Heritable Disorders of Connective Tissue

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	Mutation	Inheritance	Clinical	Hints
Ehlers Danlos syndrome (6 subtypes)	Classic- COL 5, tenascin X Hypermobility- COL3, tenascin X Vascular- COL3 Kyphoscoliosis- lysyl hydroxylase Arthrochalasia-COL1 Dermatosparaxis- Procollagen	Classic-AD Hypermobility-AD Vascular-AD Kyphoscoliosis-AR Arthrochalasia-AD Dermatosparaxis-AR	Classic-hyperextensible skin and joints, easy bruising, 'fish mouth' wide atrophic scars Hypermobility – smooth and velet like skin, joint hypermobility, pain, dislocations Vascular – thin and fragile skin, arterial and visceral rupture (GI or uterine) Kyphoscoliosis- fish mouth' wide atrophic scars, easy bruising, hypotonia in neontaes, ocular rupture, marfanoid habitus Arthrochalasia- joint hypermobility, fragile skin and extensible, congenital hip dislocation Dermatosparaxis- skin fragility, saggy redundant skin, hernias, premature rupture of fetal membranes	All subtypes AD, except 2 (kyphoscoliosis, dermatodparaxis) Important for these patients to avoid contact sports! Examine 1st degree family members!
Pseudoxanthoma Elasticum	ABCC6	AR	Yellow papules, coalescing into plaques over redundant, lax and soft skin folds, yellow papules on labial mucosa, angioid streaks in eyes, risk of miscarriages	'Plucked chicken skin'
Cutis Laxa	ELN, Fibrillin -4, Fibrillin-5	AR or AD	Sagging inelastic skin, pulmonary emphysema, urinary and gastrointestinal tract diverticuli	Great variability in subtypes clinically. 'Hound dog facies' -lack recoil -premature aged appearance -vocal cord laxity → deep voice
Others:				
Marfan syndrome	Fibrillin-1	AD	Striae, elastosis perforans serpiginosa, upward dislocation of lens, aortic aneurysm, kyphoscolsis, tall stature	Think 'upward' dislocation of lens b/c so tall
Homocystinuria	Cystathione beta synthease	AR	Downward dislocation of lens, malar flush, livedo reticularis, diffuse pigmentary dilution, marfanoid habitus, osteoporsis,	Downward dislocation of lens
Osteogenesis imperfecta	COL 1	AD	Thin skin, blue sclerae	
Buschke-Ollendorrff syndrome	LEMD3	AD	Dermatofibrosis lenticularis disseminata (connective tissue nevi), osteopoikilosis	
DeBarsy syndrome	Elastin mRNA	AR	Growth retardation, joint laxity, ocular defects, musculoskeletal abnormalities	
Williams syndrome	Allelic deletion of elastin gene	AD	Aortic stenosis, velvety skin, dysmorphic facies	

Stains for Heritable Disorders of Connective Tissue

Substance	Stain
Elastin	Verhoeff van gieson, Orecin
Calcium	Von Kossa

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References:
Bolognia, Chapter 97, Heritable Disorders of Connective Tissue.
Fitzpatick, Chapter 63.
Structure and Function of Skin course at AAD, Dr. Jouni Uitto, "Extracellular matrix in acquired and inherited skin disease."
Spitz Genodermatoses, Chapter 4: Disorders of Connective Tissue.