Bones, Eyes, and Nails

With contributions from Elise M. Herro, MD, Benjamin A. Solky, MD, and Jennifer L. Jones, MD. (Updated July 2015)*

CONDITION	INHERITANCE: GENE	BONE	EYES	NAILS
5-FU,AZT, antimalarials				Blue lunulae
Acne Fulminans		Osteolytic Lesions (sterno-clavicular)		
AEC (Ankyloblepharon filiforme adenatum-Ectodermal dysplasia-Cleft palate) [Hay-Wells Syndrome]	AD: p63	Anodontia/hypodontia	Ankyloblepharon (strands of skin), lacrimal duct abnormalities	Onychodysplasia or anonychia
Albright's Osteodystrophy		Bradymetacarpalism		
Alkaptonuria	AR: homogentisate 1,2-dioxygenase (HGO)	Severe arthropathy (larger joints)	Pingueculae, Osler's Sign (blue-gray scleral pigment)	
Allezandrini Syndrome			Unilateral retinitis pigmentosa, eyelash poliosis	
Alopecia Areata				Nail Pits, Red and Spotted Lunula
Apert's Syndrome	FGFR2	Craniosynostosis, syndactyly		One large fingernail
Argyria			Blue Sclera	Slate Blue Lunula
Arsenic poisoning, rheumatic fever, CHF				Mee's Lines (all nails)
Ataxia-Telangiectasia (Louis-Bar Syndrome)	AR: ataxia-telangiectasia mutated (ATM)		Bulbar Telangiectasia	
Bacterial Infection				Black nail (Proteus mirabilis); Green nail (Pseudomonas)
Beare-Stevenson Cutis Gyrata Syndrome	FGFR2	Craniosynostosis		
Behçet's Syndrome	A/w HLA-B51	Asymmetric, non-erosive polyarthritis	Retinal vasculitis, posterior uveitis, & hypopyon	
Bonnet Dechaune Blanc Syndrome (Wyburn-Mason)	Unknown		Retinal AVM's	
Bushke-Ollendorf Syndrome	AD: LEMD3 or MAN1	Osteopoikolosis		
Chanarin-Dorfman Syndrome (Neutral lipid storage disease with ichthyosis)	ABHD5	Short stature	Cataracts, nystagmus, ectropion	
Chédiak-Higashi Syndrome	AR: LYST		Photophobia, nystagmus, strabismus	
CHF, Connective Tissue Disease, CO Poisoning, Alopecia Areata				Red Lunula
CHIME Syndrome (Coloboma, Heart defects, Ichthyosiform Dermatosis, Mental retardation, Ear abnormalities)	AR: PIGL		Colobomas of Retina	
Cicatricial Pemphigoid	Ab against β-4-integrin		Symblepharon, scarring, blindness	
Cirrhosis, CHF, diabetes				Terry's Nails
Cockayne's Syndrome (CS)	AR: CSA: ERCC8 gene CSB: ERCC6 gene	Dwarfism; intracranial calcifications	Salt & Pepper Retinitis Pigmentosa with Optic Atrophy; Cataracts	
Coffin-Siris Syndrome		Microcephaly		5th nail dystrophy/anonychia
Congenital Contractural Arachnodactyly	AD: fibrillin 2	Arachnodactyly, scoliosis, crumpled ears		
Congenital Ichthyosiform Erythroderma (CIE) [Nonbullous CIE]	AR: transglutaminase 1 (TGM1), ALOX12B/ ALOXE3 (lipoxygenase)		Ectropion	
Congenital Onychodysplasia of the Index finger (COIF)				Anonychia
Congenital Syphilis	Early: 0-2 yrs Late: >2 yrs	Early: Wimberger's sign (sawtooth metaphysis) Late: osteochondritis, Clutton's joints (knees), Higoumenaki' sign (medial clavicle), saddle nose, saber shins, mulberry molars, Hutchinson's teeth	Late: interstitial keratitis	

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Conradi-Hünermann Syndrome (Chondrodysplasia punctata)	XLD: Emopamil-binding protein (EBP) XLR: Arylsulfatase E AR: PEX 7, DHAPAT, alkyldihydroacetone phosphate synthase	Unilateral limb shortening, Chondrodysplasia punctata (stippled epiphyses); scoliosis	Asymmetric Focal Cataracts	
Cornelia de Lange Syndrome	Sporadic (most); AD: nipped-β-like (NIPBL) and SMC1L1	Microcephaly, clinodactyly of 5th finger		
Darier-White Disease (Keratosis follicularis)	AD: ATP2A2 (encoes SERCA2)			Red and white longitudinal bands, V-nicking
Deafness, Congenital Onychodystrophy, Recessive form (DOOR)				Anonychia
Dermatomyositis				Samitz sign (cuticle fraying)
Down's Syndrome	Trisomy 21	Clinodactyly	Brushfield spots (periphery of iris)	
Dyskeratosis Congenita (Zinsser-Engman-Cole Syndrome)	XLR (*most common*): dyskerin (DKC1) AD: telomerase RNA component (TERC)	Dental caries with early tooth loss; intracranial calcification		Dystrophic with longitudinal ridges, pterygium; atrophic
EEC Syndrome (Ectrodactyly-Ectodermal Dysplasia-Cleft lip/palate Syndrome)	AD: EEC1; EEC2; EEC3 (*p63 gene - most common*)	Ectrodactyly ("lobster-claw deformity"); Hypodontia/ anodontia	Lacrimal gland/duct abnormalities	Onychodystrophy
Ehlers-Danlos VI (Kyphoscoliosis)	AR: procollagen lysyl 2-oxoglutarate 5 dioxygenase (PLOD)	Severe kyphoscoliosis	Keratoconus, ruptured globe, retinal detachment, blindness, blue sclera	
Ehlers-Danlos VIIA,B (Arthrochalasia)	AD: COL1A1 (type A) or COL1A2 (type B)	Congenital hip dislocation, scoliosis, short stature		
Ehlers-Danlos IX	XLR: lysyl oxidase	Occipital horns		
Epidermal Nevus Syndrome (Icthyosis hystrix)	Sporadic	Kyphoscoliosis, hemihypertrophy	Coloboma, corneal opacity, cortical blindness	
Fabry Disease (Angiokeratoma corporis diffusum)	XLR: α-galactosidase A (GLA)		Whorl-like corneal opacities, spoke-like cataracts	
Fanconi's Anemia	AR: FANC	Absent radius or thumb, microcephaly, growth retardation	Strabismus, retinal hemorrhages	
Fe++ Deficiency				Koilonychia
Franceschetti-Jadassohn Syndrome		Malaligned great toes		
Fungal Infection				Distal subungal (T. rubrum); Proximal white subungal (T. rubrum - often a/w HIV) Superficial (T. mentag)
Gardner's Syndrome	AD: adenomatous polyposis coli (APC)	Craniofacial osteomatosis; supernumerary teeth	Congenital Hypertrophy of Retinal Pigmented Epithelium (CHRPE)	
Gaucher's Disease	AR: acid-β-glucocidase (GBA)		Pingueculae	
Goltz's Syndrome (Focal Dermal Hypoplasia)	XLD: PORCN	Osteopathia Striata, Lobster Claw Deformity	Coloboma, microphthalmia	
Gorlin's Syndrome (Basal Cell Nevus Syndrome)	AD: PTCH1	Bifid Rib, Mandibular Keratocysts, Kyphoscoliosis, Calcified Falx Cerebri, Frontal Bossing	Hypertelorism, coloboma	
Haim-Munk Syndrome	AR: cathepsin C gene	Loss of teeth d/t severe periodontitis; arachnodactyly, acro-osteolysis		Onychogryphosis
Hallerman-Streiff Syndrome		Bird-like facies, natal teeth	Microopthalmia, Congenital Cataracts, Strabismus	
Harlequin Fetus	AR: ABCA12		Ectropion	
Hemochromatosis	AR: HFE			Koilonychia
Hermansky-Pudlak Syndrome	AR: HPS1 (*most common*) and HPS2/AP3B1		Photophobia, nystagmus, decreased visual acuity	

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Hidrotic Ectodermal Dysplasia (Clouston syndrome)	AD: connexin 30 (GJB6)	Tufting of terminal phalanges, thickened calvarium		Onychodystrophy, micronychia or anonychia, hyperconvex, brittle, paronychia
High Fever, Surgery, & Meds (chemo)				Beau's Lines
Homocystinuria	AR: cystathionine β-synthase (CBS)	Marfanoid habitus, pectus excavatum, genu valgum	Downward lens displacement, glaucoma	
Hyper-IgE Syndrome (Job Syndrome)	AD: STAT3 AR: DOK8 TYK2	Retained primary teeth and lack of secondary teeth; broad nasal bridge		
Hyperthyroidism				Koilonychia
Hypoalbuminemia, nephrotic syndrome, liver disease				Muehrcke's nails (lines disappear when squeezed)
Hypohidrotic Ectodermal Dysplasia (Christ-Siemens-Touraine syndrome)	XLR: ectodysplasin (EDA) AD/AR: NEMO	Frontal bossing, saddle nose; hypo-/anodontia, peg-shaped conical incisors and canines		Slight onychodystrophy compared to hidrotic disease
Hypomelanosis of Ito (Incontinentia pigmenti achromians)	Not inherited; mosaicism	Scoliosis, limb length discrepancy; anodontia	Strabismus, hypertelorism	
Hypothyroidism				Plummer's nails (onycholysis)
Incontinentia Pigmenti (Bloch-Sulzberger's)	XLD: NF-κB essential modulator (NEMO)	Anodontia, peg/conical teeth; Supernumerary vertebrae with extra ribs	Strabismus, Coloboma, Cataracts, Optic Atrophy	
Juvenile Xanthogranuloma (JXG)			Hyphema, Hypopyon	
KID Syndrome (Keratosis-ichthyosis-deafness)	AD and AR: GJB2 (encodes connexin 26)		Keratitis (secondary blindness may occur)	Dystrophic
Lamellar Ichthyosis	AR: transglutaminase 1 (TGM1)		Ectropion	
LEOPARD Syndrome (Moynahan)	AD: PTPN11 (encodes SHP2)	Growth retardation	Hypertelorism	Koilonychia
Lichen Planus				Dorsal Pterygium
Linear Morphea		Melorheostosis		
Lipoid Proteinosis (Urbach-Wiethe)	AR: extracellular matrix protein 1 (EM1)	Sickle-shaped beanbag calcifications in hippocampus	Eyelid "String of Pearls"	
Lymphedema-distichiasis Syndrome	AD: FOXC2		Distichiasis (double row of eyelashes) --> corneal irritation; ectropion	
Maffucci's Syndrome	Sporadic but now also parathyroid hormone receptor protein defect (PTHrP)	Enchondromas, chondrosarcoma, short stature		
Mal de Meleda	AR: secreted Ly-6/uPar related protein 1 (SLURP1)			Koilonychia; subungal hyperkeratosis
Marfan's Syndrome	AD: fibrillin-1	Marfanoid habitus: tall, arachnodactyly, pectus excavatum, high arched palate, kyphoscoliosis	Upward lens displacement	Dolionychia
McCune-Albright Syndrome	Sporadic; postzygotic somatic mutations in GNAS1	Polyostotic fibrous dysplasia		
Menkes Kinky Hair Syndrome (Occipital Horn Syndrome)	XLR: MKN or ATP7A (encodes ATPase - copper binding)	Occipital horns (exostosis), frontal bossing, wormian bodies in sagittal suture, metaphyseal widening with spurs in long bones		
Monilethrix	AD: human basic type II hair keratin genes (hHb1/KRT81, hHb6/KRT86)	Teeth abnormalities	Cataracts (rare)	Brittle
Multicentric Reticulohistiocytosis		Mutilating arthritis, accordion hand		
Multiple Endocrine Neoplasia (MEN III AKA IIb)	AD: RET proto-oncogene	Marfanoid habitus		

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Multiple myeloma				Absent lunulae
Nail-Patella Syndrome (HOOD)	AD: LMX1B	Posterior iliac horns, Absent patella	Lester iris (hyperpigmentation of pupillary margin), cataracts, glaucoma	Triangular lunula, micronychia, anonychia
Neurofibromatosis I (NF-1) [Von Recklinghausen]	AD: NF1 (encodes neurofibromin	Sphenoid wing dysplasia, scoliosis	Lisch nodules (iris hamartomas), optic gliomas, congenital glaucoma	Macronychia
Neurofibromatosis I (NF-2) [Bilateral acoustic neurofibromatosis]	AD: NF2/SCH (encodes schwannomin/merlin)		Juvenile posterior subcapsular lenticular cataracts	
Oculocutaneous Albinism (OCA)	OCA 1 - AR: tyrosinase (TYR) OCA2 (*most common*) - AR: P gene OCA3 - AR: tyrosinase related protein 1		Blue to gray-blue irides (OCA1) Blue to yellow brown irides (OCA2/3), nystagmus, photophobia, prominent red reflux, impaired visual acuity	
Osteogenesis Imperfecta	AD: genes encode type I collagen	Fragile bones (fractures) Type I: bowing of long bones, kyphoscoliosis Type II: beaded ribs, crumpled humeri and femora, abducted thighs	Blue sclera	
Pachydermoperiostosis (PDP) [Primary hypertrophic osteoarthropathy]	AD (1/3)	Periarticular and subperiosteal periostosis		Clubbing
Pachyonychia Congenita I (Jadassohn-Lewandowsky syndrome)	Type I - AD: K16/K6a			Thickened nails, pincer nails, staph/Candidal paronychia (fingers>toes)
Pachyonychia Congenita II (Jackson-Lawler)	Type II - AD: K17/K6b	Natal teeth (N.B. *oral benign leukokeratosis in PC type 1*)		Thickened nails, pincer nails, staph/Candidalparonychia (fingers>toes)
Papillon-Lefèvre Syndrome	AR: CTSC (encodes cathepsin C)	Tentorial & chondroid plexus dural calcification; alveolar bone resorption and loss of teeth		
Progeria (Hutchinson-Gilford syndrome)	AD: lamin A	Large cranium; frontal bossing, thin beaked nose, micrognathia; osteoporosis, coxa valga; delayed permanent teeth		Thin, dystrophic
Pseudoxanthoma Elasticum (PXE) [Gronblad-Strandberg]	AR (most common); AD ATP-binding cassette subfamily C member 6 (ABCC6)	Intracranial calcification	Angioid streaks (rupture in Bruch's membrane), retinal hemorrhage causing blindness	
Psoriasis				Oil spots, onycholysis, pitting
Refsum Syndrome (Phytanic acid storage disease)	AR: PAHX, PEX7		Salt & pepper retinitis pigmentosa	
Renal Disease				Lindsay's Nails
Retinoids, Indinavir, and Estrogen				Pyogenic Granuloma
Rhizomelic Dwarfism		Enchondromas		
Richner-Hanhart Syndrome (Tyrosinemia type II)	AR: tyrosine aminotransferase	Variety skeletal anomalies	Pseudoherpetic keratitis, corneal ulceration, neovascularization and blindness	
Rubenstein-Taybi Syndrome	Sporadic AD proposed: human CREB-binding protein (CREBBP)	Broad thumbs and halluces, beaked nose	Strabismus	Brachyonychia
Russell-Silver Syndrome	Sporadic	Short stature, clinodactyly of fifth finger, skeletal asymmetry		
Sarcoidosis		Lytic bone cysts of hands with honeycombed pattern		
Schopf-Sculz-Passarge Syndrome	AR	Hypodontia	Cystic eyelids	
Sjögren-Larsson Syndrome	AR: fatty aldehyde dehydrogenase (FALDH)	Scissor gait	Glistening dots retinitis pigmentosa	

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Sturge-Weber Syndrome (Encephalotrigeminal angiomatosis)	Sporadic	Tram-track (gyriform) calcifications in temporal/ occipital cortex; skeletal hypertrophy a/w capillary malformation	Ipsilateral glaucoma	
Systemic Sclerosis		Resorption of distal phalanges		Pterygium Inversum Unguis (ventral)
Trichinosis, Endocarditis & Trauma				Splinter hemorrhages
Trichorhinophalangeal Syndrome	AD: TRPS1	Cone-shaped phalangeal epiphyses; pear-shaped broad nose		Thin nails
Tuberous Sclerosis (Bourneville's syndrome)	AD or spontaneous TSC1: hamartin TSC2: tuberin	Enamel pits; phalangeal periosteal cysts; calcification of tubers in basal ganglia, subependymal nodules	Retinal hamartomas (phakomas)	Koenen's tumor (periungal fibroma), macronychia
Von Hippel-Lindau Syndrome	AD: VHL tumor suppressor		Retinal hemangioblastomas	
Waardenburg Syndrome	AD Type I: Pax3 Type II: MITF Type III: Pax 3 Type IV: SOX1O and endothelin-3		Dystopia canthorum (not type II), heterchromia irides	
Wilson's Disease (Hepatolenticular degeneration)	AR: ATB7B (encodes ATPase CU^{2+}-transporting polypeptide		Kayser-Fleischer ring (copper deposit in Descemet's membrane)	Blue lunulae
Xeroderma Pigmentosum	AR: XP (multiple variants)		Photophobia, ectropion, benign eyelid papillomas, BCC, melanoma	
X-Linked Ichthyosis	XLR: arylsulfatase C/ steroid sulfatase (STS)		Posterior comma-shaped corneal opacities (Descemet's membrane)	
Yellow Nail Syndrome	FOXC2			Yellow curved nails, absent lunula/ cuticles

Reviewed and updated July 2015 by: Alina Goldenberg, MD, Emily deGolian, MD, and Sharon Jacob, MD.