Elise M. Herro, MD, is Health Sciences Clinical Instructor, Clinician-Educator track, in the Division of Dermatology, Department of Medicine, UCLA.

Antoine Amado, MD is a Contact Dermatitis Fellow at the Cleveland Clinic, Ohio.

Sharon E. Jacob, MD, is an assistant professor of Clinical Dermatology, director of the Contact Dermatitis Clinic and Medical Student Education, Department of Dermatology and Cutaneous Surgery, University of Miami, School of Medicine, Miami, Florida.

Hypertrichosis

With contributions from Elise M. Herro, MD, Antoine Amado, MD, and Sharon E. Jacob, MD. (Updated July 2015)*

	Disorder	Inheritance	Gene Defect	Clinical Manifestations	Mechanism Hypertrichosis
Congenital (Circumscribed)	Congenital nevocellular nevus			Increased hair within the lesion	
	Smooth muscle hamartoma			Pigmented pebbly patch trunk, vellus hair hypertrichosis, pseudo-Darier sign	↑hair size & pigmentation
	Nevoid hypertrichosis (HT)			Usually solitary patch of terminal hair w/o other abnormality; anywhere on body	↑# normal hair follicles
	HT with neurofibroma			Periorbital cases	
	HT Cubiti (hairy elbows)	Sporadic ? AD/AR *somatic mosaicism		Symmetric pattern, appears during infancy, resolves partly/ completely by adolescence	High percentage of hair follicles in anagen phase
	Hemihypertrophy	?Spontaneous mutation		Terminal hair limited to hypertrophic side Assoc. Beckwith-Wiedemann synd, neurofibromatosis, Klippel-Trenaunay-Weber synd & Proteus synd, Wilms tumor, hepatoblastomas, brain tumors, adrenocortic neop, internal hemangiomas and GU malformations	↑hair shaft diameters & terminal hair follicles
	Hairy cutaneous malfor. palms & soles	AD		Patches of skin with hair follicles bilaterally on the palms and/ or soles. Vellus in women and children; males hair becomes terminal at puberty	Androgen-sensitive N hair follicles
	Spinal hypertrichosis			Excess hair over the spine: discrete patch of sacral terminal hair ["faun-tail"] or midline vellus hair ["silky down"]. Underlying spinal dysraphism [50% derm finding; 1/3 those hypertrichosis]: dermal cyst or sinus, myelomeningocele, diastematomyelia, vertebral abn, subdural or extradural lipoma. Cervical spinal hypertrichosis ~ kyphoscoliosis. MRI evaluation.	Simultaneous abn. skin and nervous tissue --> ectodermal origin
	Cervical hypertrichosis	Anterior: AR Posterior: AD, XLR		Small patch of terminal hair superior to laryngeal prominence solitary (AD) or with peripheral neuropathy (AR) and hallux valgus	
Congenital (Generalized 1°)	Congenital HT lanuginosa	AD, sporadic	Cr8q22	Lanugo hair (may be vellus) remains over the entire body after birth, sparing palms, soles & mucous membrane. Associated with dental abn.	
	Congenital Gen. HT	XL	X24-q27.1	Terminal hair on face, trunk & limbs; sparing palms, soles & mucosa	
	Ambras Syndrome		Cr8	Thicker, longer hair on face, ears, shoulders, as well as whole body, sparing glabrous regions; facial dysmorphism and dental anomalies	
	Gingival fibromatosis w HT	AD		Early childhood; hairiness on face, trunk, eyebrows + progressive gingival hyperplasia. 50% mental retardation &/ or seizures. ≠ Antiepileptics & cyclosporine	
	H Syndrome	AR	SLC29A3	(hyperpigmentation, hypertrichosis, hepatosplenomegaly, hearing loss, heart anomalies, hypogonadism, low height (short stature), hyperglycemia/diabetes mellitus, and hallux valgus/flexion contractures) -- new form of histiocytosis. Initially appear on the inner thighs and shins but may be more widespread	
	Osteochondrosyplasia W HT (Cantú Syndrome)	AR, AD	Unknown	Gen. HT, sparing glabrous skin & membranes. Also macrosomia & cardiomegaly	
	HT, pigmentary retinopathy & facial abn			Gen. HT, sparing ant. torso, palms, soles & mucous memb; hyperpigmentation face & extrem; facial abn, regional lipoatrophy, pigmentary retinopathy. ~ SMH	

Hypertrichosis

With contributions from Elise M. Herro, MD, Antoine Amado, MD, and Sharon E. Jacob, MD. (Updated July 2015)*

	Disorder	Inheritance	Gene Defect	Clinical Manifestations	Mechanism Hypertrichosis
Congenital (Generalized 2°)	Brachamann-de Lange synd (Cornelia de Lange syndrome)	AD (most cases sporadic) ---------- XL	Cr5p 13.1 NIPBL ---------- Cr Xp11.22-p11.21 SMC1L1	Thick & convergent eyebrows (synophrys) & eyelashes; low hairline; vellus HT trunk, post. neck, sacrum, elbows; cutis marmorata; severe mental retardation; upturned nostrils, depressed nasal bridge, low-set ears, small & irregular teeth, micrognathia, high palate & bifid uvula; short arms & abn hands & feet	
	Teratogens			**Fetal hydantoin syndrome**: during first 9 weeks gestation have 10% risk; HT, nail hypoplasia, cleft lip, midfacial hypoplasia, long upper lip, low birth weight. After 9 weeks LBW w/o other congenital abn. **Fetal alcohol syndorme**: during any point in pregnancy. HT [inconstant]; prenatal growth deficiency, develop. delay, mental retardation, & facial abn [microcephaly, short upturned nose, short palpebral fissures, thin upper lip, & poorly developed philtrum]	
	Lipodystrophy	AR	BSCL2 (encodes lamins) Insulin receptor gene	**Berardinelli-Seip synd**: HT scalp, face, neck & extrem. ↑age. Gen. lipoatrophy, acanthosis nigricans, hyperhidrosis, phlebomegaly, xanthomas, NIDDM, genital hypertrophy, mental retard, corneal opacities, cardiac, renal, & ovarian abn., hepatosplenomegaly **Donohue syndrome** (leprechaunism), more severe: HT face & trunk, acanthosis nigricans; loose & redundant skin. Lipoatrophy, genital hypertrophy, abdominal distension, slow growth, prominent eyes & lips, low-set ears, flattened nasal bridge. Hyperinsulinemia w/ insulin resistance.	androgen-sensitive?
	Mucopolysaccharidoses	AR except XLR in Hunter's	Hurler's: α-L-iduronidase Hunter's: iduronate sulfatase	Short stature w typical facies, skeletal deformities, hepatosplenomegaly & cardiac abn. Lanugo HT back & extrem, bushy eyebrows, low frontal hairline, abundant & coarse scalp hair. Hurler syndrome (MPS-I), Hunter (MPS-II), and Sanfilippo syndrome (MPS-III) - hair-shaft dysmorphism. All types with generalized hirsutism.	Animal std: ↑glycosaminoglycans skin
	Stiff-skin syndrome			Stony-hard skin, ↓ joint mobility, & mild HT; complication: restricted lung capacity	
	Winchester syndrome		Cr16q13 MMP2	Thickened & HT of skin, short stature with severe osteolysis carpal/tarsal bones, corneal opacifications	
	Porphyrias	CEP: AR _____ PCT: AD/sporadic/ acquired	UrogenIII synthase _____ Urogen decarboxylase	Congenital erythropoetic porphiria (CEP/Gunther disease) photosensitivity birth → vesicles & bulla, hyperpigmentation, scarring, & HT. PCT may present w/ HT (60%) face (temple areas) & upper torso [sole sympt]. HEP homozygous form of PCT - similar to CEP. HT later stages Erythropoietic protoporphyria; Hereditary coproporphyria & Variegate porphyria	
	Rubinstein-Taybi syndrome	Sporadic/ AD	Cr22q13, 16p13.3 CREBBP; EP300 (genetic heterogeneity)	HT, bird-like facies, keloids, pilomatricomas, broad thumbs/great toes, short stature, mental retardation. [cAMP-bind protein]	
	Schinzel-Giedion syndrome			HT face & limbs, depressed nasal bridge, high forehead, hypoplastic midface, club feet, abn. ribs, limbs & skull. Hypoplastic dermal ridges, seborreic rash, suscep. dermatophyte infection	
	Barber-Say syndrome	AD, XL		HT forehead, neck & back; atrophic skin, macrostomia, growth retardation & ectropion	
	Coffin-Siris syndrome	AR	Cr7q32-34?	Lumbosacral and eyebrow HT. Hypoplastic or absent fingernails & toenails (5^{th}), mental & growth retard, sparse scalp hair, joint laxity; coarse face [microcephaly, prominent lips, low nasal bridge, wide nasal tip]	
	Hemimaxillofacial dysplasia			Unilateral enlarged maxilla, hypoplastic teeth, ipsilateral HT [inconstant]	
	Craniofacial dysotosis			PDA, hypoplasia labia majora, dental & eyes abn, ↑ terminal HT limbs, back & low hair line	
	Hypomelanosis of Ito	Not inherited	Mosaicism Xp11 translocation	Hypopigmented macular patches (Blaschko lines), neurological symptoms & HT (also scalp alopecia)	
	MELAS Syndrome		Several mitochondrial tRNA genes	(Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes) Pruritus, scaling erythema neck, terminal HT legs	
Acquired (Circumscribed)	Becker nevus	Sporadic, ?paradominant		Irregular hypermelanotic patch torso, ↑hair at puberty. ↑males, solitary, acquired & unilateral. Pigmentation before HT. Histology- hamartoma **Becker nevus syndrome**: Becker nevus, ipsilateral hypoplasia shoulder girdle, arm or breast; scoliosis or vertebral abn. ≠SMH	↑# androgen receptors
	Hypertrichosis w/ local inflammation			Chemically induced dermatitis [iodine or psoralen], orthopedic casts & splints [vellous], friction [insect bites, sack bearers], thrombophlebitis, osteomyelitis, vaccination sites	Reg. effect healing Fx; Freq. scratching; ↑ reg. blood flow
	HT of the pinna	AD		Older men. In AIDS, babies with XYY synd, babies diabetic mothers, diabetics	
	Trichomegaly			Isolated HT eyelashes & in areas of linear scleroderma. HIV, SLE, Latanoprost	

Hypertrichosis

With contributions from Elise Herro, MD, Antoine Amado, MD, and Sharon Jacob, MD. (Updated July 2015)*

	Disorder	Inheritance	Gene Defect	Clinical Manifestations	Mechanism Hypertrichosis
Acquired (Generalized)	Cerebral disturbances			Gen. HT. Post viral encephalitis, posttraumatic head injury children, traumatic shock, transient diencephalic, pitituitary or hypothalamic disturbances.	Hypothalamic factors
	Acrodynia			Reaction to chronic mercury exposure. Gen. HT, erythema fingers, toes & nose; perspiration & salivation, painful hands/feet.	
	Infection			TB: transient HT children, face & limbs AIDS: HT eyelashes, eyebrows & ears	
	Malnutrition			Gen. vellus HT (marasmus, celiac dz), bulimia 36% & anorexia nervosa 77%	
	Dermatomyositis			Juvenile DM ↑hair growth face & limbs, ↑male children & Mexican ancestry. PM adult also gen. HT	
	Thyroid abnormalities			**Hypothyroidism**: HT children >adult, resolves w/ replacement Tx. **Hyperthyroidism**: Localized HT over plaques of pretibial myxedema	
	Lawrence-Seip syndrome			Lipoatrophic diabetes ~Berardinelli-Seip synd. HT after viral infection	
	Acquired porphyrias			↑hair growth [PCT 2° hexachlorobenzene exposure]	
	Acquired HT lanuginosa (Malignant down)			Assoc. malignancies lung, colon, lymphomas, Ewing's arcoma, rectum, pancreas, breast, ovary & uterus. Precede CA 1 to 2 years. New lanugo: workup	Tumor-secreted substance ↑hair growth
	POEMS syndrome (Crow-Fukase synd)			(polyneuropathy, organomegaly, endocrinopathy, M protein, skin changes) A/w plasma cell dyscrasias. Gen. HT 78-85% (lower extrem), hyperpigmentation, skin thickening, digital clubbing, cutanous glomeruloid hemangioma	
	Pharmacologic hypertrichosis			*__Phenytoin__ HT: after 2-3 m; ↑limbs, face & trunk, resolve after 1 year discont 75%. * glaucoma Tx, regional hypertrichosis: __Acetazolamide__ [children, back & legs] & __latanoprost__ topical (prostagalndine F2 analogue) eyelashes & eyelids 77 %. *__Streptomycin__ : Diff. TB. *__Cyclosporine__: HTafter organ transp. 24-94%. * __Psoralen__: HT light-exposed areas. __Diazoxide__. __Minoxidil__ ↑terminal hair growth after 4 m.	Phenytoin: unknown Latanoprost: mitogenic pathw Diazoxide: ↑follicles anagen Minoxidil: Vel to Ter hairs

Abbreviations:

AGPAT2: 1-acylglycerol-3-phosphate O-acyltransferase 2
CREBBP: Transcriptional coactivator CREB-binding protein
HET: Hepatoerythropoietic Porphyria
HT: hypertrichosis
INSR: Insulin receptor gene
MMP2: Matrix metalloproteinase-2
NIPBL: Nipped-B-like
PCT: Porphyria Cutanea Tarda
SMC1L1: Structural maintenance of chromosomes 1-like 1
UROGEN III Synthase: Uroporphyrinogen III synthase
UROGEN Decarboxylase: Uroporphyrinogen decarboxylase

References:

1. *Wendelin DS, Pope DN, Mallory SB. Hypertrichosis. J Am Acad Dermatol 2003;48:161-79.*
2. *OMIM, Online Mendelian Inheritance in Man Database. Available at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM*
3. *Polizzi A, Pavone P, Ciancio E, La Rosa C, Sorge G, Ruggieri M. Hypertrichosis cubiti (hairy elbow syndrome): a clue to a malformation syndrome. J Pediatr Endocrinol Metab 2005;18:1019-25.*
4. *Spitz JL. Genodermatoses: A Clinical Guide to Genetic Skin Disorders. New York: Lippincott, Williams & Wilkins, 2005.*
5. Molho-Pessach V, et al. H syndrome: The first 79 patients. J Am Acad Dermatol 2014;70(1):80-87.
6. Baumeister FA, et al. Ambras syndrome: delineation of a unique hypertrichosis universalis congenita and association with a balanced pericentric inversion (8) (p11.2; q22). Clin Genet. 1993 Sep;44(3):121-8. Review.

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