS*	Heparan sulfate sulfatase	
Mucopolysaccharidosis IIIB	AR	252920		17q21		N-Ac-α-D-glucosaminidase	
Mucopolysaccharidosis IIIC	AR	252930				Ac-CoA:α-glucosaminidase-N-acetyltransferase	
Mucopolysaccharidosis IIID	AR	252940		12q14	*GNS*	N-Ac-D-glucosamine-6-sulfatase	
Mucopolysaccharidosis IVA	AR	230500		16q24.3	*GALNS*	Galactose-6-sulfatase	
Mucopolysaccharidosis IVB	AR	230500		3p21.33	*GLBI*	β-Galactosidase	
Mucopolysaccharidosis VI	AR	253200		5q13.3	*ARSB*	Arylsulfatase B	
Mucopolysaccharidosis VII	AR	253200		7q21.11	*GUSB*	β-Glucuronidase	
Fucosidosis	AR	230000		1p34	*FUCA*	α-Fucosidase	
a-Mannosidosis	AR	248500		19p13.2-q12	*MAN*	α-Mannosidase	
b-Mannosidosis	AR	248510		4	*MANB*	β-Mannosidase	
Aspartylglucosaminuria	AR	208400		4q23-q27	*AgA*	Aspartyglucosaminidase	
GMI Gangliosidosis, several forms	AR	230500		3p21-p14.2	*GLB1*	β-Galactosidase	
Sialidosis, several forms	AR	256550		6p21.3	*NEU*	α-Neuraminidase	
Sialic acid storage disease	AR	269920		6q14-q15	*SIASD*		

Galactosialidosis, several forms	AR	256540	20q13.1	*PPGB*	β-Galactosidase protective protein	
Multiple sulfatase deficiency	AR	272200			Multiple sulfatases	
Mucolipidosis II	AR	252500	4q21-23	*GNPTA*	N-Ac-Glucosamine-phosphotransferase-	
Mucolipidosis III	AR	252600	4q21-23	*GNPTA*	N-Ac-Glucosamine phosphotransferase	
		See also: Groups 8,10,11,14				
23. Low birthweight slender bone group						
Type I microcephalic osteodysplastic dysplasia	AR	210710				
Type II microcephalic osteodysplastic dysplasia	AR	210720				
Microcephalic osteodysplastic dysplasia (Saul Wilson)	AR	210730				
3M syndrome	AR	273750				
24. Dysplasias with decreased bone density						
Osteogenesis imperfecta I (normal teeth)	AD	166200	17q	*COLIA1*	α(1)I procollagen	120150
Osteogenesis imperfecta I (normal teeth)		166200	7q22.1	*COLIA2*		120160
Osteogenesis imperfecta I (opalescent teeth)	AD	166240	7q22.1	*COLIA2*	α(1)I procollagen	120150
	AD	166240	7q22.1	*COLIA2*	α(2)I procollagen	120160
Osteogenesis imperfecta II	AD	166210	17q	*COLIA1*	α(1)I procollagen	120150
	AD	166210	17q22.1	*COLIA2*	α(2)I procollagen	120160
	AD	259400	17q	*COLIA1*	α(1)I procollagen	120150
Osteogenesis imperfecta III	AD	259420	17q	*COLIA1*	α(1)I procollagen	120150
	AD	259420	7q22.1	*COLIA2*	α(2)I procollagen	120160
	AR	259420	7q22.1	*COLIA2*	α(2)I procollagen	120160
	AR	259420				
Osteogenesis imperfecta IV (normal teeth)	AD	166220	7q22.1	*COLIA2*	α(2)I procollagen	120160
	AD	166220	17q	*COLIA1*	(1)I procollagen	120150
Osteogenesis imperfecta IV (opalescent teeth)	AD	166220	7q22.1	*COLIA2*	(2)I procollagen	120160
Osteogenesis imperfecta V	AD	166220	17q	*COLIA1*	(1)I procollagen	120150
Osteogenesis imperfecta VI						
Cole-Carpenter dysplasia	SP	112240				
Bruck dysplasia I	AR	259450	17p12	*TLH1*		
Bruck dysplasia II						
Singleton-Merton dysplasia	AR					
Osteopenia with radiolucent lesions of the mandible	AD	166260				
Osteoporosis-pseudoglioma dysplasia	AR	259770	11q12-q13			
Geroderma osteodysplasticum	AR	231070				
Idiopathic juvenile osteoporosis	SP	259750				
25. Dysplasias with defective mineralization						
Hypophosphatasia—perinatal lethal and infantile forms	AR	241500	1p36.1-p34	*ALPL*	Alkaline phosphatase	171760
Hypophosphatasia adult form	AD	146300	1p36.1-p34	*ALPL*	Alkaline phosphatase	171760
Hypophosphatemic rickets	XLD	307800	Xp22.2-p22.1	*PHEX*	X-linked hypophosphate mia protein	171760
	AD			*FGF23*		

TABLE I. (*Continued*)

Osteochondrodysplasia	Mode of Inheritance*	OMIM syndrome	Comments	Chromosome locus	Gene	Gene product	OMIM gene/ protein
Neonatal hyperparathyroidism	AR	239200		3q21-q24 19p13.3	*CASR*	Calcium sensor	601199
Transient neonatal hyperparathyroidism with hypocalciuric hypercalcemia	AD	145980		3q21-q24	*CASR*	Calcium sensor	601199
	AD			19p13.3			
26. *Increased bone density without modification of bone shape*							
Osteopetrosis							
Infantile form (OPB)	AR	259700		16q13	*TC1RG1*	Vacuolar protein	604592
	AR			11q13.4-q13.5	*CLCN7*	Chloride channel pump	602727
With infantile neuroaxonal dysplasia	AR?	600329					
Delayed form type I (OPA1)	AD	166600		1p21			
Delayed form type II (OPA2)	AD	166600		16p13.3			
Intermediate form (possibly heterogeneous)	AR	259710					
With ectodermal dysplasia and immune defect (OLEDAID)	XL	300301		Xq28	*IKBKG (NEMO)*	NF-kB signaling	
Dysosteosclerosis	AR	224300					
Osteomesopyknosis	AD	166450					
Cranial osteosclerosis with bamboo hair (Netherton)	AR	256500			*SPINK5*		
Pyknodysostosis	AR	265800		1q21	*CTSK*	Cathepsin K	601105
Osteosclerosis Stanescu type	AD	122900					
Osteopathia striata (isolated)	SP						
Osteopathia striata with cranial sclerosis	AD/XLD?	166500					
Melorheostosis	SP	155950					
Osteopoikilosis	AD	166700					
Mixed sclerosing bone dysplasia	SP						
27. *Increased bone density with diaphyseal involvement*							
Diaphyseal dysplasia Camurati-Engelmann	AD	131300		19q13.1-13.3	*TGFb1*	Transforming growth factor beta 1	
Diaphyseal dysplasia with anemia (Ghosal)	AR	231095					
Craniodiaphyseal dysplasia	?AR	218300 122860					
Lenz-Majewski dysplasia		151050					
Endosteal hyperostosis van Buchem type	AR	239100		17q12-q21			
Sclerosteosis	AR	269500		17q12-q21	*SOST*	Sclerostine	
Worth type	AD	144750					
Sclero-osteo-cerebellar dysplasia	AR	213002					
Kenny-Caffey dysplasia type I	AR	244460		1q42-q43			
Kenny-Caffey dysplasia type II	AD	127000					
Osteoectasia with hyperphosphatasia (Juvenile Paget disease)	AR	239000					
Diaphyseal medullary stenosis with bone malignancy	AD	112250		9p21-p22			
Oculodentoosseous dysplasia	AR	257850					
	AD	164200		6q22-23			

Trichodentoosseous dysplasia AD	AD	190320		17q21	*DLX3*	Distal-less 4 protein	
28. *Increased bone density with metaphyseal involvement*							
Pyle dysplasia	AR	269500					
Craniometaphyseal dysplasia							
Severe type	AR	218400					
Mild type	AD	123000		5p15.2-p14.2	transmembrane *ANKH*		
			See also: Group 29				
29. *Craniotubular digital dysplasias*							
Frontometaphyseal dysplasia	XLR	305620					
Osteodysplasty, Melnick-Needles	XLD	309350					
Precocious osteodysplasty (terHaar dysplasia)	AR	249420					
Otopalatodigital syndrome type I	XLD	311300		Xq28			
Otopalatodigital syndrome type II	XLR	304120					
			See also: Group 28				
30. *Neonatal severe osteosclerotic dysplasias*							
Blomstrand dysplasia	AR	215045					
Raine dysplasia	AR	259775					
Caffey disease with prenatal onset	AD ?AR	114000	See also: Mucolipidosis II				
Astley-Kendall dysplasia	AR						
31. *Disorganized development of cartilaginous and fibrous components of the skeleton*							
Dysplasia epiphysealis hemimelica	SP	127800					
Multiple cartilaginous exostoses	AD	133700		8q23-q24.1	*EXT1*	Exostosin-1	
	AD	133701		11p12-p11	*EXT2*	Exostosin-2	
	AD	600209		19p			
Enchondromatosis (Ollier)	SP	166000					
Enchondromatosis with hemagiomata (Maffucci)	SP	166000					
Spondyloenchondromatosis	AR	271550					
Spondyloenchondromatosis with basal ganglia calcification	AR						
Dysspondyloenchondromatosis							
Metachondromatosis	AD	156250					
Osteoglophonic dysplasia	AD	166250					
Genochondromatosis	AD	166000					
Carpotarsal osteochondromatosis	AD	127820					
Fibrous dysplasia (McCune-Albright and others)	SP mosaic	174800		20q13	*GNAS1*	guanine nucleotide protein, α subunit	139320
Jaffe-Campanacci type	SP						
Fibrodysplasia ossificans progressiva	AD	135100		4q27-31			112262
Cherubism	AD	118400		4p16	*SH3BP2*		
Cherubism with gingival fibromatosis	AR	135300					
32. Osteolyses							
Multicentric-hands and feet							
Multicentric carpal-tarsal osteolysis with and without nephropathy	AD	166300					

TABLE I. (*Continued*)

Osteochondrodysplasia	Mode of Inheritance*	OMIM syndrome	Comments	Chromosome locus	Gene	Gene product	OMIM gene/ protein
Winchester syndrome	AR	277950					
Torg syndrome	AR	259600		19q12-21	*MMP2*	MMP2	120360
		605156					
Distal phalanges							
Hadju-Cheney syndrome	AD	102500					
Mandibuloacral syndrome	AR	248370					
Diaphyses and metaphyses							
Familial expansile osteolysis	AD	174810		16q21.1-q22	*TNFRSF11A*	RANK	603499
Juvenile hyaline fibromatosis (includes systemic juvenile hyalinosis)	AR	228600					
		236490					
33. *Patella dysplasias*							
Nail-patella dysplasia	AD	161200		9q34.1	*LMX1B*	LIM homeodomain	602575
Patella hypoplasia/aplasia	AD			17q21-q22			
Ischiopubic patellar dysplasia	AD	147891					
Genitopatellar syndrome	AR?	606170					
Ear-patella-short stature syndrome (Meier-Gorlin)	AR	224690					
Localized Skeletal Malformations (Dysostoses)							
A. Localized disorders with predominant cranial and facial involvement							
Apert syndrome	AD	101200		10q25-q26	*FGFR2*	5351C	
Pfeiffer syndrome	AD	101600		10q25-q26	*FGFR2*		
Pfeiffer syndrome	AD	101600		8p12-p11	*FGFR1*	P252R	
Crouzon syndrome	AD	123500		10q26	*FGFR2*		
Craniosynostosis (Crouzon-like) with Acanthosis Nigricans	AD			4p16.3	*FGFR3*	A391G	
Jackson-Weiss syndrome	AD	123150		10q25-q26	*FGFR2*	P252R	
Jackson-Weiss syndrome	AD	123150		8p11	*FGFR1*		
Saethre-Chotzen syndrome	AD	101400		7p21	*TWIST*		
Craniosynostosis Muenke type	AD	602849		4p16.3	*FGFR3*	P250R	
Craniosynostosis Boston type	AD	604757		5q34	*MSX2*		
Craniosynostosis Adelaide type	AD	600593		4p16			
Craniosynostosis with polydactyly (carpenter)	AR	201000		7p21			
Antley-Bixler syndrome	AD	207410		10q26	*FGFR2*		
Craniosynostosis with cuits gyrata (Beare-Stevenson)	AD	123790		10q26	*FGFR2*		
Oral-facial-digital syndrome type I	XLR	311200		Xp22.3	*CXORF5*		
Cephalo-polysyndactyly (Greig)	AD	175700		7p13	*GLI3*		
Craniofrontonasal dysplasia	XLD	304110		Xp22			
Mandibulo-facial dysostosis (Treacher Collins)	AD	154500		5q32			
			See also: Group 19				
B. *Localized disorders with predominant axial involvement*							
Spondylocostal dysplasia	AD	277300		19q13			
Spondylocostal dysplasia	AR	277300		19q13			

COVESDEM (COsto VErtebral Segmentation DEfect with Mesomelia and peculiar face)	AR	180700	9q22
Oculo-vertebral syndrome (Weyer)	AD	193530	4p16
C. *Localized disorders with predominant involvement of the extremities*			
Isolated SHFM3	AD	600095	10q24
Isolated SHFM4	AD	605289	3q27
Syndromic SHFM1 with deafness and MR	AD	183600	7q21.3-q22.1
Isolated SHFM2	XL	313350	Xq26
Ectrodactyly-ectodermal dysplasia cleft-palate syndrome	AD	129900	7q11.2-q12.3
Symphalangism—proximal	AD	285800	17q22
Rubinstein-Taybi syndrome	?AD	180849	19p13
Coffin-Siris syndrome	AR	135900	1q21
Coffin-Siris syndrome	AR	135900	7q34
Fanconi syndrome Group A	AR	227650	16q24.3
Fanconi syndrome Group C	AR	227650	9q22.3
Fanconi syndrome Group D	AR	227650	3p22-p26
Fanconi syndrome Group E	AR	227650	6p21-p22
Fanconi syndrome Group F	AR	227650	11p15
Fanconi syndrome Group G	AR	227650	9p13
Multiple synostoses	AD	186500	17q21-q22
Hand foot genital syndrome	AD	140000	7p15
			See also: Group 17 and Group 16

*AD, autosomal dominant; AR, autosomal recessive; SP, sporadic; XLD, X-linked dominant; XLR, X-linked recessive.

4. In the short-rib dysplasia group, types I and III have been identified as different ends of the spectrum of the same disorder. Thoracolaryngopelvic dysplasia (Barnes) has been included.

6. The autosomal recessive type of multiple epiphyseal dysplasia has been included in the diastrophic dysplasia group.

10. Several newly delineated disorders have been included in the spondyloepimetaphyseal dysplasia group. These include: SEMD Handigodu type, SEMD with multiple dislocations (Hall), SEMD Pakistani type and anauxetic dysplasia.

11. Familial hip dysplasia (Beukes) has been included in the group of multiple epiphyseal dysplasia and pseudoachondroplasia.

12. In the chondrodysplasia punctata group, the brachytelephalangic type has been recognized as the same as the X-linked recessive type. Zellweger's syndrome and Vitamin K dependent coagulation defect have been excluded on the basis that they do not represent osteochondrodysplasias. CHILD- limb reduction icthyosis has been included and HEM (Greenberg dysplasia) and dappled diaphyseal dysplasia have been moved from the previous group of lethal chondrodysplasias with fragmented bones.

16. In the mesomelic group, types Kantaputra, Verloes and Savarirayan have been included.

17. The previous Group 17 has been divided into two. The new Group 17 is the acromelic dysplasias and Group 18 is acromesomelic dysplasias.

23. The low birthweight, slender bone group now incorporates microcephalic osteodysplastic dysplasia (Saul-Wilson) and the 3M syndrome.

24. Two new subtypes of osteogenesis imperfecta have been included; Type V, recognised by the presence of dislocated radial heads and hyperplastic callus formation and Type VI, diagnosed on the bone histology.

29. A new group of craniotubular digital disorders has been created and includes frontometaphyseal dysplasia, osteodysplasty (Melnick-Needles), precocious osteodysplasty (Ter Haar) and oto-palato-digital syndrome types I and II. The former group of lethal dysplasias with fragmented bones has been divided between the chondrodysplasia punctata group and the group of neonatal severe osteosclerotic dysplasias.

32. In the osteolyses group, Francois, Whyte-Hemmingway and Giacci have been excluded.

33. Several further conditions have been added to the patella dysplasia group.

A total of 33 groups have now been identified in addition to three groups of dysostoses.

The references are only relevant recent publications, mainly identifying new disorders or molecular advances. They are given under the individual groups.

REFERENCES

International Working Group on Constitutional Diseases of Bone. 1998. International nomenclature and classification of the osteochondrodysplasias. Am J Med Genet 79:376–382.

Group 10

Agarwal SS, Phadke SR, Fredlund V, Viljoen DL, Beighton P. 1997. Mseleni and Handigodu Familial Osteoarthropathies: Syndromic Identity? Am J Med Genet 72:435–439.

Nicole S, Davoine CS, Topaloglu H, Cattolico L, Barral D, Beighton P, Hamida CB, Hammouda H, Cruaud C, White PS, Samson D, Urtizberea JA, Lehmann-Horn F, Weissenbach J, Hentati F, Fontaine B. 2000. Perlecan, the major proteoglycan of basement membranes, is altered in Schwartz-Jampel syndrome (chondrodystrophic myotonia). Nat Genet 26:480–483.

Hall CM, Elcioglu N, Shaw DG. 1998. A distinct form of spondyloepimetaphyseal dysplasia with multiple dislocations. J Med Genet 35:566–572.

Horn D, Rupprecht E, Kunze J, Spranger J. 2001. Anauxetic dysplasia, a spondylometaepiphyseal dysplasia with extreme dwarfism. J Med Genet 38:262–265.

Group 11

Roby P, Eyre S, Worthington J, Ramesar R, Cilliers H, Beighton P, Grant M, Wallis G. 1999. Autosomal Dominant (Beukes) Premature Degenerative Osteoarthropathy of the Hip Joint Maps to an 11cM Region on Chromosome 4q35. Am J Hum Genet 64:904–908.

Group 12

Grange DK, Kratz LE, Braverman NE, Kelley RI. 2000. CHILD syndrome caused by deficiency of 3-beta-hydroxysteroid-delta-8, delta-7-isomerase. Am J Med Genet 90:328–335.

Chitayat D, Gruber H, Mullen BJ, Pauzner D, Costa T, Lachman R, Rimoin DL. 1993. Hydrops-ectopic calcification-moth-eaten skeletal dysplasia (Greenberg dysplasia): prenatal diagnosis and further delineation of a rare genetic disorder. Am J Med Genet 47:272–277.

Group 13

Ridanpaa M, van Eenennaam H, Pelin K, Chadwick R, Johnson C, Yuan B, van Venrooij W, Pruijn G, Salmela R, Rockas S, Makitie O, Kaitila I, de la Chapelle A. 2001. Mutations in the RNA component of RNase MRP cause a pleiotropic human disease, cartilage-hair hypoplasia. Cell 104:195–203.

Group 16

Fujimoto M, Kantaputra PN, Ikegawa S, Fukushima Y, Sonata S, Matsuo M, Ishida T, Matsumoto T, Kondo S, Tomita H, Deng HX, D'urso M, Rinaldi MM, Ventruto V, Takagi T, Nakamura Y, Niikawa N. 1998. The gene for mesomelic dysplasia Kantaputra type is mapped to chromosome 2q24-q32. J Hum Genet 43:32–36.

Savarirayan R, Cormier-Daire V, Curry CJ, Nashelsky MB, Rappaport V, Rimoin DL, Lachman RS. 2000. New mesomelic dysplasia with absent fibulae and triangular tibiae. Am J Med Genet 94:59–63.

Robertson SP, Shears DJ, Oei P, Winter RM, Scambler PJ, Aftimos S, Savarirayan R. 2000. Homozygos deletion of SHOX in a mentally retarded male with Langer mesomelic dysplasia. J Med Genet 37:959–964.

Group 17

Lim-Dunham JE, Poznanski AK, Tachdjidian MO. 1995. Christian Brachydactyly in a father and two daughters. Skeletal Radiol 24:623–625.

Group 26

Frattini A, Orchard PJ, Sobacchi C, Giliani S, Abinun M, Mattsson JP, Keeling DJ, Andersson AK, Wallbrandt P, Zecca L, Notarangelo LD, Vezzoni P, Villa A. 2000. Defects in TCIRGI subunit of the vacuolar proton pump are responsible for a subset of human autosomal recessive osteopetrosis. Nat Genet 25:343–346.

Sobacchi C, Frattini A, Orchard P, Porras O, Tezcan I, Andolina M, Babul-Hirji R, Baric I, Canham N, Chitayat D, Dupuis-Girod S, Ellis I, Etzioni A, Fasth A, Fischer A, Gerritsen B, Gulino V, Horowitz E, Klamroth V, Lanino E, Mirolo M, Musio A, Matthijs G, Nonomaya S, Notarangelo LD, Ochs HD, Superti Furga A, Valiaho J, van Hove JL, Vihinen M, Vujic D, Vezzoni P, Villa A. 2001. The mutational spectrum of human malignant autosomal recessive osteopetrosis. Hum Mol Genet 10:1767–1773.

Rees H, Ang LC, Casey R, George DH. 1995. The association of infantile neuroaxonal dystrophy and osteopetrosis: a rare autosomal recessive disorder. Pediatr Neurosurg 22:321–327.

Hu PY, Lim EJ, Ciccolella J, Strisciuglio P, Sly WS. 1997. Seven novel mutations in mutations in carbonic acid anhydrase II deficiency syndrome identified by SSCP and direct sequencing analysis. Hum Mutat 9:383–387.

Benichou O, Cleiren E, Gram J, Bollerslev J, de Vernejoul MC, Van Hul W. 2001. Mapping of autosomal dominant osteopetrosis type II (Albers-Schonberg disease) to chromosome 16p13.3. Am J Hum Genet 69:647–654.

White KE, Koller DL, Takacs I, Buckwalter KA, Foroud T, Econs MJ. 1999. Locus heterogeneity of autosomal dominant osteopetrosis (ADO). J Clin Endocrinol Metab 84:1047–1051.

Doffinger R, Smahi A, Bessia C, Geissmann F, Feinberg J, Durandy A, Bodemer C, Kenwrick S, Dupuis-Girod S, Blanche S, Wood P, Rabia SH, Headon DJ, Overbeek PA, Le Deist F, Holland SM, Belani K, Kumararatne DS, Fischer A, Shapiro R, Conley ME, Reimund E, Kalhoff H, Abinun M, Munnich A, Israel A, Courtois G, Casanova JL. 2001. X-linked anhidrotic ectodermal dysplasia with immunodeficiency is caused by impaired NF-kappaB signaling. Nat Genet 27:277–285.

John E, Kozlowski K, Masel J, Muralinath S, Vijayalakshmi G. 1996. Dysosteosclerosis. Australas Radiol 40:345–347.

Sprecher E, Chavanas S, Di Giovanna JJ, Amin S, Nielsen K, Prendiville JS, Silverman R, Esterly NB, Spraker MK, Guelig E, de Luna ML, Williams ML, Buehler B, Siegfried EC, Van Maldergem L, Pfendner E, Bale SJ, Uitto J, Hovnanian A, Richard G. 2001. The spectrum of pathogenic mutations in SPINK5 in 19 families with Netherton syndrome: implications for mutation detection and first case of prenatal diagnosis. J Invest Dermatol 117:179–187.

Motyckova G, Weilbaecher KN, Horstmann M, Rieman DJ, Fisher DZ, Fischer DE. 2001. Linking osteopetrosis and pycnodysostosis: regulation of cathepsin K expression by the microphthalmia transcription factor family. Proc Natl Acad Sci USA 98:5798–5803.

Horovitz DD, Barbosa Neto JG, Boy R, Vargas FR, Llerena Junior JC, de Almeida JC. 1995. Autosomal dominant osteosclerosis type Stanescu: the third family. Am J Med Genet 57:605–609.

Bueno AL, Ramos FJ, Bueno O, Olivares JL, Bello ML, Bueno M. 1998. Severe malformations in males from families with osteopathia striata with cranial sclerosis. Clin Genet 54:400–405.

Happle R. 2001. Buschke-Ollendorff syndrome: early, unilateral and pronounced involvement may be explained as a type 2 segmental manifestation. Eur J Dermatol 11:505.

Group 27

Kinoshita A, Saito T, Tomita H, Makita Y, Yoshida K, Ghadami M, Yamada K, Kondo S, Ikegawa S, Nishimura G, Fukushima Y, Nakagomi T, Saito H, Sugimoto T, Kamegaya M, Hisa K, Murray JC, Taniguchi N, Niikawa N, Yoshiura K. 2000. Domain-specific mutations in TGFB1 result in Camurati Engelmann disease. Nat Genet 26:19–20.

Guadami M, Makita Y, Yoshida K, Nishimura G, Fukushima Y, Wakui K, Ikegawa S, Yamada K, Kondo S, Niikawa N, Tomita HA. 2000. Genetic mapping of the Camurati-Engelmann disease locus to chromosome 19q13.1-q13.3. Am J Hum Genet 66:143–147.

Brunkow ME, Gardner JC, Van Ness J, Paeper BW, Kovacevich BR, Proll S, Skonier JE, Zhao L, Sabo PJ, Fu Y, Alisch RS, Gillet L, Colbert T, Tacconi P, Galas D, Hamersma H, Beighton P, Mulligan J. 2001. Bone dysplasia sclerosteosis results from loss of the SOST gene product, a novel cystine knot-containing protein. Am J Hum Genet 68:577–589.

Staehling-Hampton K, Proll S, Paeper BW, Zhao L, Charmley P, Brown A, Gardner JC, Galas D, Schatzman RC, Beighton P, Papapoulos S, Hamersma H, Brunkow M. 2002. A 52-kb deletion in the *SOST-MEOX1* intergenic region on 17q12-q21 is associated with van Buchem disease in the Dutch population. Am J Med Genet 110:144–152.

Van Hul W, Balemans W, van Hul E, Dikkers FG, Obee H, Stokroos RS, Hildering P, Vanhoenacker F, Van Camp G, Willems PJ. 1998. Van Buchem disease (hyperostosis corticalis generalisata) maps to chromosome 17q12-q21. Am J Hum Genet 62:391–399.

Diaz GA, Gelb BD, Ali F, Sakati N, Sanjad S, Meyer BF, Kambouris M. 1999. Sanjad-Sakati and autosomal recessive Kenny Caffey syndromes are

allelic: evidence for an ancestral founder mutation and locus refinement. Am J Med Genet 85:48–52.

Diaz GA, Khan KT, Gelb BD. 1998. The autosomal recessive Kenny Caffey syndrome locus maps to chromosome 1q42-q43. Genomics 54:13–18.

Sabry MA, Farag TI, Shaltout AA, Zaki M, Al Mazidi Z, Abulhassan SJ, Al-Torki N, Quishawi A, Al Awadi SA. 1999. Kenny Caffey syndrome: an Arab variant? Clin Genet 55:44–49.

Sabry MA, Zaki M, Shaltout A. 1998. Genotypic/phenotypic heterogeneity of Kenny Caffey syndrome. J Med Genet 35:1054–1055.

Martignetti JA, Desnick RJ, Aliprandis E, Norton KI, Hardcastle P, Nade S, Gelb BD. 1999. Diaphyseal medullary stenosis with malignant fibrous histiocytoma: a hereditary bone dysplasia/cancer syndrome maps to 9p21-22. Am J Hum Genet 64:801–807.

Martignetti JA, Gelb BD, Pierce H, Picci P, Desnick R. 2000. Malignant fibrous histiocytoma: inherited and sporadic forms have loss of heteozygosity at chromosome bands 9p21-22. Evidence for a common genetic defect. Genes, Chromosomes Cancer 27:191–195.

Gladwin A, Donnai D, Metcalfe K, Schrander-Stumpel C, Brueton L, Verloes A, Aylsworth A, Toriello H, Winter R, Dixon M. 1997. Localization of a gene for oculodentodigital syndrome to human chromosome 6q22-q24. Hum Mol Genet 6:123–127.

Boyadjiev SA, Jabs EW, LaBuda M, Jamal JE, Torbergsen T, Ptacek LJ 2nd, Rogers RC, Nyberg-Hansen R, Opjordsmoen S, Zeller CB, Stine OC, Stalker HJ, Zori RT, Shapiro RE. 1999. Linkage analysis narrows the critical region for oculodentodigital dysplasia to chromosome 6q22-q23. Genomics 58:34–40.

Price JA, Bowden DW, Wright JT, Pettenati MJ, Hart TC. 1998. Identification of a mutation in DLX3 associated with tricho-dento-osseous (TDO) syndrome. Hum Mol Genet 7:563–569.

Group 28

Reichenberger E, Tiziani V, Watanabe S, Park L, Ueki Y, Santanna C, Baur ST, Shiang R, Grange DK, Beighton P, Gardner J, Hamersma H, Sellars S, Ramesar R, Lidral AC, Sommer A, Raposo do Amaral CM, Gorlin RJ, Mulliken JB, Olsen BR. 2001. Autosomal dominant craniometaphyseal dysplasia is caused by mutations in the transmembrane protein ANK. Am J Hum Genet 68:1321–1326.

Group 31

Xu MQ, Feldman G, Le Merrer M, Shugart YY, Glaser DL, Urtizberea JA, Fardeau M, Connor JM, Triffitt J, Smith R, Shore EM, Kaplan FS. 2000. Linkage exclusion and mutational analysis of the noggin gene in patients with fibrodysplasia ossificans progressiva. Clin Genet 58: 291–298.

Feldman G, Li M, Martin S, Urbanek M, Urtizberea JA, Fardeau M, Le Merrer M, Connor JM, Triffitt J, Smith R, Muenke M, Kaplan FS, Shore EM. 2000. Fibrodysplasia ossificans progressiva, a heritable disorder of severe heterotopic ossification, maps to human chromosome 4q27-31. Am J Hum Genet 66:128–135.

Ueki Y, Tiziani V, Santanna C, Fukai N, Maulik C, Garfinkle J, Ninomiya C, do Amaral C, Peters H, Habal M, Rhee-Morris L, Doss JB, Kreiborg S, Olsen BR, Reichenberger E. 2001. Mutations in the gene encoding c-Abl-binding protein SH3BP2 cause cherubism. Nat Genet 28:125–126.

Group 32

Group Martignetti JA, Aqeel A, Sewairi WA, Boumah CE, Kambouris M, Mayouf SA, Sheth KV, Eid WA, Dowling O, Harris J, Glucksman MJ, Bahabri S, Meyer BF, Desnick RJ. 2001. Mutation of the matrix metalloproteinase 2 gene (MMP2) causes a multicentric osteolysis and arthritis syndrome. Nat Genet 28:261–265.

Group 33

McIntosh I, Dreyer SD, Clough MV, Dunston JA, Eyaid W, Roig CM, Montgomery T, Ala-Mello S, Kaitila I, Winterpacht A, Zabel B, Frydman M, Cole WG, Francomano CA, Lee B. 1998. Mutation analysis of LMX1B gene in nail-patella syndrome patients. Am J Hum Genet 63:1651–1658.

Morello R, Zhou G, Dreyer SD, Harvey SJ, Ninomiya Y, Thorner PS, Miner JH, Cole W, Winterpacht A, Zabel B, Oberg KC, Lee B. 2001. Regulation of glomerular basement membrane collagen expression by LMX1B contributes to renal disease in nail patella syndrome. Nat Genet 27:205–208.

Mangino M, Sanchez O, Torrente I, De Luca A, Capon F, Novelli G, Dallapiccola B. 1999. Localization of a gene for familial patella aplasia-hypoplasia (PTLAH) to chromosome 17q21-22. Am J Hum Genet 65: 441–447.

Cormier-Daire V, Chauvet ML, Lyonnet S, Briard ML, Munnich A, Le Merrer M. 2000. Genitopatellar syndrome: a new condition comprising absent patellae, scrotal hypoplasia, renal anomalies, facial dysmorphism and mental retardation. J Med Genet 37:520–524.

Bongers EM, Opitz JM, Fryer A, Sarda P, Hennekam RC, Hall BD, Superneau DW, Harbison M, Poss A, van Bokhoven H, Hamel BC, Knoers NV. 2001. Meier-Gorlin syndrome: report of eight additional cases and review. Am J Med Genet 102:115–124.