Table 650-1 International Society for the Study of Vascular Anomalies (ISSVA) Classification System

VASCULAR MALFORMATION	VASCULAR TUMOR
Slow-flow malformations Capillary malformation Venous malformation Lymphatic malformation Fast-flow malformations Arterial malformation Arteriovenous malformation Arteriovenous fistula Combined vascular malformations	Infantile hemangioma Congenital hemangioma Rapidly involuting congenital hemangioma Noninvoluting congenital hemangioma Kaposiform hemangioendothelioma Tufted angioma Spindle cell hemangioendothelioma Epithelioid hemangioendothelioma Other rare hemangioendotheliomas Angiosarcoma Acquired vascular tumors: pyogenic granuloma

Table 653-2 Typical Features of Segmental and Nonsegmental Vitiligo

SEGMENTAL VITILIGO	NONSEGMENTAL VITILIGO
Often begins in childhood	Can begin in childhood, but later onset is more common
Has rapid onset and stabilizes	Is progressive, with flare-ups
Involves hair compartment soon after onset	Involves hair compartment in later stages
Is usually not accompanied by other autoimmune diseases	Is often associated with personal or family history of autoimmunity
Often occurs in the face	Commonly occurs at sites sensitive to pressure and friction and prone to trauma
Is usually responsive to autologous grafting, with stable repigmentation	Frequently relapses in situ after autologous grafting
Can be difficult to distinguish from nevus depigmentosus, especially in cases with early onset	

Table 650-2 Complications of Hemangioma and Their Treatment

CLINICAL FINDING	RECOMMENDED TREATMENT
Severe ulceration/ maceration	Encourage twice-daily cleansing regimen Dilute sodium bicarbonate soaks ± Flashlamp pulsed-dye laser ± Oral corticosteroids or propranolol ± Culture-directed systemic antibiotics for infection
Bleeding (not KMP)	Gelfoam or Surgifoam or propranolol Compression therapy ± embolization
Hemangioma with ophthalmologic sequelae	Patching therapy as directed by ophthalmologist Intralesional vs oral corticosteroids vs propranolol
Subglottic hemangioma	Oral corticosteroids, propranolol, ± potassium titanyl phosphate (KtP) laser Tracheotomy if required
KMP	Corticosteroids, aminocaproic acid, vincristine, interferon-α ± embolization
High-flow hepatic hemangioma	Corticosteroids or interferon ± embolization

KMP, Kasabach-Merritt phenomenon.

Table 650-3 Clinical "Red Flags" Associated with Hemangiomas

CLINICAL FINDING	RECOMMENDED EVALUATION
Facial hemangioma involving significant area of face	Evaluate for PHACES (posterior fossa abnormalities, hemangioma, and arterial, cardiac, eye, and sternal abnormalities): MRI for orbital hemangioma ± posterior fossa malformation Cardiac, ophthalmologic evaluation Evaluate for midline abnormality: supraumbilical raphe, sternal atresia, cleft palate, thyroid abnormality
Cutaneous hemangiomas in beard distribution	Evaluate for airway hemangioma, especially if manifesting with stridor
Periocular hemangioma	MRI of orbit Ophthalmologic evaluation
Paraspinal midline vascular lesion	Ultrasonography or MRI to evaluate for occult spinal dysraphism
Hemangiomatosis (multiple small cutaneous hemangiomas)	Evaluate for parenchymal hemangiomas, especially hepatic/ central nervous system Guaiac stool test
Large hemangioma, especially hepatic	Ultrasonography with Doppler flow study MRI Thyroid function studies
Thrill and/or bruit associated with hemangioma	Consider cardiac evaluation and echocardiography to rule out diastolic reversal of flow in aorta MRI to evaluate extent and flow characteristics
Head tilting	Evaluate appropriately for specific site of lesion, and consider physical therapy evaluation
Delayed milestones	Consider side effect of corticosteroids (myopathy, weight-related) Consider side effect of interferon (especially spastic diplegia)
LUMBAR syndrome	MRI of spine, kidneys

LUMBAR, lower body infantile hemangiomas and other skin defects, urogenital anomalies and ulceration, myelopathy, boney deformities, anorectal malformations and arterial anomalies, renal anomalies.

Table 654-2 Clinical Presentation and Diagnosis of Selected Epidermolysis Bullosa Subtypes in the Neonatal Period

EB SUBTYPE (USUAL INHERITANCE)	CLINICAL FEATURES		DIAGNOSIS
	Cutaneous	Extracutaneous	
EB simplex–generalized (AD)	Mild to moderate blistering, often generalized Rare scarring, milia	Occasional mucosal blistering	EM: Intrabasal layer split IF: BPAG1 (BP230), BP-180 (BPAG2, collagen XVII), $\alpha_6\beta_4$ integrin, laminin 1, laminin 332, type IV collagen, type VII collagen (EBA antigen) at base of blister
EB simplex–localized (AD)	Mild blistering, often localized, sometimes in 1st 24 mo, but often not until later infancy or childhood Rare scarring, milia	Rare mucosal involvement	EM: Intrastratum basale split IF: Same as for EB simplex—generalized
EB simplex–Dowling-Meara (AD)	Moderate to severe blistering, which starts generalized, then is grouped (herpetiform); milia; nail dystrophy, shedding	Mild mucosal blistering	EM: Intrastratum basale split; clumped keratin filaments IF: Same as for EB simplex—generalized
Junctional EB–non-Herlitz (AR)	Moderate blistering; atrophic scars; nail dystrophy	Mild mucosal blistering; enamel hypoplasia	EM: Intralamina lucida cleavage; variable reduction in hemidesmosomes IF: Absence of staining with 19-DEJ-1 (uncein); variable staining with GB3 and other laminin 332 antibodies, including 46 and K140; BPAG1 (BP230) BP180 (BPAG2, type XVII collagen), $\alpha_6\beta_4$ integrin in blister roof; laminin 1, type IV collagen, type VII collagen (EBA antigen) at base of blister
Junctional EB–Herlitz (AR)	Severe generalized blistering that heals poorly; granulation tissue; scarring; nail dystrophy	Severe mucosal blistering; GI involvement common; laryngeal involvement with airway obstruction; urologic involvement	EM: Cleavage intralamina lucida; markedly reduced or no hemidesmosomes; absence of sub-basal dense plates IF: Absence of staining with 19-DEJ-1 (uncein) and GB3 (laminin 332) and of staining with other laminin 332 antibodies, including 46 and K140; BPAG1 (BP230) and BP180 (BPAG2, type XVII collagen) in blister roof; laminin-1, type IV collagen, and type VII collagen at base of blister
Junctional EB–pyloric atresia (AR)	Severe blistering	Polyhydramnios; pyloric atresia; urologic involvement: uretovesicular obstruction, hydronephrosis	EM: Cleavage intralamina lucida and intraplasma membrane; small hemidesmosomes IF: BPAG1 (BP230) and BP180 (BPAG2, type XVII collagen) in blister roof; laminin-1, type IV collagen, and type VII collagen at base of blister; Absence of 19-DEJ-1(uncein), $\alpha_6\beta_4$ integrin absent or reduced
Dominant dystrophic EB (AD)	Mild to moderate blistering (but may be more severe in newborn period) Milia, scarring Nail dystrophy	Mild mucosal blistering	EM: Cleavage sublamina densa; variable reduction in anchoring fibrils IF: BPAG1 (BP230), BPAG2 (BP180, type XVII collagen), $\alpha_6\beta_4$ integrin, laminin 1, type IV collagen at top of blister Staining for type VII collagen (EBA antigen) is normal, variable, or absent
Recessive dystrophic EB–Hallopeau-Siemens (AR)	Severe blistering Milia, scarring	Severe mucosal blistering; GI involvement common; urologic involvement	EM: Cleavage sublamina densa; absence of anchoring fibrils IF: BPAG1 (BP230), BP-180 (BPAG2, type XVII collagen), $\alpha_6\beta_4$ integrin, laminin 1, type IV collagen at top of blister Variability or absence of staining for type VII collagen (EBA antigen)

AD, autosomal dominant; AR, autosomal recessive; EB, epidermolysis bullosa; EBA, epidermolysis bullosa acquisita; EM, electron microscopy; GI, gastrointestinal; IF, immunohistochemical and immunofluorescence antigen mapping findings.

Table 658-1 Disorders of Cornification That Usually Manifest in the First Weeks of Life

DISORDER	INHERITANCE	CLINICAL FEATURES	MUTATION	VISUAL METHOD OF DIAGNOSIS
Harlequin ichthyosis	AR	Thick, armor-like scale with fissuring	*ABCA12*	Clinical
Collodion baby	Usually AR	Shiny collodion membrane	Various	Clinical
Recessive X-linked ichthyosis	Recessive X-linked	Collodion membrane May have genital anomalies	Steroid sulfatase	Plasma cholesterol sulfate
Lamellar ichthyosis	Usually AR	Collodion membrane	Transglutaminase I *ABCA12* *CYP4F22*	Clinical
Congenital ichthyosiform erythroderma	AR	Collodion membrane	Transglutaminase 1 *ALOX12B* *ALOXE3*	Clinical
Epidermolytic ichthyosis	AD	Scaling and blistering	Keratins 1, 10, 2e	Clinical and histologic
Ichthyosis hystrix	AD	Plaques of hyperkeratosis	Keratin 1, *GJB2*	Clinical
Familial peeling skin	AR	Superficial peeling	Unknown	Clinical and histologic
Sjögren-Larsson syndrome	AR	Variable skin thickening Mental, developmental retardation Spastic diplegia Seizures "Glistening dots"	*FAD*	Clinical and fibroblast cultures for FAD
Neutral lipid storage disease	AR	Collodion membrane or ichthyosiform erythroderma	*CGI58*	Blood smear for vacuolated polymorphonuclear leukocytes
Netherton syndrome	AR	Ichthyosiform erythroderma Scant hair, often failure to thrive	*SPINK 5* Unknown	Clinical; hair exam later in infancy Clinical and hair microscopy; hair sulfur content
Trichothiodystrophy	AR	Collodion membrane Broken hair	*XPB* *XPD*	
KID (keratitis with ichthyosis and deafness) syndrome	May be AD, AR	Erythrokeratodermatous or thick, leathery skin with stippled papules	*GJB2*	Clinical; auditory evoked potentials
CHILD (congenital hemidysplasia with ichthyosiform erythroderma and limb defects) syndrome	X-linked dominant	Alopecia Unilateral waxy yellow, scaling Hemidysplasia Limb defects	*NSDHL*	Clinical
Conradi-Hünermann syndrome	X-linked dominant	Thick, psoriasiform scale over erythroderma, patterned along Blaschko lines Proximal limb shortening	*ARSE*	Clinical
Ichthyosis follicularis	Usually X-linked recessive	Prominent follicular hyperkeratoses Alopecia Photophobia	*MBTPS2*	Clinical
CHIME (colobomas of the eyes, heart defects, ichthyosiform dermatosis, mental retardation, and ear abnormalities) syndrome	AR	Ichthyotic erythematous plaques Cardiac defects; typical facies Retinal colobomas	Unknown	Clinical
Gaucher disease	AR	Collodion membrane Hepatosplenomegaly	β-Glucocerebrosidase	Clinical; fibroblast cultures

AD, autosomal dominant; AR, autosomal recessive.; FAD, fatty aldehyde.

Table 659-1 Ehlers-Danlos Syndrome

TYPE	FORMER NAME	CLINICAL FEATURES*	INHERITANCE	OMIM†	MOLECULAR DEFECT
Classic	EDS I and II	Joint hypermobility; skin hyperextensibility; atrophic scars; smooth, velvety skin; subcutaneous spheroids	AD	130000 130010	Structure of type V collagen because of mutations in *COL5A1, COL5A2*
Hypermobility	EDS III	Joint hypermobility; some skin hyperextensibility, with or without smooth, velvety texture	AD AR	130020 225320	? Tenascin-X *(TNX)*
Vascular	EDS IV	Thin skin; easy bruising; pinched nose; acrogeria; rupture of large-caliber and medium-caliber arteries, uterus, and large bowel	AD	130050 (225350) (225360)	Deficient type III collagen *(COL3A1)*
Kyphoscoliotic	EDS VI	Joint hypermobility; congenital, progressive rupture; scoliosis; scleral fragility with globe rupture; tissue fragility, aortic dilation, MVP	AR	225400	Deficiency of lysyl hydroxylase
Arthrochalasis	EDS VII A	Joint hypermobility, severe, with subluxations, congenital hip dislocation; skin hyperextensibility; tissue fragility	AD	130060	No cleavage of amino terminus of type I procollagen because of mutations in *COL1A1* or *COL1A2*
Dermatosparaxis	EDS VII C	Severe skin fragility; decreased skin elasticity, easy bruising; hernias; premature rupture of fetal membranes	AR	225410	No cleavage of amino terminus of type I procollagen because of deficiency of peptidase
Unclassified types	EDS V	Classic features	XL	305200	?
	EDS VIII	Classic features and periodontal disease	AD	130080	?
	EDS X	Mild classic features, MVP	?	225310	?
	EDS XI	Joint instability	AD	147900	?
	EDS IX	Classic features; occipital horns	XL	309400	Allelic to Menkes syndrome
	EDS, progeroid form	Classic features and premature aging	AR	130700	Deficiency of galactosyltransferase I

*Listed in order of diagnostic importance.
†Entries in Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD). Available at: http://omim.org/
AD, autosomal dominant; AR, autosomal recessive; EDS, Ehlers-Danlos syndrome; MVP, mitral valve prolapse; XL, X-linked.

Table 668-3 Drugs for Head Lice

DRUG	RESISTANCE	FDA-APPROVED LOWER AGE OR WEIGHT LIMIT	DOSAGE AND ADMINISTRATION	COST[a]/SIZE
Ivermectin 0.5% lotion–Sklice (Sanofi Pasteur)	No[b]	6 months	Apply to dry hair and scalp for 10 min, then rinse	$257.88/4 oz
Ivermectin tablets[c]–Stromectol (Merck)	No	15 kg	200-400 µg/kg PO once; repeat 7-10 days later	9.97[d]
Spinosad 0.9% suspension–Natroba (ParaPro)	No[b]	4 yr	Apply to dry hair for 10 min, then rinse; repeat 7 days later if necessary	219.00/4 oz
Benzyl alcohol 5% lotion–Ulesfia (Shionogi)	No	6 months	Apply to dry hair for 10 min, then rinse; repeat 7 days later	52.62/8 oz
Pyrethrins with piperonyl butoxide shampoo[e,f]–Generic Rid (Bayer)	Yes	2 yr	Apply to dry hair for 10 min, then shampoo; repeat 7-10 days later	12.49/8 oz 19.99/8 oz[g]
Permethrin 1% creme rinse[e]–Generic Nix (Insight)	Yes	2 months	Apply to shampooed, towel-dried hair for 10 min, then rinse; repeat 7 days later	18.49/4 oz 19.99/4 oz[g]
Malathion 0.5% lotion– Generic Ovide (Taro)	Not in U.S.	6 yr	Apply to dry hair for 8-12 hr,[h] then shampoo; repeat 7-9 days later if necessary	152.67/2 oz 160.46/2 oz

[a]Wholesale acquisition cost (WAC). Source: PricePointRx. Reprinted with permission by FDB, Inc. All rights reserved. Copyright 2012. www.firstdatabank.com/support/drug-pricing-policy.aspx. Actual retail prices may be higher. Amount needed may vary.
[b]Product new to market: currently no reports of resistance.
[c]Not FDA-approved for treatment of head lice. Stromectol is available in 3 mg tablets.
[d]Cost of 1 dose for a 30 kg child at the lowest dosage.
[e]Available without a prescription.
[f]Products that contain benzyl alcohol as their vehicle may be more effective.
[g]Cost according to drugstore.com.
[h]One or two 20 min applications have also been effective (Meinking TL, Vicaria M, Eyerdam DH,, et al: Efficacy of a reduced application time of Ovide lotion (0.5% malathion) compared to Nix creme rinse (1% permethrin) for the treatment of head lice, Pediatr Dermatol 21:670–674, 2004.)

Table 656-2 Cutaneous Reactions to Sunlight

SUNBURN

Photoallergic drug eruptions:
- Systemic drugs include tetracyclines, psoralens, chlorothiazides, sulfonamides, barbiturates, griseofulvin, thiazides, quinidine, phenothiazines
- Topical agents include coal tar derivatives, psoralens, halogenated salicylanilides (soaps), perfume oils (e.g., oil of bergamot), sunscreens (e.g., para-aminobenzoic acid [PABA], cinnamates, benzophenones)

Phototoxic drug eruptions:
- Systemic agents include nalidixic acid, furosemide, nonsteroidal antiinflammatory agents (naproxen, piroxicam), and high doses of agents causing photoallergic eruptions
- Topical agents include 5-fluorouracial, furocoumarins (e.g., lime, lemon, carrot, celery, dill, parsnip, parsley), and high doses of agents causing photoallergic eruptions

Genetic disorders with photosensitivity:
- Xeroderma pigmentosum
- Bloom syndrome
- Cockayne syndrome
- Rothmund-Thomson syndrome
- Trichothiodystrophy
- Smith-Lemli-Opitz syndrome
- Kindler syndrome

Inborn errors of metabolism:
- Porphyrias, protoporphyria
- Hartnup disease and pellagra

Infectious diseases associated with photosensitivity:
- Recurrent herpes simplex infection
- Viral exanthems (accentuated photodistribution; e.g., varicella)

Skin disease exacerbated or precipitated by light:
- Lichen planus
- Darier disease
- Lupus erythematosus including neonatal
- Dermatomyositis
- Psoriasis
- Erythema multiforme
- Atopic dermatitis
- Hailey-Hailey disease

Deficient protection because of a lack of pigment:
- Vitiligo
- Oculocutaneous albinism
- Phenylketonuria
- Chédiak-Higashi syndrome
- Hermansky-Pudlak syndrome
- Waardenburg syndrome
- Piebaldism

Table 659-4 Mastocytosis Classification

Cutaneous mastocytosis:
1. Urticaria pigmentosa:
   (a) Classic infantile type; (b) Chronic with stem cell factor mutations
2. Diffuse cutaneous mastocytosis
3. Mastocytoma of the skin
4. Telangiectasia macularis eruptive perstans

Systemic mastocytosis (without an associated hematologic non–mast cell disorder or leukemic mast cell disease):
1. Systemic indolent mastocytosis
2. Systemic smoldering mastocytosis

Systemic mastocytosis with an associated hematologic non–mast cell disorder:
1. Myeloproliferative syndrome
2. Myelodysplastic syndrome
3. Acute myeloid leukemia
4. Non-Hodgkin lymphoma

Systemic aggressive mastocytosis
Mast cell leukemia
Mast cell sarcoma
Extracutaneous mastocytoma

Table 661-1 Causes of Hyperhidrosis

CORTICAL
Emotional
Familial dysautonomia
Congenital ichthyosiform erythroderma
Epidermolysis bullosa
Nail-patella syndrome
Jadassohn-Lewandowsky syndrome
Pachyonychia congenita
Palmoplantar keratoderma
Stroke

HYPOTHALAMIC
Drugs:
- Alcohol
- Antipyretics
- Cocaine
- Emetics
- Insulin
- Opiates (including withdrawal)
- Ciprofloxacin

Exercise
Infection:
- Defervescence
- Chronic illness

Metabolic:
- Carcinoid syndrome
- Debility
- Diabetes mellitus
- Hyperpituitarism
- Hyperthyroidism
- Hypoglycemia
- Obesity
- Pheochromocytoma
- Porphyria
- Pregnancy
- Rickets
- Infantile scurvy

Cardiovascular:
- Heart failure
- Shock
- Vasomotor
- Cold injury
- Raynaud phenomenon
- Rheumatoid arthritis

Neurologic:
- Abscess
- Familial dysautonomia
- Postencephalitic
- Tumor

Miscellaneous:
- Chédiak-Higashi syndrome
- Compensatory
- Lymphoma
- Phenylketonuria
- Vitiligo

MEDULLARY
Physiologic gustatory sweating
Encephalitis
Granulosis rubra nasi
Syringomyelia
Thoracic sympathetic trunk injury

SPINAL
Cord transection
Syringomyelia

CHANGES IN BLOOD FLOW
Maffucci syndrome
Arteriovenous fistula
Klippel-Trenaunay syndrome
Glomus tumor
Blue rubber-bleb nevus syndrome

Table 663-1 White Nail or Nail Bed Changes

DISEASE	CLINICAL APPEARANCE
Anemia	Diffuse white
Arsenic	Mees lines: transverse white lines
Cirrhosis	Terry nails: most of nail, zone of pink at distal end (see Fig. 663-3)
Congenital leukonychia (autosomal dominant; variety of patterns)	Syndrome of leukonychia, knuckle pads, deafness; isolated finding; partial white
Darier disease	Longitudinal white streaks
Half-and-half nail	Proximal white, distal pink azotemia
High fevers (some diseases)	Transverse white lines
Hypoalbuminemia	Muehrcke lines: stationary paired transverse bands
Hypocalcemia	Variable white
Malnutrition	Diffuse white
Pellagra	Diffuse milky white
Punctate leukonychia	Common white spots
Tinea and yeast	Variable patterns
Thallium toxicity (rat poison)	Variable white
Trauma	Repeated manicure: transverse striations
Zinc deficiency	Diffuse white

Table 663-3 Differential Diagnosis of Onychomycosis

Psoriasis
- As in onychomycosis: onycholysis, subungual hyperkeratosis, splinter hemorrhages, leuconychia, dystrophy
- Pitting
- Oil drop sign (a translucent yellow-red discoloration seen in the nail bed)
- Other cutaneous features of psoriasis, family history of psoriasis

Lichen planus
- Cutaneous disease at other sites
- Thin nail plate and ridging
- Dorsal pterygium—scarring at proximal aspect of nail

Trauma
- Nail plate can appear abnormal
- Nail bed should be normal
- Distal onycholysis with repeated trauma
- Single nail affected, shape of nail changed, homogenous alteration of nail color

Eczema
- Irregular buckled nails with ridging
- Cutaneous signs of eczema

Yellow nail syndrome
- Nail plate is discolored green-yellow
- Nails are hard with elevated longitudinal curvature
- Nails may be shed, painful
- Associations with bronchiectasis, lymphoedema, and chronic sinusitis

Lamellar onychoschizia (lamellar splitting)
- History of repeated soaking in water
- Usually distal portion of nail

Periungual squamous cell carcinoma/Bowens disease
- Single nail, warty changes of nail fold, ooze from edge of nail

Malignant melanoma
- Black discoloration of nail plate or nail bed
- Pigment can extend onto nail fold
- Can get associated bleeding

Myxoid (mucous) cyst
- Cyst at base of nail, groove in nail extending length of nail

Alopecia areata
- Pits, longitudinal ridging, brittleness
- Hair loss

Table 662-1 Causes of and Conditions Associated with Hypertrichosis

INTRINSIC FACTORS
Racial and familial forms such as hairy ears, hairy elbows, intraphalangeal hair, or generalized hirsutism

EXTRINSIC FACTORS
Local trauma
Malnutrition
Anorexia nervosa
Long-standing inflammatory dermatoses
Drugs: Diazoxide, phenytoin, corticosteroids, Cortisporin, cyclosporine, androgens, anabolic agents, hexachlorobenzene, minoxidil, psoralens, penicillamine, streptomycin

HAMARTOMAS OR NEVI
Congenital pigmented nevocytic nevus, hair follicle nevus, Becker nevus, congenital smooth muscle hamartoma, fawn-tail nevus associated with diastematomyelia

ENDOCRINE DISORDERS
Virilizing ovarian tumors, Cushing syndrome, acromegaly, hyperthyroidism, hypothyroidism, congenital adrenal hyperplasia, adrenal tumors, gonadal dysgenesis, male pseudohermaphroditism, non–endocrine hormone–secreting tumors, polycystic ovary syndrome

CONGENITAL AND GENETIC DISORDERS
Hypertrichosis lanuginosa, mucopolysaccharidosis, leprechaunism, congenital generalized lipodystrophy, de Lange syndrome, trisomy 18, Rubinstein-Taybi syndrome, Bloom syndrome, congenital hemihypertrophy, gingival fibromatosis with hypertrichosis, Winchester syndrome, lipoatrophic diabetes (Lawrence-Seip syndrome), fetal hydantoin syndrome, fetal alcohol syndrome, congenital erythropoietic or variegate porphyria (sun-exposed areas), porphyria cutanea tarda (sun-exposed areas), Cowden syndrome, Seckel syndrome, Gorlin syndrome, partial trisomy 3q, Ambras syndrome

Table 662-2 Disorders Associated with Alopecia and Hypotrichosis

Congenital total alopecia: Atrichia with papules, Moynahan alopecia syndrome
Congenital localized alopecia: Aplasia cutis, triangular alopecia, sebaceous nevus
Hereditary hypotrichosis: Marie-Unna syndrome, hypotrichosis with juvenile macular dystrophy, hypotrichosis–Mari type, ichthyosis with hypotrichosis, cartilage-hair hypoplasia, Hallermann-Streiff syndrome, trichorhinophalangeal syndrome, ectodermal dysplasia "pure" hair and nail and other ectodermal dysplasias
Diffuse alopecia of endocrine origin: Hypopituitarism, hypothyroidism, hypoparathyroidism, hyperthyroidism
Alopecia of nutritional origin: Marasmus, kwashiorkor, iron deficiency, zinc deficiency (acrodermatitis enteropathica), gluten-sensitive enteropathy, essential fatty acid deficiency, biotinidase deficiency
Disturbances of the hair cycle: Telogen effluvium
Toxic alopecia: Anagen effluvium
Autoimmune alopecia: Alopecia areata
Traumatic alopecia: Traction alopecia, trichotillomania
Cicatricial alopecia: Lupus erythematosus, lichen planopilaris, pseudopelade, morphea (en coup de saber) dermatomyositis, infection (kerion, favus, tuberculosis, syphilis, folliculitis, leishmaniasis, herpes zoster, varicella), acne keloidalis, follicular mucinosis, sarcoidosis
Hair shaft abnormalities: Monilethrix, pili annulati, pili torti, trichorrhexis invaginata, trichorrhexis nodosa, woolly hair syndrome, Menkes disease, trichothiodystrophy, trichodento-osseous syndrome, uncombable hair syndrome (spun-glass hair, pili trianguli et canaliculi)

Table 663-2

Large nails	Pachyonychia congenita, Rubinstein-Taybi syndrome, hemihypertrophy
Smallness or absence of nails	Ectodermal dysplasias, nail-patella, dyskeratosis congenita, focal dermal hypoplasia, cartilage-hair hypoplasia, Ellis–van Creveld, Larsen, epidermolysis bullosa, incontinentia pigmenti, Rothmund-Thomson, Turner, popliteal web, trisomy 13, trisomy 18, Apert, Gorlin-Pindborg, long arm 21 deletion, otopalatodigital, fetal alcohol, fetal hydantoin, elfin facies, anonychia, acrodermatitis enteropathica
Other	Congenital malalignment of the great toenails, familial dystrophic shedding of the nails

Bone and Joint Disorders

Table 666-1 Primary Immunodeficiencies Underlying Fungal Infections

DISEASE	ASSOCIATED INFECTIONS	IMMUNOLOGIC PHENOTYPE	GENE, TRANSMISSION
CMC			
SCID	Bacteria, viruses, fungi, mycobacteria	No T cells, with or without B and/or NK cell lymphopenia	>30 genes: *IL2RG,* X-linked; *JAK3,* autosomal recessive; RAG1, autosomal recessive; *RAG2,* autosomal recessive; *ARTEMIS,* autosomal recessive; *ADA,* autosomal recessive; *CD3,* autosomal recessive, etc.
CID		T-cell defect	
CD25 deficiency	Viruses and bacteria		*IL2RA,* autosomal recessive
NEMO or iκBγ deficiency	Pyogenic bacteria, mycobacteria, viruses		*NEMO* or *IKBG* X-linked
IκBα GOF mutation			*IKBA,* autosomal dominant
DOCK8 deficiency	Viruses, bacteria and fungi		*DOCK8,* autosomal recessive
TCR-α deficiency	Viruses and bacteria		*TCRA,* autosomal recessive
CRACM1 deficiency	Viruses, mycobacteria, bacteria and fungi		*CRACM1,* autosomal recessive
MST1/STK4 deficiency	Viruses and bacteria		*MST1/STK4,* autosomal recessive
MHC class II deficiency	Viruses, bacteria and fungi		*CIITA, RFXANK, RFXC, RFXAP,* all autosomal recessive
Idiopathic CD4 lymphopenia	*Pneumocystis, Cryptococcus,* virus	CD4 T cells <300 cells/mm^3	*UNC119,* autosomal dominant, *MAGT1* X-linked, *RAG1,* autosomal recessive
SYNDROMIC CMC			
Interleukin-12Rβ1 and interleukin-12p40 deficiencies	*Mycobacteria, Salmonella*	Deficit of interleukin-17–producing T cells	*IL12RB1,* autosomal recessive, *IL12B,* autosomal recessive
STAT3 deficiency (autosomal dominant-HIES)	*Staphylococcus aureus, Aspergillus*	Hyperimmunoglobulin E, deficit of interleukin-17–producing T cells	*STAT3,* autosomal dominant
APECED/APS-1	No	Neutralizing anti–interleukin-17A, anti–interleukin-17F, and/or anti–interleukin-22 autoantibodies	*AIRE,* autosomal recessive
CARD9 deficiency	Dermatophytes, *Candida,* brain abscess	Deficit of interleukin-17–producing T cells	*CARD9,* autosomal recessive
CMCD			
Complete interleukin-17RA deficiency	*S. aureus*	No interleukin-17 response	*IL17RA,* autosomal recessive
Partial interleukin-17F deficiency	*S. aureus*	Impaired interleukin-17F, interleukin-17A/F function	*IL17F,* autosomal dominant
STAT1 GOF mutations	Bacteria, viruses, fungi, mycobacteria	Low interleukin-17–producing T cells	*STAT1,* autosomal dominant

AIRE, autoimmune regulator; APECED, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy; APS-1, autoimmune polyendocrinopathy syndrome type 1; CARD9, caspase recruitment domain-containing protein 9; CID, combined immunodeficiency; CMC, chronic mucocutaneous candidiasis; CMCD, chronic mucocutaneous candidiasis disease; CRACM1, calcium release-activated calcium modulator 1; GOF, gain-of-function; HIES, hyperimmunoglobulin E syndrome; IκBα, inhibitor of nuclear factor of kappa light polypeptide gene enhancer in B-cells, alpha; iκBγ, inhibitor of nuclear factor of kappa light polypeptide gene enhancer in B-cells, gamma; MHC, major histocompatibility complex; MST1, macrophage stimulating 1; NEMO, nuclear factor κB essential modulator; NK, natural killer; SCID, severe combined immunodeficiency; STAT, signal transducer and activator of transcription; STK4, serine/threonine protein kinase 4; TCR, T-cell receptor.

Table 672-1 Terminologies for Deviations

TERMINOLOGY	DESCRIPTION
Congenital	Anomaly that is apparent at birth
Deformation	A normally formed structure that is pushed out of shape by mechanical forces
Deformity	A body part altered in shape from normal, outside the normal range
Developmental	A deviation that occurs over time; one that might not be present or apparent at birth
Disruption	A structure undergoing normal development that stops developing or is destroyed or removed
Dysplasia	A tissue that is abnormal or wrongly constructed
Malformation	A structure that is wrongly built; failure of embryologic development or differentiation resulting in abnormal or missing structures

Table 672-2 Skeletal Growth Considerations

- Abnormal stature can be assessed as "proportionate" or "disproportionate" based on comparing the ratio of sitting height with subischial height (lower limbs).
- Normally the arm span is almost equal to standing height.
- The head is disproportionately large at birth and ratio of head height to total height is approximately 1:4 at birth, which changes to 1:7.5 at skeletal maturity.
- Lower extremities account for approximately 15% of height at birth and 30% at skeletal maturity.
- The rate of height and growth increase is not constant and varies with growth spurts.
- By age 5 yr, birth height usually doubles and the child is approximately 60% of adult height. The child is approximately 80% of final height at 9 yr. During puberty, the standing height increases by approximately 1 cm/mo.
- Bone age is more important than chronologic age in determining future growth potential.

Table 673-3 Causes of Abnormal Gait

Limp
Pain
Torsional variations
Toe walking
Joint abnormalities
Leg-length discrepancy
Neuromuscular disorders

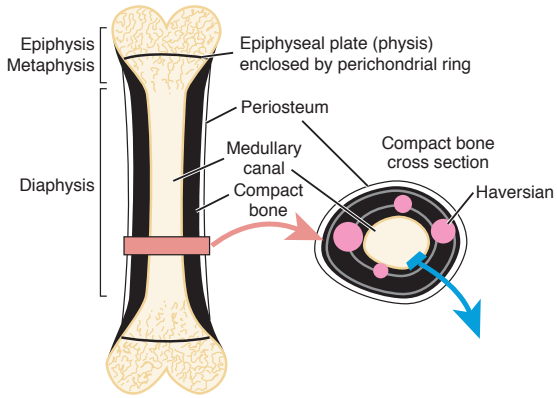

Figure 672-1 Diagram showing typical long bone divisions.

Table 672-3 Functional Milestones

MILESTONE	ACHIEVED BY
Head control	3-6 months
Sitting	6-9 months
Crawling	8 months
Pulling to stand	8-12 months
Ambulating	12-18 months

Table 673-4 Common Causes of Limping According to Age

ANTALGIC	TRENDELENBURG	LEG-LENGTH DISCREPANCY
TODDLER (1-3 YR)		
Infection Septic arthritis Hip Knee Osteomyelitis Diskitis Occult trauma Toddler's fracture Neoplasia	Hip dislocation (DDH) Neuromuscular disease Cerebral palsy Poliomyelitis	–
CHILD (4-10 YR)		
Infection Septic arthritis Hip Knee Osteomyelitis Diskitis Transient synovitis, hip LCPD Tarsal coalition Rheumatologic disorder JRA Trauma Neoplasia	Hip dislocation (DDH) Neuromuscular disease Cerebral palsy Poliomyelitis	+
ADOLESCENT (11+ YR)		
SCFE Rheumatologic disorder JRA Trauma: fracture, overuse Tarsal coalition Neoplasia		+

–, Absent; +, present; DDH, developmental dysplasia of the hip; JRA, juvenile rheumatoid arthritis; LCPD, Legg-Calvé-Perthes disease; SCFE, slipped capital femoral epiphysis.

From Thompson GH: Gait disturbances. In Kliegman RM, editor: Practical strategies of pediatric diagnosis and therapy, *Philadelphia, 1996, WB Saunders, pp. 757–778.*

Table 673-5 Differential Diagnosis of Limping

ANTALGIC GAIT
Congenital
Tarsal coalition
Acquired
Legg-Calvé-Perthes disease
Slipped capital femoral epiphysis
Trauma
Sprains, strains, contusions
Fractures
Occult
Toddler's fracture
Abuse
Neoplasia
Benign
- Unicameral bone cyst
- Osteoid osteoma

Malignant
- Osteogenic sarcoma
- Ewing sarcoma
- Leukemia
- Neuroblastoma
- Spinal cord tumors

Infectious
Septic arthritis
Reactive arthritis
Osteomyelitis
- Acute
- Subacute

Diskitis
Rheumatologic
Juvenile rheumatoid arthritis
Hip monoarticular synovitis (toxic transient synovitis)

TRENDELENBURG
Developmental
Developmental dysplasia of the hip
Leg-length discrepancy
Neuromuscular
Cerebral palsy
Poliomyelitis

Table 676-1 Causes of Leg-Length Discrepancy

CONGENITAL CAUSES
Defects in Growth
Proximal femoral focal deficiency
Congenital pseudarthrosis of the tibia
Fibular hemimelia (see Fig. 676-8)
Bone Tumors/Disease
Skeletal dysplasia
Multiple hereditary exostoses
Neurofibromatosis
Enchondromatosis (Ollier disease)
Osteogenesis imperfecta
Vascular
Klippel-Trenaunay-Weber syndrome
Russell-Silver syndrome
Miscellaneous
Congenital coxa vara
Proteus syndrome

ACQUIRED CAUSES
Trauma
Overriding fractures
Epiphyseal fractures with growth plate damage
Developmental
Developmental dysplasia of the hip
Neoplastic
Malignant tumors
Tumors across epiphysis
Neurologic
Myelodysplasia
Cerebral palsy
Infections/Inflammatory
Septic arthritis of hip
Osteomyelitis
Rheumatoid arthritis
Miscellaneous
Acquired coxa vara
Fixed pelvic obliquity in scoliosis

Table 673-6 Ashworth Scale of Spasticity

0	No increase in muscle tone
1	Slight increase in muscle tone, usually a catch or minimal resistance at end range of motion
2	Moderate tone throughout range of motion
3	Considerable increase in tone; passive range of motion difficult
4	Rigid in flexion or extension

Table 673-7 Clinical Scale of Upper-Extremity Motor Control

GRADE	DEFINITION
Grade 1	Hypotonic, no volitional motion
Grade 2	Hypertonic, no volitional motion
Grade 3	Mass flexion or extension in response to a stimulus
Grade 4	Patient can initiate movement but results in mass flexion or extension
Grade 5	Slow volitional movement; stress or rapid movement results in mass action
Grade 6	Volitional control of specific joints/muscles

Table 674-2 Differential Diagnosis of Foot Pain By Age

0-6 YR	6-12 YR	12-20 YR
Poorly fitting shoes	Poorly fitting shoes	Poorly fitting shoes
Foreign body	Sever disease	Stress fracture
Fracture	Enthesopathy (JIA)	Foreign body
Osteomyelitis	Foreign body	Ingrown toenail
Leukemia	Accessory navicular	Metatarsalgia
Puncture wound	Tarsal coalition	Plantar fasciitis
Drawing of blood	Ewing sarcoma	Osteochondroses (avascular necrosis)
Dactylitis	Hypermobile flatfoot	Freiberg
JIA	Trauma (sprains, fractures) Puncture wound	Köhler Achilles tendinitis Trauma (sprains) Plantar warts Tarsal coalition

Table 679-1 Classification of Spinal Deformities

SCOLIOSIS
Idiopathic
Infantile
Juvenile
Adolescent
Congenital
Failure of formation
  Wedge vertebrae
  Hemivertebrae
Failure of segmentation
  Unilateral bar
  Block vertebra
  Mixed
Neuromuscular
Neuropathic diseases
  Upper motor neuron
  Cerebral palsy
  Spinocerebellar degeneration (Friedreich ataxia, Charcot-Marie-Tooth disease)
  Syringomyelia
  Spinal cord tumor
  Spinal cord trauma
  Lower motor neuron
  Poliomyelitis
  Spinal muscular atrophy
Myopathies
Duchenne muscular dystrophy
Arthrogryposis
Other muscular dystrophies
Syndromes
Neurofibromatosis
Marfan syndrome
Compensatory
Leg-length discrepancy

KYPHOSIS
Postural kyphosis (flexible)
Scheuermann disease
Congenital kyphosis
  Failure of formation
  Failure of segmentation
  Mixed

Table 678-1 Differential Diagnosis of Legg-Calvé-Perthes Disease

OTHER CAUSES OF AVASCULAR NECROSIS
Sickle cell disease
Other hemoglobinopathies (e.g., thalassemia)
Chronic myelogenous leukemia
Steroid medication
Sequela of traumatic hip dislocation
Treatment of developmental dysplasia of the hip
Septic arthritis

EPIPHYSEAL DYSPLASIAS
Multiple epiphyseal dysplasia
Spondyloepiphyseal dysplasia
Mucopolysaccharidoses
Hypothyroidism

OTHER SYNDROMES
Osteochondromatosis
Metachondromatosis
Schwartz-Jampel syndrome
Trichorhinophalangeal syndrome
Maroteaux-Lamy syndrome
Martsolf syndrome

Table 679-3 Differential Diagnosis of Back Pain

INFLAMMATORY/INFECTIOUS
Diskitis
Vertebral osteomyelitis (pyogenic, tuberculous)
Spinal epidural abscess
Pyelonephritis
Pancreatitis
Psoas abscess

RHEUMATOLOGIC
Pauciarticular juvenile idiopathic arthritis
Reiter syndrome
Ankylosing spondylitis
Psoriatic arthritis

DEVELOPMENTAL
Spondylolysis
Spondylolisthesis
Scheuermann disease
Scoliosis

TRAUMATIC (ACUTE VERSUS REPETITIVE)
Hip–pelvic anomalies
Herniated disk
Overuse syndromes
Vertebral stress fractures
Upper cervical spine instability

NEOPLASTIC
Vertebral tumors
  Benign
  Eosinophilic granuloma
  Aneurysmal bone cyst
  Osteoid osteoma
  Osteoblastoma
Malignant
  Osteogenic sarcoma
  Leukemia
  Lymphoma
  Metastatic tumor
Spinal cord, ganglia, and nerve roots
  Intramedullary spinal cord tumor
  Sympathetic chain
  Ganglioneuroma
  Ganglioneuroblastoma
  Neuroblastoma

OTHER
Intraabdominal or pelvic pathology
Following lumbar puncture
Conversion reaction
Juvenile osteoporosis

Table 679-2 Conditions Associated with Hyperkyphosis

- Trauma causing spinal fractures
- Spinal infections resulting from bacterial, tuberculosis, and fungal diseases
- Metabolic diseases such as osteogenesis imperfecta or osteoporosis
- Iatrogenic (laminectomy, spinal irradiation)
- Neuromuscular diseases
- Neoplasms
- Congenital/developmental
  - Disorders of collagen such as Marfan syndrome
  - Dysplasias such as neurofibromatosis, achondroplasia, and mucopolysaccharidoses

Table 679-4 Findings Consistent with a Nonmechanical Etiology Warranting Further Evaluation

- History of trauma
- Pain that wakes the patient from sleep
- Constant pain unrelieved by rest
- Constitutional or systemic symptoms of fevers, chills, malaise, weight loss
- Any neurologic dysfunction including weakness, numbness, radicular pain, gait changes, or bowel and bladder changes
- Abnormalities in spinal alignment
- Bony tenderness to palpation or vertebral step-offs
- Significant pain with provocative tests (spinal flexion or extension)
- Positive straight-leg raise test for neurologic symptoms below the knee
- Abnormal neurologic exam

Table 680-1 Differential Diagnosis of Torticollis

CONGENITAL
Muscular torticollis
Positional deformation
Vertebral anomalies (failure segmentation, formation or both)
Unilateral atlantooccipital fusion
Klippel-Feil syndrome
Unilateral absence of sternocleidomastoid
Pterygium colli
TRAUMA
Muscular injury (cervical muscles)
Atlantooccipital subluxation
Atlantoaxial subluxation
C2-3 subluxation
Rotary subluxation
Fractures (C1, others)
INFLAMMATION
Cervical lymphadenitis
Retropharyngeal abscess
Cervical vertebral osteomyelitis or diskitis
Juvenile idiopathic arthritis
Grisel syndrome (nontraumatic rotary subluxation of the atlantoaxial joint caused by inflammation)
Upper lobe pneumonia
NEUROLOGIC
Visual disturbances (nystagmus, superior oblique or lateral rectus paresis)
Dystonic oculogyric drug reactions (phenothiazines, haloperidol, metoclopramide)
Cervical cord tumor
Posterior fossa brain tumor
Acoustic neuroma
Syringomyelia
Wilson disease
Dystonia musculorum deformans
OTHER
Acute cervical disk calcification
Sandifer syndrome (gastroesophageal reflux, hiatal hernia)
Benign paroxysmal torticollis
Bone tumors (eosinophilic granuloma, osteoid osteoma)
Soft-tissue tumor
Psychogenic

Table 680-2 Causes of Pediatric Cervical Instability

CAUSES	SUBTYPES
Congenital	Cranio-occipital defects (occipital vertebrae, basilar impression, occipital dysplasias, condylar hypoplasia, occipitalized atlas) Atlantoaxial defects (aplasia of atlas arch, aplasia of odontoid process) Subaxial anomalies (failure of segmentation and/or fusion, spina bifida, spondylolisthesis) Syndromic disorders (i.e., Down syndrome, Klippel-Feil syndrome, 22q11.2 deletion syndrome, Larsen syndrome, Marfan syndrome, Ehlers-Danlos syndrome)
Acquired	Trauma Infection (pyogenic/granulomatous) Tumor (including neurofibromatosis) Inflammatory conditions (i.e., juvenile idiopathic arthritis) Osteochondrodysplasias (i.e., achondroplasia, diastrophic dysplasia, metatropic dysplasia, spondyloepiphyseal dysplasia) Storage disorders (i.e., mucopolysaccharidoses) Metabolic disorders (rickets) Miscellaneous (including osteogenesis imperfecta, postsurgery)

Chapter 682

Arthrogryposis

Helen M. Horstmann, Christine M. Conroy, and Richard S. Davidson

Table 682-2 Current Labels and OMIM Numbers for the Distal Arthrogryposis Syndromes

SYNDROME	OMIM NUMBER
Distal arthrogryposis type 1	108120
Distal arthrogryposis type 2A (Freeman-Sheldon syndrome)	193700
Distal arthrogryposis type 2B (Sheldon-Hall syndrome)	601680
Distal arthrogryposis type 3 (Gordon syndrome)	114300
Distal arthrogryposis type 4 (scoliosis)	609128
Distal arthrogryposis type 5 (ophthalmoplegia, ptosis)	108145
Distal arthrogryposis type 6 (sensorineural hearing loss)	108200
Distal arthrogryposis type 7 (trismus-pseudocamptodactyly)	158300
Distal arthrogryposis type 8 (autosomal dominant multiple pterygium syndrome)	178110
Distal arthrogryposis type 9 (congenital contractural arachnodactyly)	121050
Distal arthrogryposis type 10 (congenital plantar contractures)	187370

From Bamshad M, Van Heest AE, Pleasure D: Arthrogryposis: a review and update. J Bone Joint Surg Am *91 Suppl 4:40–46, 2009, Table 1, p. 43.*

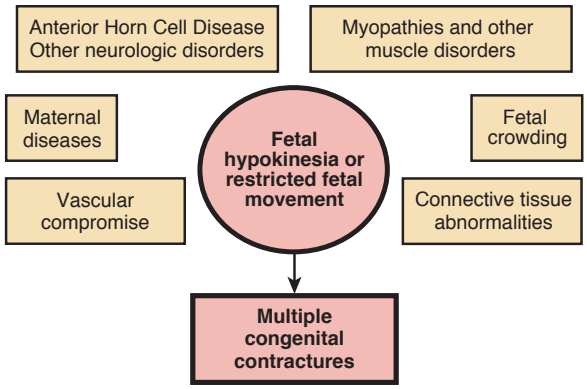

Figure 682-1 Etiology of arthrogryposis. *(Modified from Hall JG: Arthrogryposis multiplex congenital: Etiology, genetics, classification, diagnostic approach, and general aspects.* J Pediatr Orthop B *6:159–166, 1996.)*

Table 682-1 Associated Etiologies of Arthrogryposis

ARTHROGRYPOSIS CAUSED BY NERVOUS SYSTEM DISORDERS
- Focal anterior horn cell deficiency
- Generalized anterior horn cell deficiency
- Structural brain disorder/damage
- Uncertain location

(Spastic conditions are excluded)

DISTAL ARTHROGRYPOSIS SYNDROMES
- Type I dominant distal
- Type IIa dominant distal (Gordon syndrome)
- Type IIe distal
- Digitotalar dysmorphism
- Trismus pseudocamptodactyly
- Distal distribution, type not specified

PTERYGIUM SYNDROMES
- Multiple pterygium syndrome
- Lethal multiple pterygium syndrome
- Popliteal pterygium syndrome
- Ptosis, scoliosis, pterygia
- Antecubital webbing syndrome (Liebenberg)

MYOPATHIES
- Emery-Dreifuss muscular dystrophy
- Hypotonia, myopathy, mild contractures

ABNORMALITIES OF JOINTS AND CONTIGUOUS TISSUE
- Congenital contractural arachnodactyly
- Freeman-Sheldon syndrome
- Laxity or hypertonicity with intrauterine dislocation and contractures
- Larsen syndrome
- Spondyloepimetaphyseal dysplasia with joint laxity
- Trisomy 18, extended breech position with bilateral hip dislocation
- Siblings with bifid humeri, hypertelorism, and hip and knee joint dislocations

SKELETAL DISORDERS
- Diastrophic dysplasia
- Parastremmatic dysplasia
- Kniest dysplasia
- Metatropic dysplasia
- Campomelic dysplasia
- Schwartz syndrome
- Fetal alcohol syndrome with synostoses
- Osteogenesis imperfecta with bowing/contractures

INTRAUTERINE/MATERNAL FACTORS
- Fetal alcohol syndrome with contractures
- Infections
- Untreated maternal systemic lupus erythematosus
- Intrauterine fetal constraint
- Deformity (pressure)
- Amniotic fluid leakage
- Multiple pregnancies
- Intrauterine tumors
- Disruption (bands)

MISCELLANEOUS
- Pseudotrisomy 18 with contractures
- Roberts pseudothalidomide syndrome
- Deafness with distal contractures
- VACTERL association
- Multiple abnormalities and contractures not otherwise specified
- ARC

SINGLE JOINT
- Campomelia
- Symphalangism
- "Trigger" finger

ARC, arthrogryposis, renal tubular acidosis, cholestasis; VACTERL, vertebral defects, imperforate anus, congenital heart disease, tracheoesophageal fistula, renal and limb defects.

Modified from Mennen U, Van Heest A, Ezaki MB, et al: Arthrogryposis multiplex congenita. J Hand Surg Br *30:5:468–474, 2005. Copyright 2005 The British Society for Surgery of the Hand.*

Table 687-1 Staging of Overuse Injuries

GRADE	GRADING SYMPTOMS	TREATMENT
I	Pain only after activity Does not interfere with performance or intensity Generalized tenderness Disappears before next session	Modification of activity, consider cross-training, home rehabilitation program
II	Minimal pain with activity Does not interfere with performance More localized tenderness	Modification of activity, cross-training, home rehabilitation program
III	Pain interferes with activity and performance Definite area of tenderness Usually disappears between sessions	Significant modification of activity, strongly encourage cross-training, home rehabilitation program, and outpatient physical therapy
IV	Pain with activities of daily living Pain does not disappear between sessions Marked interference with performance and training intensity	Discontinue activity temporarily, cross-training only, oral analgesic, home rehabilitation program, and intensive outpatient physical therapy
V	Pain interferes with activities of daily living Signs of tissue injury (e.g., edema) Chronic or recurrent symptoms	Prolonged discontinuation of activity, cross-training only, oral analgesic, home rehabilitation program, and intensive outpatient physical therapy

Table 701-1 Osteogenesis Type, Gene Defects, and Phenotypes

OSTEOGENESIS IMPERFECTA TYPE	GENE DEFECT	PHENOTYPE
DOMINANT INHERITANCE		
Classical Sillence Types		
I	*COL1A1* null allele	Mild, nondeforming
II	*COL1A1* or *COL1A2*	Lethal perinatal
III	*COL1A1* or *COL1A2*	Progressively deforming
IV	*COL1A1* or *COL1A2*	Moderately deforming
COL1-Mutation Negative		
V	*IFITM5*	Distinct histology
RECESSIVE INHERITANCE		
Mineralization Defect		
VI	*SERPINF1*	Distinct histology
3-Hydroxylation Defects		
VII	*CRTAP*	Severe to lethal
VIII	*LEPRE1*	Severe to lethal
IX	*PPIB*	Moderate to lethal
Chaperone Defects		
X	*SERPINH1*	Severe
XI	*FKBP10*	Progressive deforming, Bruck syndrome 1
C-Propeptide Cleavage Defect		
XII	*BMP1*	Severe, high bone mass case
UNCLASSIFIED		
Zinc-finger transcription factor defect	*SP7*	Moderate
Cation channel defect	*TMEM38B*	Moderate to severe
WNT signaling pathway defect	*WNT1*	Moderate, progressively deforming

From Marini JC, Blissett AR: New genes in bone development: what's new in osteogenesis imperfecta. J Clin Endocrinol Metab *98:3095–3103, 2013, Table 1, p. 3096.*

Table 702-1 Diagnostic Criteria for Marfan Syndrome

In the absence of a family history of MFS, a diagnosis can be established in 4 distinct scenarios:
1. Aortic root Z score >2 *and* ectopia Lentis*
2. Aortic root Z score >2 *and* a bona fide *FBN1* mutation
3. Aortic root Z score >2 *and* a systemic score >7*
4. Ectopia lentis *and* a bona fide *FBN1* mutation known to cause aortic disease

In the presence of a family history of MFS, a diagnosis can be established in the presence of:
1. Ectopia lentis
2. A systemic score >7*
3. Aortic root Z score >2 if older than 20 yr or >3 if younger than 20 yr*

In the absence of a family history of MFS, alternative diagnoses include:
1. Ectopia lentis ± systemic score *and FBN1* mutation not known to associate with aortic aneurysm or no *FBN1* mutation = ectopia lentis syndrome
2. Aortic root Z score <2 *and* a systemic score >5 (with at least 1 skeletal feature) without ectopia lentis = MASS (mitral valve prolapse, myopia, borderline and nonprogressive aortic enlargement, and nonspecific skin and skeletal findings) phenotype
3. Mitral valve prolapse *and* aortic root Z score <2 *and* a systemic score <5 without ectopia lentis = mitral valve prolapse syndrome

*Denotes caveat that features suggestive of an alternative diagnosis must be excluded and appropriate alternative molecular testing should be performed.

Table 702-2 Scoring of Systemic Features in Points

- Wrist *and* thumb sign = 3 (wrist *or* thumb sign = 1)
- Pectus carinatum deformity = 2 (pectus excavatum or chest asymmetry = 1)
- Hind foot deformity = 2 (plain pes planus = 1)
- Pneumothorax = 2
- Dural ectasia = 2
- Protrusio acetabuli = 2
- Reduced US:LS *and* increased arm:height *and* no severe scoliosis = 1
- Scoliosis or thoracolumbar kyphosis = 1
- Reduced elbow extension = 1
- Facial features (3/5) = 1 (dolichocephaly, enophthalmos, down-slanting palpebral fissures, midface hypoplasia, retrognathia)
- Skin striae = 1
- Myopia >3 diopters = 1
- Mitral valve prolapse (all types) = 1

Maximum total: 20 points; score ≥7 indicates systemic involvement.
US:LS, upper segment:lower segment ratio.

Table 689-1 Return to Play (RTP) Table

NO CONTRAINDICATION TO RTP	
Healed fractures including:	Healed C1 or C2 fracture with normal cervical spine range of motion (ROM)
	Healed subaxial fracture without sagittal plane deformity
	Asymptomatic clay-shoveler's (C7) spinous process avulsion fracture
Congenital conditions	Klippel-Feil (single-level anomaly not C0/C1 articulation)
	Spina bifida occulta
Degenerative/ postsurgical conditions	Cervical disc disease (no change in baseline neurologic status)
	Single-level anterior cervical fusion (ACF) with/without instrumentation
	Single- or multiple-level posterior cervical laminotomy
Recurrent stingers	Less than 3 episodes lasting <24 hr
	Must have full cervical range of motion
	No persisting neurologic deficit
Transient quadriparesis	Single episode
	Full cervical range of motion
	Normal neurologic exam
	No radiologic instability
	Normal spinal reserve (as evidenced on MRI)
RELATIVE CONTRAINDICATION TO RTP	
Stingers/Burners	Prolonged symptomatic burner/stinger
	Three or more stingers
Transient quadriparesis	Transient quadriparesis lasting >24 hr
	More than 1 episode with symptoms of any duration
Postsurgical	Healed 2-level ACF
	Posterior cervical fusion (PCF) with/ without instrumentation
ABSOLUTE CONTRAINDICATION TO RTP	
Transient quadriparesis and any 1 or more of:	Cervical myelopathy
	Continued neck discomfort
	Reduced ROM
	Neurologic deficit from baseline after injury
Surgical procedures	C1 + C2 fusion
	Cervical laminectomy
	Three-level ACF or PCF
Soft-tissue injuries	Asymptomatic ligamentous laxity (>11 degrees of kyphotic deformity)
	C1 + C2 hypermobility with anterior dens >3.5 mm (adult), >4 mm (child), i.e., Down syndrome (see Chapter 680)
	Symptomatic cervical disc herniation
Other conditions including:	Spear tackler's spine
	Multilevel Klippel-Feil anomaly (see Chapter 680)
	Healed subaxial fracture with sagittal kyphosis coronal plane abnormality, or cord encroachment
	Ankylosing spondylitis
	Rheumatoid arthritis with spinal abnormalities
	Spinal cord abnormality (cord edema, compression, etc.)
	Arnold-Chiari syndrome
	Basilar invagination
	Occipital-C1 assimilation (occipitalization or connection)
	Spinal stenosis (canal width <13 mm between C3 and C7)

Adapted from Cantu R, Li YM, Abdulhamid M, Chin LS: Return to play after cervical spine injury in sports. Curr Sports Med Rep *12:14–17, 2013.*

Table 694-2 Major Problems Associated with Skeletal Dysplasias

PROBLEM	EXAMPLE
Lethality*	Thanatophoric dysplasia
Associated anomalies†	Ellis-van Creveld syndrome
Short stature	Common to almost all
Cervical spine dislocations	Larsen syndrome
Severe limb bowing	Metaphyseal dysplasia, Schmid type
Spine curvatures	Metatropic dysplasia
Clubfeet	Diastrophic dysplasia
Fractures	Osteogenesis imperfecta
Pneumonias, aspirations	Camptomelic dysplasia
Spinal cord compression	Achondroplasia
Joint problems (hips, knees)	Most skeletal dysplasias
Hearing loss	Common (greatest with cleft palate)
Myopia/cataracts	Stickler syndrome
Immunodeficiency‡	Cartilage-hair hypoplasia, Schimke immunoosseous dysplasia
Poor body image	Variable, but common to all
Sex reversal	Camptomelic dysplasia

*Mostly a result of severely reduced size of thorax.

Table 694-5 Usually Nonlethal Dwarfing Conditions Recognizable at Birth or Within 1st Few Mo of Life

MOST COMMON
Achondroplasia
Osteogenesis imperfecta (types I, III, IV)
Spondyloepiphyseal dysplasia congenita
Diastrophic dysplasia
Ellis-van Creveld syndrome
LESS COMMON
Chondrodysplasia punctata (some forms)
Kniest dysplasia
Metatropic dysplasia
Langer mesomelic dysplasia

Table 694-3 Associated Anomalies in Skeletal Dysplasias

ANOMALY	EXAMPLE
Heart defects	Ellis-van Creveld syndrome, Jeune syndrome
Polydactyly	Short rib polydactyly, Majewski type
Cleft palate	Diastrophic dysplasia
Ear cysts	Diastrophic dysplasia
Spinal cord compression	Achondroplasia
Encephalocele	Dyssegmental dysplasia
Hemivertebrae	Dyssegmental dysplasia
Micrognathia	Camptomelic dysplasia
Nail dysplasia	Ellis-van Creveld syndrome
Conical teeth, oligodontia	Ellis-van Creveld syndrome
Multiple oral frenula	Ellis-van Creveld syndrome
Dentinogenesis imperfecta	Osteogenesis imperfecta
Pretibial skin dimples	Camptomelic dysplasia
Cataracts, retinal detachment	Stickler syndrome
Intestinal atresia	Saldino-Noonan
Renal cysts	Saldino-Noonan
Camptodactyly	Diastrophic dysplasia
Craniosynostosis	Thanatophoric dysplasia
Ichthyosis	Chondrodystrophia punctata
Hitchhiker thumb	Diastrophic dysplasia
Sparse scalp hair	Cartilage-hair hypoplasia
Hypertelorism	Robinow syndrome
Hypoplastic nasal bridge	Acrodysostosis
Clavicular agenesis	Cleidocranial dysplasia
Genital hypoplasia	Robinow syndrome
Tail	Metatropic dysplasia
Omphalocele	Beemer-Langer syndrome
Blue sclera	Osteogenesis imperfecta

Table 694-4 Lethal Neonatal Dwarfism

USUALLY FATAL*
Achondrogenesis (different types)
Thanatophoric dysplasia
Short rib polydactyly (different types)
Homozygous achondroplasia
Camptomelic dysplasia
Dyssegmental dysplasia, Silverman-Handmaker type
Osteogenesis imperfecta, type II
Hypophosphatasia (congenital form)
Chondrodysplasia punctata (rhizomelic form)
OFTEN FATAL
Asphyxiating thoracic dystrophy (Jeune syndrome)
OCCASIONALLY FATAL
Ellis-van Creveld syndrome
Diastrophic dysplasia
Metatropic dwarfism
Kniest dysplasia

*A few prolonged survivors have been reported in most of these disorders.

Table 702-4 Differential Diagnosis of Marfan Syndrome

DIFFERENTIAL DIAGNOSIS	CARDIAC FEATURES	VASCULAR FEATURES	SYSTEMIC FEATURES
AORTIC ANEURYSM SYNDROMES			
Loeys-Dietz syndrome (MIM 609192)	Patent ductus arteriosus Atrial septal defect Bicuspid aortic valve	Aortic root aneurysm Arterial tortuosity Widespread aneurysms Vascular dissection at relatively young ages and small aortic dimensions	Hypertelorism Cleft palate Broad or bifid uvula Craniosynostosis Midface hypoplasia Blue sclerae Arachnodactyly Pectus deformity Scoliosis Joint hypermobility Pes planus Rarely Easy bruising Dystrophic scars Translucent skin Rarely developmental delay
Familial thoracic aortic aneurysm (MIM 132900)	Generally none Rare forms with patent ductus arteriosus	Aortic root aneurysm Ascending aortic aneurysm	Generally none Rarely livedo reticularis and iris flocculi
Shprintzen-Goldberg syndrome (MIM 182212)	None	Aortic root aneurysm	Hypertelorism Craniosynostosis Arched palate Arachnodactyly Pectus deformity Scoliosis Joint hypermobility Developmental delay
Bicuspid aortic valve with aortic aneurysm (MIM: 109730)	Bicuspid aortic valve	Aortic root aneurysm Ascending aortic aneurysm	
Ehlers-Danlos syndrome, type IV (MIM: 130050)	Mitral valve prolapse	Aneurysm and rupture of any medium to large muscular artery No predisposition for aortic root enlargement	Joint hypermobility Atrophic scars Translucent skin Easy bruising Hernias Rupture of hollow organs
ECTOPIA LENTIS SYNDROMES			
Familial ectopia lentis (MIM 129600)	None	None	Nonspecific skeletal features
Homocystinuria (MIM 236200)	Mitral valve prolapse	Intravascular thrombosis	Tall stature Ectopia lentis Long-bone overgrowth Developmental delay
SYNDROMES WITH SYSTEMIC MANIFESTATIONS OF MFS			
MASS phenotype (MIM 604308)	Mitral valve prolapse	Borderline or nonprogressive	Nonspecific skin and skeletal findings Myopia

Table 703-2 Clinical Variants of Rickets and Related Conditions

TYPE	SERUM CALCIUM LEVEL	SERUM PHOSPHORUS LEVEL	ALKALINE PHOSPHATASE ACTIVITY	URINE CONCENTRATION OF AMINO ACIDS	GENETICS	GENE DEFECT KNOWN
CALCIUM DEFICIENCY WITH SECONDARY HYPERPARATHYROIDISM [DEFICIENCY OF VITAMIN D; LOW 25(OH)D AND NO STIMULATION OF HIGHER $1,25(OH)_2D$ VALUES]						
Lack of Vitamin D						
Lack of exposure to sunlight	N or L	L	E	E		
Dietary deficiency of vitamin D	N or L	L	E	E		
Congenital	N or L	L	E	E		
Other Deficiencies						
Malabsorption of vitamin D	N or L	L	E	E		
Liver diseases	N or L	L	E	E		
Anticonvulsant drug	N or L	L	E	E		
Renal osteodystrophy	N or L	E	E	V		
Vitamin D–dependent type I	L	N or L	E	E	AR	Y
PRIMARY PHOSPHATE DEFICIENCY (NO SECONDARY HYPERPARATHYROIDISM)						
Genetic Primary Hypophosphatemia	N	L	E	N	XI, AD, AR	Y
X-linked hypophosphatemic rickets					XL	Y
Autosomal dominant hypophosphatemic rickets					AD	Y
Autosomal recessive hypophosphatemic rickets					AR	Y
Fanconi Syndrome						
Cystinosis	N	L	E	E	AR	Y
Tyrosinosis	N	L	E	E	AR	Y
Lowe syndrome	N	L	E	E	XR	Y
Acquired	N	L	E	E		
Phosphate Deficiency or Malabsorption						
Parenteral hyperalimentation	N	L	E	N		
Low phosphate intake	N	L	E	N		
Other						
Renal tubular acidosis, type II proximal	N	L	E	N		Y
Tumor-induced osteomalacia	N	L	E	N		Y
END-ORGAN RESISTANCE TO $1,25(OH)_2D_3$						
Vitamin D-dependent type II (several variants)	L	L or N	E	E	AR	Y
RELATED CONDITIONS RESEMBLING RICKETS						
Hypophosphatasia	N	N	L	Phosphoethanolamine elevated	AR	Y
Metaphyseal Dysostosis						
Jansen type		N	E	N	AD	Y
Schmid type		N	E	N	AD	Y

AD, autosomal dominant; AR, autosomal recessive; E, elevated; L, low; N, normal; V, variable; XL, X-linked; Y, yes.

Table 715-1 Prognosticating in Myelomeningocele

MOTOR LEVEL SPINAL CORD SEGMENT	CRITICAL MOTOR FUNCTION PRESENT	MOBILITY: SCHOOL AGE	RANGE: ADULT	ACTIVITY: ADOLESCENT
T12	Totally paralyzed lower limbs	Standing brace, wheelchair	Wheelchair	Wheelchair, no ambulation
L1-2	Hip flexor muscles	Crutches, braces, wheelchair	Wheelchair, household ambulation	Wheelchair, nonfunctional ambulation
L3-4	Quadriceps muscles	Crutches, braces, household ambulation, wheelchair	Crutches, household ambulation, wheelchair	50% Wheelchair, household ambulation with crutches
L5	Medical hamstrings, anterior tibial muscles	Crutches, braces, community ambulation	Crutches, community ambulation	Community ambulation with crutches
S1	Lateral hamstring and peroneal muscles	Community ambulation	Community ambulation	Community ambulation 50% crutch or cane
S2-3	Mild loss of intrinsic foot muscles possible	Normal	Normal	Limited endurance because of late foot deformities

From Braddon RL, editor: Physical medicine & rehabilitation, *ed 4, Philadelphia, 2011, WB Saunders, Table 54-1, p. 1284.*

Table 707-1 Risks for Osteoporosis

ENDOCRINE DISORDERS
Female Hypogonadism
Turner syndrome
Hypothalamic amenorrhea (athletic triad)
Anorexia nervosa
Premature and primary ovarian failure
Depot medroxyprogesterone acetate therapy
Estrogen receptor α *(ESR1)* mutations
Hyperprolactinemia
Male Hypogonadism
Primary gonadal failure (Klinefelter syndrome)
Secondary gonadal failure (idiopathic hypogonadotropic hypogonadism)
Delayed puberty
Hyperthyroidism
Hyperparathyroidism
Hypercortisolism (therapeutic or Cushing disease)
Growth hormone deficiency
Thyrotoxicosis

INFLAMMATORY DISORDERS
Dermatomyositis
Chronic hepatitis
Systemic lupus erythematosus

GASTROINTESTINAL DISORDERS
Malabsorption syndromes (cystic fibrosis, celiac disease, biliary atresia)
True or perceived milk intolerance
Inflammatory bowel disease
Chronic obstructive jaundice
Primary biliary cirrhosis and other cirrhoses
Alactasia
Subtotal gastrectomy

BONE MARROW DISORDERS
Bone marrow transplant
Lymphoma
Leukemia
Hemolytic anemias (sickle cell anemia, thalassemia)
Systemic mastocytosis

CONNECTIVE TISSUE/BONE DISORDERS
Juvenile osteoporosis
Osteogenesis imperfecta
Ehlers-Danlos syndrome
Marfan syndrome
Homocystinuria
Fibrous dysplasia
Previous or recurrent low impact fractures
Early onset osteoporosis with *WNT1* mutations
X-linked osteoporosis with fractures with *PLS3* mutations

DRUGS
Alcohol
Heparin
Glucocorticosteroids
Thyroxine
Anticonvulsants
Gonadotropin-releasing hormone agonists
Cyclosporine
Chemotherapy
Cigarettes

MISCELLANEOUS DISORDERS
Immobilization (cerebral palsy, spinal muscular atrophy, Duchenne dystrophy)
Rheumatoid arthritis
Renal disease
Glycogen storage disease type 1
Chronic hepatitis
Low calcium dietary intake
Gaucher disease
Severe congenital neutropenia

Table 723-1 Diseases Caused By Agents of Chemical and Biologic Terrorism, Classified By Syndrome

	NEUROMUSCULAR SYMPTOMS PROMINENT	RESPIRATORY SYMPTOMS PROMINENT	DERMATOLOGIC FINDINGS PROMINENT
Sudden-onset	Nerve agents	Chlorine Phosgene Cyanide	Mustard Lewisite
Delayed-onset	Botulism	Anthrax Plague Tularemia Ricin	Smallpox

Rehabilitation Medicine and Others

Table 712-1 Dosing Guidelines, Pharmacologic Actions, and Adverse Event Profile of Commonly Prescribed Oral Antispasmodic Medications for Children

ORAL MEDICATION (DOSE/FREQ., AGE/ WEIGHT RANGE)	MODE OF ACTION	ADVERSE EVENTS/PRECAUTIONS
Baclofen (0.125-1 mg/kg/day) *Dosing guideline* *2-7 yr* 2.5-10 mg tid-qid (10-40 mg/day) *8-12 yr* 5-15 mg tid-qid (15-60 mg/day) *12-16 yr* 5-20 mg tid-qid (20-80 mg/day) *Note:* Caution advised with renal impairment, consider reducing dose.	Centrally acting, structural analog of γ-aminobutyric acid (GABA), binds to $GABA_B$ receptors of presynaptic excitatory interneurons (and postsynaptic primary afferents) causing presynaptic inhibition of monosynaptic/polysynaptic spinal reflexes. Rapid absorption, blood level peaks in 1 hr, half-life 5.5 hr. Renal (70-80% unchanged) and hepatic (15%) excretion.	Central nervous system (CNS) depression (sedation, drowsiness, fatigue), nausea, headache, dizziness, confusion, euphoria, hallucinations, hypotonia, ataxia, paresthesias. **Note: Abrupt withdrawal** may cause seizures, hallucinations, rebound muscle spasms, and hyperpyrexia.
Diazepam (0.12-0.8 mg/kg/day) *Dosing guideline* 6 mo-12 yr 0.12-0.8 mg/kg/day PO divided q6-8h >12 yr 2-10 mg PO bid-qid *Note:* Prescription of a *qhs* dose only or proportionately larger dose at bedtime may limit excessive daytime sedation.	Centrally acting; binds to $GABA_A$ receptors mediating presynaptic inhibition in brainstem reticular formation and spinal polysynaptic pathways. Rapid absorption; blood level peaks in 1 hr, with half-life of 30-60 hr. Metabolized in liver, producing pharmacologically active metabolites with long duration of action. Increased potential for adverse effects with low albumin levels as a result of being 98% protein bound.	CNS depression (sedation, impaired memory and attention), ataxia. Dependence/potential for substance abuse/ overdose. Withdrawal syndrome (including anxiety, agitation, irritability, tremor, muscle twitching, nausea, insomnia, seizures, hyperpyrexia).
Dantrolene Sodium (3-12 mg/kg/day) *Dosing guideline (for children >5 yr old):* *6-8 mg/kg/day PO divided bid-qid* In children >5 yr old Start 0.5 mg/kg qd-bid for 7 days, then 0.5 mg/kg tid for 7 days, then 1 mg/kg tid for 7 days, then 2 mg/kg tid to a maximum of 12 mg/kg/day or 400 mg/day.	Peripheral action, blocking release of calcium from sarcoplasmic reticulum with uncoupling of nerve excitation and skeletal muscle contraction. Blood level peaks in 3-6 hr (active metabolite 4-8 hr), with half-life of approximately 15 hr. Metabolized largely in liver, with 15-25% of nonmetabolized drug excreted in urine.	Malaise, fatigue, nausea, vomiting, diarrhea, muscle weakness with high dose. *Note:* Hepatotoxicity (baseline liver function tests **must** be checked prior to starting dantrolene, tested weekly during dose titration, and regularly every 1-2 mo thereafter). Drug *should be discontinued* promptly if liver enzymes become elevated.
Tizanidine *Dosing guideline* In children <10 yr: Commence 1 mg orally at bedtime initially, increasing to 0.3-0.5 mg/ kg in 4 divided doses. In children >10 yr: Commence 2 mg orally at bedtime initially, increased according to response, maximum 24 mg/day in 3-4 divided doses.	Centrally acting, α_2-adrenoceptor agonist activity at both spinal and supraspinal sites. Prevents release of excitatory amino acids, facilitating presynaptic inhibition. Good oral absorption, blood level peaks in 1-2 hr, with a half-life of 2.5 hr. Extensive first-pass hepatic metabolism with urinary excretion of inactive metabolites.	Dry mouth, drowsiness, tiredness, headache, dizziness, insomnia, anxiety, aggression, mood swings, visual hallucinations, risk of hypotension (although 10 times less antihypertensive potency than clonidine), nausea, vomiting, and constipation. Liver function tests should be monitored at baseline, 1, 3, and 6 mo. Then periodically.
Clonidine *Dosing guideline* 0.025-0.1 mg in 2-3 divided doses. *Note:* A retrospective chart review of literature about clonidine in children reported an average dosage based on weight was 0.02-0.03 mg/kg/day (0.4-0.5 mg/day), with a range of 0.0014-0.15 mg/kg/day.	Centrally acting, mixed α-adrenoceptor agonist with predominant α_2 activity causing membrane hyperpolarization at multiple sites in brain, brainstem, and dorsal horns of spinal cord. Inhibition of substance P may also contribute to tone reduction via an antinociceptive effect. Rapidly absorbed orally, blood level peaks in 1-1.5 hr, with a half-life of 6-20 hr.	Drowsiness, dry mouth, bradycardia, orthostatic hypotension. Abrupt cessation may result in rebound hypertension.

Table 720-3 Differential Characteristics of Mercury Exposure

	ELEMENTAL	INORGANIC (SALT)	ORGANIC (ALKYL)
Primary route of exposure	Inhalation	Oral	Oral
Primary tissue distribution	CNS, kidney	Kidney	CNS, kidney, liver
Clearance	Renal, GI	Renal, GI	Methyl: GI Aryl: renal, GI
Clinical effects:			
CNS	Tremor	Tremor, erethism (irritability)	Paresthesias, ataxia, tremor, tunnel vision, dysarthria
Pulmonary	+++	—	—
Gastrointestinal	+	+++ (caustic)	+
Renal	+	+++ (acute tubular necrosis)	+
Acrodynia	+	++	—
Therapy	BAL, DMSA	BAL, DMSA	DMSA (early)

BAL, British antilewisite; CNS, central nervous system; DMSA, 2,3-dimercaptosuccinic acid; GI, gastrointestinal; +, mild; ++, moderate; +++, severe.

Table 719-1 Effects of Selected Chemical Pollutants on Infants and Children

CHEMICAL POLLUTANT	EFFECT(S)
Air pollution	Asthma, other respiratory diseases, sudden infant death syndrome
Asbestos	Mesothelioma and lung cancer
Benzene, nitrosamine, vinyl chloride, ionizing radiation	Cancer
Diethylstilbestrol	Adenocarcinoma of the vagina after intrauterine exposure
Environmental tobacco smoke	Increased risk of sudden infant death syndrome and asthma
Ethyl alcohol	Fetal alcohol syndrome after intrauterine exposure
Lead	Neurobehavioral toxicity from low-dose exposure
Methyl mercury	Developmental neurotoxicity
Organophosphate insecticides	Developmental neurotoxicity
Polychlorinated biphenyls	Developmental neurotoxicity
Polybrominated diphenyl ethers	Developmental neurotoxicity
Phthalates	Developmental neurotoxicity and reproductive impairment
Thalidomide	Phocomelia after intrauterine exposure
Trichloroethylene	Elevated risk of leukemia after intrauterine exposure

Table 720-1 Effects of Arsenic on Organ Systems

ORGAN SYSTEM	EFFECTS OF ARSENIC
Gastrointestinal system	Submucosal vesicles, watery or bloody diarrhea, severe hematemesis
Cardiovascular system	Reduced myocardial contractility, prolonged QT intervals, tachyarrhythmias
	Vasodilation, hypotension
Kidneys	Hematuria, proteinuria, acute tubular necrosis
Nervous system	Toxic encephalopathy with seizures, cerebral edema, and coma
	Chronic exposure: peripheral painful sensorimotor neuropathy
Hematologic and lymphatic system	Anemia and thrombocytopenia; acute hemolysis with arsine gas
Liver	Fatty degeneration with central necrosis
Skin	Desquamation, alopecia, hyperkeratosis, nail changes
	Chronic exposure: hyperkeratosis, hyperpigmentation
Teratogenic	Neural tube defects in the fetus
Oncologic	Urologic cancer, other malignancies

Table 720-2 Acceptable and Toxic Levels of Arsenic and Mercury

	ARSENIC	MERCURY
Molecular weight	74.9 Da	200.59 Da
Acceptable blood level	<5 μg/L (<0.665 nmol/L)	<10 μg/L (<50 nmol/L)
Acceptable urine level	<50 μg/L (<6.65 nmol/L) 24 hr urine sample	<20 μg/L (<100 nmol/L)
Intervene at blood level		>35 μg/L (>175 nmol/L)
Intervene at urine level	>100 μg/L (>13.3 nmol/L) 24 hr urine sample	>150 μg/L (>750 nmol/L)

Table 721-4 Chelation Therapy

NAME	SYNONYM	DOSE	TOXICITY
Succimer	Chemet, 2,3-dimercaptosuccinic acid (DMSA)	350 mg/m^2 body surface area/dose ***(not 10 mg/kg)*** q8h, PO for 5 days, then q12h for 14 days	Gastrointestinal distress, rashes; elevated LFTs, depressed white blood cell count
Edetate*	$CaNa_2EDTA$ (calcium disodium edetate), versenate	1,000-1,500 mg/m^2 body surface area/day; IV infusion—continuous or intermittent; IM divided q6h or q12h for 5 days	Proteinuria, pyuria, rising blood urea nitrogen/creatinine—all rare Hypercalcemia if too rapid an infusion Tissue inflammation if infusion infiltrates
British antilewisite (BAL)	Dimercaprol	300-500 mg/m^2 body surface area/day; **IM only** divided q4h for 3-5 days. Only for BLL ≥70 μg/dL	Gastrointestinal distress, altered mentation; elevated LFTs, hemolysis if glucose-6-phosphate dehydrogenase deficiency; no concomitant iron treatment
D-Pen	Penicillamine	10 mg/kg/day for 2 wk increasing to 25-40 mg/kg/day; oral, divided q12h. For 12-20 wk	Rashes, fever; blood dyscrasias, elevated LFTs, proteinuria Allergic cross reactivity with penicillin

*Always given as the calcium salt; never as the sodium salt without calcium.
BLL, blood lead level; IM, intramuscularly; IV, intravenously; LFT, liver function test; PO, by mouth.
From Markowitz ME: Lead poisoning, Pediatr Rev *21:327–335, 2000.*

Table 723-3 Critical Chemical Agents of Terrorism

AGENT	TOXICITY	CLINICAL FINDINGS	ONSET	DECONTAMINATION*	MANAGEMENT
NERVE AGENTS					
Tabun, sarin, soman, VX	Anticholinesterase: muscarinic, nicotinic, central nervous system effects	Vapor: miosis, rhinorrhea, dyspnea Liquid: diaphoresis, vomiting Both: coma, paralysis, seizures, apnea	Seconds: vapor Minutes to hours: liquid	Vapor: fresh air, remove clothes, wash hair Liquid: remove clothes, wash skin, hair with copious soap and water, ocular irrigation	ABCs. Atropine: 0.05 mg/kg IV†, IM‡ (min: 0.1 mg, max: 5 mg), repeat q2-5 min prn for marked secretions, bronchospasm Pralidoxime: 25 mg/kg IV, IM§ (max: 1 g IV; 2 g IM), may repeat within 30-60 min prn, then again q1h for 1 or 2 doses prn for persistent weakness, high atropine requirement Diazepam: 0.3 mg/kg (max: 10 mg) IV; lorazepam: 0.1 mg/kg IV, IM (max: 4 mg); midazolam: 0.2 mg/kg (max: 10 mg) IM prn for seizures or severe exposure
VESICANTS					
Mustard	Alkylation	Skin: erythema, vesicles Eye: inflammation Respiratory tract: inflammation	Hours	Skin: soap and water Eyes: water (effective only if done within minutes of exposure)	Symptomatic care
Lewisite	Arsenical		Immediate pain		Possibly British antilewisite (BAL) 3 mg/kg IM q4-6h for systemic effects of lewisite in severe cases
PULMONARY AGENTS					
Chlorine, phosgene	Liberate hydrochloric acid, alkylation	Eye, nose, and throat irritation (especially chlorine) Respiratory: bronchospasm, pulmonary edema (especially phosgene)	Minutes: eye, nose, and throat irritation, bronchospasm Hours: pulmonary edema	Fresh air Skin: water	Symptomatic care (see text)
CYANIDE					
	Cytochrome oxidase Inhibition: cellular anoxia, lactic acidosis	Tachypnea, coma, seizures, apnea	Seconds	Fresh air	ABCs, 100% oxygen
				Skin: soap and water	Na bicarbonate prn metabolic acidosis; hydroxycobalamin 70 mg/kg IV (max: 5 g) *or* nitrite/thiosulfate, given as follows (see text): *Na nitrite (3%): dose (mL/kg)* (max: 10 mL) — *Estimated hemoglobin concentration (g/dL)* 0.27 — 10 0.33 — 12 (estimated for average child) 0.39 — 14 followed by Na thiosulfate (25%): 1.65 mL/kg (max: 50 mL)

*Decontamination, especially for patients with significant nerve agent or vesicant exposure, should be performed by healthcare providers garbed in adequate personal protective equipment. For emergency department staff, this equipment consists of a nonencapsulated, chemically resistant body suit, boots, and gloves with a full-face air-purifier mask/hood.

†Intraosseous route is likely equivalent to intravenous.

‡Atropine might have some benefit via endotracheal tube or inhalation, as might aerosolized ipratropium. See also Table 723-4.

§Pralidoxime is reconstituted to 50 mg/mL (1 g in 20 mL water) for IV administration, and the total dose infused over 30 min, or may be given by continuous infusion (loading dose 25 mg/kg over 30 min, and then 10 mg/kg/hr). For IM use, it might be diluted to a concentration of 300 mg/mL (1 g added to 3 mL water—by analogy to the U.S. Army's Mark 1 autoinjector concentration), to effect a reasonable volume for injection. See also Table 723-4.

ABCs, airway, breathing, and circulatory support; max, maximum; min, minimum; prn, as needed.

Adapted from Henretig FH, Cieslak TJ, Eitzen EM: Biological and chemical terrorism, J Pediatr *141:311–326, 2002.*

Table 724-2 Microorganisms Associated with Bites

DOG BITES
Staphylococcus species
Streptococcus species
Eikenella species
Pasteurella species
Proteus species
Klebsiella species
Haemophilus species
Enterobacter species
Capnocytophaga canimorsus
Bacteroides species
Moraxella species
Corynebacterium species
Neisseria species
Fusobacterium species
Prevotella species
Porphyromonas species

CAT BITES
Pasteurella species
Actinomyces species
Propionibacterium species
Bacteroides species
Fusobacterium species
Clostridium species
Wolinella species
Peptostreptococcus species
Staphylococcus species
Streptococcus species

HERBIVORE BITES
Actinobacillus lignieresii
Actinobacillus suis
Pasteurella multocida
Pasteurella caballi
Staphylococcus hyicus subsp. *hyicus*

SWINE BITES
Pasteurella aerogenes
Pasteurella multocida
Bacteroides species
Proteus species
Actinobacillus suis
Streptococcus species
Flavobacterium species
Mycoplasma species

RODENT BITES—RAT BITE FEVER
Streptobacillus moniliformis
Spirillum minus

PRIMATE BITES
Bacteroides species
Fusobacterium species
Eikenella corrodens
Streptococcus species
Enterococcus species
Staphylococcus species
Enterobacteriaceae
Simian herpesvirus

LARGE REPTILE (CROCODILE, ALLIGATOR) BITES
Aeromonas hydrophila
Pseudomonas pseudomallei
Pseudomonas aeruginosa
Proteus species
Enterococcus species
Clostridium species

Table 724-3 Prophylactic Management of Human or Animal Bite Wounds to Prevent Infection

CATEGORY OF MANAGEMENT	MANAGEMENT
Cleansing	Remove visible dirt. Cleanse the wound surface with soap and water, saline, 1% povidone–iodine, or 1% benzalkonium chloride. Irrigate with a copious volume of sterile saline solution by high-pressure syringe irrigation.* Do not irrigate puncture wounds; Standard Precautions should be used.
Wound culture	No, for fresh wounds, unless signs of infection exist. Yes for wounds that appear infected.†
Diagnostic Imaging	Indicated for penetrating injuries overlying bones or joints, for suspected fracture, or to assess foreign body inoculation.
Debridement	Remove superficial devitalized tissue.
Operative debridement and exploration	Yes if any of the following: • Extensive wounds (devitalized tissue) • Involvement of the metacarpophalangeal joint (clenched-fist injury) • Cranial bites by large animal
Wound closure	Yes for selected fresh, nonpuncture bite wounds.
Assess tetanus immunization status	Yes.
Assess risk of rabies from animal bites	Yes.
Assess risk of hepatitis B virus infection from human bites	Yes.
Assess risk of human immunodeficiency virus from human bites	Yes.
Initiate antimicrobial therapy	Yes for: • Moderate or severe bite wounds, especially if edema or crush injury is present • Puncture wounds, especially if penetration of bone, tendon sheath, or joint has occurred • Face, hand, foot, and genital bites • Wounds in immunocompromised and asplenic persons • Wounds with signs of infection
Follow-up	Inspect wound for signs of infection within 48 hr

*Use of an 18-gauge needle with a large-volume syringe is effective. Antimicrobial or antiinfective solutions offer no advantage and may increase tissue irritation.

†Both aerobic and anaerobic bacterial culture should be performed.