**3122 Part XXXI** ◆ The Skin

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| **Table 650-1** | International Society for the Study of Vascular Anomalies (ISSVA) Classification System |
| **VASCULAR**  **MALFORMATION VASCULAR TUMOR** | |
| Slow-flow malformations Infantile hemangioma Capillary malformation Congenital hemangioma Venous malformation Rapidly involuting congenital Lymphatic malformation hemangioma  Fast-flow malformations Noninvoluting congenital Arterial malformation hemangioma  Arteriovenous malformation Kaposiform hemangioendothelioma Arteriovenous fistula Tufted angioma  Combined vascular Spindle cell hemangioendothelioma malformations Epithelioid hemangioendothelioma  Other rare hemangioendotheliomas Angiosarcoma  Acquired vascular tumors: pyogenic granuloma | |

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| **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.

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| **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 Evaluate for airway hemangioma,  in beard distribution 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.

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| **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 | | |

**Chapter 654** ◆ Vesiculobullous Disorders **3145**

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| **Table 654-2** Clinical | Presentation and Diagnosis of Selected Epidermolysis Bullosa Subtypes in the Neonatal Period | |
| **EB SUBTYPE (USUAL INHERITANCE)** | **CLINICAL FEATURES**  **Cutaneous Extracutaneous** | **DIAGNOSIS** |
| EB simplex– generalized (AD) | Mild to moderate blistering, Occasional mucosal blistering often generalized  Rare scarring, milia | EM: Intrabasal layer split  IF: BPAG1 (BP230), BP-180 (BPAG2, collagen  XVII), α6β4 integrin, laminin 1, laminin 332, type IV collagen, type VII collagen (EBA antigen) at base of blister |
| EB simplex–localized (AD) | Mild blistering, often Rare mucosal involvement localized, sometimes in 1st  24 mo, but often not until later infancy or childhood  Rare scarring, milia | EM: Intrastratum basale split  IF: Same as for EB simplex—generalized |
| EB simplex–Dowling- Meara (AD) | Moderate to severe blistering, Mild mucosal blistering which starts generalized,  then is grouped (herpetiform); milia; nail dystrophy, shedding | EM: Intrastratum basale split; clumped keratin filaments  IF: Same as for EB simplex—generalized |
| Junctional EB–non- Herlitz (AR) | Moderate blistering; atrophic Mild mucosal blistering; enamel scars; nail dystrophy 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), α6β4 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 Severe mucosal blistering; GI that heals poorly; involvement common; laryngeal granulation tissue; scarring; involvement with airway  nail dystrophy 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), α6β4 integrin absent or reduced |
| Dominant dystrophic EB (AD) | Mild to moderate blistering Mild mucosal blistering (but may be more severe in  newborn period) Milia, scarring  Nail dystrophy | EM: Cleavage sublamina densa; variable reduction in anchoring fibrils  IF: BPAG1 (BP230), BPAG2 (BP180, type XVII  collagen), α6β4 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 Severe mucosal blistering; GI  Milia, scarring involvement common; urologic involvement | EM: Cleavage sublamina densa; absence of anchoring fibrils  IF: BPAG1 (BP230), BP-180 (BPAG2, type XVII  collagen), α6β4 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.

**Chapter 658** ◆ Disorders of Keratinization **3169**

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| **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.

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| **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)*  Deficient type III collagen  *(COL3A1)* |
| 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) |
| 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 | | EDS V | Classic features  Classic features and periodontal disease  Mild classic features, MVP Joint instability  Classic features; occipital horns Classic features and premature  aging | XL | 305200 | ? |
| EDS VIII | AD | 130080 | ? |
| types | |
|  | | EDS X | ? | 225310 | ? |
|  | | EDS XI | AD | 147900 | ? |
|  | | EDS IX | XL | 309400 | Allelic to Menkes syndrome |
|  | | EDS, progeroid form | 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.

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| **Table 668-3** | Drugs for Head Lice | | | | |
| **DRUG** | | **RESISTANCE** | **FDA-APPROVED LOWER AGE OR WEIGHT LIMIT** | **DOSAGE AND ADMINISTRATION** | **COSTa/SIZE** |
| Ivermectin 0.5% lotion–Sklice (Sanofi Pasteur) | | Nob | 6 months | Apply to dry hair and scalp for 10 min, then rinse | $257.88/4 oz |
| Ivermectin tabletsc–Stromectol (Merck) | | No | 15 kg | 200-400 μg/kg PO once; repeat 7-10 days later | 9.97d |
| Spinosad 0.9% suspension–Natroba (ParaPro) | | Nob | 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 shampooe,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 ozg |
| Permethrin 1% creme rinsee– 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 ozg |
| 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 |

aWholesale acquisition cost (WAC). Source: PricePointRx. Reprinted with permission by FDB, Inc. All rights reserved. Copyright 2012. [www.firstdatabank.com/support/](http://www.firstdatabank.com/support/) drug-pricing-policy.aspx. Actual retail prices may be higher. Amount needed may vary.

bProduct new to market: currently no reports of resistance.

cNot FDA-approved for treatment of head lice. Stromectol is available in 3 mg tablets.

dCost of 1 dose for a 30 kg child at the lowest dosage.

eAvailable without a prescription.

fProducts that contain benzyl alcohol as their vehicle may be more effective.

gCost according to drugstore.com.

hOne 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.)

**Chapter 659** ◆ Diseases of the Dermis **3183**

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

Cutaneous Reactions to Sunlight

**Table 656-2**

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| **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 | | 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 |
| 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 | |
| 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 |

Cutaneous mastocytosis:

1. Urticaria pigmentosa:

(a) Classic infantile type; (b) Chronic with stem cell factor mutations

1. Diffuse cutaneous mastocytosis
2. Mastocytoma of the skin
3. 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

Mastocytosis Classification

**Table 659-4**

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

Differential Diagnosis of Onychomycosis

**Table 663-3**

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| **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 |

|  |  |
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| **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** | |
| Congenital Diseases with Nail Defects  Pachyonychia congenita, Rubinstein-Taybi | | |
| Large nails  Smabasllennecses orf nails | | | syndrome, hemihypertrophy |  |
| 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 |  |
| Congenital malalignment of the great toenails, familial dystrophic shedding of the nails |  |
| Other | | |
|  |  |

# Bone and Joint Disorders

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| **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  CD25 deficiency  NEMO or iκBγ deficiency | Viruses and bacteria Pyogenic bacteria,  mycobacteria, viruses  Viruses, bacteria and fungi  Viruses and bacteria Viruses, mycobacteria,  bacteria and fungi Viruses and bacteria Viruses, bacteria and  fungi  *Pneumocystis, Cryptococcus*, virus | T-cell defect | *IL2RA,* autosomal recessive  *NEMO* or *IKBG* X-linked |
| IκBα GOF mutation DOCK8 deficiency |  | *IKBA,* autosomal dominant  *DOCK8,* autosomal recessive |
| TCR-α deficiency CRACM1 deficiency |  | *TCRA,* autosomal recessive  *CRACM1,* autosomal recessive |
| MST1/STK4 deficiency MHC class II deficiency  Idiopathic CD4 lymphopenia | CD4 T cells <300 cells/mm3 | *MST1/STK4,* autosomal recessive  *CIITA, RFXANK, RFXC, RFXAP,* all  autosomal recessive  *UNC119,* autosomal dominant, *MAGT1*  X-linked, *RAG1,* autosomal recessive |
| SYNDROMIC CMC  Interleukin-12Rβ1 and interleukin-12p40 deficiencies  STAT3 deficiency (autosomal dominant- HIES)  APECED/APS-1  CARD9 deficiency | *Mycobacteria, Salmonella*  *Staphylococcus aureus, Aspergillus*  No  Dermatophytes, *Candida*, brain abscess | Deficit of interleukin-17– producing T cells  Hyperimmunoglobulin E, deficit of interleukin-17–producing T cells  Neutralizing anti–interleukin-17A, anti–interleukin-17F, and/or anti–interleukin-22 autoantibodies  Deficit of interleukin-17– producing T cells | *IL12RB1,* autosomal recessive, *IL12B,*  autosomal recessive  *STAT3,* autosomal dominant  *AIRE,* autosomal recessive  *CARD9,* autosomal recessive |
| CMCD  Complete interleukin-17RA deficiency  Partial interleukin-17F deficiency  STAT1 GOF mutations | *S. aureus*  *S. aureus*  Bacteria, viruses, fungi, mycobacteria | No interleukin-17 response  Impaired interleukin-17F, interleukin-17A/F function  Low interleukin-17–producing T cells | *IL17RA,* autosomal recessive *IL17F,* autosomal dominant *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.

Epiphysis Metaphysis

|  |  |  |
| --- | --- | --- |
| **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 |

Epiphyseal plate (physis) enclosed by perichondrial ring

Diaphysis

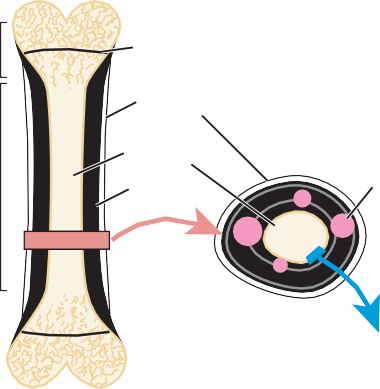
Periosteum Medullary

canal

Compact bone

Compact bone cross section

Haversian

**Figure 672-1** Diagram showing typical long bone divisions.

Limp Pain

Torsional variations Toe walking

Joint abnormalities Leg-length discrepancy

Neuromuscular disorders

Causes of Abnormal Gait

**Table 673-3**

|  |  |  |  |
| --- | --- | --- | --- |
| **Table 672-3** | Functional Milestones | | |
| **MILESTONE**  Head control Sitting Crawling | |  | **ACHIEVED BY** |
| 3-6 months |
| 6-9 months |
| 8 months |
| Pulling to stand | | 8-12 months |
| Ambulating | | 12-18 months |

|  |  |  |  |
| --- | --- | --- | --- |
| **Table 673-4** | Commo | n 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 | |  | + |

* 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.

Skeletal Growth Considerations

**Table 672-2**

−, 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.*

|  |  |
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| **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 | |

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| **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 | |

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| **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 | |

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| **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 |

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| **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 | |

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* 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

Conditions Associated with Hyperkyphosis

**Table 679-2**

* 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

Findings Consistent with a Nonmechanical Etiology Warranting Further Evaluation

**Table 679-4**

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| **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 |

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| **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 | |

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| **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 | |

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| **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 | |

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| **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) | |

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Chapter **682**

**Arthrogryposis**

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

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| **Table 682-2** | Current Labels and OMIM Numbers for the Distal Arthrogryposis Syndromes |
| **OMIM**  **SYNDROME NUMBER** | |
| Distal arthrogryposis type 1 108120 | |
| Distal arthrogryposis type 2A (Freeman-Sheldon 193700 syndrome) | |
| 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- 158300 pseudocamptodactyly) | |
| Distal arthrogryposis type 8 (autosomal dominant 178110 multiple pterygium syndrome) | |
| Distal arthrogryposis type 9 (congenital contractural 121050 arachnodactyly) | |
| Distal arthrogryposis type 10 (congenital plantar 187370 contractures) | |

*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.*

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| **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 | |

Anterior Horn Cell Disease Other neurologic disorders

Myopathies and other muscle disorders

Maternal diseases

Fetal crowding

Vascular compromise

Connective tissue abnormalities

**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.)*

**Fetal hypokinesia or restricted fetal movement**

**Multiple congenital contractures**

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.*

**Chapter 687** ◆ Management of Musculoskeletal Injury **3337**

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| **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 |

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| **Table 701-1** | Osteogenesis Type, Gene Defects, and Phenotypes | | |
| **OSTEOGENESIS IMPERFECTA TYPE** | | **GENE DEFECT** | **PHENOTYPE** |
| DOMINANT INHERITANCE  *Classical Sillence Types*  I II III IV  *COL1-Mutation Negative*  V | | *COL1A1* null allele *COL1A1* or *COL1A2 COL1A1* or *COL1A2 COL1A1* or *COL1A2*  *IFITM5* | Mild, nondeforming Lethal perinatal Progressively deforming Moderately deforming  Distinct histology |
| RECESSIVE INHERITANCE  *Mineralization Defect*  VI  *3-Hydroxylation Defects*  VII VIII IX  *Chaperone Defects*  X XI  *C-Propeptide Cleavage Defect*  XII | | *SERPINF1*  *CRTAP LEPRE1 PPIB*  *SERPINH1 FKBP10*  *BMP1* | Distinct histology  Severe to lethal Severe to lethal Moderate to lethal  Severe  Progressive deforming, Bruck syndrome 1  Severe, high bone mass case |
| UNCLASSIFIED  Zinc-finger transcription factor defect Cation channel defect  WNT signaling pathway defect | | *SP7 TMEM38B WNT1* | Moderate Moderate to severe  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.*

**Chapter 689** ◆ Cervical Spinal Injuries **3353**

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| **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.

* 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

Scoring of Systemic Features in Points

**Table 702-2**

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

*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.*

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| **Table 689-1** | **Return to Play (RTP) Table** |
| NO CONTRAINDICATION TO RTP  Healed fractures Healed C1 or C2 fracture with normal including: 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/ Cervical disc disease (no change in postsurgical conditions 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 Cervical myelopathy  and any 1 or more of: 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 Spear tackler’s spine  including: 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) | |

**3364 Part XXXII** ◆ Bone and Joint Disorders

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| **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.

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| **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 | |

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| **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 | |

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| **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.

**3388 Part XXXII** ◆ Bone and Joint Disorders

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| **Table 702-4** Differential Diagnosis of Marfan Syndrome | | | |
| **DIFFERENTIAL DIAGNOSIS** | **CARDIAC FEATURES** | **VASCULAR FEATURES** | **SYSTEMIC FEATURES** |
| AORTIC ANEURYSM SYNDROMES  Loeys-Dietz syndrome (MIM 609192)  Familial thoracic aortic aneurysm (MIM 132900)  Shprintzen-Goldberg syndrome (MIM 182212) | Patent ductus arteriosus Atrial septal defect Bicuspid aortic valve  Generally none  Rare forms with patent ductus arteriosus  None | Aortic root aneurysm Arterial tortuosity Widespread aneurysms  Vascular dissection at relatively young ages and small aortic dimensions  Aortic root aneurysm Ascending aortic aneurysm  Aortic root aneurysm | 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 Generally none  Rarely livedo reticularis and iris flocculi  Hypertelorism Craniosynostosis Arched palate Arachnodactyly Pectus deformity Scoliosis  Joint hypermobility Developmental delay |
| Bicuspid aortic valve with aortic aneurysm (MIM: 109730)  Ehlers-Danlos syndrome, type IV (MIM: 130050) | Bicuspid aortic valve Mitral valve prolapse | Aortic root aneurysm Ascending aortic aneurysm 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 |

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| **Table 703-2** Clinical Variants of Rickets and Related Conditions | | | | | |
| **SERUM CALCIUM**  **TYPE 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  Liver diseases N or L  Anticonvulsant drug N or L  Renal osteodystrophy N or L  Vitamin D–dependent type I L | L L L E  N or L | E E E E E | E E E V E | AR | Y |
| PRIMARY PHOSPHATE DEFICIENCY (NO SECONDARY HYPERPARATHYROIDISM)  *Genetic Primary Hypophosphatemia* N L E X-linked hypophosphatemic rickets  Autosomal dominant hypophosphatemic rickets  Autosomal recessive hypophosphatemic rickets  *Fanconi Syndrome*  Cystinosis N L E  Tyrosinosis N L E  Lowe syndrome N L E  Acquired N L E  *Phosphate Deficiency or Malabsorption*  Parenteral hyperalimentation N L E  Low phosphate intake N L E  *Other*  Renal tubular acidosis, type II proximal N L E  Tumor-induced osteomalacia N L E | | | N  E E E E  N N  N N | XI, AD, AR XL  AD AR  AR AR XR | Y Y Y  Y  Y Y Y  Y Y |
| END-ORGAN RESISTANCE TO 1,25(OH)2D3  Vitamin D-dependent type II (several L variants) | L or N | E | E | AR | Y |
| RELATED CONDITIONS RESEMBLING RICKETS  Hypophosphatasia N  *Metaphyseal Dysostosis*  Jansen type Schmid type | N  N N | L  E E | Phosphoethanolamine elevated  N N | AR  AD AD | Y  Y Y |

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

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| **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.*

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| **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 | | 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 |
| INFLAMMATORY DISORDERS  Dermatomyositis Chronic hepatitis  Systemic lupus erythematosus | |
| 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 |
| 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 | |

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| **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

**3404 Part XXXIII** ◆ Rehabilitation Medicine

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| **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 GABAB 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 GABAA 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, α2-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 α2 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. |

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| **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.

**3424 Part XXXIV** ◆ Environmental Health Hazards

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| **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 |

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| **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 |

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| **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) |

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| **Table 721-4** | Chelation Therapy | | | |
| **NAME** | | **SYNONYM** | **DOSE** | **TOXICITY** |
| Succimer | | Chemet, 2,3-dimercaptosuccinic acid (DMSA) | 350 mg/m2 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\* | | CaNa2EDTA (calcium disodium edetate), versenate | 1,000-1,500 mg/m2 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/m2 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.*

**Chapter 723** ◆ Biologic and Chemical Terrorism **3445**

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| **Table 723-3** Critical Chemical Agents of Terrorism | | | | |
| **AGENT TOXICITY** | **CLINICAL FINDINGS** | **ONSET** | **DECONTAMINATION**\* | **MANAGEMENT** |
| NERVE AGENTS  Tabun, sarin, Anticholinesterase: soman, VX 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  Lewisite Arsenical | Skin: erythema, vesicles  Eye: inflammation Respiratory tract:  inflammation | Hours  Immediate pain | Skin: soap and water Eyes: water (effective only if done within  minutes of exposure) | Symptomatic care  Possibly British antilewisite (BAL) 3 mg/kg IM q4-6h for systemic  effects of lewisite in severe cases |
| PULMONARY AGENTS  Chlorine, Liberate phosgene 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  Skin: soap and water | ABCs, 100% oxygen  Na bicarbonate prn metabolic acidosis; hydroxycobalamin 70 mg/ kg IV (max: 5 g) *or* nitrite/thiosulfate, given as follows (see text):  *Na nitrite (3%): Estimated dose (mL/kg) hemoglobin*  (max: 10 mL) *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.*

**Chapter 724** ◆ Animal and Human Bites **3449**

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| **Table 724-2** | Microorganisms Associated with Bites | |
| DOG BITES | | SWINE BITES |
| *Staphylococcus* species | | *Pasteurella aerogenes* |
| *Streptococcus* species | | *Pasteurella multocida* |
| *Eikenella* species | | *Bacteroides* species |
| *Pasteurella* species | | *Proteus* species |
| *Proteus* species | | *Actinobacillus suis* |
| *Klebsiella* species | | *Streptococcus* species |
| *Haemophilus* species | | *Flavobacterium* species |
| *Enterobacter* species | | *Mycoplasma* species |
| *Capnocytophaga canimorsus Bacteroides* species *Moraxella* species *Corynebacterium* species *Neisseria* 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 |
| *Fusobacterium* species | |
| *Prevotella* species | |
| *Porphyromonas* species | |
| CAT BITES | |
| *Pasteurella* species | |
| *Actinomyces* species | |
| *Propionibacterium* species | |
| *Bacteroides* species | |
| *Fusobacterium* species | |
|  |
| *Clostridium* species | | LARGE REPTILE (CROCODILE, |
| *Wolinella* species | |
| ALLIGATOR) BITES |
| *Peptostreptococcus* species | |
| *Aeromonas hydrophila* |
| *Staphylococcus* species | | *Pseudomonas pseudomallei* |
| *Streptococcus* species | | *Pseudomonas aeruginosa* |
| *Proteus* species *Enterococcus* species *Clostridium* species |
| HERBIVORE BITES  *Actinobacillus lignieresii Actinobacillus suis* | |
| *Pasteurella multocida* | |  |
| *Pasteurella caballi* | |  |
| *Staphylococcus hyicus* subsp. | |  |
| *hyicus* | |  |

|  |  |  |
| --- | --- | --- |
| **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 Yes if any of the following:  and exploration • 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.