

Get Full Access and More at

ExpertConsult.com

Kliegman | Stanton | St Geme | Schor

Nelson

TEXTBOOK *of*
PEDIATRICS

20
EDITION

Volume 1

EDITION

ICS
0

Volume 2

ELSEVIER

ELSEVIER

Nelson Tables



Nelson Tables

Nelson
TEXTBOOK *of*

EDITION 20

PEDIATRICS
Tables

Prepared and Edited By

**Dr. Ahmed Mohammed
Abd Elsattar
Al-Azhar University**

نَسْأَلُكُمُ الْدِيَارَ

CONTENTS

Growth, Development and Behaviour	1
Nutrition	37
Electrolyte and Acid-Base Disorders	50
Pediatric Drug Therapy	57
The Acutely Ill Child	63
Human Genetics	79
Metabolic Disorders	91
The Newborn Infant	109
Adolescent Development	142
Immunology	148
Allergic Disorders	162
Rheumatic Diseases of Childhood	191
Infectious Diseases	212
The Digestive System	300
Respiratory System	341
The Cardiovascular System	366
Diseases of the Blood	393
Cancer and Benign Tumors	411
Nephrology	428
Gynecologic Problems of Childhood	445
The Endocrine System	450
The Nervous System	477
Disorders of the Eye	546
The Ear	555
The Skin	563
Bone and Joint Disorders	571
Rehabilitation Medicine and others	583

Growth, Development and Behaviour

NEWBORN	NUTRITION	DIARRHEA	PNEUMONIA
Breastfeeding promotion including initiation			
	Improved water source, sanitation, and hygiene Preventive vitamin A supplementation Preventive zinc supplementation		
Periconceptional folic acid supplementation or fortification Multiple micronutrient/iron-folate supplementation in pregnancy Maternal balanced energy protein supplementation Maternal calcium supplementation			
ORS Antibiotics for dysentery		ORS Antibiotics for dysentery	
Case management of pneumonia			Case management of pneumonia
IPTp case management, Syphilis detection and treatment Tetanus toxoid vaccination Diabetes case management Fetal growth restriction detection Hypertensive disease prevention and case management Induction of labor for pregnancies after 41 weeks Active management of the third stage of labor Clean birth practices Labor and delivery management ANS for preterm labor Antibiotics for preterm premature rupture of membranes Immediate assessment and stimulation Neonatal resuscitation Thermal care Chlorhexidine cord application Clean postnatal practices Hospital care of preterm babies including Kangaroo mother care	Appropriate complementary feeding Management of moderate acute malnutrition Management of severe acute malnutrition	Zinc for treatment of diarrhea Rotavirus vaccine	Hib vaccine Pneumococcal vaccine

ANS, antenatal corticosteroid treatment; Hib, *Haemophilus influenzae* type b; IPTp, intermittent preventive treatment of malaria for pregnant women.

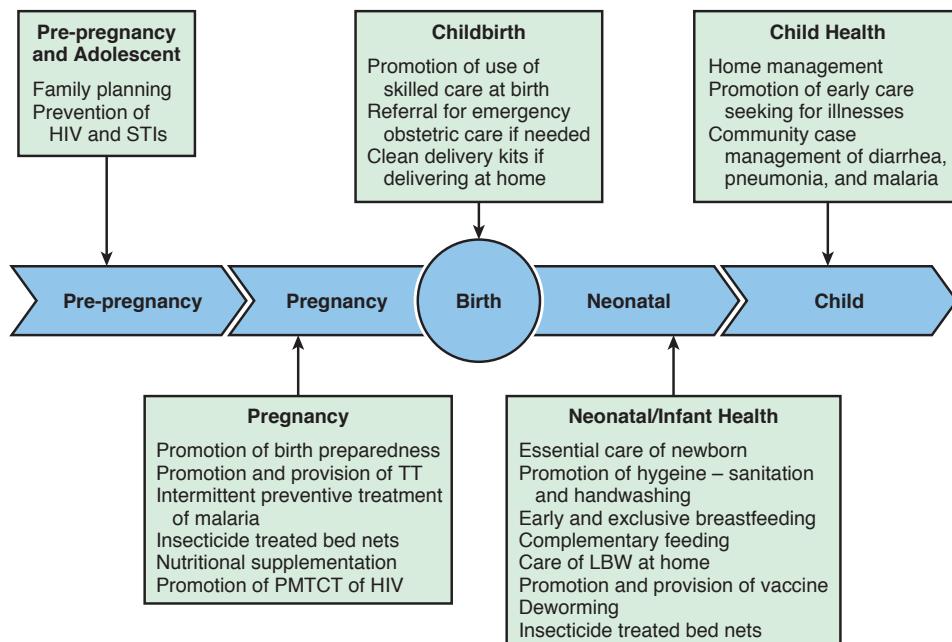
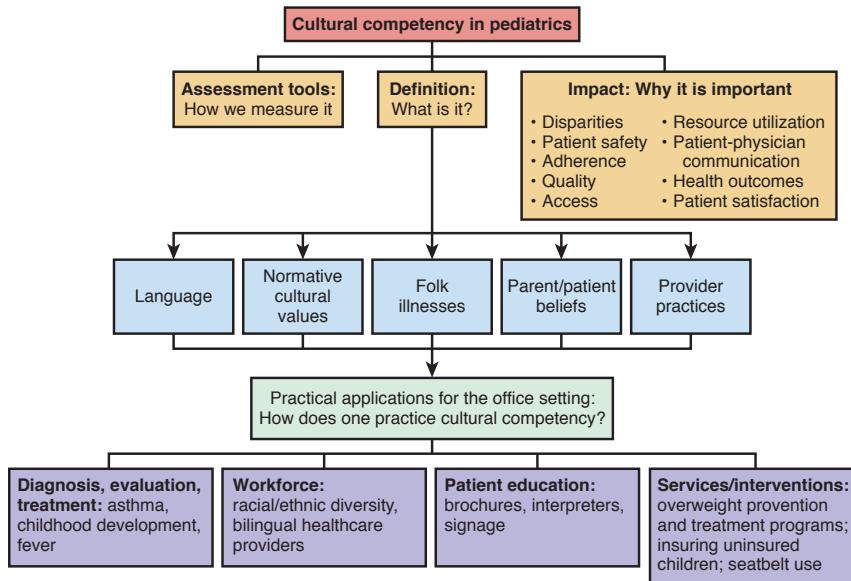


Figure 1-13 Neonatal and child health interventions: delivered by community health workers.

36 Part I ◆ The Field of Pediatrics



Conceptual framework for cultural competency in pediatrics: (1) what is known about the impact of cultural competency on general pediatric care; (2) the domains of cultural competency; and (3) practical applications of cultural competency for general pediatricians

Figure 4-1 Components of cultural competency in pediatric practice. (From Brotanek JM, Seeley CE, Flores G: The importance of cultural competency in general pediatrics, *Curr Opin Pediatr* 20:711-718, 2008, Fig. 1, p. 712.)

Table 4-3 Home Remedies for Fever, Colic, and Teething Among African-Americans			
CONDITION	REMEDY	KNOWLEDGE, % (N = 107)	USE, % (N = 107)
Fever	Acetaminophen*	98	77.6
	Cool bath*	85	48.3
	Isopropyl alcohol*	71	38.3
	Cool drinks/popsicles†	11.2	0
	Undress child†	10.3	0
	Ibuprofen†	10.3	0
	Warm feet†	8.4	0
Colic	Potatoes or onions in socks†	6.5	0
	Catnip*	34.6	8.4
	Senna extract*	25.2	4.7
	Other (asafetida, paregoric, or bicarbonate)†	13.1	0
	Chamomile*	7.5	0
	Walk†	6.5	0
	Cigarette smoke†	5.6	0
	Simethicone drops†	4.7	0
	Vacuum/steam†	3.7	0
	Cover head†	3.7	0
	Massage†	2.8	0
	Gripe water*	1.9	0
Teething	Nonprescription benzocaine gel*	97.2	57
	Teething object†	35.2	7.5
	Whiskey*	34.6	1.9
	Penny*	16.8	0
	Ice cubes/popsicles†	13.3	0
	Egg†	11.4	0
	Spices (asafetida, cloves, or vanilla)†	4.8	0

*Responses given in closed-ended questions.

†Responses given in open-ended questions.

From Smitherman LC, Janisse J, Mathur A: The use of folk remedies among children in an urban black community: remedies for fever, colic and teething, *Pediatrics* 115:297-304, 2005, Table 2.

66 Part II ◇ Growth, Development, and Behavior

MILESTONE	AVERAGE AGE OF ATTAINMENT (MO)	DEVELOPMENTAL IMPLICATIONS
GROSS MOTOR		
Holds head steady while sitting	2	Allows more visual interaction
Pulls to sit, with no head lag	3	Muscle tone
Brings hands together in midline	3	Self-discovery of hands
Asymmetric tonic neck reflex gone	4	Can inspect hands in midline
Sits without support	6	Increasing exploration
Rolls back to stomach	6.5	Truncal flexion, risk of falls
Walks alone	12	Exploration, control of proximity to parents
Runs	16	Supervision more difficult
FINE MOTOR		
Grasps rattle	3.5	Object use
Reaches for objects	4	Visuomotor coordination
Palmar grasp gone	4	Voluntary release
Transfers object hand to hand	5.5	Comparison of objects
Thumb-finger grasp	8	Able to explore small objects
Turns pages of book	12	Increasing autonomy during book time
Scribbles	13	Visual-motor coordination
Builds tower of 2 cubes	15	Uses objects in combination
Builds tower of 6 cubes	22	Requires visual, gross, and fine motor coordination
COMMUNICATION AND LANGUAGE		
Smiles in response to face, voice	1.5	More active social participant
Monosyllabic babble	6	Experimentation with sound, tactile sense
Inhibits to "no"	7	Response to tone (nonverbal)
Follows one-step command with gesture	7	Nonverbal communication
Follows one-step command without gesture	10	Verbal receptive language (e.g., "Give it to me")
Says "mama" or "dada"	10	Expressive language
Points to objects	10	Interactive communication
Speaks first real word	12	Beginning of labeling
Speaks 4-6 words	15	Acquisition of object and personal names
Speaks 10-15 words	18	Acquisition of object and personal names
Speaks 2-word sentences (e.g., "Mommy shoe")	19	Beginning grammaticalization, corresponds with 50 word vocabulary
COGNITIVE		
Stares momentarily at spot where object disappeared	2	Lack of object permanence (out of sight, out of mind [e.g., yarn ball dropped])
Stares at own hand	4	Self-discovery, cause and effect
Bangs 2 cubes	8	Active comparison of objects
Uncovers toy (after seeing it hidden)	8	Object permanence
Egocentric symbolic play (e.g., pretends to drink from cup)	12	Beginning symbolic thought
Uses stick to reach toy	17	Able to link actions to solve problems
Pretend play with doll (e.g., gives doll bottle)	17	Symbolic thought

Table 10-2 Emerging Patterns of Behavior During the 1st Yr of Life*

NEONATAL PERIOD (1ST 4 WK)	
Prone:	Lies in flexed attitude; turns head from side to side; head sags on ventral suspension
Supine:	Generally flexed and a little stiff
Visual:	May fixate face on light in line of vision; "doll's-eye" movement of eyes on turning of the body
Reflex:	Moro response active; stepping and placing reflexes; grasp reflex active
Social:	Visual preference for human face
AT 1 MO	
Prone:	Legs more extended; holds chin up; turns head; head lifted momentarily to plane of body on ventral suspension
Supine:	Tonic neck posture predominates; supple and relaxed; head lags when pulled to sitting position
Visual:	Watches person; follows moving object
Social:	Body movements in cadence with voice of other in social contact; beginning to smile
AT 2 MO	
Prone:	Raises head slightly farther; head sustained in plane of body on ventral suspension
Supine:	Tonic neck posture predominates; head lags when pulled to sitting position
Visual:	Follows moving object 180 degrees
Social:	Smiles on social contact; listens to voice and coos
AT 3 MO	
Prone:	Lifts head and chest with arms extended; head above plane of body on ventral suspension
Supine:	Tonic neck posture predominates; reaches toward and misses objects; waves at toy
Sitting:	Head lag partially compensated when pulled to sitting position; early head control with bobbing motion; back rounded
Reflex:	Typical Moro response has not persisted; makes defensive movements or selective withdrawal reactions
Social:	Sustained social contact; listens to music; says "aah, ngah"
AT 4 MO	
Prone:	Lifts head and chest, with head in approximately vertical axis; legs extended
Supine:	Symmetric posture predominates, hands in midline; reaches and grasps objects and brings them to mouth
Sitting:	No head lag when pulled to sitting position; head steady, tipped forward; enjoys sitting with full truncal support
Standing:	When held erect, pushes with feet
Adaptive:	Sees raisin, but makes no move to reach for it
Social:	Laughs out loud; may show displeasure if social contact is broken; excited at sight of food
AT 7 MO	
Prone:	Rolls over; pivots; crawls or creep-crawls (Knobloch)
Supine:	Lifts head; rolls over; squirms
Sitting:	Sits briefly, with support of pelvis; leans forward on hands; back rounded
Standing:	May support most of weight; bounces actively
Adaptive:	Reaches out for and grasps large object; transfers objects from hand to hand; grasp uses radial palm; rakes at raisin
Language:	Forms polysyllabic vowel sounds
Social:	Prefers mother; babbles; enjoys mirror; responds to changes in emotional content of social contact
AT 10 MO	
Sitting:	Sits up alone and indefinitely without support, with back straight
Standing:	Pulls to standing position; "cruises" or walks holding on to furniture
Motor:	Creeps or crawls
Adaptive:	Grasps objects with thumb and forefinger; pokes at things with forefinger; picks up pellet with assisted pincer movement; uncovers hidden toy; attempts to retrieve dropped object; releases object grasped by other person
Language:	Repetitive consonant sounds ("mama," "dada")
Social:	Responds to sound of name; plays peek-a-boo or pat-a-cake; waves bye-bye
AT 1 YR	
Motor:	Walks with one hand held; rises independently, takes several steps (Knobloch)
Adaptive:	Picks up raisin with unassisted pincer movement of forefinger and thumb; releases object to other person on request or gesture
Language:	Says a few words besides "mama," "dada"
Social:	Plays simple ball game; makes postural adjustment to dressing

*Data are derived from those of Gesell (as revised by Knobloch), Shirley, Provence, Wolf, Bailey, and others.

Data from Knobloch H, Stevens F, Malone AF: Manual of developmental diagnosis, Hagerstown, MD, 1980, Harper & Row.

68 Part II ◆ Growth, Development, and Behavior

Table 10-3 Time of Appearance in X-Rays of Centers of Ossification in Infancy and Childhood		
BOYS—AGE AT APPEARANCE*	BONES AND EPIPHYSEAL CENTERS	GIRLS—AGE AT APPEARANCE*
HUMERUS, HEAD		3 wk
3 wk		
CARPAL BONES		
2 mo ± 2 mo	Capitate	2 mo ± 2 mo
3 mo ± 2 mo	Hamate	2 mo ± 2 mo
30 mo ± 16 mo	Triangular [†]	21 mo ± 14 mo
42 mo ± 19 mo	Lunate [†]	34 mo ± 13 mo
67 mo ± 19 mo	Trapezium [†]	47 mo ± 14 mo
69 mo ± 15 mo	Trapezoid [†]	49 mo ± 12 mo
66 mo ± 15 mo	Scapoid [†]	51 mo ± 12 mo
No standards available	Pisiform [†]	No standards available
METACARPAL BONES		
18 mo ± 5 mo	II	12 mo ± 3 mo
20 mo ± 5 mo	III	13 mo ± 3 mo
23 mo ± 6 mo	IV	15 mo ± 4 mo
26 mo ± 7 mo	V	16 mo ± 5 mo
32 mo ± 9 mo	I	18 mo ± 5 mo
FINGERS (EPIPHYSIS)		
16 mo ± 4 mo	Proximal phalanx, 3rd finger	10 mo ± 3 mo
16 mo ± 4 mo	Proximal phalanx, 2nd finger	11 mo ± 3 mo
17 mo ± 5 mo	Proximal phalanx, 4th finger	11 mo ± 3 mo
19 mo ± 7 mo	Distal phalanx, 1st finger	12 mo ± 4 mo
21 mo ± 5 mo	Proximal phalanx, 5th finger	14 mo ± 4 mo
24 mo ± 6 mo	Middle phalanx, 3rd finger	15 mo ± 5 mo
24 mo ± 6 mo	Middle phalanx, 4th finger	15 mo ± 5 mo
26 mo ± 6 mo	Middle phalanx, 2nd finger	16 mo ± 5 mo
28 mo ± 6 mo	Distal phalanx, 3rd finger	18 mo ± 4 mo
28 mo ± 6 mo	Distal phalanx, 4th finger	18 mo ± 5 mo
32 mo ± 7 mo	Proximal phalanx, 1st finger	20 mo ± 5 mo
37 mo ± 9 mo	Distal phalanx, 5th finger	23 mo ± 6 mo
37 mo ± 8 mo	Distal phalanx, 2nd finger	23 mo ± 6 mo
39 mo ± 10 mo	Middle phalanx, 5th finger	22 mo ± 7 mo
152 mo ± 18 mo	Sesamoid (adductor pollicis)	121 mo ± 13 mo
HIP AND KNEE		
Usually present at birth	Femur, distal	Usually present at birth
Usually present at birth	Tibia, proximal	Usually present at birth
4 mo ± 2 mo	Femur, head	4 mo ± 2 mo
46 mo ± 11 mo	Patella	29 mo ± 7 mo
FOOT AND ANKLE [‡]		

Values represent mean ± standard deviation, when applicable.

*To nearest month.

[†]Except for the capitate and hamate bones, the variability of carpal centers is too great to make them very useful clinically.

[‡]Standards for the foot are available, but normal variation is wide, including some familial variants, so this area is of little clinical use.

The norms present a composite of published data from the Fels Research Institute, Yellow Springs, OH (Pyle SI, Sontag L: AJR Am J Roentgenol 49:102, 1943), and unpublished data from the Brush Foundation, Case Western Reserve University, Cleveland, OH, and the Harvard School of Public Health, Boston, MA. Compiled by Lieb, Buehl, and Pyle.

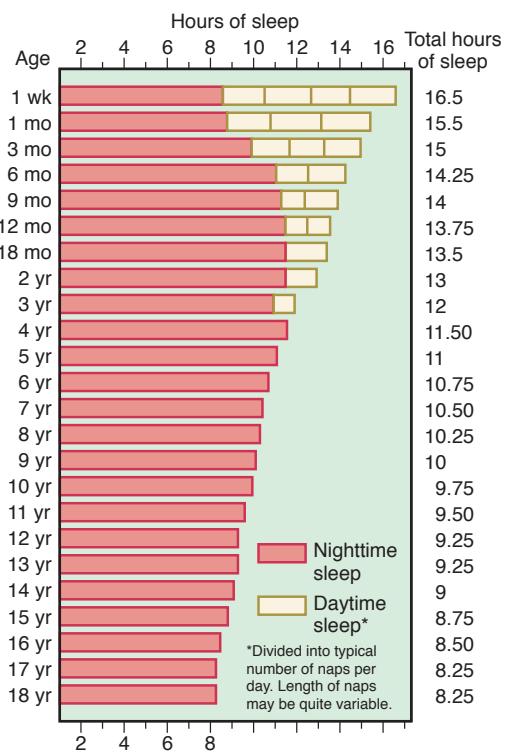


Figure 10-2 Typical sleep requirements in children. (From Ferber R: Solve your child's sleep problems, New York, 1985, Simon & Schuster.)

Table 15-1 Growth and Caloric Requirements

AGE	APPROXIMATE DAILY WEIGHT GAIN (g)	APPROXIMATE MONTHLY WEIGHT GAIN	GROWTH IN LENGTH (cm/mo)	GROWTH IN HEAD CIRCUMFERENCE (cm/mo)	RECOMMENDED DAILY ALLOWANCE (kcal/kg/day)
0-3 mo	30	2 lb	3.5	2.00	115
3-6 mo	20	1.25 lb	2.0	1.00	110
6-9 mo	15	1 lb	1.5	0.50	100
9-12 mo	12	13 oz	1.2	0.50	100
1-3 yr	8	8 oz	1.0	0.25	100
4-6 yr	6	6 oz	3 cm/yr	1 cm/yr	90-100

Adapted from National Research Council, Food and Nutrition Board: Recommended daily allowances, Washington, DC, 1989, National Academy of Sciences; Frank D, Silva M, Needlman R: Failure to thrive: myth and method, Contemp Pediatr 10:114, 1993.

Table 15-3 Chronology of Human Dentition of Primary or Deciduous and Secondary or Permanent Teeth

	Calcification		Age at Eruption		Age at Shedding	
	BEGINS AT	COMPLETE AT	MAXILLARY	MANDIBULAR	MAXILLARY	MANDIBULAR
PRIMARY TEETH						
Central incisors	5th fetal mo	18-24 mo	6-8 mo	5-7 mo	7-8 yr	6-7 yr
Lateral incisors	5th fetal mo	18-24 mo	8-11 mo	7-10 mo	8-9 yr	7-8 yr
Cuspids (canines)	6th fetal mo	30-36 mo	16-20 mo	16-20 mo	11-12 yr	9-11 yr
First molars	5th fetal mo	24-30 mo	10-16 mo	10-16 mo	10-12 yr	10-12 yr
Second molars	6th fetal mo	36 mo	20-30 mo	20-30 mo	10-12 yr	11-13 yr
SECONDARY TEETH						
Central incisors	3-4 mo Max, 10-12 mo	9-10 yr 10-11 yr	7-8 yr 8-9 yr	6-7 yr 7-8 yr		
Lateral incisors	Mand, 3-4 mo					
Cuspids (canines)	4-5 mo	12-15 yr	11-12 yr	9-11 yr		
First premolars (bicuspids)	18-21 mo	12-13 yr	10-11 yr	10-12 yr		
Second premolars (bicuspids)	24-30 mo	12-14 yr	10-12 yr	11-13 yr		
First molars	Birth	9-10 yr	6-7 yr	6-7 yr		
Second molars	30-36 mo	14-16 yr	12-13 yr	12-13 yr		
Third molars	Max, 7-9 yr Mand, 8-10 yr	18-25 yr	17-22 yr	17-22 yr		

Mand, Mandibular; Max, maxillary.

Adapted from a chart prepared by P.K. Losch, Harvard School of Dental Medicine, who provided the data for this table.

100 Part II ◆ Growth, Development, and Behavior

Table 16-3 Red Flags in Developmental Screening and Surveillance

These indicators suggest that development is seriously disordered and that the child should be promptly referred to a developmental or community pediatrician.

Note: Most children do not have "red flags" and thus require quality screening to detect any problems.

POSITIVE INDICATORS (THE PRESENCE OF ANY OF THE FOLLOWING)

Loss of developmental skills at any age

Parental or professional concerns about vision, fixing, or following an object or a confirmed visual impairment at any age (simultaneous referral to pediatric ophthalmology)

Hearing loss at any age (simultaneous referral for expert audiologic or ear, nose, and throat assessment)

Persistently low muscle tone or floppiness

No speech by 18 mo, especially if the child does not try to communicate by other means such as gestures (simultaneous referral for urgent hearing test)

Asymmetry of movements or other features suggestive of cerebral palsy, such as increased muscle tone

Persistent toe walking

Complex disabilities

Head circumference above the 99.6th centile or below 0.4th centile. Also, if circumference has crossed 2 centiles (up or down) on the appropriate chart or is disproportionate to parental head circumference

An assessing clinician who is uncertain about any aspect of assessment but thinks that development may be disordered

NEGATIVE INDICATORS (ACTIVITIES THAT THE CHILD CANNOT DO)

Sit unsupported by 12 mo

Walk by 18 mo (boys) or 2 yr (girls) (check creatine kinase urgently)

Walk other than on tiptoes

Run by 2.5 yr

Hold object placed in hand by 5 mo (corrected for gestation)

Reach for objects by 6 mo (corrected for gestation)

Point at objects to share interest with others by 2 yr

From Bellman M, Byrne O, Sege R: Developmental assessment of children. BMJ 346:31–36, 2013.

Table 16-4 Resources for Developmental–Behavioral Screening/Surveillance in Primary Care

DEVELOPMENTAL–BEHAVIORAL PROMOTION AND PARENT TRAINING

Kids' Health

From the Nemours Foundation, this site has a well-visit guide for each age, anticipatory guidance information, and an easily searchable database for handouts (in English and Spanish) on health and safety, emotional and social development and positive parenting for babies through adolescence.

Reach Out and Read

Offers parenting handouts on how to share books, literacy milestones, and guidance for professionals. Tabs within the site include: Parents and Educators Home, Importance of Reading Aloud, Literacy Milestones, Reading Tips, Books for Children, and Books for Parents.

American Academy of Pediatrics (Information for Families)

The AAP has numerous handouts that can be downloaded for free and available in multiple languages. Provides information on a variety of topics including health conditions, safety and prevention, mental health issues from birth through adolescence.

American Academy of Child and Adolescent Psychiatry

AACAP was one of the first professional organizations to develop handouts for families. These are freely downloadable and cover a wide range of topics as divorce, sleep problems, specific mental health diagnoses, help for military families, and how and where to find a psychiatrist. Handouts are written in many different languages including Spanish, Malaysian, Urdu, Arabic, Icelandic, Polish, and Hebrew. Other site research reviews for professionals, video clips, and links to other resources.

REFERRAL LINKS

American Academy of Pediatrics: Find a Pediatrician

Helps locate developmental-behavioral, neurodevelopmental, general and other subspecialty pediatricians.

Individuals with Disabilities Education Act

Provides links to state, regional and local early intervention programs under the Individuals with Disabilities Education Act, and testing services for young children with suspected or known to have disabilities go to

Early Head Start and Head Start

Provides links to local programs including services for migrant workers, tribal councils, etc.

INTERVENTION SERVICES FOR OLDER CHILDREN

To refer children 3 yr of age and older for evaluations, contact the school district's department of psychology or special education.

For after school/tutoring programs, check with the child's school of zone, and see the websites of the Boys and Girls Club and the YWCA.

TRAINING AND IMPLEMENTATION PLANNING

Medical Home Initiative

From the AAP and focused on coordinated care for children with special healthcare needs, the site has training materials, rating scales, an e-mail announcement list for providers, how-to information, etc. Medical Home also sponsors several conferences each year.

Harvard University

Includes a helpful video showing providers who, although reluctant to try quality screening, found use of tools far more sensitive and less than time-consuming. The site also provides a helpful implementation guide.

PEDStest.org

Includes downloadable implementation planning forms, workflow charts, two-way consent forms, longitudinal problem checklists, age-specific encounter forms, training guides, slide shows, freely downloadable risk and resilience measures, mental health and academic screens for older children, videos offering a rationale for screening, information about tools, guidance on billing and coding, and links to parenting resources in multiple languages.

Table 17-1 Conditions That Do and Do Not Require Exclusion from Group Childcare Settings

CONDITIONS THAT REQUIRE EXCLUSION	COMMENTS
If any of these 3 key criteria for exclusion of children who are ill are met, the child should be temporarily excluded, regardless of the type of illness:	
Illness preventing the child from participating comfortably in activities as determined by the childcare provider	Providers should specify in their policies, approved by the facilities' healthcare consultant, what severity level of illness the facility can manage, and how much and what types of illness will be addressed: <ul style="list-style-type: none">• Severity level 1 consists of children whose health condition is accompanied by high interest and complete involvement in activity associated with an absence of symptoms of illness (such as children recovering from pinkeye, rash, or chickenpox), but who need further recuperation time• Severity level 2 encompasses children whose health condition is accompanied by a medium activity level because of symptoms (such as children with low-grade fever, children at the beginning of an illness, and children in the early recovery period of an illness)• Severity level 3 is composed of children whose health condition is accompanied by a low activity level because of symptoms that preclude much involvement
Illness resulting in a greater need for care than the childcare staff can provide without compromising the health and safety of the other children as determined by the childcare provider	
Illness that poses a risk of spread of harmful diseases to others	
In addition to the above key criteria, temporary exclusion is recommended when the child has any of the following conditions:	
Fever (temperature above 38°C [101°F] orally, above 38.9°C [102°F] rectally, or above 37.8°C [100°F] or higher taken axillary [armpit] or measured by an equivalent method) and behavior change or other signs and symptoms (e.g., sore throat, rash, vomiting, diarrhea)	Accompanied by behavior changes or other signs or symptoms of illness until medical professional evaluation finds the child able to be included at the facility
Acute change in behavior including lethargy/lack of responsiveness, inexplicable irritability or persistent crying, difficult breathing, or having a quickly spreading rash	Until evaluation by a medical professional finds the child able to be included at the facility
Diarrhea (defined by watery stools or decreased form of stool that is not associated with changes of diet). Exclusion is required for all diapered children whose stool is not contained in the diaper and toilet-trained children if the diarrhea is causing soiled pants or clothing	Readmission after diarrhea can occur when diapered children have their stool contained by the diaper (even if the stools remain loose) and when toilet-trained children are continent. Special circumstances that require specific exclusion criteria include the following: <ul style="list-style-type: none">• Toxin-producing <i>Escherichia coli</i> or <i>Shigella</i> infection, until stools are formed and test results of 2 stool cultures obtained from stools produced 24-hr apart do not detect these organisms• <i>Salmonella</i> serotype Typhi infection, until diarrhea resolves and, in children younger than age 5 yr, 3 negative stool cultures obtained with 24-hr-intervals are obtained
Blood or mucus in stool	Not explained by dietary change, medication, or hard stools
Vomiting illness	More than 2 times in the previous 24 hr, unless the vomiting is determined to be caused by a noninfectious condition and the child remains adequately hydrated
Abdominal pain	Persistent (continues more than 2 hr) or intermittent associated with fever or other signs or symptoms
Mouth sores with drooling	Unless the child's primary care provider or local health department authority states that the child is noninfectious
Rash with fever or behavior changes	Until the primary care provider has determined that the illness is not an infectious disease
Active tuberculosis	Until the child's primary care provider or local health department states child is on appropriate treatment and can return
Impetigo	Until treatment has been started
Streptococcal pharyngitis (i.e., strep throat or other streptococcal infection)	Until 24 hr after treatment has been started
Purulent conjunctivitis	Defined as pink or red conjunctiva with white or yellow eye discharge, until after treatment has been initiated
Pediculosis (head lice)	Until after the first treatment Note: Exclusion is not necessary before the end of the program day
Scabies	Until after treatment has been given

Continued

104 Part II ◆ Growth, Development, and Behavior
Table 17-1 Conditions That Do and Do Not Require Exclusion from Group Childcare Settings—cont'd

CONDITIONS THAT REQUIRE EXCLUSION	COMMENTS
Varicella-zoster (chickenpox)	Until all lesions have dried or crusted (usually 6 days after onset of rash)
Rubella	Until 6 days after onset of rash
Pertussis	Until 5 days of appropriate antibiotic treatment
Mumps	Until 5 days after onset of parotid gland swelling
Measles	Until 4 days after onset of rash
Hepatitis A virus	Until 1 wk after onset of illness or jaundice if the child's symptoms are mild or as directed by the health department
Any child determined by the local health department to be contributing to the transmission of illness during an outbreak	
CONDITIONS THAT DO NOT REQUIRE EXCLUSION	COMMENTS
Common colds, runny noses	Regardless of color or consistency of nasal discharge
A cough not associated with an infectious disease or a fever	
Watery, yellow or white discharge or crusting eye discharge without fever, eye pain, or eyelid redness	
Presence of bacteria or viruses in urine or feces in the absence of illness symptoms, like diarrhea	Exceptions include children infected with highly contagious organisms capable of causing serious illness
Pink eye (bacterial conjunctivitis) indicated by pink or red eyelids after sleep	If 2 unrelated children in the same program have conjunctivitis, the organism causing the conjunctivitis may have a higher risk for transmission and a child healthcare professional should be consulted.
Fever without any signs or symptoms of illness in children who are older than 6 mo regardless of whether acetaminophen or ibuprofen was given	If the child is behaving normally but has a fever of below 38.9°C (102°F) rectally or the equivalent, the child should be monitored, but does not need to be excluded for fever alone
Rash without fever and without behavioral changes	
Lice or nits	Exclusion for treatment of an active lice infestation may be delayed until the end of the day
Ringworm	Exclusion for treatment may be delayed until the end of the day
Molluscum contagiosum	Do not require exclusion or covering of lesions
Thrush (i.e., white spots or patches in the mouth or on the cheeks or gums)	
Fifth disease	Once the rash has appeared
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) without an infection or illness that would otherwise require exclusion	Known MRSA carriers or colonized individuals should not be excluded
Cytomegalovirus infection	
Chronic hepatitis B infection	
HIV infection	
Asymptomatic children who have been previously evaluated and found to be shedding potentially infectious organisms in the stool	Children who are continent of stool or who are diapered with formed stools that can be contained in the diaper may return to care
Children with chronic infections conditions that can be accommodated in the program according to the legal requirement of federal law in the Americans with Disabilities Act	The act requires that childcare programs make reasonable accommodations for children with disabilities and/or chronic illnesses, considering each child individually

Adapted from American Academy of Pediatrics, American Public Health Association, National Resource Center for Health and Safety in Child Care and Early Education: Stepping stones to caring for our children: national health and safety performance standards: guidelines for early care and education programs, third edition, Elk Grove Village, IL, 2013, Authors, pp 46–52, available at: <http://nrckids.org/index.cfm/products/stepping-stones-to-caring-for-our-children-3rd-edition-ss3/stepping-stones-to-caring-for-our-children-3rd-edition-ss3/>

Table 19-1 Normal Developmental Changes in Children's Sleep

AGE CATEGORY	SLEEP DURATION AND SLEEP PATTERNS	ADDITIONAL SLEEP ISSUES	SLEEP DISORDERS
Newborn (0-2 mo)	Total sleep: 10-19 hr per 24 hr (average = 13-14.5 hr), may be higher in premature babies Bottlefed babies generally sleep for longer periods (2-5 hr bouts) than breastfed babies (1-3 hr) Sleep periods are separated by 1-2 hr awake No established nocturnal-diurnal pattern in the 1st few wk; sleep is evenly distributed throughout the day and night, averaging 8.5 hr at night and 5.75 hr during the day	The American Academy of Pediatrics issued a formal recommendation in 2005 advocating against bed sharing in the 1st yr of life, instead encouraging proximate but separate sleeping surfaces for mother and infant. Safe sleep practices for infants: <ul style="list-style-type: none">• Place the baby on his or her back to sleep at night and during nap times• Place the baby on a firm mattress with a well-fitting sheet in a safety-approved crib• Do not use pillows or comforters• Cribs should not have corner posts over $\frac{1}{6}$ in high or decorative cutouts• Make sure the baby's face and head stay uncovered and clear of blankets and other coverings during sleep	Most sleep issues that are perceived as problematic at this stage represent a discrepancy between parental expectations and developmentally appropriate sleep behaviors Newborns who are noted by parents to be extremely fussy and persistently difficult to console are more likely to have underlying medical issues, such as colic, gastroesophageal reflux, and formula intolerance
Infant (2-12 mo)	Total sleep: average is 12-13 hr (note that there is great individual variability in sleep times during infancy) Nighttime: average is 9-10 hr Naps: average is 3-4 hr	Sleep regulation or self-soothing involves the infant's ability to negotiate the sleep-wake transition, both at sleep onset and following normal awakenings throughout the night. The capacity to self-soothe begins to develop in the 1st 12 wk of life, and is a reflection of both neurodevelopmental maturation and learning Sleep consolidation, or "sleeping through the night," is usually defined by parents as a continuous sleep episode without the need for parental intervention (e.g., feeding, soothing) from the child's bedtime through the early morning. Infants develop the ability to consolidate sleep between 6 wk and 3 mo	Behavioral insomnia of childhood; sleep onset association type Sleep-related rhythmic movements (head banging, body rocking)
Toddler (1-3 yr)	Total sleep: average is 11-13 hr Nighttime: average is 9.5-10.5 hr Naps: average is 2-3 hr; decrease from 2 naps to 1 at average age of 18 mo	Cognitive, motor, social, language developmental issues impact on sleep Nighttime fears develop; transitional objects, bedtime routines important	Behavioral insomnia of childhood, sleep onset association type Behavioral insomnia of childhood, limit setting type
Preschool (3-5 yr)	Nighttime: average is 9-10 hr Naps decrease from 1 nap to no nap Overall, 26% of 4 yr olds and just 15% of 5 yr olds nap	Persistent cosleeping tends to be highly associated with sleep problems in this age group Sleep problems may become chronic	Behavioral insomnia of childhood, limit setting type Sleepwalking Sleep terrors Nighttime fears/nightmares Obstructive sleep apnea
Middle childhood (6-12 hr)	9-11 hr	School and behavior problems may be related to sleep problems Media and electronics, such as television, computer, video games, and the Internet increasingly compete for sleep time Irregularity of sleep-wake schedules reflects increasing discrepancy between school and non-school night bedtimes and wake times	Nightmares Obstructive sleep apnea Insufficient sleep
Adolescence (>12 yr)	Average sleep duration 7-7.5 hr; only 20% of adolescents overall get the recommended 9-9.25 hr of sleep Later bedtimes; increased discrepancy sleep patterns weekdays/weekends	Puberty-mediated phase delay (later sleep onset and wake times), relative to sleep-wake cycles in middle childhood Earlier required wake times Environmental competing priorities for sleep	Insufficient sleep Delayed sleep phase disorder Narcolepsy Restless legs syndrome/periodic limb movement disorder

Table 19-3 Basic Principles of Healthy Sleep for Adolescents

1. **Wake up and go to bed at about the same time every night.** Bedtime and wake-up time should not differ from school to non-school nights by more than approximately 1 hr.
2. **Avoid sleeping in on weekends** to "catch up" on sleep. This makes it more likely that you will have problems falling asleep.
3. If you take **naps**, they should be **short** (no more than 1 hr) and **scheduled in the early to midafternoon**. However, if you have a problem with falling asleep at night, **napping** during the day may make it worse and should be avoided.
4. **Spend time outside** every day. Exposure to sunlight helps to keep your body's internal clock on track.
5. **Exercise regularly.** Exercise may help you fall asleep and sleep more deeply.
6. **Use your bed for sleeping only.** Don't study, read, listen to music, watch television, etc., on your bed.
7. Make the 30-60 minutes before a **quiet or wind-down time**. Relaxing, calm, enjoyable activities, such as reading a book or listening to calm music, help your body and mind slow down enough to let you get to sleep. Don't study, watch exciting/scary movies, exercise, or get involved in "energizing" activities just before bed.
8. Eat regular meals and **don't go to bed hungry**. A light snack before bed is a good idea; eating a full meal in the hour before bed is not.
9. **Avoid** eating or drinking products containing **caffeine** from dinner time on. These include caffeinated sodas, coffee, tea, and chocolate.
10. **Do not use alcohol.** Alcohol disrupts sleep and may cause you to awaken throughout the night.
11. **Smoking disturbs sleep.** Don't smoke at least 1 hr before bed (and preferably, not at all!).
12. Don't use **sleeping pills, melatonin, or other nonprescription sleep aids** to help you sleep unless specifically recommended by your doctor. These can be dangerous, and the sleep problems often return when you stop taking the medicine.

Table 19-4 Anatomic Factors That Predispose to Obstructive Sleep Apnea and Hypoventilation in Children**NOSE**

Anterior nasal stenosis
Choanal stenosis/atresia
Deviated nasal septum
Seasonal or perennial rhinitis
Nasal polyps, foreign body, hematoma, mass lesion

NASOPHARYNGEAL AND OROPHARYNGEAL

Adenotonsillar hypertrophy
Macroglossia
Cystic hygroma
Velopharyngeal flap repair
Cleft palate repair
Pharyngeal mass lesion

CRANIOFACIAL

Micrognathia/retrognathia
Midface hypoplasia (e.g., trisomy 21, Crouzon, Apert syndrome)
Mandibular hypoplasia (Pierre Robin sequence, Treacher Collins, Cornelia de Lange)
Craniofacial trauma
Skeletal and storage diseases
Achondroplasia
Storage diseases (e.g., glycogen, Hunter, Hurler syndrome)

Table 19-5 American Academy of Pediatrics Clinical Practice Guideline: Diagnosis and Management of Childhood Obstructive Sleep Apnea Syndrome (September 2012)

Key Action Statement 1: Screening for OSAS

As part of routine health maintenance visits, clinicians should inquire whether the child or adolescent snores. If the answer is affirmative or if a child or adolescent presents with signs or symptoms of OSAS, clinicians should perform a more focused evaluation. (Evidence Quality: Grade B; Recommendation Strength: Recommendation.)

Key Action Statement 2A: Polysomnography

If a child or adolescent snores on a regular basis and has any of the complaints or findings of OSAS, clinicians should either (1) obtain a polysomnogram (Evidence Quality A; Key Action strength: Recommendation) or (2) refer the patient to a sleep specialist or otolaryngologist for a more extensive evaluation (Evidence quality D; Key Action strength: Option). (Evidence Quality: Grade A for polysomnography, Grade D for specialist referral; Recommendation Strength: Recommendation.)

Key Action Statement 2B: Alternative Testing

If polysomnography is not available, then clinicians may order alternative diagnostic tests, such as nocturnal video recording, nocturnal oximetry, daytime nap polysomnography, or ambulatory polysomnography. (Evidence Quality: Grade C; Recommendation Strength: Option.)

Key Action Statement 3: Adenotonsillectomy

If a child is determined to have OSAS, has a clinical examination consistent with adenotonsillar hypertrophy, and does not have a contraindication to surgery, the clinician should recommend adenotonsillectomy as the first line of treatment. If the child has OSAS but does not have adenotonsillar hypertrophy, other treatment should be considered (see Key Action Statement 6). Clinical judgment is required to determine the benefits of adenotonsillectomy compared with other treatments in obese children with varying degrees of adenotonsillar hypertrophy. (Evidence Quality: Grade B; Recommendation Strength: Recommendation.)

Key Action Statement 4: High-Risk Patients Undergoing Adenotonsillectomy

Clinicians should monitor high-risk patients undergoing adenotonsillectomy as inpatients postoperatively. (Evidence Quality: Grade B; Recommendation Strength: Recommendation.)

Key Action Statement 5: Reevaluation

Clinicians should clinically reassess all patients with OSAS for persisting signs and symptoms after therapy to determine whether further treatment is required. (Evidence Quality: Grade B; Recommendation Strength: Recommendation.)

Key Action Statement 5B: Reevaluation of High-Risk Patients

Clinicians should reevaluate high-risk patients for persistent OSAS after adenotonsillectomy, including those who had a significantly abnormal baseline polysomnogram, have sequelae of OSAS, are obese, or remain symptomatic after treatment, with an objective test (see Key Action Statement 2) or refer such patients to a sleep specialist. (Evidence Quality: Grade B; Recommendation Strength: Recommendation.)

Key Action Statement 6: CPAP

Clinicians should refer patients for CPAP management if symptoms/signs or objective evidence of OSAS persists after adenotonsillectomy or if adenotonsillectomy is not performed. (Evidence Quality: Grade B; Recommendation Strength: Recommendation.)

Key Action Statement 7: Weight Loss

Clinicians should recommend weight loss in addition to other therapy if a child/adolescent with OSAS is overweight or obese. (Evidence Quality: Grade C; Recommendation Strength: Recommendation.)

Key Action Statement 8: Intranasal Corticosteroids

Clinicians may prescribe topical intranasal corticosteroids for children with mild OSAS in whom adenotonsillectomy is contraindicated or for children with mild postoperative OSAS. (Evidence Quality: Grade B; Recommendation Strength: Option.)

Adapted from Marcus CL, Brooks LJ, Draper KA, et al: Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics* 130:576-584, 2012.

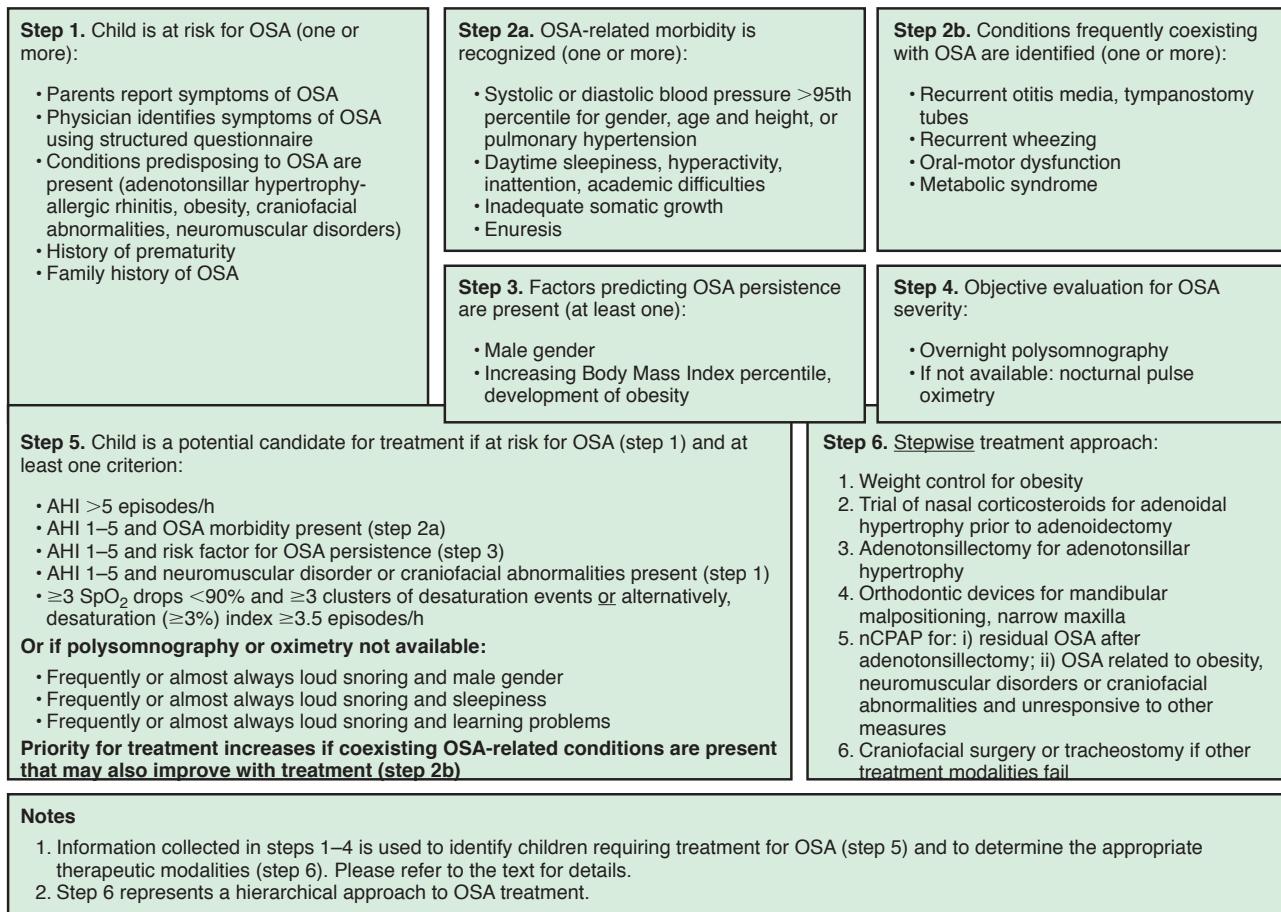
Algorithm for the Diagnosis and Treatment of Pediatric OSA

Figure 19-1 Algorithm for the diagnosis and treatment of pediatric OSA. (From Kaditis A, Kheirandish-Gozal L, Gozal D: Algorithm for the diagnosis and treatment of pediatric OSA: a proposal of two pediatric sleep centers, *Sleep Med* 13(3):217–227, 2012, Figure 1.)

Table 21-3 Medications for ADHD Symptoms

NAME	FDA APPROVED (AGE RANGE IN YEARS)	TARGET SYMPTOMS	USUAL DAILY DOSAGE RANGE	SUGGESTED TOP END OF DAILY DOSAGE RANGE
STIMULANTS				
<i>Long Acting</i>				
Methylphenidate (Concerta)	ADHD (6 and up)	Inattention Hyperactivity Impulsivity	6-12: 18-54 mg >12: 18-72 mg	6-12: 54 mg >12: 72 mg
Dexmethylphenidate (Focalin XR)	ADHD (6 and up)	Inattention Hyperactivity Impulsivity	Child: 5-30 mg	Child: 30 mg
Amphetamine combination (Adderall XR)	ADHD (6 and up)	Inattention Hyperactivity Impulsivity	6-12: 5-10 mg >12: 10-20 mg	6-12: 30 mg >12: 40 mg
Dextroamphetamine (Dexedrine Spansule)	ADHD (6 and up)	Inattention Hyperactivity Impulsivity	5-40 mg	40 mg
<i>Intermediate Acting</i>				
Methylphenidate (Metadate CD, Metadate ER, Ritalin LA, Ritalin SR)	ADHD (6 and up)	Inattention Hyperactivity Impulsivity	10-60 mg	60 mg
<i>Short Acting</i>				
Dexmethylphenidate (Focalin)	ADHD (6 and up)	Inattention Hyperactivity Impulsivity	2.5-20 mg	20 mg
Methylphenidate (Ritalin, Methyltin)	ADHD (6 and up)	Inattention Hyperactivity Impulsivity	5-30 mg	60 mg
Amphetamine combination (Adderall)	ADHD (3 and up)	Inattention Hyperactivity Impulsivity	3-5: 2.5-40 mg >6: 5-40 mg	40 mg
Dextroamphetamine (Dexedrine)	ADHD (6 and up)	Inattention Hyperactivity Impulsivity	2.5-40 mg	40 mg
SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITOR				
Atomoxetine (Strattera)	ADHD (6 and up)	Inattention Hyperactivity Impulsivity	<70 kg: 0.5-1.2 mg/kg >70 kg: 40-80 mg	<70 kg: 1.4 mg/kg >70 kg: 100 mg
α-AGONISTS				
Clonidine (Catapres)	Not approved for ADHD in children & adolescents	Inattention Hyperactivity Impulsivity	27-40.5 kg: 0.05-0.2 mg 40.5-45 kg: 0.05-0.3 mg >45 kg: 0.05-0.4 mg	27-40.5 kg: 0.2 mg 40.5-45 kg: 0.3 mg >45 kg: 0.4 mg
Clonidine (Kapvay)	ADHD (6-17)	Inattention Hyperactivity Impulsivity	0.1-0.4 mg/day	0.4 mg
Guanfacine (Tenex)	Not approved for ADHD in children & adolescents	Inattention Hyperactivity Impulsivity	27-40.5 kg: 0.5-2 mg 40.5-45 kg: 0.5-3 mg >45 kg: 0.5-4 mg	27-40.5 kg: 2 mg 40.5-45 kg: 3 mg >45 kg: 4 mg
Guanfacine (Intuniv)	ADHD (6-17)	Inattention Hyperactivity Impulsivity	1-4 mg	4 mg

ADHD, attention-deficit/hyperactivity disorder.

130 Part III ◆ Behavioral and Psychiatric Disorders

Table 21-4 Medications for Depression and Anxiety Symptoms				
NAME	FDA APPROVED (AGE RANGE IN YEARS)	TARGET SYMPTOMS	USUAL DAILY DOSAGE RANGE	SUGGESTED TOP END OF DAILY DOSAGE
SELECTIVE SEROTONIN REUPTAKE INHIBITORS				
Citalopram (Celexa)	Not approved for anxiety & depression in children & adolescents	Depression Anxiety Obsessions/compulsions	20-40 mg	40 mg
Escitalopram (Lexapro)	Depression (12-17)	Depression Anxiety Obsessions/compulsions	10-20 mg	20 mg
Fluoxetine (Prozac)	Depression (8-17) OCD (7-17)	Depression Anxiety Obsessions/compulsions	10-60 mg	60 mg
Sertraline (Zoloft)	OCD (6-17)	Depression Anxiety Obsessions/compulsions	25-200 mg	200 mg
TRICYCLIC ANTIDEPRESSANTS				
Clomipramine (Anafranil)	OCD (10-17)	Obsessions/compulsions	25-100 mg	Lesser of 200 mg or 3 mg/kg
ATYPICAL ANTIDEPRESSANTS				
Bupropion (Wellbutrin XL)	Not approved for depression in children & adolescents	Depression	150-300 mg	450 mg
Venlafaxine (Effexor XR)	Not approved for anxiety & depression in children & adolescents	Depression Anxiety	75-225 mg	225 mg
ANXIOLYTIC AGENTS				
Lorazepam (Ativan)	Not approved for anxiety	Anxiety	0.5-6 mg	10 mg
Clonazepam (Klonopin)	Not approved for panic in children & adolescents	Panic	0.5-1 mg	4 mg
Buspirone (BuSpar)	Not approved for anxiety & depression in children & adolescents	Anxiety	15-30 mg	60 mg
Hydroxyzine (Atarax, Vistaril)	Anxiety	Anxiety	50 mg >6: 50-100 mg	<6: 2 mg/kg 50 mg >6: 100 mg

ADHD: attention-deficit/hyperactivity disorder; OCD: obsessive-compulsive disorder.

132 Part III ◆ Behavioral and Psychiatric Disorders

Table 21-6 Medications for Mania				
	FDA APPROVED (AGE RANGE IN YEARS)	TARGET SYMPTOMS	USUAL DAILY DOSAGE RANGE	SUGGESTED TOP END OF DAILY DOSAGE
MOOD STABILIZERS				
Lithium carbonate (Eskalith, Eskalith CR, Lithobid)	Bipolar disorder (12-17)	Mania Depression	<22 kg: 600 mg 22-41 kg: 900 mg >41 kg: 1200 mg	1800 mg
Divalproex (Depakote, Depakote ER)	Not approved for mania in children & adolescents	Mania	Teen: 10-60 mg/kg (Blood valproic acid level 50-100 µg/mL)	60 mg/kg
ATYPICAL ANTIPSYCHOTICS				
Aripiprazole (Abilify)	Bipolar disorder (10-17) Schizophrenia (13-17) Irritability in autism (6-17)	Irritability Psychosis Mania Aggression Agitation	2-30 mg	30 mg Autism: 15 mg
Risperidone (Risperdal)	Bipolar disorder (10-17) Schizophrenia (13-17) Irritability in autism (5-17)	Psychosis Mania Aggression Agitation Irritability	0.5-6 mg Autism: 15-20 kg: 0.25 mg-0.5 mg >20 kg: 0.5-1 mg	Bipolar & Schizophrenia: 6 mg Autism: 3 mg

Table 21-5 Medications for Psychosis and Agitation

NAME	FDA APPROVED (AGE RANGE IN YEARS)	TARGET SYMPTOMS	USUAL DAILY DOSAGE RANGE	SUGGESTED TOP END OF DAILY DOSAGE
ATYPICAL ANTIPSYCHOTICS				
Aripiprazole (Abilify)	Bipolar disorder (10-17) Schizophrenia (13-17) Irritability in autism (6-17)	Psychosis Mania Irritability Aggression Agitation	2-30 mg qd	30 mg Autism: 15 mg
Olanzapine (Zyprexa)	Bipolar disorder (13-17) Schizophrenia (13-17)	Psychosis Mania Agitation	2.5-10 mg qd	20 mg
Quetiapine (Seroquel)	Bipolar disorder (10-17) Schizophrenia (13-17)	Psychosis Mania Agitation	Bipolar: 400-600 mg Schizophrenia: 400-800 mg	Bipolar: 600 mg Schizophrenia: 800 mg
Risperidone (Risperdal)	Bipolar disorder (10-17) Schizophrenia (13-17) Irritability in autism (5-17)	Psychosis Mania Aggression Agitation Irritability	0.5-6 mg Autism: 15-20 kg: 0.25 mg-0.5 mg >20 kg: 0.5-1 mg	Bipolar & Schizophrenia: 6 mg Autism: 3 mg
Ziprasidone (Geodon)	Not approved for psychosis, mania, aggression, or agitation in children & adolescents	Psychosis Mania Agitation	40-160 mg	200 mg
TYPICAL ANTIPSYCHOTICS				
Haloperidol (Haldol)	Psychosis (3-17) Tourette (3-17) Severe behavioral disorders (3-17) Agitation (3-17)	Psychosis Mania Aggression Agitation	3-12: 0.05-0.15 mg/kg >12: 0.5-5 mg Agitation: 3-12: 0.01-0.03 mg/kg >12: 0.5-10 mg	3-12: 0.15 mg/kg/day >12: maximum 100 mg for severe refractory cases

Table 22-4 DSM-5 Diagnostic Criteria for Factitious Disorders**Factitious Disorder Imposed on Self**

- A. Falsification of physical or psychological signs or symptoms, or induction of injury or disease, associated with identified deception.
- B. The individual presents himself or herself to others as ill, impaired, or injured.
- C. The deceptive behavior is evident even in the absence of obvious external rewards.
- D. The behavior is not better explained by another mental disorder, such as delusional disorder or another psychotic disorder.

Factitious Disorder Imposed on Another (Previously Factitious Disorder by Proxy)

- A. Falsification of physical or psychological signs or symptoms, or induction of injury or disease, in another, associated with identified deception.
- B. The individual presents another individual (victim) to others as ill, impaired or injured.
- C. The deceptive behavior is evident even in the absence of obvious external rewards.
- D. The behavior is not better explained by another mental disorder, such as delusional disorder or another psychotic disorder.

Note: The perpetrator, not the victim, receives this diagnosis

Adapted from the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, (Copyright 2013). American Psychiatric Association, p. 324.

Table 22-1 DSM-5 Diagnostic Criteria for Conversion Disorder or Functional Neurologic Symptom Disorder

- A. One or more symptoms or deficits affecting voluntary motor or sensory function.
 - B. Clinical findings provide evidence of incompatibility between the symptom and recognized neurologic or medical conditions.
 - C. The symptom or deficit is not better explained by another medical or mental disorder.
 - D. The symptom or deficit causes clinically significant distress or impairment in social, occupational, or other important areas of functioning or warrants medical evaluation.
- Specify symptom type: weakness or paralysis, abnormal movements, swallowing symptoms, speech symptom, attacks/seizures, or anesthesia/sensory loss, special sensory symptom (visual, olfactory, or hearing), or mixed symptoms.

Adapted from the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, (Copyright 2013). American Psychiatric Association, p. 318.

Table 22-2 DSM-5 Diagnostic Criteria for Somatic Symptom Disorder

- A. One or more somatic symptoms that are distressing or result in significant disruption of daily life.
- B. Excessive thoughts, feelings or behaviors related to the somatic symptoms or associated health concerns as manifested by at least one of the following:
 - 1. Disproportionate and persistent thoughts about the seriousness of one's symptoms.
 - 2. Persistent high level of anxiety about health and symptoms.
 - 3. Excessive time and energy devoted to these symptoms or health concerns.
- C. Although any 1 somatic symptom may not be continuously present, the state of being symptomatic is persistent.

Specify if:

With predominant pain (previously known as pain disorder in DSM IV-TR): for individuals whose somatic symptoms predominantly involve pain.

Persistent: A persistent course is characterized by severe symptoms, marked impairment, and long duration (more than 6 mo).

Adapted from the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, (Copyright 2013). American Psychiatric Association, p. 311.

Table 22-5 DSM-5 Diagnostic Criteria for Other Specified/Unspecified Somatic Symptom and Related Disorders

Other Specified

This category applies to presentations in which symptoms characteristic of a somatic symptom and related disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but do not meet full criteria for any of the disorders in the somatic symptom and related disorders diagnostic class.

Examples of presentations that can be specified using the "other specified" designation include the following:

1. Brief somatic symptom disorder: Duration of symptoms is <6 mo.
2. Brief illness anxiety disorder: Duration of symptoms is <6 mo.
3. Illness anxiety disorder without excessive health-related behaviors: Criterion D for illness anxiety disorder is not met.
4. Pseudocyesis: A false belief of being pregnant that is associated with objective signs and reported symptoms of pregnancy.

Unspecified

This category applies to presentations in which symptoms characteristic of a somatic symptom and related disorder that cause clinically significant distress or impairment in functioning predominate but do not meet criteria for any of the other disorders in the somatic symptom and related disorders diagnostic class.

Table 22-3 DSM-5 Diagnostic Criteria for Psychological Factors Affecting Other Medical Conditions

- A. A medical symptom or condition (other than a mental disorder) is present.
- B. Psychological or behavioral factors adversely affect the medical condition in 1 of the following ways:
 1. The factors have influenced the course of the medical condition as shown by a close temporal association between the psychological factors and the development or exacerbation of, or delayed recovery from, the medical condition.
 2. The factors interfere with the treatment of the medical condition (e.g., poor adherence).
 3. The factors constitute additional well-established health risks for the individual.
 4. The factors influence the underlying pathophysiology, precipitating or exacerbating symptoms or necessitating medical attention.
- C. The psychological and behavioral factors in Criterion B are not better explained by another mental disorder (e.g., panic disorder, major depressive disorder, posttraumatic stress disorder).

Adapted from the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, (Copyright 2013). American Psychiatric Association, p. 322.

Table 24-1 DSM-5 Diagnostic Criteria for Tic Disorders

Note: A tic is a sudden, rapid, recurrent, nonrhythmic motor movement or vocalization.

TOURETTE'S DISORDER

- A. Both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently.
- B. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset.
- C. Onset is before age 18 years.
- D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).

PERSISTENT (CHRONIC) MOTOR OR VOCAL TIC DISORDER

- A. Single or multiple motor or vocal tics have been present during the illness, but not both motor and vocal.
- B. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset.
- C. Onset is before age 18 years.
- D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).
- E. Criteria have never been met for Tourette's disorder.

Specify if:

With motor tics only

With vocal tics only

PROVISIONAL TIC DISORDER

- A. Single or multiple motor and/or vocal tics.
- B. The tics have been present for less than 1 year since first tic onset.
- C. Onset is before age 18 years.
- D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).
- E. Criteria have never been met for Tourette's disorder or persistent (chronic) motor or vocal tic disorder.

Table 24-3 Diagnostic Criteria Proposed for Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS)

CRITERION	DESCRIPTION
I.	Abrupt, dramatic onset of obsessive-compulsive disorder or severely restricted food intake
II.	Concurrent presence of additional neuropsychiatric symptoms, with similarly severe and acute onset, from at least 2 of the following 7 categories (see text for full description): <ol style="list-style-type: none"> 1. Anxiety 2. Emotional lability and/or depression 3. Irritability, aggression and/or severely oppositional behaviors 4. Behavioral (developmental) regression 5. Deterioration in school performance 6. Sensory or motor abnormalities 7. Somatic signs and symptoms, including sleep disturbances, enuresis or urinary frequency
III.	Symptoms are not better explained by a known neurologic or medical disorder, such as Sydenham chorea, systemic lupus erythematosus, Tourette disorder or others. Note: The diagnostic work-up of patients suspected of PANS must be comprehensive enough to rule out these and other relevant disorders. The nature of the co-occurring symptoms will dictate the necessary assessments, which may include MRI scan, lumbar puncture, electroencephalogram or other diagnostic tests.

From the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, (Copyright 2013). American Psychiatric Association, p. 81.

Table 24-2 Repetitive Movements of Childhood

	DESCRIPTION	TYPICAL DISORDERS WHERE PRESENT
Tics	Sudden rapid, recurrent, nonrhythmic, stereotyped, vocalization or motor movement	Transient tics, Tourette disorder, persistent tic disorder
Dystonia	Involuntary, sustained, or intermittent muscle contractions that cause twisting and repetitive movements, abnormal postures, or both	DYT1 Gene, Wilson, myoclonic dystonia, extrapyramidal symptoms caused by dopamine blocking agents
Chorea	Involuntary, random, quick, jerking movements, most often of the proximal extremities, that flow from joint to joint. Movements are abrupt, nonrepetitive, and arrhythmic and have variable frequency and intensity	Sydenham chorea, Huntington chorea
Stereotypies	Stereotyped, rhythmic, repetitive movements or patterns of speech, with lack of variation over time	Autism, stereotypic movement disorder, intellectual disability
Compulsions	A repetitive, excessive, meaningless activity or mental exercise that a person performs in an attempt to avoid distress or worry	Obsessive-compulsive disorder, anorexia, body dysmorphic disorder, trichotillomania, excoriation disorder
Myoclonus	Shock-like involuntary muscle jerk that may affect a single body region, one side of the body, or the entire body; may occur as a single jerk or repetitive jerks	Hiccups, hypnic jerks, Lennox-Gastaut syndrome, juvenile myoclonic epilepsy, mitochondrial encephalopathies, metabolic disorders
Akathisia	Unpleasant sensations of "inner" restlessness, often prompting movements in an effort to reduce the sensations	Extrapyramidal adverse effects from dopamine blocking agents; anxiety
Volitional behaviors	Behavior that may be impulsive or due to boredom like tapping peers, making sounds (animal noises)	Attention-deficit/hyperactivity disorder, oppositional defiant disorder, sensory integration disorders

Adapted from Murphy TK, Lewin AB, Storch EA, et al: Practice parameter for the assessment and treatment of children and adolescents with chronic tic disorders, J Am Acad Child Adolesc Psychiatry 52(12):1341–1359, 2013.

Table 26-1 DSM-5 Diagnostic Criteria for Major Depressive Episode

- A. Five (or more) of the following symptoms have been present during the same 2 wk period and represent a change from previous functioning; at least 1 of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
1. Depressed most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). **Note:** In children and adolescents, can be irritable mood.
 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
 3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. **Note:** In children, consider failure to make expected weight gain.
 4. Insomnia or hypersomnia nearly every day.
 5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
 6. Fatigue or loss of energy nearly every day.
 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The episode is not attributable to the physiological effects of a substance or to another medical condition.
- Note:** Criteria A-C represent a major depressive episode.
- D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizopreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
- E. There has never been a manic episode or a hypomanic episode.

Table 26-2 DSM-5 Diagnostic Criteria for Persistent Depressive Disorder

- A. Depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others, for at least 2 yr.
- Note:** In children and adolescents, mood can be irritable and duration must be at least 1 yr.
- B. Presence, while depressed, of 2 (or more) of the following:
1. Poor appetite or overeating.
 2. Insomnia or hypersomnia.
 3. Low energy or fatigue.
 4. Low self-esteem.
 5. Poor concentration or difficulty making decisions.
 6. Feelings of hopelessness.
- C. During the 2 yr period (1 yr for children or adolescents) of the disturbance, the individual has never been without the symptoms in Criteria A and B for more than 2 mo at a time.
- D. Criteria for a major depressive disorder may be continuously present for 2 yr.
- E. There has never been a manic episode or a hypomanic episode, and criteria have never been met for cyclothymic disorder.
- F. The disturbance is not better explained by a persistent schizoaffective disorder, schizophrenia, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder.
- G. The symptoms are not attributable to the physiologic effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hypothyroidism).
- H. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- Note:** Because the criteria for a major depressive episode include 4 symptoms that are absent from the symptom list for persistent depressive disorder (dysthymia), a very limited number of individuals will have depressive symptoms that have persisted longer than 2 yr but will not meet criteria for persistent depressive disorder. If full criteria for a major depressive episode have been met at some point during the current episode of illness, they should be given a diagnosis of major depressive disorder. Otherwise, a diagnosis of other specified depressive disorder or unspecified depressive disorder is warranted.

Table 28-1 DSM-5 Diagnostic Criteria for Anorexia Nervosa

- A. Restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health. Significantly low weight is defined as a weight that is less than minimally normal or, for children and adolescents, less than that minimally expected.
- B. Intense fear of gaining weight or of becoming fat, or persistent behavior that interferes with weight gain, even though at a significantly low weight.
- C. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight.

Specify whether:

Restricting type (ICD-10-CM code F50.01): During the last 3 mo, the individual has not engaged in recurrent episodes of binge eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas). This subtype describes presentations in which weight loss is accomplished primarily through dieting, fasting, and/or excessive exercise.

Binge-eating/purging type (ICD-10-CM code F50.02): During the last 3 mo, the individual has engaged in recurrent episodes of binge eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas).

Specify if:

In partial remission: After full criteria for anorexia nervosa were previously met, Criterion A (low body weight) has not been met for a sustained period, but either Criterion B (intense fear of gaining weight or becoming fat or behavior that interferes with weight gain) or Criterion C (disturbances in self-perception of weight and shape) is still met.

In full remission: After full criteria for anorexia nervosa were previously met, none of the criteria have been met for a sustained period of time.

Specify current severity:

The minimum level of severity is based, for adults, on current body mass index (BMI) (see below) or, for children and adolescents, on BMI percentile. The ranges below are derived from World Health Organization categories for thinness in adults; for children and adolescents, corresponding BMI percentiles should be used. The level of severity may be increased to reflect clinical symptoms, the degree of functional disability, and the need for supervision.

Mild: $BMI \geq 17 \text{ kg/m}^2$

Moderate: $BMI 16\text{--}16.99 \text{ kg/m}^2$

Severe: $BMI 15\text{--}15.99 \text{ kg/m}^2$

Extreme: $BMI < 15 \text{ kg/m}^2$

Table 28-2 DSM-5 Diagnostic Criteria for Bulimia Nervosa

- A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
 - 1. Eating, in a discrete period of time (e.g., within any 2 hr period), an amount of food that is definitely larger than what most individuals would eat in a similar period of time under similar circumstances.
 - 2. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating).
- B. Recurrent inappropriate compensatory behaviors in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, or other medications; fasting; or excessive exercise.
- C. The binge eating and inappropriate compensatory behaviors both occur, on average, at least once a week for 3 mo.
- D. Self-evaluation is unduly influenced by body shape and weight.
- E. The disturbance does not occur exclusively during episodes of anorexia nervosa.

Specify if:

In partial remission: After full criteria for bulimia nervosa were previously met, some, but not all, of the criteria have been met for a sustained period of time.

In full remission: After full criteria for bulimia nervosa were previously met, none of the criteria have been met for a sustained period of time.

Specify current severity:

The minimum level of severity is based on the frequency of inappropriate compensatory behaviors (see below). The level of severity may be increased to reflect other symptoms and the degree of functional disability.

Mild: An average of 1-3 episodes of inappropriate compensatory behaviors per week.

Moderate: An average of 4-7 episodes of inappropriate compensatory behaviors per week.

Severe: An average of 8-13 episodes of inappropriate compensatory behaviors per week.

Extreme: An average of 14 or more episodes of inappropriate compensatory behaviors per week.

Adapted from the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, (Copyright 2013). American Psychiatric Association, p. 345.

Table 28-3 DSM-5 Diagnostic Criteria for Avoidant/Restrictive Food Intake Disorder

- A. An eating or feeding disturbance (e.g., apparent lack of interest in eating or food; avoidance based on the sensory characteristics of food; concern about aversive consequences of eating) as manifested by persistent failure to meet appropriate nutritional and/or energy needs associated with one (or more) of the following:
 - 1. Significant weight loss (or failure to achieve expected weight gain or faltering growth in children).
 - 2. Significant nutritional deficiency.
 - 3. Dependence on enteral feeding or oral nutritional supplements.
 - 4. Marked interference with psychosocial functioning.
- B. The disturbance is not better explained by lack of available food or by an associated culturally sanctioned practice.
- C. The eating disturbance does not occur exclusively during the course of anorexia nervosa or bulimia nervosa, and there is no evidence of a disturbance in the way in which one's body weight or shape is experienced.
- D. The eating disturbance is not attributable to a concurrent medical condition or not better explained by another mental disorder. When the eating disturbance occurs in the context of another condition or disorder, the severity of the eating disturbance exceeds that routinely associated with the condition or disorder and warrants additional clinical attention.

Specify if:

In remission: After full criteria for avoidant/restrictive food intake disorder were previously met, the criteria have not been met for a sustained period of time.

Table 28-4 Eating and Weight Control Habits Commonly Found in Children and Adolescents with an Eating Disorder

HABIT	Prominent Feature		Clinical Comments Regarding Eating Disorder Habits	
	ANOREXIA NERVOSA	BULIMIA NERVOSA	ANOREXIA NERVOSA	BULIMIA NERVOSA
Overall intake	Inadequate energy (calories), although volume of food and beverages may be high because of very low caloric density of intake as a result of "diet" and nonfat choices	Variable, but calories normal to high; intake in binges often "forbidden" food or drink that differs from intake at meals	Consistent inadequate caloric intake leading to wasting of the body is an essential feature of diagnosis	Inconsistent balance of intake, exercise and vomiting, but severe caloric restriction is short-lived
Food	Counts and limits calories, especially from fat; Emphasis on "healthy food choices" with reduced caloric density Monotonous, limited "good" food choices, often leading to vegetarian or vegan diet Strong feelings of guilt after eating more than planned leads to exercise and renewed dieting	Aware of calories and fat, but less regimented in avoidance than AN Frequent dieting interspersed with overeating, often triggered by depression, isolation, or anger	Obsessive-compulsive attention to nutritional data on food labels and may have "logical" reasons for food choices in highly regimented pattern, such as sports participation or family history of lipid disorder	Choices less structured, with more frequent diets
Beverages	Water or other low- or no-calorie drinks; nonfat milk	Variable, diet soda common; may drink alcohol to excess	Fluids often restricted to avoid weight gain	Fluids ingested to aid vomiting or replace losses
Meals	Consistent schedule and structure to meal plan Reduced or eliminated caloric content, often starting with breakfast, then lunch, then dinner Volume can increase with fresh fruits, vegetables, and salads as primary food sources	Meals less regimented and planned than in AN; more likely impulsive and unregulated, often eliminated following a binge-purge episode	Rigid adherence to "rules" governing eating leads to sense of control, confidence, and mastery	Elimination of a meal following a binge-purge only reinforces the drive for binge later in the day
Snacks	Reduced or eliminated from meal plan	Often avoided in meal plans, but then impulsively eaten	Snack foods removed early because "unhealthy"	Snack "comfort foods" can trigger a binge
Dieting	Initial habit that becomes progressively restrictive, although often appearing superficially "healthy" Beliefs and "rules" about the patient's idiosyncratic nutritional requirements and response to foods are strongly held	Initial dieting gives way to chaotic eating, often interpreted by the patient as evidence of being "weak" or "lazy"	Distinguishing between healthy meal planning with reduced calories and dieting in ED may be difficult	Dieting tends to be impulsive and short-lived, with "diets" often resulting in unintended weight gain
Binge eating	None in restrictive subtype, but an essential feature in binge-purge subtype	Essential feature, often secretive Shame and guilt prominent afterward	Often "subjective" (more than planned but not large)	Relieves emotional distress, may be planned
Exercise	Characteristically obsessive-compulsive, ritualistic, and progressive May excel in dance, long-distance running	Less predictable May be athletic, or may avoid exercise entirely	May be difficult to distinguish active thin vs. ED	Males often use exercise as means of "purging"
Vomiting	Characteristic of binge-purge subtype May chew, then spit out, rather than swallow, food as a variant	Most common habit intended to reduce effects of overeating Can occur after meal as well as a binge	Physiologic and emotional instability prominent	Strongly "addictive" and self-punishing, but does not eliminate calories ingested—many still absorbed
Laxatives	If used, generally to relieve constipation in restrictive subtype, but as a cathartic in binge-purge subtype	Second most common habit used to reduce or avoid weight gain, often used in increasing doses for cathartic effect	Physiologic and emotional instability prominent	Strongly "addictive," self-punishing, but ineffective means to reduce weight (calories are absorbed in the small intestine, but laxatives work in the colon)
Diet pills	Very rare, if used; more common in binge-purge subtype	Used to either reduce appetite or increase metabolism	Use of diet pills implies inability to control eating	Control over eating may be sought by any means

AN, anorexia nervosa; BN, bulimia nervosa; ED, eating disorder.

Table 28-5 Symptoms Commonly Reported by Patients with an Eating Disorder

SYMPTOMS	Diagnosis		CLINICAL COMMENTS REGARDING ED SYMPTOMS
	ANOREXIA NERVOSA	BULIMIA NERVOSA	
Body image	Feels fat, even with extreme emaciation, often with specific body distortions (e.g., stomach, thighs); Strong drive for thinness, with self-efficacy closely tied to appraisal of body shape, size, and/or weight	Variable body image distortion and dissatisfaction, but drive for thinness is less than the desire to avoid gaining weight	Challenging a patient's body image is both ineffective and counter-therapeutic clinically Accepting the patient's expressed body image but noting its discrepancy with symptoms and signs reinforces concept that patient can "feel" fat but also "be" too thin and unhealthy
Metabolism	Hypometabolic symptoms include feeling cold, tired, and weak and lacking energy May be both bothersome and reinforcing	Variable, depending on balance of intake and output and hydration	Symptoms are evidence of body's "shutting down" in an attempt to conserve calories with an inadequate diet Emphasizing reversibility of symptoms with healthy eating and weight gain can motivate patients to cooperate with treatment
Skin	Dry skin, delayed healing, easy bruising, goose flesh Orange-yellow skin on hands	No characteristic symptom, self-injurious behavior may be seen	Skin lacks good blood flow and the ability to heal in low weight Carotenemia with large intake of β-carotene foods; reversible
Hair	Lanugo-type hair growth on face and upper body Slow growth and increased loss of scalp hair	No characteristic symptom	Body hair growth conserves energy Scalp hair loss can worsen during refeeding "telogen effluvium" (resting hair is replaced by growing hair) Reversible with continued healthy eating
Eyes	No characteristic symptom	Subconjunctival hemorrhage	Caused by increased intrathoracic pressure during vomiting
Teeth	No characteristic symptom	Erosion of dental enamel erosion Decay, fracture, and loss of teeth	Intraoral stomach acid resulting from vomiting etches dental enamel, exposing softer dental elements
Salivary glands	No characteristic symptom	Enlargement (no to mild tenderness)	Caused by chronic binge eating and induced vomiting, with parotid enlargement more prominent than submandibular; reversible
Heart	Dizziness, fainting in restrictive subtype Palpitations more common in binge-purge subtype	Dizziness, fainting, palpitations	Dizziness and fainting due to postural orthostatic tachycardia and dysregulation at hypothalamic and cardiac level with weight loss, as a result of hypovolemia with binge-purge Palpitations and arrhythmias often caused by electrolyte disturbance Symptoms reverse with weight gain and/or cessation of binge-purge
Abdomen	Early fullness and discomfort with eating Constipation Perceives contour as "fat," often preferring well-defined abdominal musculature	Discomfort after a binge Cramps and diarrhea with laxative abuse	Weight loss is associated with reduced volume and tone of GI tract musculature, especially the stomach Laxatives may be used to relieve constipation or as a cathartic Symptom reduction with healthy eating can take weeks to occur
Extremities and musculoskeletal	Cold, blue hands and feet	No characteristic symptoms Self-cutting or burning on wrists or arms	Energy-conserving low body temperature with slow blood flow most notable peripherally Quickly reversed with healthy eating
Nervous system	No characteristic symptom	No characteristic symptom	Neurologic symptoms suggest a diagnosis other than an ED
Mental status	Depression, anxiety, obsessive-compulsive symptoms, alone or in combination	Depression; PTSD; borderline personality disorder traits	Underlying mood disturbances can worsen with dysfunctional weight control practices and can improve with healthy eating AN patients might report emotional "numbness" with starvation, preferable to emotionality associated with healthy eating

AN, anorexia nervosa; BN, bulimia nervosa; ED, eating disorder; GI, gastrointestinal; PTSD, posttraumatic stress disorder.

Table 28-6 Signs Commonly Found in Patients with Eating Disorders Relative to Prominent Feature of Weight Control

PHYSICAL SIGN	Prominent Feature		CLINICAL COMMENTS RELATED TO EATING DISORDER SIGNS
	RESTRICTIVE INTAKE	BINGE EATING/PURGING	
General appearance	Thin to cachetic, depending on balance of intake and output Might wear bulky clothing to hide thinness and might resist being examined	Thin to overweight, depending on the balance of intake and output through various means	Examine in hospital gown Weight loss more rapid with reduced intake and excessive exercise Binge eating can result in large weight gain, regardless of purging behavior Appearance depends on balance of intake and output and overall weight control habits
Weight	Low and falling (if previously overweight may be normal or high); may be falsely elevated if patient drinks fluids or adds weights to body before being weighed	Highly variable, depending on balance of intake and output and state of hydration Falsification of weight is unusual	Weigh in hospital gown with no underwear, after voiding (measure urine SG) Remain in gown until physical exam completed to identify possible fluid loading (low urine SG, palpable bladder) or adding weights to body
Metabolism	Hypothermia: temp < 35.5°C (95.9°F), pulse < 60 beats/min Slowed psychomotor response with very low core temperature	Variable, but hypometabolic state is less common than in AN	Hypometabolism related to disruption of hypothalamic control mechanisms as a result of weight loss Signs of hypometabolism (cold skin, slow capillary refill, acrocyanosis) most evident in hands and feet, where energy conservation is most active
Skin	Dry Increased prominence of hair follicles Orange or yellow hands	Calluses over proximal knuckle joints of hand (Russell's sign)	Carotenemia with large intake of β-carotene foods Russell's sign: maxillary incisors abrasion develops into callus with chronic digital pharyngeal stimulation, usually on dominant hand
Hair	Lanugo-type hair growth on face and upper body Scalp hair loss, especially prominent in parietal region	No characteristic sign	Body hair growth conserves energy Scalp hair loss "telogen effluvium" can worsen weeks after refeeding begins, as hair in resting phase is replaced by growing hair
Eyes	No characteristic sign	Subconjunctival hemorrhage	Increased intrathoracic pressure during vomiting
Teeth	No characteristic sign	Eroded dental enamel and decayed, fractured, missing teeth	Perimolysis, worse on lingual surfaces of maxillary teeth, is intensified by brushing teeth without preceding water rinse
Salivary glands	No characteristic sign	Enlargement, relatively nontender	Parotid > submandibular involvement with frequent and chronic binge eating and induced vomiting
Throat	No characteristic sign	Absent gag reflex	Extinction of gag response with repeated pharyngeal stimulation
Heart	Bradycardia, hypotension, and orthostatic pulse differential > 25 beats/min	Hypovolemia if dehydrated	Changes in AN resulting from central hypothalamic and intrinsic cardiac function Orthostatic changes less prominent if athletic, more prominent if associated with purging
Abdomen	Scaphoid, organs may be palpable but not enlarged, stool-filled left lower quadrant	Increased bowel sounds if recent laxative use	Presence of organomegaly requires investigation to determine cause Constipation prominent with weight loss
Extremities and musculoskeletal system	Cold, acrocyanosis, slow capillary refill Edema of feet Loss of muscle, subcutaneous, and fat tissue	No characteristic sign, but may have rebound edema after stopping chronic laxative use	Signs of hypometabolism (cold) and cardiovascular dysfunction (slow capillary refill and acrocyanosis) in hands and feet Edema, caused by capillary fragility more than hypoproteinemia in AN, can worsen in early phase of refeeding
Nervous system	No characteristic sign	No characteristic sign	Water loading before weigh-ins can cause acute hyponatremia
Mental status	Anxiety about body image, irritability, depressed mood, oppositional to change	Depression, evidence of PTSD, more likely suicidal than AN	Mental status often improves with healthier eating and weight; SSRIs only shown to be effective for BN

AN, anorexia nervosa; BN, bulimia nervosa; PTSD, posttraumatic stress disorder; SG, specific gravity; SSRI, selective serotonin reuptake inhibitor.

Table 30-1 DSM-5 Diagnostic Criteria for Autism Spectrum Disorder

- A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history:
 - 1. Deficits in social-emotional reciprocity.
 - 2. Deficits in nonverbal communicative behaviors used for social interaction.
 - 3. Deficits in developing, maintaining, and understanding relationships.
- B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history:
 - 1. Stereotyped or repetitive motor movements, use of objects, or speech.
 - 2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior.
 - 3. Highly restricted, fixated interests that are abnormal in intensity or focus.
 - 4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment.
- C. Symptoms must be present in the early developmental period (may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).
- D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
- E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay.

Table 30-4 Medical and Genetic Evaluation of Children with Autism Spectrum Disorder

Recommended evaluations
Careful physical examination to identify dysmorphic physical features
Macrocephaly
Wood's lamp examination for tuberous sclerosis
Formal audiologic evaluation
Lead test; repeat periodically in children with pica
Chromosomal microarray
Consider if results of above evaluation are normal and if accompanying intellectual impairment
FISH test for region 15q11q13 to rule out duplications in Prader-Willi/Angelman syndrome
Fluorescence in situ hybridization (FISH) test for telomeric abnormalities
Test for mutations in MECP2 gene (Rett syndrome) in females
DNA testing for fragile X syndrome
Metabolic testing to consider based on clinical features (emesis, hypotonia, lethargy, ataxia, coarse facial features of a storage disease, multiple organs involved)
Fasting blood glucose
Plasma amino acids
Ammonia and lactate
Fatty acid profile, paroxysmal
Carnitine
Acylcarnitine, quantitative
Homocysteine
Urine amino acids
Urine organic acids
Urine purine/pyrimidines
Urine acylglycine, random
Plasma 7-dehydrocholesterol (Smith-Lemli-Opitz disease screening)
Medical testing to consider based on clinical features
Complete blood cell count
Liver enzymes
Biotinidase
Thyroxine, thyroid-stimulating hormone
Ceruloplasmin/serum copper
EEG if the following clinical features are noted
Clinically observable seizures
History of significant regression in social or communication functioning

Table 30-5 Level of Evidence for Pharmacologic Treatment of Target Symptoms in Autism Spectrum Disorder

CLASS	AGENT	PRIMARY TARGET SYMPTOM(S)	LEVEL OF EVIDENCE
α_2 -Agonist	Clonidine Guanfacine	Hyperactivity Hyperactivity	Insufficient Insufficient
Antipsychotics	Aripiprazole Haloperidol Risperidone Risperidone Olanzapine	Irritability, hyperactivity, stereotypy Behavioral symptoms Irritability, hyperactivity Repetitive behavior, stereotypy Global functioning	Established Established Established Preliminary Insufficient
Mood stabilizers	Divalproex sodium/Valproic acid Lamotrigine Levetiracetam	Irritability, repetitive behavior Irritability, social behavior Irritability	Insufficient Insufficient Insufficient
Norepinephrine reuptake inhibitors	Atomoxetine	Hyperactivity	Preliminary
Serotonin reuptake inhibitors	Citalopram Fluoxetine Clomipramine	Repetitive behavior Repetitive behavior Repetitive behavior, stereotypy, irritability, hyperactivity	Insufficient Insufficient Insufficient
Stimulants	Methylphenidate	Hyperactivity	Promising
Miscellaneous	Amantadine Naltrexone Naltrexone Pentoxifylline	Hyperactivity, irritability Social behavior, communication, indiscriminant learning, SIB Hyperactivity Irritability, social withdrawal	Insufficient Insufficient Preliminary Preliminary

Established, >2 strong studies or >4 adequate studies in separate settings; Insufficient, lack of research or mixed outcomes; Preliminary, >1 adequate study; Promising, >2 adequate studies.

Adapted from Siegel M, Beaulieu AA. Psychotropic medications in child with autism spectrum disorders: A systematic review and synthesis for evidenced based practice. J Autism Dev Disord 42(8):1592–1605, 2012.

Table 30-2 Signs and Symptoms of Possible Autism in Preschool Children (or Equivalent Mental Age)

Social interaction and reciprocal communication behaviors	Eye contact, pointing, and other gestures
Spoken language	<ul style="list-style-type: none"> Reduced or absent use of gestures and facial expressions to communicate (although may place an adult's hand on objects) Reduced and poorly integrated gestures, facial expressions, body orientation, eye contact (looking at people's eyes when speaking), and speech used in social communication Reduced or absent social use of eye contact (assuming adequate vision) Reduced or absent "joint attention" (when 1 person alerts another to something by means of gazing, finger pointing, or other verbal or nonverbal indication for the purpose of sharing interest). This would be evident in the child from lack of: <ul style="list-style-type: none"> Gaze switching Following a point (looking where the other person points to—may look at hand) Using pointing at or showing objects to share interest
Responding to others	<ul style="list-style-type: none"> Absent or delayed response to name being called, despite normal hearing Reduced or absent responsive social smiling Reduced or absent responsiveness to other people's facial expressions or feelings Unusually negative response to the requests of others ("demand avoidance" behavior) Rejection of cuddles initiated by parent or carer, although the child himself or herself may initiate cuddles
Interacting with others	<ul style="list-style-type: none"> Reduced or absent awareness of personal space, or unusually intolerant of people entering their personal space Reduced or absent social interest in others, including children of his or her own age—may reject others; if interested in others, he or she may approach others inappropriately, seeming to be aggressive or disruptive Reduced or absent imitation of others' actions Reduced or absent initiation of social play with others, plays alone Reduced or absent enjoyment of situations that most children like—for example, birthday parties Reduced or absent sharing of enjoyment
	Ideas and imagination
	<ul style="list-style-type: none"> Reduced or absent imagination and variety of pretend play
	Unusual or restricted interests and/or rigid and repetitive behaviors
	<ul style="list-style-type: none"> Repetitive "stereotypical" movements such as hand flapping; body rocking while standing; spinning; finger flicking Repetitive or stereotyped play—for example, opening and closing doors Over focused or unusual interests Excessive insistence on following own agenda Extremes of emotional reactivity to change or new situations; insistence on things being "the same" Over-reaction or under-reaction to sensory stimuli, such as textures, sounds, smells Excessive reaction to the taste, smell, texture, or appearance of food, or having extreme food fads

From Baird G, Douglas HR, Murphy MS: Recognizing and diagnosing autism in children and young people: summary of NICE guidance. *BMJ* 343:d6360, 2011, Box 1, p. 901.

Table 30-3 DSM-5 Severity Levels for Autism Spectrum Disorder

SEVERITY LEVEL	SOCIAL COMMUNICATION	RESTRICTED, REPETITIVE BEHAVIORS
Level 3 "Requiring very substantial support"	Severe deficits in verbal and nonverbal social communication skills cause severe impairments in functioning, very limited initiation of social interactions, and minimal response to social overtures from others. <i>For example</i> , a person with few words of intelligible speech who rarely initiates interaction and, when he or she does, makes unusual approaches to meet needs only and responds to only very direct social approaches	Inflexibility of behavior, extreme difficulty coping with change, or other restricted/repetitive behaviors markedly interfere with functioning in all spheres. Great distress/difficulty changing focus or action.
Level 2 "Requiring substantial support"	Marked deficits in verbal and nonverbal social communication skills; social impairments apparent even with supports in place; limited initiation of social interactions; and reduced or abnormal responses to social overtures from others. <i>For example</i> , a person who speaks simple sentences, whose interaction is limited to narrow special interests, and who has markedly odd nonverbal communication	Inflexibility of behavior, difficulty coping with change, or other restricted/repetitive behaviors appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress and/or difficulty changing focus or action.
Level 1 "Requiring support"	Without supports in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful responses to social overtures of others. May appear to have decreased interest in social interactions. <i>For example</i> , a person who is able to speak in full sentences and engages in communication but whose to-and-fro conversation with others fails, and whose attempts to make friends are odd and typically unsuccessful	Inflexibility of behavior causes significant interference with functioning in one or more contexts. Difficulty switching between activities. Problems of organization and planning hamper independence.

From the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (Copyright 2013). American Psychiatric Association, p. 52.

Table 33-1 DSM-5 Diagnostic Criteria for Attention-Deficit/Hyperactivity Disorder**DIAGNOSTIC CRITERIA**

1. A persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):

1. **Inattention:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:
 - **Note:** The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.
 - 1. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or during other activities (e.g., overlooks or misses details, work is inaccurate).
 - 2. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading).
 - 3. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction).
 - 4. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., starts tasks but quickly loses focus and is easily sidetracked).
 - 5. Often has difficulty organizing tasks and activities (e.g., difficulty managing sequential tasks; difficulty keeping materials and belongings in order; messy, disorganized work; has poor time management; fails to meet deadlines).
 - 6. Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework; for older adolescents and adults, preparing reports, completing forms, reviewing lengthy papers).
 - 7. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).
 - 8. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts).
 - 9. Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments).

2. **Hyperactivity and impulsivity:** Six (or more) of the following symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities:

- **Note:** The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.
 1. Often fidgets with or taps hands or feet or squirms in seat.
 2. Often leaves seat in situations when remaining seated is expected (e.g., leaves his or her place in the classroom, in the office or other workplace, or in other situations that require remaining in place).
 3. Often runs about or climbs in situations where it is inappropriate. (**Note:** In adolescents or adults, may be limited to feeling restless.)
 4. Often unable to play or engage in leisure activities quietly.
 5. Is often "on the go," acting as if "driven by a motor" (e.g., is unable to be or uncomfortable being still for extended time, as in restaurants, meetings; may be experienced by others as being restless or difficult to keep up with).
 6. Often talks excessively.
 7. Often blurts out an answer before a question has been completed (e.g., completes people's sentences; cannot wait for turn in conversation).
 8. Often has difficulty waiting his or her turn (e.g., while waiting in line).
 9. Often interrupts or intrudes on others (e.g., butts into conversations, games, or activities; may start using other people's things without asking or receiving permission; for adolescents and adults, may intrude into or take over what others are doing).
2. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.
 3. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities).
 4. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.
 5. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

Specify whether:

- **Combined presentation:** If both Criterion A1 (inattention) and Criterion A2 (hyperactivity-impulsivity) are met for the past 6 months.
- **Predominantly inattentive presentation:** If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity-impulsivity) is not met for the past 6 months.
- **Predominantly hyperactive/impulsive presentation:** If Criterion A2 (hyperactivity-impulsivity) is met and Criterion A1 (inattention) is not met for the past 6 months.

Specify if:

- **In partial remission:** When full criteria were previously met, fewer than the full criteria have been met for the past 6 months, and the symptoms still result in impairment in social, academic, or occupational functioning.

Specify current severity:

- **Mild:** Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning.
- **Moderate:** Symptoms or functional impairment between "mild" and "severe" are present.
- **Severe:** Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.

Table 33-2 Differences Between U.S. and European Criteria for ADHD or HKD	
DSM-5 ADHD	ICD-10 HKD
SYMPTOMS	
Either or both of following: At least 6 of 9 inattentive symptoms At least 6 of 9 hyperactive or impulsive symptoms	All of following: At least 6 of 8 inattentive symptoms At least 3 of 5 hyperactive symptoms At least 1 of 4 impulsive symptoms
PERVASIVENESS	
Some impairment from symptoms is present in >1 setting	Criteria are met for >1 setting

ADHD, attention-deficit/hyperactivity disorder; DSM-5, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*; HKD, hyperkinetic disorder; ICD-10, *International Classification of Diseases, 10th edition*.

Adapted from Biederman J, Faraone S: Attention-deficit hyperactivity disorder, *Lancet* 366:237–248, 2005.

Table 33-3 Differential Diagnosis of Attention-Deficit/Hyperactivity Disorder	
PSYCHOSOCIAL FACTORS	
Response to physical or sexual abuse	
Response to inappropriate parenting practices	
Response to parental psychopathology	
Response to acculturation	
Response to inappropriate classroom setting	
DIAGNOSES ASSOCIATED WITH ADHD BEHAVIORS	
Fragile X syndrome	
Fetal alcohol syndrome	
Pervasive developmental disorders	
Obsessive-compulsive disorder	
Gilles de la Tourette syndrome	
Attachment disorder with mixed emotions and conduct	
MEDICAL AND NEUROLOGIC CONDITIONS	
Thyroid disorders (including general resistance to thyroid hormone)	
Heavy metal poisoning (including lead)	
Adverse effects of medications	
Effects of abused substances	
Sensory deficits (hearing and vision)	
Auditory and visual processing disorders	
Neurodegenerative disorder, especially leukodystrophies	
Posttraumatic head injury	
Postencephalitic disorder	

Note: Coexisting conditions with possible ADHD presentation include oppositional defiant disorder, anxiety disorders, conduct disorder, depressive disorders, learning disorders, and language disorders. Presence of 1 or more of the symptoms of these disorders can fall within the spectrum of normal behavior, whereas a range of these symptoms may be problematic but fall short of meeting the full criteria for the disorder.

From Reiff MI, Stein MT: Attention-deficit/hyperactivity disorder evaluation and diagnosis: a practical approach in office practice, *Pediatr Clin North Am* 50:1019–1048, 2003. Adapted from Reiff MI: Attention-deficit/hyperactivity disorders. In Bergman AB, editor: 20 Common problems in pediatrics, New York, 2001, McGraw-Hill, p 273.

Table 36-1 Identification of Cause in Children with Severe Intellectual Disability		
CAUSE	EXAMPLES	PERCENT OF TOTAL
Chromosomal disorder	Trisomies 21, 18, 13, Deletion 1p36 Klinefelter syndrome Wolf Hirschhorn syndrome	~20
Genetic syndrome	Fragile X syndrome Prader-Willi syndrome Rett syndrome	~20
Nonsyndromic autosomal mutations	Variations in copy number, de novo mutations in SYNGAP1, GRIK2, TUSC3, oligosaccharyl transferase, and others	~10
Developmental brain abnormality	Hydrocephalus ± meningocele, lissencephaly	~8
Inborn errors of metabolism or neurodegenerative disorder	PKU, Tay-Sachs, various storage diseases	~7
Congenital infections	HIV, toxoplasmosis, rubella, CMV, syphilis, herpes simplex	~3
Familial intellectual disability	Environment, syndromic, or genetic	~5
Perinatal causes	HIE, meningitis, IVH, PVL, fetal alcohol syndrome	4
Postnatal causes	Trauma (abuse), meningitis, hypothyroidism	~4
Unknown	Cerebral palsy	20

CMV, Cytomegalovirus; HIE, hypoxic ischemic encephalopathy; HIV, human immunodeficiency virus; IVH, intraventricular hemorrhage; PKU, phenylketonuria; PVL, periventricular leukomalacia.

Modified from Stromme P, Hayberg G: Aetiology in severe and mild mental retardation: a population based study of Norwegian children, *Dev Med Child Neurol* 42:76–86, 2000.

Table 33-4 Medications Used in the Treatment of Attention-Deficit/Hyperactivity Disorder

GENERIC NAME	BRAND NAME	DURATION	DOSAGE RANGE	SIDE EFFECTS
METHYLPHENIDATE				
Immediate-release	Ritalin, Methylin	3-4 hr	5, 10, 20 mg tabs	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics, priapism
Extended-release	Metadate ER, Methylin ER,	4-6 hr	10, 20 mg extended- release tabs	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics, priapism
	Metadate-CD	8-10 hr	10, 20, 30 mg extended- release caps	
	Ritalin LA Concerta	8-10 hr 10-12 hr	20, 30, 40 mg caps 18, 27, 36, 54 mg caps	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics
Sustained-release	Ritalin SR, Methylphenidate SR	4-6 hr	20 mg sustained- release tabs	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics, priapism
Transdermal system	Daytrana	≥12 hr	Patch	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics, priapism
DEXMETHYLPHENIDATE				
	Focalin	4-6 hr	2.5, 5, 10 mg tabs	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics
Extended-release	Focalin XR	6-8 hr		Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics
DEXTRAMPHETAMINE				
Short-acting	Dexedrine, DextroStat	4-6 hr	5, 10, 15 mg tabs	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics
Intermediate-acting	Dexedrine, Spansule	6-8 hr	5, 10, 20 mg tabs	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics
Lisdexamfetamine	Vyvanse	≤12 hr	30 mg, 50 mg, 70 mg tablets	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics
MIXED AMPHETAMINE SALTS				
Intermediate-acting	Adderall	4-6 hr	5, 10, 20 mg tabs	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics
Extended-release	Adderall XR	8-12 hr	5, 10, 15, 20, 25, 30 mg caps	Moderate appetite suppression, mild sleep disturbances, transient weight loss, irritability, emergence of tics
ATOMOXETINE				
Extended-release	Strattera	12 hr	10, 18, 25, 40, 60 mg caps	Nervousness, sleep problems, fatigue, stomach upset, dizziness, dry mouth
Bupropion Bupropion	Wellbutrin Wellbutrin SR, Wellbutrin XL	4-5 hr	100, 150 mg tabs 100, 150, 200 mg tabs	Can lead in rare cases to severe liver injury or to suicidal ideation Difficulty sleeping, headache, seizures
TRICYCLIC ANTIDEPRESSANTS				
Imipramine	Tofranil	Variable	See Table 21-4	Nervousness, sleep problems, fatigue, stomach upset, dizziness, dry mouth, accelerated heart rate
Desipramine* Nortriptyline	Norpramin Aventyl, Pamelor			
α-AGONISTS				
Clonidine	Catapres, Kapvay	6-12 hr	3-10 µg/kg/day bid-qid	Sedation, depression, dry mouth, rebound hypertension on discontinuing, confusion
Guanfacine	Tenex, Intuniv	6-12 hr	1, 2, 3 mg tabs	Hypotension, lightheadedness

cap, capsule; tab, tablet.

*Associated with deaths from cardiac problems. Not recommended for children.

Table 36-2 Common Presentations of Intellectual Disability By Age

AGE	AREA OF CONCERN
Newborn	Dysmorphic syndromes, (multiple congenital anomalies), microcephaly Major organ system dysfunction (e.g., feeding and breathing)
Early infancy (2-4 mo)	Failure to interact with the environment Concerns about vision and hearing impairments
Later infancy (6-18 mo)	Gross motor delay
Toddlers (2-3 yr)	Language delays or difficulties
Preschool (3-5 yr)	Language difficulties or delays Behavior difficulties, including play Delays in fine motor skills: cutting, coloring, drawing
School age (>5 yr)	Academic underachievement Behavior difficulties (attention, anxiety, mood, conduct, etc.)

208 Part IV ◆ Learning Disorders

Table 35-1 Normal Language Milestones	
HEARING AND UNDERSTANDING	TALKING
BIRTH TO 3 MONTHS Startles to loud sounds Quiets or smiles when spoken to Seems to recognize your voice and quiets if crying Increases or decreases sucking behavior in response to sound	Makes pleasure sounds (cooing, gooing) Cries differently for different needs Smiles when sees you
4-6 MO Moves eyes in direction of sounds Responds to changes in tone of your voice Notices toys that make sounds Pays attention to music	Babbling sounds more speech-like, with many different sounds, including <i>p, b, and m</i> Vocalizes excitement and displeasure Makes gurgling sounds when left alone and when playing with you
7 MO-1 YEAR Enjoys games such as peekaboo and pat-a-cake Turns and looks in direction of sounds Listens when spoken to Recognizes words for common items, such as cup, shoe, and juice Begins to respond to requests (<i>Come here. Want more?</i>)	Babbling has both long and short groups of sounds, such as <i>tata upup bibibibi</i> . Uses speech or noncrying sounds to get and keep attention Imitates different speech sounds Has 1 or 2 words (<i>bye-bye, Dada, Mama</i>), although they might not be clear
1-2 YR Points to a few body parts when asked Follows simple commands and understands simple questions (<i>Roll the ball. Kiss the baby. Where's your shoe?</i>) Listens to simple stories, songs, and rhymes Points to pictures in a book when named	Says more words every month Uses some 1-2 word questions (<i>Where kitty? Go bye-bye? What's that?</i>) Puts 2 words together (<i>more cookie, no juice, mommy book</i>) Uses many different consonant sounds at the beginning of words
2-3 YR Understands differences in meaning (e.g., go-stop, in-on, big-little, up-down) Follows 2-step requests (<i>Get the book and put it on the table.</i>)	Has a word for almost everything Uses 2-3 word "sentences" to talk about and ask for things Speech is understood by familiar listeners most of the time Often asks for or directs attention to objects by naming them
3-4 YR Hears you when you call from another room Hears television or radio at the same loudness level as other family members Understands simple who, what, where, why questions	Talks about activities at school or at friends' homes Usually understood by people outside the family Uses a lot of sentences that have ≥4 words Usually talks easily without repeating syllables or words
4-5 YR Pays attention to a short story and answers simple questions about it Hears and understands most of what is said at home and in school	Voice sounds as clear as other children's Uses sentences that include details (<i>I like to read my books.</i>) Tells stories that stick to a topic Communicates easily with other children and adults Says most sounds correctly except a few, such as <i>l, s, r, v, z, ch, sh, and th</i> Uses the same grammar as the rest of the family

Adapted from American Speech-Language-Hearing Association, 2005. <http://www.asha.org/public/speech/development/chart.htm>.

Table 35-3 Speech and Language Screening		
REFER FOR SPEECH-LANGUAGE EVALUATION IF:		
AT AGE	RECEPTIVE	EXPRESSIVE
15 mo	Does not look/point at 5-10 objects	Is not using 3 words
18 mo	Does not follow simple directions ("get your shoes")	Is not using Mama, Dad, or other names
24 mo	Does not point to pictures or body parts when they are named	Is not using 25 words
30 mo	Does not verbally respond or nod/shake head to questions	Is not using unique 2-word phrases, including noun-verb combinations
36 mo	Does not understand prepositions or action words; does not follow 2-step directions	Has a vocabulary of <200 words; does not ask for things; echolalia to questions; language regression after attaining 2-word phrases

Table 36-3 Suggested Evaluation of the Child with Intellectual Disability/Global Developmental Delay

TEST	COMMENT
In-depth history	Includes pre-, peri-, and postnatal events (including seizures); developmental attainments; and 3-generation pedigree in family history
Physical examination	Particular attention to minor or subtle abnormalities; neurologic examination for focal and skull abnormalities Behavioral phenotype
Vision and hearing evaluation	Essential to detect and treat; can mask as developmental delay
Gene microarray analysis	A 7.8% yield overall (10% in syndromic and 6.5% in nonsyndromic intellectual disability) Better resolution than Karyotype. May identify up to twice as many abnormalities as karyotyping. Excellent in detecting de novo microdeletions or microduplications
Karyotype	Yield 4% in global developmental delay/intellectual disability Best for inversions and balanced insertions, reciprocal translocations, and polyploidy
Fragile X screen	Combined yield 2% Preselection on clinical grounds can increase yield to 7.6%
X-linked candidate intellectual disability genes	May explain up to 10% of intellectual disability Yield may be as high as 42% if there is a definite family history and as high as 17% from a possibly linked kindred
Exomic gene sequencing	Detects inherited and de novo point mutations especially in nonsyndromic severe intellectual disability
Neuroimaging	MRI preferred. Positives increased by abnormalities of skull contour or microcephaly and macrocephaly, or focal neurologic examination. Overall has a higher yield Identification of specific etiologies is rare. Most conditions that are found do not alter the treatment plan. Need to weigh risk of sedation against possible yield
Thyroid (T_4 , TSH)	Near 0% in settings with universal newborn screening program
Serum lead	If there are identifiable risk factors for excessive environmental lead exposure
Metabolic testing	Yield 0.2-4.6% based on clinical indicators and tests performed Urine organic acids, plasma amino acids, ammonia, lactate, and a capillary blood gas. Focused testing based on clinical findings is warranted Tandem mass spectrometry newborn screening has allowed for identification of many disorders in perinatal period and have decreased yield in older children. Other disorders have emerged; e.g., congenital disorders of glycosylation and disorders of creatine synthesis and transport
MECP2 for Rett syndrome	1.5% of females with severe intellectual disability 0.5% of males
EEG	May be deferred in absence of history of seizures
Repeated history and physical examination	Can give time for maturation of physical and behavioral phenotype. New technology may be available for evaluation

EEG, Electroencephalogram; CGH, comparative genomic hybridization; MECP2, methyl CpG binding protein 2; T_4 , thyroxine; TSH, thyroid-stimulating hormone.

Based on Michelson DJ, Shevell MI, Sherr EH, et al: Evidence report: Genetic and metabolic testing on children with global developmental delay: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of Child Neurology. *Neurology* 77:1629-35, 2011; Curry CJ, Stevenson RE, Aughton D, et al: Evaluation of mental retardation: recommendations of a Consensus Conference: American College of Medical Genetics. *Am J Med Genet* 12:72:468-477, 1997. Shapiro BK, Batshaw ML: Mental retardation. In Burg FD, Ingelfinger JR, Polin RA, et al: *Gellis and Kagan's current pediatric therapy*, ed 18, Philadelphia, 2005, WB Saunders, used with permission; and Shevell M, Ashwal S, Donley D, et al: Practice parameter: evaluation of the child with global developmental delay, *Neurology* 60:367-380, 2003.

250 Part V ◆ Children with Special Needs

Table 41-1 Historical Factors About the Period After the Neonatal Period to Be Considered in an Evaluation of Growth Failure Using a Biopsychosocial Model	
BIOLOGICAL SPHERE <p>Frequency and source of routine medical care Growth measurements Immunization status Medical illnesses Hospitalizations Medications Allergies—medications, food, other Surgeries Injuries, including bruises on infants Feeding issues—vigorous or difficult feeder Breastfeeding:<ul style="list-style-type: none">• Milk letdown• Sense of fullness/emptying• Frequency and duration of feedings• Maternal observation of baby swallowing• Maternal diet and medical problems while breastfeedingFormula feeding:<ul style="list-style-type: none">• Type• Method of mixing (concentration)• Frequency and quantity of feedingsOther intake in first few months of life, such as:<ul style="list-style-type: none">• Water• Juice• Tea• Soda• CerealSleep schedule Baby's temperament Developmental milestones Use of alternative or complementary medicines</p>	PSYCHOSOCIAL SPHERES <p>Provision of baby care, especially feeding Maternal sleep deprivation Postnatal depression or other mental illness Type and amount of social support Availability of respite for mother Involvement of father and/or other intimate partner Intimate partner violence Financial resources, including money for baby supplies Enrollment in governmental aid programs Parental reaction to fussing/crying Who lives with baby Reactions of others in the home to the baby Parental employment Use of daycare or babysitting Caregiver perception of weight gain and general appearance</p>

From Jenny C: Child abuse and neglect: diagnosis, treatment, and evidence, Philadelphia, 2011, Elsevier/Saunders, p. 554, Table 57-5.

Table 41-2 Diagnostic Classification of Causes and Selected Examples of Failure to Thrive	
INADEQUATE INTAKE <p>Inadequate food offered<ul style="list-style-type: none">• Food insecurity• Poor knowledge of child's needs• Formula dilution or excessive juice• Breastfeeding difficulties• Medical child abuse/caregiver fabricated illness (Munchausen by proxy)• Medical neglect• Food fads including "rice" milk as substitute for formula or cow milkChild not taking enough food<ul style="list-style-type: none">• Oromotor dysfunction, neurologic disease• Developmental delay• Behavioral feeding problem (altered oromotor sensitivity, pain and conditioned aversion)• Anorexia from systemic causesEmesis<ul style="list-style-type: none">• Pyloric stenosis• Gastroesophageal reflux• Eosinophilic esophagitis• Vascular rings• Malrotation with intermittent volvulus• Increased intracranial pressure and other neurologic disorders• Inborn errors of metabolism• Ruminant• Cyclic vomiting</p>	MALABSORPTION <p>Cystic fibrosis Celiac disease Hepatobiliary disease Food protein allergy, insensitivity, or intolerance Infection (giardiasis) Short gut syndrome</p> INCREASED METABOLIC DEMAND <p>Insulin resistance (intrauterine growth restriction) Congenital infections (human immunodeficiency virus, TORCHES) Syndromes (Russell-Silver, Turner, Down) Malignancy Chronic disease (cardiac, pulmonary, renal) Metabolic disorders Immunodeficiency/autoinflammatory disorders Endocrine (diabetes mellitus, diabetes insipidus, hyperthyroidism)</p>

TORCHES, toxoplasma, other agents, rubella, cytomegalovirus, herpes simplex.

Data from Jaffe A: Failure to thrive: current clinical concepts, Pediatr Rev 32:100-108, 2011.

Table 41-3 Failure to Thrive: Differential Diagnosis by System

PSYCHOSOCIAL/BEHAVIORAL	GASTROINTESTINAL
Inadequate diet because of poverty/food insufficiency, errors in food preparation	Pyloric stenosis Gastroesophageal reflux Repair of tracheoesophageal fistula Malrotation Malabsorption syndromes Celiac disease Milk intolerance: lactose, protein Pancreatic insufficiency syndromes (cystic fibrosis) Chronic cholestasis Inflammatory bowel disease Chronic congenital diarrhea states Short bowel syndrome Pseudobstruction Hirschsprung disease Food allergy
Poor parenting skills (lack of knowledge of sufficient diet)	
Child/parent interaction problems (autonomy struggles, coercive feeding, maternal depression)	
Food refusal	
Rumination	
Parental cognitive or mental health problems	
Child abuse or neglect; emotional deprivation	
NEUROLOGIC	CARDIAC
Cerebral palsy	Cyanotic heart lesions Congestive heart failure Vascular rings
Hypothalamic and other central nervous system tumors (diencephalic syndrome)	
Neuromuscular disorders	
Neurodegenerative disorders	
RENAL	PULMONARY/RESPIRATORY
Recurrent urinary tract infection	Severe asthma Cystic fibrosis; bronchiectasis Chronic respiratory failure Bronchopulmonary dysplasia Adenoid/tonsillar hypertrophy Obstructive sleep apnea
Renal tubular acidosis	
Renal failure	
ENDOCRINE	MISCELLANEOUS
Diabetes mellitus	Collagen-vascular disease Malignancy Primary immunodeficiency Transplantation
Diabetes insipidus	
Hypothyroidism/hyperthyroidism	
Growth hormone deficiency	
Adrenal insufficiency	
GENETIC/METABOLIC/CONGENITAL	INFECTIONS
Sickle cell disease	Perinatal infection (TORCHES) Occult/chronic infections Parasitic infestation Tuberculosis HIV
Inborn errors of metabolism (organic acidosis, hyperammonemia, storage disease)	
Fetal alcohol syndrome	
Skeletal dysplasias	
Chromosomal disorders	
Multiple congenital anomaly syndromes (VATER, CHARGE)	

CHARGE, coloboma, heart disease, atresia choanae, retarded growth and retarded development and/or central nervous system anomalies, genital hypoplasia, and ear anomalies and/or deafness; TORCHES, toxoplasma, other agents, rubella, cytomegalovirus, herpes simplex; VATER, vertebral defects, imperforate anus, tracheoesophageal fistula, and radial and renal dysplasia.

Table 41-4 Approach to Failure to Thrive Based on Signs and Symptoms

HISTORY/PHYSICAL EXAMINATION	DIAGNOSTIC CONSIDERATION
Spitting, vomiting, food refusal	Gastroesophageal reflux, chronic tonsillitis, food allergies, eosinophilic esophagitis
Diarrhea, fatty stools	Malabsorption, intestinal parasites, milk protein intolerance, pancreatic insufficiency, celiac disease, immunodeficiency, inflammatory bowel disease
Snoring, mouth breathing, enlarged tonsils	Adenoid hypertrophy, obstructive sleep apnea
Recurrent wheezing, pulmonary infections	Asthma, aspiration, food allergy, cystic fibrosis, immunodeficiency
Recurrent infections	HIV or congenital immunodeficiency diseases, anatomic defects
Travel to/from developing countries	Parasitic or bacterial infections of the gastrointestinal tract

Table 41-5 Approach to Physical Examination	
Vital signs	Blood pressure, if over 2 yr, temperature, pulse, respirations, oxygen saturation, anthropometry (growth percentiles, body mass index)
General appearance	Activity, affect, posture
Skin	Hygiene, rashes, trauma (bruises, burns, scars)
Head	Hair whorls, color and pluckability of hair, occipital alopecia, fontanel size and patency, frontal bossing, sutures, shape, facial dysmorphisms, philtrum
Eyes	Ptosis, strabismus, fundoscopic examination where possible, palpebral fissures, conjunctival pallor, icterus, cataracts
Ears	External form, rotation, tympanic membranes
Mouth, nose, throat	Thinness of lip, hydration, dental eruption and hygiene caries, glossitis, cheilosis, gum bleeding, marked tonsillar enlargement
Neck	Hairline, masses, lymphadenopathy
Cardiovascular	Evidence of congestive heart failure, cyanosis
Abdomen	Protuberance, hepatosplenomegaly, masses
Genitalia	Malformations, hygiene, trauma
Rectum	Fissures, trauma, hemorrhoids
Extremities	Edema, dysmorphisms, rachitic changes, nails and nail beds
Neurologic	Cranial nerves, reflexes, tone, retention of primitive reflexes, quality of voluntary movement

Table 43-4 Key Elements of Effective Symptom Management	
	Establish and periodically revisit goals of care and ensure that goals are communicated to entire care team.
	Anticipate and plan for symptoms before they occur.
	Assess the child for symptoms regularly, using consistent and developmentally appropriate assessment tools.
• Utilize self-report, if the child is able to reliably report symptoms.	
• Evaluate all aspects of the symptom, including quality, frequency, duration, and intensity.	
	Consider the holistic nature of symptoms.
• Explore the meaning that symptoms may have for families in their social, cultural, religious context.	
• Assess distress caused by the symptom.	
• Evaluate the degree of functional impairment from the symptom.	
	Understand the pathophysiology of the symptom and establish a complete differential diagnosis.
	Treat the underlying cause if possible, weighing benefits and risks, in the context of goals of care.
	Choose the least-invasive route for medications—by mouth whenever possible.
	Prescribe regular medications for constant symptoms, and consider prn doses for breakthrough or uncontrolled symptoms.
	Consider both pharmacologic and nonpharmacologic approaches.
	Reassess the symptom and response to interventions regularly.
• For refractory symptoms, revisit the differential diagnosis and review potentially contributing factors.	
• Effective interventions relieve the symptom and reduce distress and functional impairment.	
	Partner with families to identify and address any barriers to optimal control of symptoms.
	Address spiritual, emotional, and existential suffering in addition to physical suffering as these are often interrelated.

Table 43-5 | Guidelines for Pain Management

Utilize nonopioid analgesics as monotherapy for mild pain and together with opioids for more severe pain.

- Nonopioid analgesics include acetaminophen, nonsteroidal antiinflammatory drugs (NSAIDs), salicylates, and selective cyclooxygenase (COX-2) inhibitors.

For moderate or severe pain, start with a short-acting opioid at regular intervals.

- When dose requirements have stabilized, consider converting opioid to a long-acting formulation with doses available for breakthrough or uncontrolled pain, as needed.
- For uncontrolled pain, increase opioid dose by 30-50%; for severe pain increase by 50-100%.
- Avoid codeine and opioids with mixed agonist activity (e.g., butorphanol, pentazocine).

Administer medications via the simplest, most effective, and least-distressing route.

Dispel the myth that strong medications should be saved for extreme situations or the very end of life.

- Opioids do not have a "ceiling effect," and escalating symptoms may be treated with an increase in dose.

Clarify for families the differences between tolerance, physical dependence, and addiction.

Anticipate and treat/prevent common analgesic side effects (gastritis with NSAIDs; constipation, pruritus, nausea, sedation with opioids).

- Always initiate a bowel regimen to prevent constipation when starting opioids.

Consider a stimulant for opioid-induced somnolence.

Puritus rarely indicates a true allergy. If not responsive to an antihistamine, consider low-dose naloxone or switching opioids.

Consider switching to a different opioid for intolerable side effects or neurotoxicity (e.g., myoclonus).

Use an equianalgesic conversion table when switching opioids, and account for incomplete cross-tolerance.

Consider the use of adjuvant drugs for specific pain syndromes, and for their opioid-sparing effect:

- Antidepressants (e.g., amitriptyline, nortriptyline) and anticonvulsants (e.g., gabapentin, carbamazepine, topiramate) for neuropathic pain.

Steroids or NSAIDs for bone pain.

Sedatives and hypnotics for anxiety and muscle spasm.

- To enhance analgesia from opioids, consider clonidine or ketamine.

Use topical local anesthetics (lidocaine, prilocaine, bupivacaine) when possible.

Consider anesthetic blocks for regional pain.

Consider palliative radiation therapy.

Consider psychological approaches (e.g., cognitive or behavioral therapy) and integrative therapies (e.g., acupuncture, massage).

Table 43-6 Pharmacologic Approach to Symptoms Commonly Experienced by Children with Life-Threatening Illness

SYMPTOM	MEDICATION	STARTING DOSE	COMMENTS
Pain—mild	Acetaminophen Ibuprofen	15 mg/kg po q 4 hr, max 4 g/day 10 mg/kg po q 6 hr	Available po (including liquid), pr, IV PO (including liquid) only; avoid if risk of bleeding; use only in infants ≥6 mo. Use with caution in congestive heart failure. Chewable tablets contain phenylalanine
	Trilisate	10-15 mg/kg po tid	Trilisate may have less antiplatelet activity and therefore pose less risk for bleeding than other salicylates. Salicylates, however, have been associated with Reye syndrome in children <2 yr
Pain—moderate/ severe	Morphine immediate release (i.e., MSIR)	0.3 mg/kg po q 4 hr if <50 kg; 5-10 mg po q 4 hr ^{*†}	Also available in IV/SQ formulation ^{‡§}
	Oxycodone	0.1 mg/kg po q 4 hr if <50 kg; 5-10 mg po q 4 hr if >50 kg ^{*†}	No injectable formulation ^{‡§}
	Hydromorphone	0.05 mg/kg po q 4 hr if <50 kg; 1-2 mg po q 4 hr if >50 kg ^{*†}	Also available in IV/SQ formulation. Injectable form very concentrated, facilitating subcutaneous delivery ^{‡§}
	Fentanyl Methadone	0.5-1.5 µg/kg IV/SQ q 30 min ^{*†} Starting dose 0.1-0.2 mg/kg po bid. May give tid if needed. Recommend consultation with experienced clinician for equivalence dosing from other opioids. ^{*†}	Rapid infusion may cause chest wall rigidity ^{‡§} Only opioid with immediate and prolonged effect available as a liquid; do not adjust dose more often than every 72 hr as prolonged biologic half-life > than therapeutic half-life. Knowledge of the pharmacokinetics of methadone is needed for converting to and from doses of other opioids. Also available IV/SQ. May cause QT interval prolongation (consider ECG), especially in adults on >200 mg/day or in those at risk for QT prolongation. Interacts with several antiretrovirals [§]
	MS Contin Kadian (contains sustained- release pellets), Avinza (contains immediate and extended release beads) Oramorph OxyContin Transdermal fentanyl patch	Total daily dose of MSIR divided bid-tid	Do not crush MS Contin. For those unable to swallow pills, Kadian and Avinza capsules may be opened and contents mixed with food but cannot be chewed. Kadian contents may be mixed in 10 mL water and given via 16-French G-tube. Avoid alcohol with Avinza. Larger dose formulation may not be suitable for small children [§]
Pain—sustained release	Oramorph OxyContin Transdermal fentanyl patch	Total daily dose of oxycodone divided bid-tid Divide 24-hr po morphine dose by 2 to determine starting dose of transdermal fentanyl. There is no data on the equianalgesic conversion from transdermal fentanyl to any oral opioid	Do not crush [§] Smallest patch size may be too high for small children. For children >2 yr. Apply to upper back in young children. Patch may not be cut. Typically for patients on at least 60 mg morphine/day or its equivalent. Not appropriate when dosage changes are frequent or for opioid-naïve patients. Fever >40°C results in higher serum concentrations [§]
	Nortriptyline	0.5 mg/kg po at bedtime to maximum of 150 mg/day	Fewer anticholinergic side effects than amitriptyline. May cause constipation, sedation, postural hypotension, dry mouth. May cause QT interval prolongation (consider ECG). At higher doses monitor ECG and plasma levels
	Gabapentin	Start at 5 mg/kg/day at bedtime and gradually increase to 10-15 mg/kg/day divided tid; titrate up by 5 mg/kg/day every 3-4 days as needed but not to exceed 50-75 mg/kg/day (3600 mg/day)	May cause neuropsychiatric events in children (aggression, emotional lability, hyperkinesia), usually mild but may require discontinuation of gabapentin. May cause dizziness, drowsiness, tremor, nystagmus, ataxia, swelling
	Pregabalin	Start at 1 mg/kg/dose po at bedtime for 3 days, then increase to 1 mg/kg/dose bid. Increase every 3 days to 3 mg/kg/dose po bid (maximum: 6 mg/kg/dose)	
	Methadone	See previous listing	See previous listing
Dyspnea	Morphine, immediate release (i.e., MSIR)	0.1 mg/kg po q 4 hr prn ^{*†}	All opioids may relieve dyspnea. For dyspnea, the starting dose is 30% of the dose that would be administered for pain [§]
	Lorazepam	0.025-0.05 mg/kg IV/po q 6 hr, up to 2 mg/ dose	See previous listing

Table 43-6 Pharmacologic Approach to Symptoms Commonly Experienced by Children with Life-Threatening Illness—cont'd

SYMPTOM	MEDICATION	STARTING DOSE	COMMENTS
Respiratory secretions	Scopolamine patch	1.5 mg patch, change q 72 hr	Excessive drying of secretions can cause mucus plugging of airways. Good for motion-induced nausea and vomiting. Handling patch and contacting eye may cause anisocoria and blurry vision. May fold patches but do not cut them. Anticholinergic side effects possible
	Glycopyrrolate	0.04-0.1 mg/kg po q 4-8 hr	Powerful antusalagogue. Excessive drying of secretions can cause mucus plugging of airways. Anticholinergic side effects possible. Quaternary ammonium structure limits its ability to cross lipid membranes, such as the blood-brain barrier (in contrast to atropine, scopolamine and hyoscyamine sulfate), so may exert fewer central anticholinergic effects
	Hyoscyamine sulfate Atropine	4 gtt po q 4 hr prn if <2 yr; 8 gtt po q 4 hr prn if 2-12 yr; do not exceed 24 gtt/24 hr 1-2 gtt SL q 4-6 hr prn	Anticholinergic side effects possible, including sedation. May be given sublingually Give 0.5% ophthalmic drops sublingually
Nausea	Metoclopramide	0.1-0.2 mg/kg/dose q 6 hr, up to 10 mg/dose (prokinetic and mild nausea dosing). For chemotherapy-associated nausea 0.5-1 mg/kg q 6 hr prn po/IV/SC, give with diphenhydramine and continue diphenhydramine for 24 hr after last dose of high-dose metoclopramide to prevent extrapyramidal reaction	Helpful when dysmotility is an issue; may cause extrapyramidal reactions, particularly in children following IV administration of high doses. Contraindicated in complete bowel obstruction or pheochromocytoma
	Ondansetron	0.15 mg/kg dose IV/po q 8 hr prn. No single intravenous dose should exceed 16 mg because of risk of QT prolongation	Significant experience in pediatrics. Good empiric therapy for nausea in palliative care population. Oral dissolving tablet contains phenylalanine. Higher doses used with chemotherapy although single 32 mg IV dose is no longer available (risk for QT prolongation). Consider ECG monitoring in patients with electrolyte abnormalities, congestive heart failure, bradycardias, or in patients on other medications with the potential to cause QT prolongation
	Dexamethasone Lorazepam Dronabinol	0.1 mg/kg/dose tid po/IV; max dose 10 mg/day See previous listing 2.5-5 mg/m ² /dose q 3-4 hr	Also helpful with hepatic capsular distention, bowel wall edema, anorexia, increased intracranial pressure. May cause mood swings or psychosis See previous listing Available in 2.5- and 5-mg capsules. May remove liquid contents from capsules for children who cannot swallow capsules. Avoid in patients with sesame oil hypersensitivity or history of schizophrenia. May cause euphoria, dysphoria or other mood changes. Tolerance to central nervous system side effects usually develops in 1-3 days of continuous use. Avoid in patients with depression or mania
Anxiety	Scopolamine patch	See previous listing	See previous listing
	Lorazepam	See previous listing	See previous listing
Agitation	Haloperidol	0.01 mg/kg po tid prn for acute onset: 0.025-0.050 mg/kg po, may repeat 0.025 mg/kg in 1 hr prn	May cause extrapyramidal reactions, which can be reversed with diphenhydramine or Cogentin. Safety not established in children <3 yr
Sleep disturbance/ insomnia	Lorazepam Trazodone	See previous listing Children 6-18 yr: 0.75-1 mg/kg/dose, given bid-tid if needed If >18 yr, start at 25-50 mg/dose, given bid-tid if needed	See previous listing Potentially arrhythmogenic
Fatigue	Methylphenidate	0.3 mg/kg/dose titrated as needed, up to 60 mg/day	Rapid antidepressant effect; also improves cognition. Administer before meals to avoid appetite suppression. Use with caution in children at risk for cardiac arrhythmia. Available as liquid and chewable tablet

Continued

264 Part V ◆ Children with Special Needs

Table 43-6 Pharmacologic Approach to Symptoms Commonly Experienced by Children with Life-Threatening Illness—cont'd

SYMPTOM	MEDICATION	STARTING DOSE	COMMENTS
Pruritus	Diphenhydramine	0.5-1 mg/kg q 6 hr IV/po (100 mg max per day)	May reverse phenothiazine-induced dystonic reactions. Topical formulation on large areas of the skin or open area may cause toxic reactions. May cause paradoxical reaction in young children
	Hydroxyzine	0.5-1 mg/kg q 6 hr IV/po (600 mg maximum per day)	
Constipation	Docusate MiraLAX	40-150 mg/day po in 1-4 divided doses <5 yr: $\frac{1}{2}$ scoop (8.5 g) in 4 oz of water daily >5 yr: 1 scoop (17 g) in 8 oz of water daily	Stool softener available as liquid or capsule Tasteless powder may be mixed in beverage of choice. Now available nonprescription
	Lactulose	5-10 mL po up to q 2 hr until bowel movement	Bowel stimulant; dosing q 2 hr may cause cramping
	Senna Dulcolax	2.5 mL po daily (for children weighing >27 kg) 3-12 yr: 5-10 mg po daily >12 yr: 5-15 mg po daily	Bowel stimulant; available as granules Available in oral or rectal formulation
	Pediatric Fleet's Enema	2.5 oz pediatric enema for children 2-11 yr; adult enema for children ≥12 yr	May repeat ×1 if needed. Do not use in neutropenic patients
	Methylnaltrexone	10-20 kg: 2 mg SC 21-33 kg: 4 mg SC 34-46 kg: 6 mg SC 47-62 kg: 8 mg SC 63-114 kg: 12 mg SC ≥155 kg: 0.15 mg/kg SC Administer 1 dose every other day as needed; maximum of 1 dose per 24 hr	A peripherally acting opioid antagonist for opioid-induced constipation. Usually works within 30-60 minutes of administration
Muscle spasm	Diazepam	0.5 mg/kg/dose IV/po q 6 hr prn; initial dose for children <5 yr is 5 mg dose; for children ≥5 yr dose is 10 mg/dose	May be irritating if given by peripheral IV
	Baclofen	5 mg po tid, increase by 5 mg/dose as needed	Helpful with neuropathic pain and spasticity; abrupt withdrawal may result in hallucinations and seizures; not for children <10 yr
Seizures	Lorazepam	0.1 mg/kg IV/po/SL/PR; repeat q 10 min ×2	May be given pr as Diastat (0.2 mg/kg/dose q 15 minutes ×3 doses)
	Diazepam	0.1 mg/kg q 6 hr (max 5 mg/dose if <5 yr; max 10 mg/dose if ≥5 yr)	
Neuroirritability	Gabapentin Clonidine	See previous listing Starting dose: 0.05 mg/day. May increase every 3-5 days by 0.05 mg/day to 3-5 µg/kg/day given in divided doses 3-4 times/day; maximum dose is 0.3 mg/day May switch from oral to transdermal route once optimal oral dose is established; Transdermal dose is equivalent to the total oral daily dose (e.g., if total oral dose is 0.1 mg/day, apply 1 patch (delivers 0.1 mg/day). Change patch every 7 days.	Transdermal patch may contain metal (e.g., aluminum) that may cause burns if worn during MRI scan. Remove patch prior to MRI. Patch may be cut into quarter or half fractions based on dose needed
	Clonazepam	<10 yr or <30 kg Initial dose: 0.01-0.03 mg/kg/day divided tid; ≥10 yr (≥30 kg) Initial dose: up to 0.25 mg po tid; may increase by 0.5-1 mg/day every 3 days Maintenance dose: 0.05-0.2 mg/kg/day up to 20 mg/day	
Anorexia	Megestrol acetate	10 mg/kg/day in 1-4 divided doses, may titrate up to 15 mg/kg/day or 800 mg/day	For children >10 yr. Acute adrenal insufficiency may occur with abrupt withdrawal after long-term use. Use with caution in patients with diabetes mellitus or history of thromboembolism. May cause photosensitivity
	Dronabinol Cyproheptadine	See previous listing Children ≥2 yr and adolescents: 0.08 mg/kg po q 8 hr; if no benefit in 5 days, increase dose by 0.04-0.08 mg/kg/dose maximum daily dose: ≤6 yr: 12 mg/day; 7-14 yr: 16 mg/day; ≥15 yr: 32 mg/day	

*Infants <6 mo should receive 25-30% of the usual opioid starting dose.

¹Although the usual opioid starting dose is presented, dose may be titrated as needed. There is no ceiling/maximum dose for opioids.

²Breakthrough dose is 10% of 24 hr dose. See Chapter 62 for information regarding titration of opioids.

³Side effects from opioids include constipation, respiratory depression, pruritus, nausea, urinary retention, physical dependence.

ECG, electrocardiogram; gt, drops; hr, hour; IV, intravenously; po, by mouth; pr, rectally; prn, as needed; SC, subcutaneously; SL, sublingually.

Adapted from Ullrich C, Wolfe J: Pediatric pain and symptom control. In Walsh TD, Caraceni AT, Fainsinger R, et al: *Palliative medicine*, Philadelphia, 2008, Saunders, pp. 1101-1102, Table 198.3.

Table 43-7 Nonpharmacologic Approach to Symptoms Commonly Experienced by Children with Life-Threatening Illness

SYMPTOM	APPROACH TO MANAGEMENT
Pain	Prevent pain when possible by limiting unnecessary painful procedures, providing sedation, and giving pre-emptive analgesia prior to a procedure (e.g., including sucrose for procedures in neonates) Address coincident depression, anxiety, sense of fear or lack of control Consider guided imagery, relaxation, hypnosis, art/pet/play therapy, acupuncture/acupressure, biofeedback, massage, heat/cold, yoga, transcutaneous electric nerve stimulation, distraction
Dyspnea or air hunger	Suction secretions if present, positioning, comfortable loose clothing, fan to provide cool, blowing air Limit volume of IV fluids, consider diuretics if fluid overload/pulmonary edema present Behavioral strategies including breathing exercises, guided imagery, relaxation, music, distraction
Fatigue	Sleep hygiene (establish a routine, promote habits for restorative sleep) Regular, gentle exercise; Prioritize or modify activities Address potentially contributing factors (e.g., anemia, depression, side effects of medications) Aromatherapy*: peppermint, rosemary, basil
Nausea/vomiting	Consider dietary modifications (bland, soft, adjust timing/volume of foods or feeds) Aromatherapy*: ginger, peppermint, lavender acupuncture/acupressure
Constipation	Increase fiber in diet, encourage fluids, ambulation (if possible)
Oral lesions/dysphagia	Oral hygiene and appropriate liquid, solid and oral medication formulation (texture, taste, fluidity). Treat infections, complications (mucositis, pharyngitis, dental abscess, esophagitis) Oropharyngeal motility study and speech (feeding team) consultation
Anorexia/cachexia	Manage treatable lesions causing oral pain, dysphagia, or anorexia. Support caloric intake during phase of illness when anorexia is reversible. Acknowledge that anorexia/cachexia is intrinsic to the dying process and may not be reversible Prevent/treat coexisting constipation
Pruritus	Moisturize skin Trim child's nails to prevent excoriation Try specialized antiitch lotions Apply cold packs Counterstimulation, distraction, relaxation
Diarrhea	Evaluate/treat if due to obstipation Assess and treat infection Dietary modification
Depression	Psychotherapy, behavioral techniques, setting attainable daily goals Aromatherapy*: bergamot, lavender
Anxiety	Psychotherapy (individual and family), behavioral techniques Aromatherapy*: clary sage, angelica, mandarin, lavender
Agitation/terminal restlessness	Evaluate for organic or drug causes Educate family Orient and reassure child; provide calm, nonstimulating environment, use familiar music, verse, voice, touch Aromatherapy*: frankincense, ylang ylang

*Best if aromatherapy is administered by a practitioner trained in aromatherapy.

From Sourkes B, Frankel L, Brown M, et al: Food, toys, and love: pediatric palliative care, *Curr Probl Pediatr Adolesc Health Care* 35:345-392, 2005.

Nutrition

Table 45-2

Conditions for Which Human Milk Has Been Suggested to Possibly Have a Protective Effect

Acute disorders	Crohn disease
Diarrhea	Childhood cancer
Otitis media	Lymphoma
Urinary tract infection	Leukemia
Necrotizing enterocolitis	Recurrent otitis media
Septicemia	Allergy
Infant botulism	Obesity and overweight
Insulin-dependent diabetes mellitus	Hospitalizations
Celiac disease	Infant mortality

Table 45-1

Selected Beneficial Properties of Human Milk Compared to Infant Formula

Secretory IgA	Specific antigen-targeted antiinfective action
Lactoferrin	Immunomodulation, iron chelation, antimicrobial action, antiadhesive, trophic for intestinal growth
κ-Casein	Antiadhesive, bacterial flora
Oligosaccharides	Prevention of bacterial attachment
Cytokines	Antiinflammatory, epithelial barrier function
Growth factors	
Epidermal growth factor	Luminal surveillance, repair of intestine
Transforming growth factor (TGF)	Promotes epithelial cell growth (TGF-β) Suppresses lymphocyte function (TGF-β)
Nerve growth factor	Promotes neural growth
Enzymes	
Platelet-activating factor-acetylhydrolase	Blocks action of platelet-activating factor
Glutathione peroxidase	Prevents lipid oxidation
Nucleotides	Enhance antibody responses, bacterial flora

Adapted from Hamosh M: Bioactive factors in human milk, *Pediatr Clin North Am* 48:69–86, 2001.

Table 45-3

Absolute and Relative Contraindications to Breastfeeding Because of Maternal Health Conditions

MATERNAL HEALTH CONDITION	DEGREE OF RISK
HIV and HTLV infection	In the United States, breastfeeding is contraindicated In other settings, health risks of not breastfeeding must be weighed against the risk of transmitting virus to the infant
Tuberculosis infection	Breastfeeding is contraindicated until completion of approximately 2 wk of appropriate maternal therapy
Varicella-zoster infection	Infant should not have direct contact to active lesions Infant should receive immune globulin
Herpes simplex infection	Breastfeeding is contraindicated with active herpetic lesions of the breast
CMV infection	May be found in milk of mothers who are CMV seropositive Transmission through human milk causing symptomatic illness in term infants is uncommon
Hepatitis B infection	Infants routinely receive hepatitis B immune globulin and hepatitis B vaccine if mother is HbsAg positive No delay in initiation of breastfeeding is required
Hepatitis C infection	Breast-feeding is not contraindicated
Alcohol intake	Limit maternal alcohol intake to <0.5 g/kg/day (for a woman of average weight, this is the equivalent of 2 cans of beer, 2 glasses of wine, or 2 oz of liquor)
Cigarette smoking	Discourage cigarette smoking, but smoking is not a contraindication to breastfeeding
Chemotherapy, radiopharmaceuticals	Breastfeeding is generally contraindicated

Table 45-4

Recommendations on Breastfeeding Management for Healthy Term Infants

1. Exclusive breastfeeding for about 6 months
 - Breastfeeding preferred; alternatively expressed mother's milk, or donor breast milk
 - To continue for at least the first year and beyond as long as mutually desired by mother and child
 - Complementary foods rich in iron and other micronutrients should be introduced at about 6 mo of age
2. Peripartum policies and practices that optimize breastfeeding initiation and maintenance should be compatible with the AAP and Academy of Breastfeeding Medicine Model Hospital Policy and include the following:
 - Direct skin-to-skin contact with mothers immediately after delivery until the first feeding is accomplished and encouraged throughout the postpartum period
 - Delay in routine procedures (weighing, measuring, bathing, blood tests, vaccines, and eye prophylaxis) until after the first feeding is completed
 - Delay in administration of intramuscular vitamin K until after the first feeding is completed but within 6 hr of birth
 - Ensure 8-12 feedings at the breast every 24 hr
 - Ensure formal evaluation and documentation of breastfeeding by trained caregivers (including position, latch, milk transfer, examination) at least once for each nursing shift
 - Give no supplements (water, glucose water, commercial infant formula, or other fluids) to breastfeeding newborn infants unless medically indicated using standard evidence-based guidelines for the management of hyperbilirubinemia and hypoglycemia
 - Avoid routine pacifier use in the postpartum period
 - Begin daily oral vitamin D drops (400 IU) at hospital discharge
3. All breastfeeding infants should be seen by a pediatrician within 48 to 72 hr after discharge from the hospital
 - Evaluate hydration (elimination patterns)
 - Evaluate body weight gain (body weight loss no more than 7% from birth and no further weight loss by day 5; assess feeding and consider more frequent follow-up)
 - Discuss maternal/infant issues
 - Observe feeding
4. Mother and infant should sleep in proximity to each other to facilitate breastfeeding
5. Pacifier should be offered, while placing infant in back-to-sleep-position, no earlier than 3 to 4 weeks of age and after breastfeeding has been established

Table 46-2 Classification of Undernutrition		
CLASSIFICATION	INDEX	GRADING
Gomez (underweight)	90-75% of median weight-for-age 75-60% <60%	Grade 1 (mild) Grade 2 (moderate) Grade 3 (severe)
Waterlow (wasting)	90-80% of median weight-for-height <70%	Mild Severe
Waterlow (stunting)	95-90% of median height-for-age 90-85% <85%	Mild Moderate Severe
WHO (wasting)	<-2 to >-3 SD weight-for-height <-3	Moderate Severe
WHO (stunting)	<-2 to >-3 SD height-for-age <-3	Moderate Severe
WHO (wasting) (for age group 6-59 mo)	115-125 mm mid-upper arm circumference <115 mm	Moderate Severe

SITE	SIGNS
Face	Moon face (kwashiorkor), simian facies (marasmus)
Eye	Dry eyes, pale conjunctiva, Bitot spots (vitamin A), periorbital edema
Mouth	Angular stomatitis, cheilitis, glossitis, spongy bleeding gums (vitamin C), parotid enlargement
Teeth	Enamel mottling, delayed eruption
Hair	Dull, sparse, brittle hair, hypopigmentation, flag sign (alternating bands of light and normal color), broomstick eyelashes, alopecia
Skin	Loose and wrinkled (marasmus), shiny and edematous (kwashiorkor), dry, follicular hyperkeratosis, patchy hyper- and hypopigmentation (crazy paving or flaky paint dermatoses), erosions, poor wound healing
Nails	Koilonychia, thin and soft nail plates, fissures, or ridges
Musculature	Muscle wasting, particularly buttocks and thighs; Chvostek or Trousseau sign (hypocalcemia)
Skeletal	Deformities, usually as a result of calcium, vitamin D, or vitamin C deficiencies
Abdomen	Distended: hepatomegaly with fatty liver; ascites may be present
Cardiovascular	Bradycardia, hypotension, reduced cardiac output, small vessel vasculopathy
Neurologic	Global developmental delay, loss of knee and ankle reflexes, impaired memory
Hematologic	Pallor, petechiae, bleeding diathesis
Behavior	Lethargic, apathetic, irritable on handling

From Grover Z, Ee LC: Protein energy malnutrition, *Pediatr Clin N Am* 56:1055-1068, 2009.

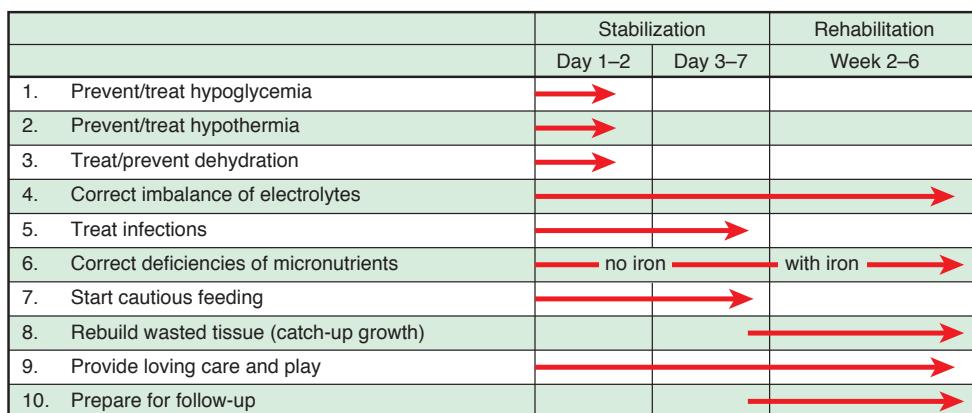


Figure 46-6 The 10 steps of treatment for severe acute malnutrition and their approximate time frames.

Table 46-7 Emergency Treatment in Severe Malnutrition

CONDITION	IMMEDIATE ACTION
Shock • lethargic or unconscious and cold hands Plus either: • slow capillary refill (longer than 3 sec) or • weak fast pulse	<ol style="list-style-type: none"> Give oxygen Give sterile 10% glucose (5 mL/kg) by IV Give IV fluid at 15 mL/kg over 1 hr, using: <ul style="list-style-type: none"> Ringers lactate with 5% dextrose or half-normal saline with 5% dextrose or half-strength Darrow solution with 5% dextrose if all of the above are unavailable, Ringer lactate Measure and record pulse and respirations at the start and every 10 minutes <p>If there are signs of improvement (pulse and respiration rates fall) repeat IV 15 mL/kg for 1 more hr. Then switch to oral or nasogastric rehydration with ReSoMal, 5-10 mL/kg in alternate hr (see Table 46-8 step 3)</p> <p>If there are no signs of improvement assume septic shock and:</p> <ol style="list-style-type: none"> Give maintenance fluid IV (4 mL/kg/hr) while waiting for blood Order 10 mL/kg fresh whole blood and transfuse slowly over 3 hr. If signs of heart failure, give 5-7 mL/kg packed cells rather than whole blood Give furosemide 1 mL/kg IV at the start of the transfusion
Hypoglycemia Blood glucose less than 3 mmol/L	See Table 46-8 step 1 for treatment
Severe dehydration	Do not give IV fluids except in shock See Table 46-8 step 3 for treatment
Very severe anemia Hb less than 4 g/dL	If very severe anemia (or Hb 4-6 g/dL AND respiratory distress): <ol style="list-style-type: none"> Give whole blood 10 mL/kg slowly over 3 hr. If signs of heart failure, give 5-7 mL/kg packed cells rather than whole blood Give furosemide 1 mL/kg IV at the start of the transfusion
Emergency eye care Corneal ulceration	If corneal ulceration: <ol style="list-style-type: none"> Give vitamin A immediately (age <6 mo 50,000 IU, 6-12 mo 100,000 IU, >12 mo 200,000 IU) Instill 1 drop atropine (1%) into affected eye to relax the eye and prevent the lens from pushing out

Table 46-8 Therapeutic Directives for Stabilization

STEP	PREVENTION	TREATMENT
1. Prevent/treat hypoglycemia blood glucose <3 mmol/L	Avoid long gaps without food and minimize need for glucose: <ol style="list-style-type: none"> Feed immediately Feed every 3 hr day and night (2 hr if ill) Feed on time Keep warm Treat infections (they compete for glucose) <p>Note: Hypoglycemia and hypothermia often coexist, and are signs of severe infection</p>	<p>If conscious:</p> <ol style="list-style-type: none"> 10% glucose (50 mL), or a feed (see step 7), or 1 teaspoon sugar under the tongue-whichever is quickest Feed every 2 hr for at least the first day. Initially give $\frac{1}{4}$ of feed every 30 min Keep warm Start broad-spectrum antibiotics <p>If unconscious:</p> <ol style="list-style-type: none"> Immediately give sterile 10% glucose (5 mL/kg) by IV Feed every 2 hr for at least first day. Initially give $\frac{1}{4}$ of feed every 30 min. Use nasogastric (NG) tube if unable to drink Keep warm. Start broad-spectrum antibiotics
2. Prevent/treat hypothermia axillary <35°C (95°F); rectal <35.5°C (95.9°F)	Keep warm and dry and feed frequently <ol style="list-style-type: none"> Avoid exposure Dress warmly, including head and cover with blanket Keep room hot; avoid draughts Change wet clothes and bedding Do not bathe if very ill Feed frequently day and night Treat infections 	Actively rewarm <ol style="list-style-type: none"> Feed Skin-to-skin contact with carer ("kangaroo technique") or dress in warmed clothes, cover head, wrap in warmed blanket and provide indirect heat (e.g. heater; transwarmer mattress; incandescent lamp) Monitor temperature hourly (or every 30 min if using heater) Stop rewarming when rectal temperature is 36.5°C (97.7°F)
3. Prevent/treat dehydration	Replace stool losses <ol style="list-style-type: none"> Give ReSoMal after each watery stool. ReSoMal (37.5 mmol Na/L) is a low-sodium rehydration solution for malnutrition 	Do not give IV fluids unless the child is in shock <ol style="list-style-type: none"> Give ReSoMal 5 mL/kg every 30 min for first 2 hr orally or NG tube Then give 5-10 mL/kg in alternate hours for up to 10 hr. Amount depends on stool loss and eagerness to drink. Feed in the other alternate hour Monitor hourly and stop if signs of overload develop (pulse rate increases by 25 beats/min and respiratory rate by 5 breaths/min; increasing edema; engorged jugular veins) Stop when rehydrated (3 or more signs of hydration: less thirsty, passing urine, skin pinch less slow, eyes less sunken, moist mouth, tears, less lethargic, improved pulse and respiratory rate).

Continued

304 Part VI ◆ Nutrition

Table 46-8 Therapeutic Directives for Stabilization—cont'd

STEP	PREVENTION	TREATMENT
4. Correct electrolyte imbalance—deficit of potassium and magnesium, excess sodium		<p>1. Give extra potassium (4 mmol/kg/day) and magnesium (0.6 mmol/kg/day) for at least 2 wk (see Table 46-12) Note: Potassium and magnesium are already added in NutriSet F75 and F100 packets</p>
5. Prevent/treat infections	Minimize risk of cross-infection 1. Avoid overcrowding 2. Wash hands 3. Give measles vaccine to unimmunized children age >6 mo	Infections are often silent. Starting on the first day, give broad-spectrum antibiotics to all children. 1. For antibiotic choices/schedule see Table 46-9 2. Ensure all doses are given, and given on time 3. Cover skin lesions so they do not become infected Note: Avoid steroids as they depress immune function
6. Correct micronutrient deficiencies	Note: Folic acid, multivitamins, zinc, copper, and other trace minerals are already added in NutriSet F75 and F100 packets	Do not give iron in the stabilization phase 1. Give vitamin A on day 1 (under 6 mo 50,000 units; 6-12 mo 100,000 units; >12 mo 200,000 units) if child has any eye signs of vitamin A deficiency or has had recent measles. Repeat this dose on days 2 and 14 2. Folic acid 1 mg (5 mg on day 1) 3. Zinc (2 mg/kg/day) and copper (0.3 mg/kg/day). These are in the electrolyte/mineral solution and Combined Mineral Vitamin mix (CMV) and can be added to feeds and ReSoMal 4. Multivitamin syrup or CMV
7. Start cautious feeding		1. Give 8-12 small feeds of F75 to provide 130 mL/kg/day, 100 kcal/kg/day and 1-1.5 g protein/kg/day 2. If gross edema, reduce volume to 100 mL/kg/day 3. Keep a 24-hr intake chart. Measure feeds carefully. Record leftovers 4. If child has poor appetite, coax and encourage to finish the feed. If unfinished, reoffer later. Use NG tube if eating 80% or less of the amount offered 5. If breastfed, encourage continued breastfeeding but also give F75 6. Transfer to F100 when appetite returns (usually within 1 wk) and edema has been lost or is reduced 7. Weigh daily and plot weight.

Table 46-9 Recommended Antibiotics*

	GIVE
If no complications	Amoxicillin oral 25 mg/kg twice daily for 5 days
If complications (shock, hypoglycemia, hypothermia, skin lesions, respiratory or urinary tract infections, or lethargy/sickly)	Gentamicin (7.5 mg/kg IV or IM) once daily for 7 days and Ampicillin (50 mg/kg IV or IM) every 6 hr for 2 days, then oral amoxicillin (25-40 mg/kg) every 8 hr for 5 days

*Local resistance patterns may require these to be adjusted. Ensure that there is Gram-negative cover.

If specific infections are identified, add appropriate antibiotics.

For persistent diarrhea/small bowel overgrowth, add metronidazole (7.5 mg/kg oral) every 8 hr for 7 days.

Table 46-10 Recipes for Milk Formulas F75 and F100

	F75 ^b (STARTER)	F75 ^c (STARTER) (CEREAL-BASED)	F100 ^d (CATCH-UP)
Dried skimmed milk (g)	25	25	80
Sugar (g)	100	70	50
Cereal flour (g)	—	35	—
Vegetable oil (g)	30	30	60
Electrolyte/mineral solution (mL) ^a	20	20	20
Water: make up to (mL)	1000	1000	1000
Content/100 mL			
Energy (kcal)	75	75	100
Protein (g)	0.9	1.1	2.9
Lactose (g)	1.3	1.3	4.2
Potassium (mmol)	4.0	4.2	6.3
Sodium (mmol)	0.6	0.6	1.9
Magnesium (mmol)	0.43	0.46	0.73
Zinc (mg)	2.0	2.0	2.3
Copper (mg)	0.25	0.25	0.25
% Energy from protein	5	6	12
% Energy from fat	32	32	53
Osmolality (mOsm/L)	413	334	419

Whisk at high speed to prevent oil from separating out.

^aSee Table 46-12 for recipe, or use commercially available therapeutic Combined Mineral Vitamin mix (CMV).

^bA comparable F75 can be made from 35 g dried whole milk, 100 g sugar, 20 g oil, 20 mL electrolyte/mineral solution, and water to 1000 mL; or from 300 mL full cream cow's milk, 100 g sugar, 20 g oil, 20 mL electrolyte/mineral solution, and water to 1000 mL.

^cThis lower-osmolality formula may be helpful for children with dysentery or persistent diarrhea. Cook for 4 min.

^dA comparable F100 can be made from 110 g dried whole milk, 50 g sugar, 30 g oil, 20 mL electrolyte/mineral solution, and water to 1000 mL; or from 880 mL full cream cow's milk, 75 g sugar, 20 g oil, 20 mL electrolyte/mineral solution, and water to 1000 mL.

Table 46-11 Recipe for Rehydration Solution for Malnutrition (ReSoMal)

INGREDIENT	AMOUNT
Water	2 L
WHO-ORS	One 1-L sachet*
Sucrose	50 g
Electrolyte/mineral solution†	mL

ReSoMal contains 37.5 mmol sodium and 40 mmol potassium/L

*Sachet contains 2.6 g sodium chloride, 2.9 g trisodium citrate, 1.5 g potassium chloride, 13.5 g glucose.

†See Table 46-12 for recipe, or use commercially available therapeutic Combined Mineral Vitamin mix (CMV).

Table 46-12 Recipe for Concentrated Electrolyte/Mineral Solution*

INGREDIENT	g	mol/20 mL
Potassium chloride: KCl	224.0	24 mmol
Tripotassium citrate	81.0	2 mmol
Magnesium chloride: MgCl ₂ ·6H ₂ O	76.0	3 mmol
Zinc acetate: Zn acetate·2H ₂ O	8.2	300 μmol
Copper sulfate: CuSO ₄ ·5H ₂ O	1.4	45 μmol
Water: make up to	2500 mL	

Add 20 mL when preparing 1 L of feed or ReSoMal.

*Make fresh each month. Use cooled boiled water.

Table 46-13 Clinical Signs and Symptoms of Refeeding Syndrome

HYPOPHOSPHATEMIA	HYPOKALEMIA	HYPOMAGNESEMIA	VITAMIN/THIAMINE DEFICIENCY	SODIUM RETENTION	HYPERGLYCEMIA
Cardiac	Cardiac	Cardiac	Encephalopathy	Fluid overload	Cardiac
Hypotension	Arrhythmias	Arrhythmias	Lactic acidosis	Pulmonary edema	Hypotension
Decreased stroke volume	Respiratory Failure	Neurologic Weakness	Death	Cardiac compromise	Respiratory Failure
Respiratory	Neurologic	Tremor			Hypercapnia
Impaired diaphragm contractility	Weakness	Tetany			Failure
Dyspnea	Paralysis	Seizures			Other
Respiratory failure	Gastrointestinal	Altered mental status			Ketoacidosis
Neurologic	Nausea	Coma			Coma
Paresthesia	Vomiting	Gastrointestinal			Dehydration
Weakness	Constipation	Nausea			Impaired immune function
Confusion	Muscular	Vomiting			
Disorientation	Rhabdomyolysis	Diarrhea			
Lethargy	Muscle necrosis	Other			
Areflexic paralysis	Other	Refractory hypokalemia and hypocalcemia			
Seizures	Death	Death			
Coma					
Hematologic					
Leukocyte dysfunction					
Hemolysis					
Thrombocytopenia					
Other					
Death					

Data from Kraft MD, Btaiche IF, Sacks GS: Review of RFS, Nutr Clin Pract 20:625–633, 2005. From Fuentebella J, Kerner JA: Refeeding syndrome, Pediatr Clin North Am 56:1201–1210, 2009.

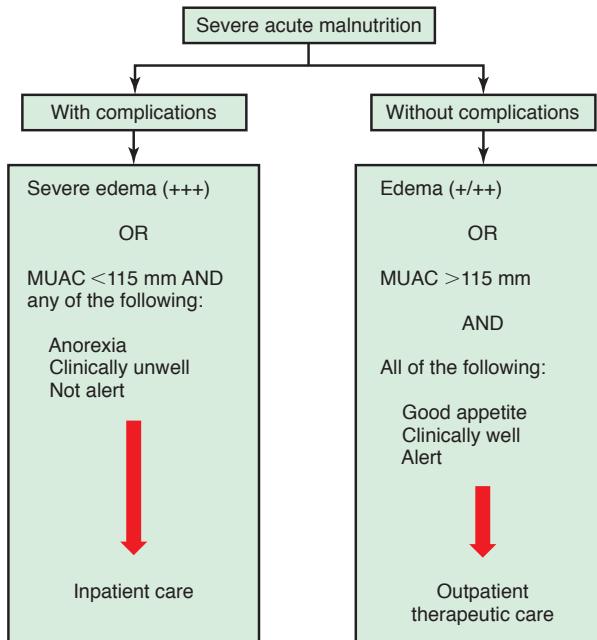


Figure 46-7 Flow diagram for inpatient and outpatient care in the child with severe acute malnutrition. MUAC, Mid upper arm circumference.

Table 47-1 Endocrine and Genetic Causes of Obesity

DISEASE	SYMPTOMS	LABORATORY
ENDOCRINE		
Cushing syndrome	Central obesity, hirsutism, moon face, hypertension	Dexamethasone suppression test
GH deficiency	Short stature, slow linear growth	Evoked GH response, IGF-1
Hyperinsulinism	Nesidioblastosis, pancreatic adenoma, hypoglycemia, Mauriac syndrome	Insulin level
Hypothyroidism	Short stature, weight gain, fatigue, constipation, cold intolerance, myxedema	TSH, FT ₄
Pseudohypoparathyroidism	Short metacarpals, subcutaneous calcifications, dysmorphic facies, mental retardation, short stature, hypocalcemia, hyperphosphatemia	Urine cAMP after synthetic PTH infusion
GENETIC		
Alstrom syndrome	Cognitive impairment, retinitis pigmentosa, diabetes mellitus, hearing loss, hypogonadism, retinal degeneration	ALMS1 gene
Bardet-Biedl syndrome	Retinitis pigmentosa, renal abnormalities, polydactyly, hypogonadism	BBS1 gene
Biemond syndrome	Cognitive impairment, iris coloboma, hypogonadism, polydactyly	
Carpenter syndrome	Polydactyly, syndactyly, cranial synostosis, mental retardation	Mutations in the RAB23 gene, located on chromosome 6 in humans
Cohen syndrome	Mid-childhood-onset obesity, short stature, prominent maxillary incisors, hypotonia, mental retardation, microcephaly, decreased visual activity	Mutations in the VPS13B gene (often called the COH1 gene) at locus 8q22
Deletion 9q34	Early-onset obesity, mental retardation, brachycephaly, synophrys, prognathism, behavior and sleep disturbances	Deletion 9q34
Down syndrome	Short stature, dysmorphic facies, mental retardation	Trisomy 21
ENPP1 gene mutations	Insulin resistance, childhood obesity	Gene mutation on chromosome 6q
Fröhlich syndrome	Hypothalamic tumor	
FTO gene polymorphism	Dysregulation of orexigenic hormone acyl-ghrelin, poor postprandial appetite suppression	Homozygous for FTO AA allele
Leptin or leptin receptor gene deficiency	Early-onset severe obesity, infertility (hypogonadotropic hypogonadism)	Leptin
Melanocortin 4 receptor gene mutation	Early-onset severe obesity, increased linear growth, hyperphagia, hyperinsulinemia	MC4R mutation
Prader-Willi Syndrome	Most common known genetic cause of obesity Homozygous worse than heterozygous	
Proopiomelanocortin deficiency	Neonatal hypotonia, slow infant growth, small hands and feet, mental retardation, hypogonadism, hyperphagia leading to severe obesity, paradoxically elevated ghrelin	Partial deletion of chromosome 15 or loss of paternally expressed genes
Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD)	Obesity, red hair, adrenal insufficiency, hyperproinsulinemia Often confused with congenital central hypoventilation syndrome (CCHS), presentation ≥1.5 yr with weight gain, hyperphagia, hypoventilation, cardiac arrest, central diabetes insipidus, hypothyroidism, growth hormone deficiency, pain insensitivity, hypothermia, precocious puberty, neural crest tumors	Loss-of-function mutations of the POMC gene Unknown genes May be a paraneoplastic disorder
Turner syndrome	Ovarian dysgenesis, lymphedema, web neck, short stature, cognitive impairment	XO chromosome

cAMP, cyclic adenosine monophosphate; FT₄, free thyroxine; GH, growth hormone; IGF, insulin-like growth factor; PTH, parathyroid hormone; TSH, thyroid-stimulating hormone.

312 Part VI ◆ Nutrition

Table 47-2 Obesity-Associated Comorbidities		
DISEASE	POSSIBLE SYMPTOMS	LABORATORY CRITERIA
CARDIOVASCULAR		
Dyslipidemia	HDL <40, LDL >130, total cholesterol >200	Fasting total cholesterol, HDL, LDL, triglycerides
Hypertension	SBP >95% for sex, age, height	Serial testing, urinalysis, electrolytes, blood urea nitrogen, creatinine
ENDOCRINE		
Type 2 diabetes mellitus	Acanthosis nigra, polyuria, polydipsia	Fasting blood glucose >110, hemoglobin A _{1c} , insulin level, C-peptide, oral glucose tolerance test
Metabolic syndrome	Central adiposity, insulin resistance, dyslipidemia, hypertension, glucose intolerance	Fasting glucose, LDL and HDL cholesterol
Polycystic ovary syndrome	Irregular menses, hirsutism, acne, insulin resistance, hyperandrogenemia	Pelvic ultrasound, free testosterone, LH, FSH
GASTROINTESTINAL		
Gallbladder disease	Abdominal pain, vomiting, jaundice	Ultrasound
Nonalcoholic fatty liver disease (NAFLD)	Hepatomegaly, abdominal pain, dependent edema, ↑ transaminases Can progress to fibrosis, cirrhosis	AST, ALT, ultrasound, CT, or MRI
NEUROLOGIC		
Pseudotumor cerebri	Headaches, vision changes, papilledema	Cerebrospinal fluid opening pressure, CT, MRI
Migraines	Hemicrania, headaches	None
ORTHOPEDIC		
Blount disease (tibia vara)	Severe bowing of tibia, knee pain, limp	Knee x-rays
Musculoskeletal problems	Back pain, joint pain, frequent strains or sprains, limp, hip pain, groin pain, leg bowing	X-rays
Slipped capital femoral epiphysis	Hip pain, knee pain, limp, decreased mobility of hip	Hip x-rays
PSYCHOLOGICAL		
Behavioral complications	Anxiety, depression, low self-esteem, disordered eating, signs of depression, worsening school performance, social isolation, problems with bullying or being bullied	Child Behavior Checklist, Children's Depression Inventory, Peds QL, Eating Disorder Inventory 2, subjective ratings of stress and depression, Behavior Assessment System for Children, Pediatric Symptom Checklist
PULMONARY		
Asthma	Shortness of breath, wheezing, coughing, exercise intolerance	Pulmonary function tests, peak flow
Obstructive sleep apnea	Snoring, apnea, restless sleep, behavioral problems	Polysomnography, hypoxia, electrolytes (respiratory acidosis with metabolic alkalosis)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CT, computed tomography; FSH, follicle-stimulating hormone; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LH, luteinizing hormone; MRI, magnetic resonance imaging; Peds QL, Pediatric Quality of Life Inventory; SBP, systolic blood pressure.

Table 47-6 | Proposed Suggestions for Preventing Obesity**PREGNANCY**

Normalize body mass index before pregnancy.
Do not smoke.
Maintain moderate exercise as tolerated.
In gestational diabetics, provide meticulous glucose control.
Gestational weight gain within the Institute of Medicine (IOM) recommendations.

POSTPARTUM AND INFANCY

Breastfeeding: exclusive for 4-6 mo, continue with other foods for 12 mo.
Postpone the introduction of baby foods to 4-6 mo and juices to 12 mo.

FAMILIES

Eat meals as a family in a fixed place and time.
Do not skip meals, especially breakfast.
No television during meals.
Use small plates, and keep serving dishes away from the table.
Avoid unnecessary sweet or fatty foods and sugar-sweetened drinks.
Remove televisions from children's bedrooms; restrict times for television viewing and video games.
Do not use food as a reward.

SCHOOLS

Eliminate candy and cookie sales as fundraisers.
Review the contents of vending machines and replace with healthier choices; eliminate sodas.
Avoid financial support for sports teams from beverage and food industries.
Install water fountains and hydration stations.
Educate teachers, especially physical education and science faculty, about basic nutrition and the benefits of physical activity.
Educate children from preschool through high school on appropriate diet and lifestyle.
Mandate minimum standards for physical education, including 60 min of strenuous exercise 5 times weekly.
Encourage "the walking school bus": groups of children walking to school with adult supervision.

COMMUNITIES

Increase family-friendly exercise and safe play facilities for children of all ages.
Develop more mixed residential-commercial developments for walkable and bicyclable communities.
Discourage the use of elevators and moving walkways.
Provide information on how to shop and prepare healthier versions of culture-specific foods.

HEALTHCARE PROVIDERS

Explain the biologic and genetic contributions to obesity.
Give age-appropriate expectations for body weight in children.
Work toward classifying obesity as a disease to promote recognition, reimbursement for care, and willingness and ability to provide treatment.

INDUSTRY

Mandate age-appropriate nutrition labeling for products aimed at children (e.g., red light/green light foods, with portion sizes).
Encourage marketing of interactive video games in which children must exercise in order to play.
Use celebrity advertising directed at children for healthful foods to promote breakfast and regular meals.
Reduce portion size (drinks and meals).

GOVERNMENT AND REGULATORY AGENCIES

Classify childhood obesity as a legitimate disease.
Find novel ways to fund healthy lifestyle programs (e.g., with revenues from food and drink taxes).
Subsidize government-sponsored programs to promote the consumption of fresh fruits and vegetables.
Provide financial incentives to industry to develop more healthful products and to educate the consumer on product content.
Provide financial incentives to schools that initiate innovative physical activity and nutrition programs.
Allow tax deductions for the cost of weight loss and exercise programs.
Provide urban planners with funding to establish bicycle, jogging, and walking paths.
Ban advertising of fast foods, nonnutritious foods, and sugar-sweetened beverages directed at preschool children, and restrict advertising to school-age children.
Ban toys as gifts to children for purchasing fast foods.

Adapted from Speiser PW, Rudolf MCJ, Anhalt H, et al: Consensus statement: childhood obesity, J Clin Endocrinol Metab 90:1871–1887, 2005.

Table 47-7 | Anticipatory Guidance: Establishing Healthy Eating Habits in Children

Do not punish a child during mealtimes with regard to eating. The emotional atmosphere of a meal is very important. Interactions during meals should be pleasant and happy.
Do not use foods as rewards.
Parents, siblings, and peers should model healthy eating, tasting new foods, and eating a well-balanced meal.
Children should be exposed to a wide range of foods, tastes, and textures.
New foods should be offered multiple times. Repeated exposure leads to acceptance and liking.
Forcing a child to eat a certain food will decrease the child's preference for that food. Children's wariness of new foods is normal and should be expected. Offering a variety of foods with low-energy density helps children balance energy intake.
Parents should control what foods are in the home. Restricting access to foods in the home will increase rather than decrease a child's desire for that food.
Children tend to be more aware of satiety than adults, so allow children to respond to satiety, and stop eating. Do not force children to "clean their plate."

Adapted from Benton D: Role of parents in the determination of food preferences of children and the development of obesity, Int J Obes Relat Metab Disord 28:858–869, 2004. Copyright 2004. Reprinted by permission from Macmillan Publishers Ltd.

Table 49-1 Water-Soluble Vitamins						
NAMES AND SYNONYMS	BIOCHEMICAL ACTION	EFFECTS OF DEFICIENCY	TREATMENT OF DEFICIENCY	CAUSES OF DEFICIENCY	DIETARY SOURCES	RDA* BY AGE
Thiamine (vitamin B ₁)	Coenzyme in carbohydrate metabolism Nucleic acid synthesis Neurotransmitter synthesis	Neurologic (dry beriberi): irritability, peripheral neuritis, muscle tenderness, ataxia Cardiac (wet beriberi): tachycardia, edema, cardiomegaly, cardiac failure	3-5 mg/day PO thiamine for 6 wk	Polished rice-based diets Malabsorptive states Severe malnutrition Malignancies Alcoholism	Meat, especially pork; fish; liver Rice (unmilled), wheat germ; enriched cereals; legumes	0-6 mo: 0.2 mg/day 7-12 mo: 0.3 mg/day 1-3 yr: 0.5 mg/day 4-8 yr: 0.6 mg/day 9-13 yr: 0.9 mg/day 14-18 yr: Girls: 1.0 mg/day Boys: 1.2 mg/day
Riboflavin (vitamin B ₂)	Constituent of flavoprotein enzymes important in oxidation-reduction reactions: amino acid, fatty acid, and carbohydrate metabolism and cellular respiration	Glossitis, photophobia, lacrimation, corneal vascularization, poor growth, cheilosis	3-10 mg/day PO riboflavin	Severe malnutrition Malabsorptive states Prolonged treatment with phenothiazines, probenecid, or OCPs	Milk, milk products, eggs, fortified cereals, green vegetables	0-6 mo: 0.3 mg/day 7-12 mo: 0.4 mg/day 1-3 yr: 0.5 mg/day 4-8 yr: 0.6 mg/day 9-13 yr: 0.9 mg/day 14-18 yr: Girls: 1.0 mg/day Boys: 1.3 mg/day
Niacin (vitamin B ₃)	Constituent of NAD and NADP, important in respiratory chain, fatty acid synthesis, cell differentiation, and DNA processing	Pellagra manifesting as diarrhea, symmetric scaly dermatitis in sun-exposed areas, and neurologic symptoms of disorientation and delirium	50-300 mg/day PO niacin	Predominantly maize-based diets Anorexia nervosa Carcinoid syndrome	Meat, fish, poultry Cereals, legumes, green vegetables	0-6 mo: 2 mg/day 7-12 mo: 4 mg/day 1-3 yr: 6 mg/day 4-8 yr: 8 mg/day 9-13 yr: 12 mg/day 14-18 yr: Girls: 14 mg/day Boys: 16 mg/day
Pyridoxine (vitamin B ₆)	Constituent of coenzymes for amino acid and glycogen metabolism, heme synthesis, steroid action, neurotransmitter synthesis	Irritability, convulsions, hypochromic anemia Failure to thrive Oxaluria	5-25 mg/day PO for deficiency states 100 mg IM or IV for pyridoxine-dependent seizures	Prolonged treatment with INH, penicillamine, OCPs	Fortified ready-to-eat cereals, meat, fish, poultry, liver, bananas, rice, potatoes	0-6 mo: 0.1 mg/day 7-12 mo: 0.3 mg/day 1-3 yr: 0.5 mg/day 4-8 yr: 0.6 mg/day 9-13 yr: 1.0 mg/day 14-18 yr: Girls: 1.2 mg/day Boys: 1.3 mg/day

Continued

Table 51-4 Laboratory Findings in Various Disorders Causing Rickets								
DISORDER	Ca	Pi	PTH	25-(OH)D	1,25-(OH) ₂ D	Alk Phos	URINE Ca	URINE Pi
Vitamin D deficiency	N, ↓	↓	↑	↓	↓, N, ↑	↑	↓	↑
Chronic kidney disease	N, ↓	↑	↑	N	↓	↑	N, ↓	↓
Dietary Pi deficiency	N	↓	N, ↓	N	↑	↑	↑	↓
Tumor-induced rickets	N	↓	N	N	RD	↑	↓	↑
Fanconi syndrome	N	↓	N	N	RD or ↑	↑	↓ or ↑	↑
Dietary Ca deficiency	N, ↓	↓	↑	N	↑	↑	↓	↑

↓, decreased; ↑, increased; ↑↑, extremely increased; 1,25-(OH)₂D, 1,25-dihydroxyvitamin D; 25-OHD, 25-hydroxyvitamin D; ADHR, autosomal dominant hypophosphatemic rickets; Alk Phos, alkaline phosphatase; ARHR, autosomal recessive hypophosphatemic rickets; Ca, calcium; HHRH, hereditary hypophosphatemic rickets with hypercalcioria; N, normal; Pi, inorganic phosphorus; PTH, parathyroid hormone; RD, relatively decreased (because it should be increased given the concurrent hypophosphatemia); VDDR, vitamin D-dependent rickets; XLH, X-linked hypophosphatemic rickets.

324 Part VI ◆ Nutrition

Table 49-1 Water-Soluble Vitamins—cont'd

NAMES AND SYNONYMS	BIOCHEMICAL ACTION	EFFECTS OF DEFICIENCY	TREATMENT OF DEFICIENCY	CAUSES OF DEFICIENCY	DIETARY SOURCES	RDA* BY AGE
Biotin	Cofactor for carboxylases, important in gluconeogenesis, fatty acid and amino acid metabolism	Scaly periorificial dermatitis, conjunctivitis, alopecia, lethargy, hypotonia, and withdrawn behavior	1-10 mg/day PO biotin	Consumption of raw eggs for prolonged periods Parenteral nutrition with infusates lacking biotin Valproate therapy	Liver, organ meats, fruits	0-6 mo: 5 µg/day 7-12 mo: 6 µg/day 1-3 yr: 8 µg/day 4-8 yr: 12 µg/day 9-13 yr: 20 µg/day 14-18 yr: 25 µg/day
Pantothenic acid (vitamin B ₅)	Component of coenzyme A and acyl carrier protein involved in fatty acid metabolism	Experimentally produced deficiency in humans: irritability, fatigue, numbness, paresthesias (burning feet syndrome), muscle cramps		Isolated deficiency extremely rare in humans	Beef, organ meats, poultry, seafood, egg yolk Yeast, soybeans, mushrooms	0-6 mo: 1.7 mg/day 7-12 mo: 1.8 mg/day 1-3 yr: 2 mg/day 4-8 yr: 3 mg/day 9-13 yr: 4 mg/day 14-18 yr: 5 mg/day
Folic acid	Coenzymes in amino acid and nucleotide metabolism as an acceptor and donor of one-carbon units	Megaloblastic anemia Growth retardation, glossitis Neural tube defects in progeny	0.5-1 mg/day PO folic acid	Malnutrition Malabsorptive states Malignancies Hemolytic anemias Anticonvulsant therapy	Enriched cereals, beans, leafy vegetables, citrus fruits, papaya	0-6 mo: 65 µg/day 7-12 mo: 80 µg/day 1-3 yr: 150 µg/day 4-8 yr: 200 µg/day 9-13 yr: 300 µg/day 14-18 yr: 400 µg/day
Cobalamin (vitamin B ₁₂)	As deoxyadenosylcobalamin, acts as cofactor for lipid and carbohydrate metabolism As methylcobalamin, important for conversion of homocysteine to methionine and folic acid metabolism	Megaloblastic anemia, irritability, developmental delay, developmental regression, involuntary movements, hyperpigmentation	1,000 µg IM vitamin B ₁₂	Vegan diets Malabsorptive states Crohn disease Intrinsic factor deficiency (pernicious anemia)	Organ meats, sea foods, poultry, egg yolk, milk, fortified ready-to-eat cereals	0-6 mo: 0.4 µg/day 7-12 mo: 0.5 µg/day 1-3 yr: 0.9 µg/day 4-8 yr: 1.2 µg/day 9-13 yr: 1.8 µg/day 14-18 yr: 2.4 µg/day
Ascorbic acid (vitamin C)	Important for collagen synthesis, metabolism of cholesterol and neurotransmitters Antioxidant functions and nonheme iron absorption	Scurvy manifesting as irritability, tenderness and swelling of legs, bleeding gums, petechiae, ecchymoses, follicular hyperkeratosis, and poor wound healing	100-200 mg/day PO ascorbic acid for up to 3 mo	Predominantly milk-based (non-human milk) diets Severe malnutrition	Citrus fruits and fruit juices, peppers, berries, melons, tomatoes, cauliflower, leafy green vegetables	0-6 mo: 40 mg/day 7-12 mo: 50 mg/day 1-3 yr: 15 mg/day 4-8 yr: 25 mg/day 9-13 yr: 45 mg/day 14-18 yr: Girls: 65 mg/day Boys: 75 mg/day

*For healthy breastfed infants, the values represent adequate intakes, that is, the mean intake of apparently "normal" infants.

INH, isoniazid; NAD, nicotinamide adenine dinucleotide; NADP, nicotinamide adenine dinucleotide phosphate; OCP, oral contraceptive pill; RDA, recommended dietary allowance.

Source: Dietary Reference Intakes (DRIs): Recommended dietary allowances and adequate intakes, vitamins. Food and Nutrition Board, Institute of Medicine, National Academies. Available from: <http://fnic.nal.usda.gov/dietary-guidance/dietary-reference-intakes/dri-tables>.

Table 51-5 Biochemical Changes in Genetic Causes of Rickets

	SERUM BIOCHEMISTRY						URINE BIOCHEMISTRY			OTHER FEATURES
	Phosphate	Calcium	PTH	25OH D	1,25(OH) ₂ D	FGF23	Alk Phos	Phosphate	Calcium	
HYPOCALCEMIC VITAMIN D PATHWAY DEFECTS										
Vitamin D deficiency	Variable	High	Low	Very low	Normal or high	Might be increased	NA	Increased	Low	Variable aminoaciduria
VDDR1A	Low	High	Low	Very low	Variable	NA	Increased	Increased	Low	25OH D does not increase after vitamin D dosing
VDDR2A	Low	High	Low	Normal or high	High	NA	Increased	Increased	Low	25OH D does increase after vitamin D dosing
VDDR2B	Low	High	Low	Normal or high	High	NA	Increased	Increased	Low	—
HYPOPHOSPHATEMIC RICKETS WITH RAISED FGF23										
XLH	Low	Normal or slightly high	Normal	Low	High	Increased	Increased	Variable	Urine calcium : creatinine used in monitoring therapy	
ADHR	Normal	Normal	Normal	Low	High	Increased	Increased	Variable	—	
ARHR1	Low	Normal	Normal	Low	High	Increased	Increased	Variable	—	
ARHR2	Low	Normal	Normal	Low	High	Increased	Increased	Variable	—	
HYPOPHOSPHATEMIC RICKETS WITHOUT RAISED FGF23										
Dent's disease*	Low	Normal	Normal	Normal	Normal	Normal	Increased	High	Low molecular weight proteinuria	
HHRH	Low	Normal	Normal	Normal	Normal	Normal	Increased	High	No loss of low molecular weight protein	
α Klotho mutation	Low	Normal	Normal	Normal	Normal	Normal	Increased	Variable	—	
OTHER INHERITED RACHITIC DISORDERS										
HPP (severe)	High	High	Low	Normal	Normal	Normal	Very low	Normal or high	High	Raised concentrations of mineralization inhibitors
HPP (mild)	Normal or high	Normal or high	Low or normal	Normal	Normal	Normal	Low	Normal	Variable	Raised concentrations of mineralization inhibitors

From Elder CJ, Bishop NJ. Rickets. Lancet 383:1665-1674, 2014.

PTH, parathyroid hormone; 25OH D, calcidiol; 1,25(OH)₂D, calcitriol; FGF23, fibroblast growth factor 23; Alk phos, alkaline phosphatase; NA, data not available; VDDR1B, vitamin D-dependent rickets due to defects in CYP2R1 encoding vitamin D-25-hydroxylase; VDDR1A, vitamin D-dependent rickets due to defects in CYP2R2B; VDDR2B, vitamin D-dependent rickets due to defects in VDR encoding the vitamin D receptor; VDDR2A, vitamin D-dependent rickets due to defects in hNRNPF1 and hNRNPF2; XLH, X-linked hypophosphatemic rickets due to mutations in PHEX; ADHR, autosomal dominant hypophosphatemic rickets due to mutations in FGF23; ARHR1, autosomal recessive hypophosphatemic rickets due to mutations in DMP1; ARHR2, autosomal recessive hypophosphatemic rickets due to mutations in ENPP1; HHRH, hereditary hypophosphatemic rickets with hypercalcuria due to mutations in SLC34A3; HPP, hypophosphatasia.

*Dent's disease is due to mutations in CLCNs.

344 Part VI ◆ Nutrition

Table 54-1 Trace Elements				
ELEMENT	PHYSIOLOGY	EFFECTS OF DEFICIENCY	EFFECTS OF EXCESS	DIETARY SOURCES
Chromium	Potentiates the action of insulin	Impaired glucose tolerance, peripheral neuropathy, and encephalopathy	Unknown	Meat, grains, fruits, and vegetables
Copper	Absorbed via specific intestinal transporter Circulates bound to ceruloplasmin Enzyme cofactor (superoxide dismutase, cytochrome oxidase, and enzymes involved in iron metabolism and connective tissue formation)	Microcytic anemia, osteoporosis, neutropenia, neurologic symptoms, depigmentation of hair and skin	Acute: nausea, emesis, abdominal pain, coma, and hepatic necrosis Chronic toxicity (liver and brain injury) occurs in Wilson disease (see Chapter 357.2) and secondary to excess intake (see Chapter 357.3)	Vegetables, grains, nuts, liver, margarine, legumes, corn oil
Fluoride	Incorporated into bone	Dental caries (see Chapter 312)	Chronic: dental fluorosis (see Chapter 307)	Toothpaste, fluoridated water
Iodine	Component of thyroid hormone (see Chapter 564)	Hypothyroidism (see Chapters 566 and 568)	Hypothyroidism and goiter (see Chapters 566 and 568); maternal excess can cause congenital hypothyroidism and goiter (see Chapter 568.1)	Saltwater fish, iodized salt
Iron	Component of hemoglobin, myoglobin, cytochromes, and other enzymes	Anemia (see Chapter 456), decreased alertness, impaired learning	Acute (see Chapter 63): nausea, vomiting, diarrhea, abdominal pain, and hypotension Chronic excess usually secondary to hereditary disorders (see Chapters 463.9 and 357.4); causes organ dysfunction	Meat, fortified foods Deficiency can also result from blood loss (hookworm infestation, menorrhagia)
Manganese	Enzyme cofactor	Hypercholesterolemia, weight loss, decreased clotting proteins*	Neurologic manifestations, cholestatic jaundice	Nuts, meat, grains, tea
Molybdenum	Enzyme cofactor (xanthine oxidase and others)	Tachycardia, tachypnea, night blindness, irritability, coma*	Hyperuricemia and increased risk of gout	Legumes, grains, liver
Selenium	Enzyme cofactor (prevents oxidative damage)	Cardiomyopathy (Keshan disease), myopathy	Nausea, diarrhea, neurologic manifestations, nail and hair changes, garlic odor	Meat, seafood, whole grains, garlic
Zinc	Enzyme cofactor Constituent of zinc-finger proteins, which regulate gene transcription	Decreased growth, dermatitis of extremities and around orifices, impaired immunity, poor wound healing, hypogonadism, diarrhea Supplements beneficial in diarrhea and improve neurodevelopmental outcomes	Abdominal pain, diarrhea, vomiting Can worsen copper deficiency	Meat, shellfish, whole grains, legumes, cheese

*These deficiency states have been reported only in case reports associated with parenteral nutrition or highly unusual diets.

Electrolyte and Acid-Base Disorders

Table 55-1 Causes of Hypernatremia

EXCESSIVE SODIUM	
Improperly mixed formula	
Excess sodium bicarbonate	
Ingestion of seawater or sodium chloride	
Intentional salt poisoning (child abuse or Munchausen syndrome by proxy)	
Intravenous hypertonic saline	
Hyperaldosteronism	
WATER DEFICIT	
Nephrogenic diabetes insipidus	
Acquired	
X-linked (OMIM 304800)	
Autosomal recessive (OMIM 222000)	
Autosomal dominant (OMIM 125800)	
Central diabetes insipidus	
Acquired	
Autosomal recessive (OMIM 125700)	
Autosomal dominant (OMIM 125700)	
Wolfram syndrome (OMIM 222300/598500)	
Increased insensible losses	
Premature infants	
Radiant warmers	
Phototherapy	
Inadequate intake:	
Ineffective breastfeeding	
Child neglect or abuse	
Adipsia (lack of thirst)	
WATER AND SODIUM DEFICITS	
Gastrointestinal losses	
Diarrhea	
Emesis/nasogastric suction	
Osmotic cathartics (lactulose)	
Cutaneous losses	
Burns	
Excessive sweating	
Renal losses	
Osmotic diuretics (mannitol)	
Diabetes mellitus	
Chronic kidney disease (dysplasia and obstructive uropathy)	
Polyuric phase of acute tubular necrosis	
Postobstructive diuresis	

OMIM, database number from the Online Mendelian Inheritance in Man (<http://www.ncbi.nlm.nih.gov/omim>).

Table 55-2 Causes of Hyponatremia

PSEUDOHYponATREMIA	
Hyperlipidemia	
Hyperproteinemia	
HYPEROSMOLALITY	
Hyperglycemia	
Iatrogenic (mannitol, sucrose, glycine)	
HYPovOLEMIC HYponATREMIA	
EXTRARENAL LOSSES	
Gastrointestinal (emesis, diarrhea)	
Skin (sweating or burns)	
Third space losses (bowel obstruction, peritonitis, sepsis)	
RENAL LOSSES	
Thiazide or loop diuretics	
Osmotic diuresis	
Postobstructive diuresis	
Polyuric phase of acute tubular necrosis	
Juvenile nephronophthisis (OMIM 256100/606966/602088/604387/611498)	
Autosomal recessive polycystic kidney disease (OMIM 263200)	
Tubulointerstitial nephritis	
Obstructive uropathy	
Cerebral salt wasting	
Proximal (type II) renal tubular acidosis (OMIM 604278)*	
Lack of aldosterone effect (high serum potassium):	
Absence of aldosterone (e.g., 21-hydroxylase deficiency [OMIM 201910])	
Pseudohypoaldosteronism type I (OMIM 264350/177735)	
Urinary tract obstruction and/or infection	
EUVOLEMIC HYponATREMIA	
Syndrome of inappropriate antidiuretic hormone secretion	
Nephrogenic syndrome of inappropriate antidiuresis (OMIM 304800)	
Desmopressin acetate	
Glucocorticoid deficiency	
Hypothyroidism	
Water intoxication:	
Iatrogenic (excess hypotonic intravenous fluids)	
Feeding infants excessive water products	
Swimming lessons	
Tap water enema	
Child abuse	
Psychogenic polydipsia	
Diluted formula	
Beer potomania	
Exercise-induced hyponatremia	
HYPERVOLEMIC HYponATREMIA	
Heart failure	
Cirrhosis	
Nephrotic syndrome	
Acute, chronic kidney injury	
Capillary leak caused by sepsis	
Hypoalbuminemia caused by gastrointestinal disease (protein-losing enteropathy)	

*Most cases of proximal renal tubular acidosis are not caused by this primary genetic disorder. Proximal renal tubular acidosis is usually part of Fanconi syndrome, which has multiple etiologies.

OMIM, database number from the Online Mendelian Inheritance in Man (<http://www.ncbi.nlm.nih.gov/omim>).

Table 55-5 Causes of Hypokalemia

SPURIOUS
High white blood cell count
TRANSCELLULAR SHIFTS
Alkalemia
Insulin
α-Adrenergic agonists
Drugs/toxins (theophylline, barium, toluene, cesium chloride, hydroxychloroquine)
Hypokalemic periodic paralysis (OMIM 170400)
Thyrotoxic periodic paralysis
Refeeding syndrome
DECREASED INTAKE
Anorexia nervosa
EXTRARENAL LOSSES
Diarrhea
Laxative abuse
Sweating
Sodium polystyrene sulfonate (Kayexalate) or clay ingestion
RENAL LOSSES
With metabolic acidosis
Distal renal tubular acidosis (OMIM 179800/602722/267300)
Proximal renal tubular acidosis (OMIM 604278)*
Ureterosigmoidostomy
Diabetic ketoacidosis
Without specific acid-base disturbance
Tubular toxins: amphotericin, cisplatin, aminoglycosides
Interstitial nephritis
Diuretic phase of acute tubular necrosis
Postobstructive diuresis
Hypomagnesemia
High urine anions (e.g., penicillin or penicillin derivatives)
With metabolic alkalosis
Low urine chloride
Emesis or nasogastric suction
Chloride-losing diarrhea (OMIM 214700)
Cystic fibrosis (OMIM 219700)
Low-chloride formula
Posthypercapnia
Previous loop or thiazide diuretic use
High urine chloride and normal blood pressure
Gitelman syndrome (OMIM 263800)
Bartter syndrome (OMIM 607364/602522/241200/601678)
Autosomal dominant hypoparathyroidism (OMIM 146200)
EAST syndrome (OMIM 612780)
Loop and thiazide diuretics
High urine chloride and high blood pressure
Adrenal adenoma or hyperplasia
Glucocorticoid-remediable aldosteronism (OMIM 103900)
Renovascular disease
Renin-secreting tumor
17β-Hydroxylase deficiency (OMIM 202110)
11β-Hydroxylase deficiency (OMIM 202010)
Cushing syndrome
11β-Hydroxysteroid dehydrogenase deficiency (OMIM 218030)
Licorice ingestion
Liddle syndrome (OMIM 177200)

*Most cases of proximal renal tubular acidosis are not caused by this primary genetic disorder. Proximal renal tubular acidosis is usually part of Fanconi syndrome, which has multiple etiologies.

EAST, epilepsy, ataxia, sensorineural hearing loss, and tubulopathy; OMIM, database number from the Online Mendelian Inheritance in Man (<http://www.ncbi.nlm.nih.gov/omim>).

Table 55-4 Causes of Hyperkalemia

SPURIOUS LABORATORY VALUE
Hemolysis
Tissue ischemia during blood drawing
Thrombocytosis
Leukocytosis
Familial pseudohyperkalemia (OMIM 609153/611184/612126)
INCREASED INTAKE
Intravenous or oral
Blood transfusions
TRANSCELLULAR SHIFTS
Acidosis
Rhabdomyolysis
Tumor lysis syndrome
Tissue necrosis
Hemolysis/hematomas/gastrointestinal bleeding
Succinylcholine
Digitalis intoxication
Fluoride intoxication
β-Adrenergic blockers
Exercise
Hyperosmolality
Insulin deficiency
Malignant hyperthermia (OMIM 145600/601887)
Hyperkalemic periodic paralysis (OMIM 170500)
DECREASED EXCRETION
Renal failure
Primary adrenal disease:
Acquired Addison disease
21-Hydroxylase deficiency (OMIM 201910)
3β-Hydroxysteroid dehydrogenase deficiency (OMIM 201810)
Lipoid congenital adrenal hyperplasia (OMIM 201710)
Adrenal hypoplasia congenita (OMIM 300200)
Aldosterone synthase deficiency (OMIM 203400/610600)
Adrenoleukodystrophy (OMIM 300100)
Hyporeninemic hypoaldosteronism:
Urinary tract obstruction
Sickle cell disease (OMIM 603903)
Kidney transplant
Lupus nephritis
Renal tubular disease:
Pseudohypoaldosteronism type I (OMIM 264350/177735)
Pseudohypoaldosteronism type II (OMIM 145260)
Bartter syndrome, type 2 (OMIM 241200)
Urinary tract obstruction
Kidney transplant
Medications:
Angiotensin-converting enzyme inhibitors
Angiotensin II blockers
Potassium-sparing diuretics
Calcineurin inhibitors
Nonsteroidal antiinflammatory drugs
Trimethoprim
Heparin
Drospirenone (in some oral contraceptives)

Table 55-3 Diagnostic Criteria for Syndrome of Inappropriate Antidiuretic Hormone Secretion

Absence of:
Renal, adrenal, or thyroid insufficiency
Heart failure, nephrotic syndrome, or cirrhosis
Diuretic ingestion
Dehydration
Urine osmolality >100 mOsm/kg (usually > plasma)
Serum osmolality <280 mOsm/kg and serum sodium <135 mEq/L
Urine sodium >30 mEq/L
Reversal of "sodium wasting" and correction of hyponatremia with water restriction

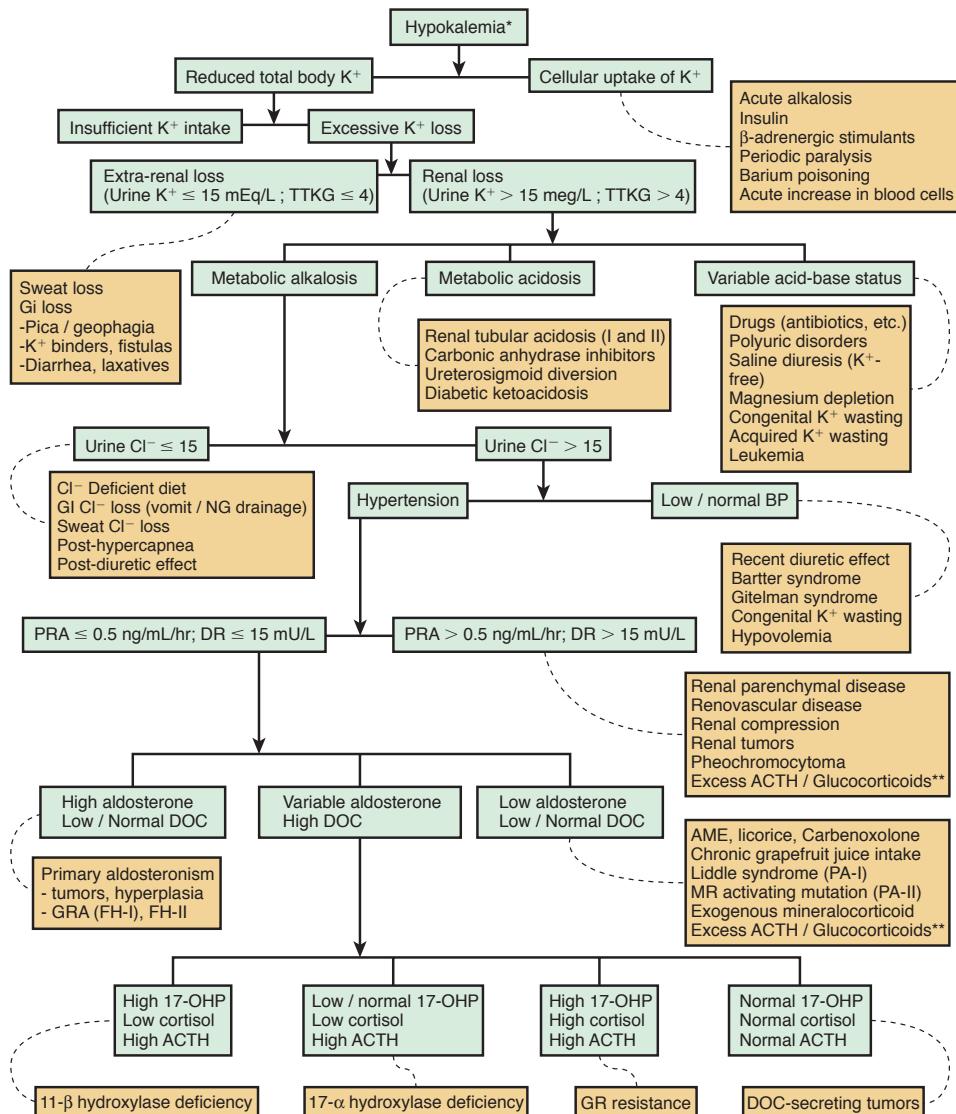


Figure 55-5 Diagnostic algorithm to evaluate persistent hypokalemia. *Spurious hypokalemia must be excluded. **Hypokalemia is uncommon in uncomplicated edematous disorders and in conditions associated with excessive glucocorticosteroids. Conditions associated with high circulating levels of glucocorticosteroids often have normal renin activity. 17-OHP, 17-hydroxyprogesterone; ACTH, adrenocorticotrophic hormone; AME, apparent mineralocorticoid excess; BP, blood pressure; Cl-, chloride; DOC, 11-deoxycorticosterone; DR, direct renin assay; GI, gastrointestinal; FH-II, familial hyperaldosteronism type II; GR, glucocorticoid receptor; GRA (FH-I), glucocorticoid remediable aldosteronism (familial hyperaldosteronism type I); K+, potassium; MR, mineralocorticoid receptor; PA-I, pseudoaldosteronism type I; PA-II, pseudoaldosteronism type II; PRA, plasma renin activity; TTKG, transtubular potassium gradient. (From Shoemaker LR, Eaton BV, Buchino JJ: A three-year-old with persistent hypokalemia, *J Pediatr* 151:696–699, 2007.)

Table 55-7 Causes of Hypomagnesemia**GASTROINTESTINAL DISORDERS**

- Diarrhea
- Nasogastric suction or emesis
- Inflammatory bowel disease
- Celiac disease
- Cystic fibrosis
- Intestinal lymphangiectasia
- Small bowel resection or bypass
- Pancreatitis
- Protein-calorie malnutrition
- Hypomagnesemia with secondary hypocalcemia (OMIM 602014)*

RENAL DISORDERS

- Medications
 - Amphotericin
 - Cisplatin
 - Cyclosporin
 - Loop diuretics
 - Mannitol
 - Pentamidine
 - Proton pump inhibitors
 - Aminoglycosides
 - Thiazide diuretics
 - Epidermal growth factor receptor inhibitors
- Diabetes
- Acute tubular necrosis (recovery phase)
- Postobstructive nephropathy
- Chronic kidney diseases
 - Interstitial nephritis
 - Glomerulonephritis
 - Post-renal transplantation
- Hypercalcemia
- Intravenous fluids
- Primary aldosteronism
- Genetic diseases
 - Gitelman syndrome (OMIM 263800)
 - Bartter syndrome (OMIM 607364/601678)
 - Familial hypomagnesemia with hypercalciuria and nephrocalcinosis (OMIM 248250)
 - Familial hypomagnesemia with hypercalciuria, nephrocalcinosis, and severe ocular involvement (OMIM 248190)
 - Autosomal recessive renal magnesium wasting with normocalciuria (OMIM 611718)
 - Renal cysts and diabetes syndrome (OMIM 137920)
 - Autosomal dominant hypomagnesemia (OMIM 160120/613882/154020)
 - EAST syndrome (OMIM 612780)
 - Autosomal dominant hypoparathyroidism (OMIM 146200)
 - Mitochondrial disorders (OMIM 500005)

MISCELLANEOUS CAUSES

- Poor intake
- Hungry bone syndrome
- Insulin administration
- Pancreatitis
- Intrauterine growth retardation
- Infants of diabetic mothers
- Exchange transfusion

*This disorder is also associated with renal magnesium wasting.

EAST, epilepsy, ataxia, sensorineurial hearing loss, and tubulopathy; OMIM, database number from the Online Mendelian Inheritance in Man (<http://www.ncbi.nlm.nih.gov/omim>).

Table 55-9 Causes of Hypophosphatemia**TRANSCELLULAR SHIFTS**

- Glucose infusion
- Insulin
- Refeeding
- Total parenteral nutrition
- Respiratory alkalosis
- Tumor growth
- Bone marrow transplantation
- Hungry bone syndrome

DECREASED INTAKE

- Nutritional
- Premature infants
- Low phosphorus formula
- Antacids and other phosphate binders

RENAL LOSSES

- Hyperparathyroidism
- Parathyroid hormone-related peptide
- X-linked hypophosphatemic rickets (OMIM 307800)
- Overproduction of fibroblast growth factor-23
- Tumor-induced rickets
- McCune-Albright syndrome
- Epidermal nevus syndrome
- Neurofibromatosis
- Autosomal dominant hypophosphatemic rickets (OMIM 193100)
- Autosomal recessive hypophosphatemic rickets (OMIM 241520)
- Fanconi syndrome
- Dent disease (OMIM 300009/300555)
- Hypophosphatemic rickets with hypercalciuria (OMIM 241530)
- Hypophosphatemic nephrolithiasis/osteoporosis type 1 (OMIM 612286)
- Hypophosphatemic nephrolithiasis/osteoporosis type 2 (OMIM 612287)
- Volume expansion and intravenous fluids
- Metabolic acidosis
- Diuretics
- Glycosuria
- Glucocorticoids
- Kidney transplantation

MULTIFACTORIAL

- Vitamin D deficiency
- Vitamin D-dependent rickets type 1 (OMIM 264700)
- Vitamin D-dependent rickets type 2 (OMIM 277440)
- Alcoholism
- Sepsis
- Dialysis

Table 55-10 Causes of Hyperphosphatemia**TRANSCELLULAR SHIFTS**

- Tumor lysis syndrome
- Rhabdomyolysis
- Acute hemolysis
- Diabetic ketoacidosis and lactic acidosis

INCREASED INTAKE

- Enemas and laxatives
- Cow's milk in infants
- Treatment of hypophosphatemia
- Vitamin D intoxication

DECREASED EXCRETION

- Renal failure
- Hypoparathyroidism or pseudohypoparathyroidism (OMIM 146200/603233/103580/241410/203330)
- Acromegaly
- Hyperthyroidism
- Tumoral calcinosis with hyperphosphatemia (OMIM 211900)

OMIM, database number from the Online Mendelian Inheritance in Man (<http://www.ncbi.nlm.nih.gov/omim>).

Table 55-13 Causes of Metabolic Acidosis**NORMAL ANION GAP**

Diarrhea

Renal tubular acidosis (RTA):

Distal (type I) RTA (OMIM 179800/602722/267300)*

Proximal (type II) RTA (OMIM 604278)^tHyperkalemic (type IV) RTA (OMIM 201910/264350/177735/145260)^t

Urinary tract diversions

Posthypocapnia

Ammonium chloride intake

INCREASED ANION GAP**Lactic acidosis**

Tissue hypoxia

Shock

Hypoxemia

Severe anemia

Liver failure

Malignancy

Intestinal bacterial overgrowth

Inborn errors of metabolism

Medications

Nucleoside reverse transcriptase inhibitors

Metformin

Propofol

Ketoacidosis

Diabetic ketoacidosis

Starvation ketoacidosis

Alcoholic ketoacidosis

Kidney failure**Poisoning**

Ethylene glycol

Methanol

Salicylate

Toluene

Paraldehyde

*Along with these genetic disorders, distal RTA may be secondary to renal disease or medications.

^tMost cases of proximal RTA are not caused by this primary genetic disorder. Proximal RTA is usually part of Fanconi syndrome, which has multiple etiologies.

^tHyperkalemic RTA can be secondary to a genetic disorder (some of the more common are listed) or other etiologies.

OMIM, database number from the Online Mendelian Inheritance in Man

Table 55-11**Appropriate Compensation During Simple Acid-Base Disorders****DISORDER****EXPECTED COMPENSATION**Metabolic acidosis $\text{PCO}_2 = 1.5 \times [\text{HCO}_3^-] + 8 \pm 2$ Metabolic alkalosis PCO_2 increases by 7 mm Hg for each 10 mEq/L increase in serum $[\text{HCO}_3^-]$ **RESPIRATORY ACIDOSIS**Acute $[\text{HCO}_3^-]$ increases by 1 for each 10 mm Hg increase in PCO_2 Chronic $[\text{HCO}_3^-]$ increases by 3.5 for each 10 mm Hg increase in PCO_2 **RESPIRATORY ALKALOSIS**Acute $[\text{HCO}_3^-]$ falls by 2 for each 10 mm Hg decrease in PCO_2 Chronic $[\text{HCO}_3^-]$ falls by 4 for each 10 mm Hg decrease in PCO_2 **Table 55-12** Normal Values of Arterial Blood Gases

pH 7.35-7.45

 $[\text{HCO}_3^-]$ 20-28 mEq/L PCO_2 35-45 mm Hg**Table 55-14** Causes of Metabolic Alkalosis**CHLORIDE-RESPONSIVE (URINARY CHLORIDE <15 MEQ/L)**

Gastric losses

Emesis

Nasogastric suction

Diuretics (loop or thiazide)

Chloride-losing diarrhea (OMIM 214700)

Chloride-deficient formula

Cystic fibrosis (OMIM 219700)

Post-hypercapnia

CHLORIDE-RESISTANT (URINARY CHLORIDE >20 MEQ/L)

High blood pressure

Adrenal adenoma or hyperplasia

Glucocorticoid-remediable aldosteronism (OMIM 103900)

Renovascular disease

Renin-secreting tumor

17 β -Hydroxylase deficiency (OMIM 202110)11 β -Hydroxylase deficiency (OMIM 202010)

Cushing syndrome

11 β -Hydroxysteroid dehydrogenase deficiency (OMIM 218030)

Licorice ingestion

Liddle syndrome (OMIM 177200)

Normal blood pressure

Gitelman syndrome (OMIM 263800)

Bartter syndrome (OMIM 607364/602522/241200/601678)

Autosomal dominant hypoparathyroidism (OMIM 146200)

EAST syndrome (OMIM 612780)

Base administration

EAST, epilepsy, ataxia, sensorineural hearing loss, and tubulopathy;

OMIM, database number from the Online Mendelian Inheritance in Man

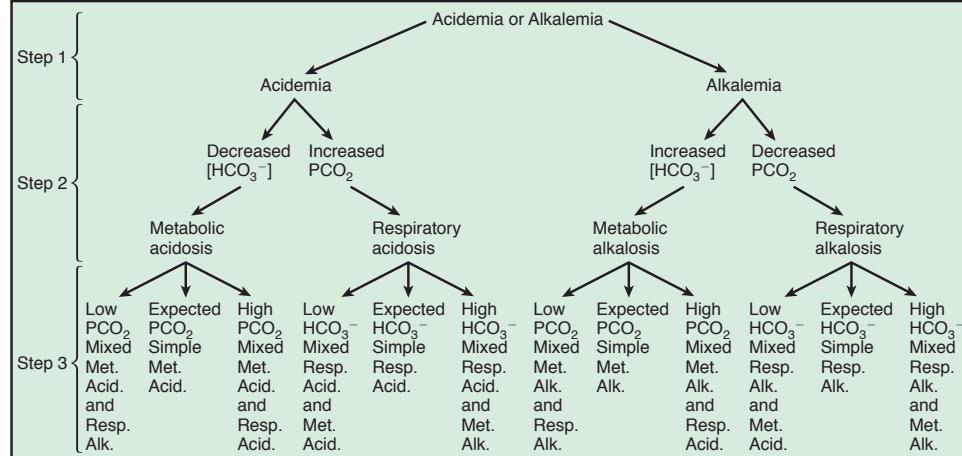


Figure 55-9 Three-step process for interpreting acid-base disturbances. In step 1, determine whether the pH is low (acidemia) or high (alkalemia). In step 2, establish an explanation for the acidemia or alkalemia. In step 3, calculate the expected compensation (see Table 55-11) and determine whether a mixed disturbance is present. Met. Acid., metabolic acidosis; Met. Alk., metabolic alkalosis; Resp. Acid., respiratory acidosis; Resp. Alk., respiratory alkalosis.

Table 55-15 Causes of Respiratory Acidosis**CENTRAL NERVOUS SYSTEM DEPRESSION**

- Encephalitis
- Head trauma
- Brain tumor
- Central sleep apnea
- Primary pulmonary hypoventilation (Ondine curse)
- Stroke
- Hypoxic brain damage
- Obesity-hypoventilation (Pickwickian syndrome)
- Increased intracranial pressure
- Medications
 - Narcotics
 - Barbiturates
 - Anesthesia
 - Benzodiazepines
 - Propofol
 - Alcohols

DISORDERS OF THE SPINAL CORD, PERIPHERAL NERVES, OR NEUROMUSCULAR JUNCTION

- Diaphragmatic paralysis
- Guillain-Barré syndrome
- Poliomyelitis
- Spinal muscular atrophies
- Tick paralysis
- Botulism
- Myasthenia
- Multiple sclerosis
- Spinal cord injury
- Medications
 - Vecuronium
 - Aminoglycosides
 - Organophosphates (pesticides)

RESPIRATORY MUSCLE WEAKNESS

- Muscular dystrophy
- Hypothyroidism
- Malnutrition
- Hypokalemia
- Hypophosphatemia
- Medications
 - Succinylcholine
 - Corticosteroids

PULMONARY DISEASE

- Pneumonia
- Pneumothorax
- Asthma
- Bronchiolitis
- Pulmonary edema
- Pulmonary hemorrhage
- Acute respiratory distress syndrome
- Neonatal respiratory distress syndrome
- Cystic fibrosis
- Bronchopulmonary dysplasia
- Hypoplastic lungs
- Meconium aspiration
- Pulmonary thromboembolus
- Interstitial fibrosis

UPPER AIRWAY DISEASE

- Aspiration
- Laryngospasm
- Angioedema
- Obstructive sleep apnea
- Tonsillar hypertrophy
- Vocal cord paralysis
- Extrinsic tumor
- Extrinsic or intrinsic hemangioma

MISCELLANEOUS

- Flail chest
- Cardiac arrest
- Kyphoscoliosis
- Decreased diaphragmatic movement due to ascites or peritoneal dialysis

Table 55-16 Causes of Respiratory Alkalosis**HYPOXEMIA OR TISSUE HYPOXIA**

- Pneumonia
- Pulmonary edema
- Cyanotic heart disease
- Congestive heart failure
- Asthma
- Severe anemia
- High altitude
- Laryngospasm
- Aspiration
- Carbon monoxide poisoning
- Pulmonary embolism
- Interstitial lung disease
- Hypotension

LUNG RECEPTOR STIMULATION

- Pneumonia
- Pulmonary edema
- Asthma
- Pulmonary embolism
- Hemothorax
- Pneumothorax
- Respiratory distress syndrome (adult or infant)

CENTRAL STIMULATION

- Central nervous system disease
 - Subarachnoid hemorrhage
 - Encephalitis or meningitis
 - Trauma
 - Brain tumor
 - Stroke
 - Fever
 - Pain
 - Anxiety (panic attack)
 - Psychogenic hyperventilation or anxiety
 - Liver failure
 - Sepsis
 - Pregnancy
 - Mechanical ventilation
 - Hyperammonemia
 - Extracorporeal membrane oxygenation or hemodialysis
- Medications
 - Salicylate intoxication
 - Theophylline
 - Progesterone
 - Exogenous catecholamines
 - Caffeine

Table 57-4 Treatment of Hypernatremic Dehydration

Restore intravascular volume:

Normal saline: 20 mL/kg over 20 min (repeat until intravascular volume restored)

Determine time for correction on basis of initial sodium concentration:

[Na] 145-157 mEq/L: 24 hr

[Na] 158-170 mEq/L: 48 hr

[Na] 171-183 mEq/L: 72 hr

[Na] 184-196 mEq/L: 84 hr

Administer fluid at constant rate over time for correction:

Typical fluid: 5% dextrose + half-normal saline (with 20 mEq/L KCl unless contraindicated)

Typical rate: 1.25-1.5 times maintenance

Follow serum sodium concentration

Adjust fluid on basis of clinical status and serum sodium concentration:

Signs of volume depletion: administer normal saline (20 mL/kg)

Sodium decreases too rapidly; either:

 Increase sodium concentration of intravenous fluid

 Decrease rate of intravenous fluid

Sodium decreases too slowly; either:

 Decrease sodium concentration of intravenous fluid

 Increase rate of intravenous fluid

Replace ongoing losses as they occur

Table 56-1 Goals of Maintenance Fluids

Prevent dehydration
Prevent electrolyte disorders
Prevent ketoacidosis
Prevent protein degradation

Table 57-1 Clinical Evaluation of Dehydration

Mild dehydration (<5% in an infant; <3% in an older child or adult): Normal or increased pulse; decreased urine output; thirsty; normal physical findings

Moderate dehydration (5-10% in an infant; 3-6% in an older child or adult): Tachycardia; little or no urine output; irritable/lethargic; sunken eyes and fontanel; decreased tears; dry mucous membranes; mild delay in elasticity (skin turgor); delayed capillary refill (>1.5 sec); cool and pale

Severe dehydration (>10% in an infant; >6% in an older child or adult): Peripheral pulses either rapid and weak or absent; decreased blood pressure; no urine output; very sunken eyes and fontanel; no tears; parched mucous membranes; delayed elasticity (poor skin turgor); very delayed capillary refill (>3 sec); cold and mottled; limp; depressed consciousness

Table 56-2 Body Weight Method for Calculating Daily Maintenance Fluid Volume

BODY WEIGHT	FLUID PER DAY
0-10 kg	100 mL/kg
11-20 kg	1,000 mL + 50 mL/kg for each kg >10 kg
>20 kg	1,500 mL + 20 mL/kg for each kg >20 kg*

*The maximum total fluid per day is normally 2,400 mL.

Table 56-3 Hourly Maintenance Water Rate

For body weight of 0-10 kg: 4 mL/kg/hr
For body weight of 10-20 kg: 40 mL/hr + 2 mL/kg/hr × (wt – 10 kg)
For body weight of >20 kg: 60 mL/hr + 1 mL/kg/hr × (wt – 20 kg)*

*The maximum fluid rate is normally 100 mL/hr.

Table 56-4 Composition of Intravenous Solutions

FLUID	[Na]	[Cl ⁻]	[K ⁺]	[Ca ²⁺]	[LACTATE-]
Normal saline (0.9% NaCl)	154	154	—	—	—
Half-normal saline (0.45% NaCl)	77	77	—	—	—
0.2 normal saline (0.2% NaCl)	34	34	—	—	—
Ringer lactate	130	109	4	3	28

Table 57-3 Monitoring Therapy

Vital signs:
Pulse
Blood pressure
Intake and output:
Fluid balance
Urine output
Physical examination:
Weight
Clinical signs of depletion or overload
Electrolytes

Pediatric Drug Therapy

434 Part VIII ◆ Pediatric Drug Therapy

Table 62-3 Commonly Used Nonopioid Medications

MEDICATION	DOSAGE	COMMENT(S)
Acetaminophen	10-15 mg/kg PO q4h 10 mg/kg IV q4h 15 mg/kg IV q6h 10 mg/kg IV q6h (<2 yr) 20-30 mg/kg/PR q4h 40 mg/kg/PR q6-8h Maximum daily dosing: 90 mg/kg/24 hr (children) 60 mg/kg/24 hr (<2 yr) 30-45 mg/kg/24 hr (neonates)	Little antiinflammatory action; no antiplatelet or adverse gastric effects; overdosing can produce fulminant hepatic failure
Aspirin	10-15 mg/kg PO q4h Maximum daily dosing: 120 mg/kg/24 hr (children)	Antiinflammatory; prolonged antiplatelet effects; may cause gastritis; associated with Reye syndrome
Ibuprofen	8-10 mg/kg PO q6h	Antiinflammatory; transient antiplatelet effects; may cause gastritis; extensive pediatric safety experience
Naprosyn	5-7 mg/kg PO q8-12h	Antiinflammatory; transient antiplatelet effects; may cause gastritis; more prolonged duration than that of ibuprofen
Ketorolac	Loading dose 0.5 mg/kg, then 0.25-0.3 mg/kg IV q6h to a maximum of 5 days; maximum dose 30 mg loading with maximum dosing of 15 mg q6h	Antiinflammatory; reversible antiplatelet effects; may cause gastritis; useful for short-term situations in which oral dosing is not feasible
Celecoxib	3-6 mg/kg PO q12-24h	Antiinflammatory; no antiplatelet or gastric effects; cross-reactivity with sulfa allergies
Choline magnesium salicylate	10-20 mg/kg PO q8-12h	Weak antiinflammatory; lower risk of bleeding and gastritis than with conventional NSAIDs
Nortriptyline, amitriptyline, desipramine	0.1-0.5 mg/kg PO qhs	For neuropathic pain; facilitates sleep; may enhance opioid effect; may be useful in sickle cell pain; risk of dysrhythmia in prolonged QTc syndrome; may cause fatal dysrhythmia in overdose; FDA says agents may enhance suicidal ideation
Gabapentin	100 mg bid or tid titrated to up to 3,600 mg/24 hr	For neuropathic pain; associated with sedation, dizziness, ataxia, headache, and behavioral changes
Quetiapine, risperidone, chlorpromazine, haloperidol	Quetiapine: 6.25 or 12.5 mg PO qd (hs); may use q6h prn acute agitation with pain. Escalate dose to 25 mg/dose if needed. Risperidone: useful for PDD spectrum or tic disorder and chronic pain; 0.25-1 mg (in 0.25-mg increments) qd or bid; see PDR for other dosing.	Useful when arousal is amplifying pain; often used when patient first starting SSRI and then weaned after at least 2 wk; check for normal QTc before initiating; side effects include extrapyramidal reactions (diphenhydramine may be used to treat) and sedation; in high doses, can lower the seizure threshold
Fluoxetine	10-20 mg PO qd (usually in morning)	SSRI for children with anxiety disorders in which arousal amplifies sensory signaling; useful in PDD spectrum disorders in very low doses; best to use in conjunction with psychiatric evaluation
Sucrose solution via pacifier or gloved finger	<i>Preterm infants (gestational age):</i> 28 wk: 0.2 mL swabbed into mouth 28-32 wk: 0.2-2 mL, depending on suck/swallow >32 wk: 2 mL <i>Term infants:</i> 1.5-2 mL PO over 2 min	Allow 2 min before starting procedure; analgesia may last up to 8 min; the dose may be repeated once

FDA, U.S. Food and Drug Administration; IV, intravenous(ly); NSAIDs, nonsteroidal antiinflammatory drugs; PDD, pervasive developmental disorder; PDR, *Physicians' Desk Reference*; PR, per rectum; QTc, corrected QT interval on an electrocardiogram; SSRI, selective serotonin reuptake inhibitor.

Table 62-4 Pediatric Dosage Guidelines for Opioid Analgesics

DRUG	EQUIANALGESIC DOSES		PARENTERAL DOSING (WEIGHT)		IV:PO DOSE RATIO	ORAL DOSING (WEIGHT)		COMMENTS
	IV	ORAL	<50 kg	>50 kg		<50 kg	>50 kg	
Fentanyl	10 µg	100 µg	0.5-1 µg/kg q1-2h	0.5-1 µg/kg/hr	0.5-1 µg/kg/hr	Oral transmucosal: 1:10 Transdermal: 1:1	Oral transmucosal: 10 µg/kg Transdermal: 12.5-50 µg/hr	Transdermal patches available; patch reaches steady state at 24 hr and should be changed q72h
Hydrocodone	N/A	1.5 mg	N/A	N/A	N/A	0.15 mg/kg	10 mg	Weak opioid; only available in form with acetaminophen
Hydromorphone	0.2 mg	0.6 mg	0.01 mg q2-4h 0.002 mg/kg/hr	0.01 mg q2-4h 0.002 mg/kg/hr	1:3	0.04-0.08 mg/kg q3-4h	2-4 mg q3-4h	5x the potency of morphine; no histamine release and fewer adverse events than morphine
Meperidine	10 mg	30 mg	0.5 mg/kg q2-4h	0.5 mg/kg q2-4h	1:4	2-3 mg/kg q3-4h	100-150 mg q3-4h	Primary use in low doses is for treatment of rigors and shivering after anesthesia or with amphotericin or blood products Not appropriate for repeated dosing
Methadone	1 mg	2 mg	0.1 mg/kg q8-24h	0.1 mg/kg q8-24h	1:2	0.2 mg/kg q8-12h PO; available as liquid or tablet	2.5 mg tid	Duration 12-24 hr; useful in certain types of chronic pain; requires additional vigilance, because it will accumulate over 72 hr and produce delayed sedation
Morphine	1 mg	3 mg	0.05 mg/kg q2-4h 0.01-0.03 mg/kg/hr	Bolus: 5-8 mg q2-4h	1:3	Immediate release: 0.3 mg/kg q3-4h Sustained release: 20-35 kg: 10-15 mg q8-12h 35-50 kg: 15-30 mg q8-12h	15-20 mg q3-4h Sustained release: 30-90 mg q8-12h	When patients who are tolerant to opioids are switched to methadone, they show incompletely cross-tolerance and improved efficacy; because it is associated with prolonged QTc, monitoring is needed for children on high and extended dosing
Oxycodeone	N/A	3 mg	N/A	N/A	N/A	0.1-0.2 mg q3-4h; available in liquid (1 mg/mL)	Immediate release: 5-10 mg q4h Sustained release: 10-120 mg q8-12h	Potent opioid for moderate/severe pain; may cause histamine release Sustained-release form must be swallowed whole; if crushed, becomes immediate-acting, leading to acute overdose

N/A, not available.

Table 63-2 Selected Historical and Physical Findings in Poisoning

SIGN	TOXIN
ODOR	
Bitter almonds	Cyanide
Acetone	Isopropyl alcohol, methanol, paraldehyde, salicylates
Alcohol	Ethanol
Wintergreen	Methyl salicylate
Garlic	Arsenic, thallium, organophosphates, selenium
OCULAR SIGNS	
Miosis	Opioids (except propoxyphene, meperidine, and pentazocine), organophosphates and other cholinergics, clonidine, phenothiazines, sedative-hypnotics, olanzapine
Mydriasis	Anticholinergics (e.g., antihistamines, TCAs, atropine), sympathomimetics (cocaine, amphetamines, PCP) postanoxic encephalopathy, opiate withdrawal
Nystagmus	Anticonvulsants, sedative-hypnotics, alcohols, PCP, ketamine, dextromethorphan
Lacration	Organophosphates, irritant gas or vapors
Retinal hyperemia	Methanol
CUTANEOUS SIGNS	
Diaphoresis	Cholinergics (organophosphates), sympathomimetics, withdrawal syndromes
Alopecia	Thallium, arsenic
Erythema	Boric acid, elemental mercury, cyanide, carbon monoxide, disulfiram, scombroid, anticholinergics, vancomycin
Cyanosis (unresponsive to oxygen)	Methemoglobinemia (e.g., benzocaine, dapsone, nitrites, phenazopyridine), amiodarone, silver
ORAL SIGNS	
Salivation	Organophosphates, salicylates, corrosives, ketamine, PCP, strychnine
Oral burns	Corrosives, oxalate-containing plants
Gum lines	Lead, mercury, arsenic, bismuth
GASTROINTESTINAL SIGNS	
Diarrhea	Antimicrobials, arsenic, iron, boric acid, cholinergics, colchicine, opioid withdrawal
Hematemesis	Arsenic, iron, caustics, NSAIDs, salicylates
Constipation	Lead
CARDIAC SIGNS	
Tachycardia	Sympathomimetics, anticholinergics, antidepressants, antipsychotics, methylxanthines (theophylline, caffeine), salicylates, cellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide), withdrawal (ethanol, sedatives, clonidine, opioids), serotonin syndrome, neuroleptic malignant syndrome
Bradycardia	β Blockers, calcium channel blockers, digoxin, clonidine, organophosphates, opioids, sedative-hypnotics
Hypertension	Sympathomimetics, anticholinergics, monoamine oxidase inhibitors, serotonin syndrome, neuroleptic malignant syndrome, clonidine withdrawal
Hypotension	β Blockers, calcium channel blockers, cyclic antidepressants, iron, antipsychotics, barbiturates, clonidine, opioids, arsenic, amatoxin mushrooms, cellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide), snake envenomation
RESPIRATORY SIGNS	
Depressed respirations	Opioids, sedative-hypnotics, alcohol, clonidine, barbiturates
Tachypnea	Salicylates, sympathomimetics, caffeine, metabolic acidosis, carbon monoxide, hydrocarbon aspiration
CENTRAL NERVOUS SYSTEM SIGNS	
Ataxia	Alcohols, anticonvulsants, sedative-hypnotics, lithium, dextromethorphan, carbon monoxide, inhalants
Coma	Opioids, sedative-hypnotics, anticonvulsants, antidepressants, antipsychotics, ethanol, anticholinergics, clonidine, GHB, alcohols, salicylates, barbiturates
Seizures	Sympathomimetics, anticholinergics, antidepressants (especially TCAs, bupropion, venlafaxine), cholinergics (organophosphates), isoniazid, camphor, lindane, salicylates, lead, nicotine, tramadol, water hemlock, withdrawal
Delirium/psychosis	Sympathomimetics, anticholinergics, LSD, PCP, hallucinogens, lithium, dextromethorphan, steroids, withdrawal
Peripheral neuropathy	Lead, arsenic, mercury, organophosphates

GHB, γ-hydroxybutyrate; LSD, lysergic acid diethylamide; NSAID, nonsteroidal antiinflammatory drug; PCP, phencyclidine; TCA, tricyclic antidepressant.

452 Part VIII ◆ Pediatric Drug Therapy

Table 63-4 Mini-Toxidromes

TOXIDROMES	SYMPTOMS AND SIGNS	EXAMPLES
α_1 Antagonists	CNS depression, tachycardia, miosis	Chlorpromazine, quetiapine, clozapine, olanzapine, risperidone
α_2 Agonist	CNS depression, bradycardia, hypertension (early), hypotension (late), miosis	Clonidine, oxymetazoline, tetrahydrozoline, tizanidine
Clonus/myoclonus	CNS depression, myoclonic jerks, clonus, hyperreflexia	Carisoprodol, lithium, serotonergic agents, bismuth, organic lead, organic mercury
Sodium channel blockers	CNS toxicity, wide QRS	Cyclic antidepressants and structurally related agents, propoxyphene, quinidine/quinine, amantadine, antihistamines, bupropion, cocaine
Potassium channel blockers	CNS toxicity, long QT	Butyrophenones, methadone, phenothiazines, zippersidone

CNS, central nervous system.

From Ruha AM, Levine M: Central nervous system toxicity. *Emerg Med Clin North Am* 32(1):205–221, 2014, Table 2, p. 208.**Table 63-5** Screening Laboratory Clues in Toxicologic Diagnosis

ANION GAP METABOLIC ACIDOSIS (MNEMONIC = MUDPILES CAT)
Methanol, metformin
Uremia
Diabetic ketoacidosis
Propylene glycol
Isoniazid, iron, massive ibuprofen
Lactic acidosis
Ethylene glycol
Salicylates
Cellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide)
Alcoholic ketoacidosis
Tylenol
ELEVATED OSMOLAR GAP
Alcohols: ethanol, isopropyl, methanol, ethylene glycol
HYPOGLYCEMIA (MNEMONIC = HOBBIES)
Hypoglycemics, oral: sulfonylureas, meglitinides
Other: quinine, unripe ackee fruit
Beta Blockers
Insulin
Ethanol
Salicylates (late)
HYPERGLYCEMIA
Salicylates (early)
Calcium channel blockers
Caffeine
HYPOCALCEMIA
Ethylene glycol
Fluoride
RHABDOMYOLYSIS
Neuroleptic malignant syndrome, serotonin syndrome
Statins
Mushrooms (<i>Tricholoma equestre</i>)
Any toxin causing prolonged immobilization (e.g., opioids, antipsychotics) or excessive muscle activity or seizures (e.g., sympathomimetics)
RADIOPAQUE SUBSTANCE ON KUB (MNEMONIC = CHIPPED)
Chloral hydrate, calcium carbonate
Heavy metals (lead, zinc, barium, arsenic, lithium, bismuth)
Iron
Phenothiazines
Play-Doh, potassium chloride
Enteric-coated pills
Dental amalgam, drug packets

KUB, kidney-ureter-bladder radiograph.

Table 63-6 Electrocardiographic Findings in Poisoning

PR INTERVAL PROLONGATION
Digoxin
Lithium
QRS PROLONGATION
Tricyclic antidepressants
Diphenhydramine
Carbamazepine
Cardiac glycosides
Chloroquine, hydroxychloroquine
Cocaine
Lamotrigine
Quinidine, quinine, procainamide, disopyramide
Phenothiazines
Propoxyphene
Propranolol
Bupropion, venlafaxine (rare)
QTc PROLONGATION*
Amiodarone
Antipsychotics (typical and atypical)
Arsenic
Cisapride
Citalopram and other SSRIs
Clarithromycin, erythromycin
Disopyramide, dofetilide, ibutilide
Fluconazole, ketoconazole, itraconazole
Methadone
Pentamidine
Phenothiazines
Sotalol

*This is a select list of important toxins; other medications are also associated with QTc prolongation.

SSRI, selective serotonin reuptake inhibitor.

Table 63-7 Common Antidotes for Poisoning

POISON	ANTIDOTE	DOSAGE	ROUTE	ADVERSE EFFECTS, WARNINGS, COMMENTS
Acetaminophen	N-Acetylcysteine (Mucomyst)	140 mg/kg loading, followed by 70 mg/kg q4h	PO	Vomiting (patient-tailored regimens are the norm)
	N-Acetylcysteine (Acetadote)	150 mg/kg over 1 hr, followed by 50 mg/kg over 4 hr, followed by 100 mg/kg over 16 hr	IV	Anaphylactoid reactions (most commonly seen with loading dose) (Higher doses of the infusion are often recommended depending upon the acetaminophen level and the degree of injury)
Anticholinergics	Physostigmine	0.02 mg/kg over 5 min; may repeat q5-10min to 2 mg max	IV/IM	Bradycardia, seizures, bronchospasm Note: Do not use if conduction delays on ECG
Benzodiazepines	Flumazenil	0.2 mg over 30 sec; if response is inadequate, repeat q1min to 1 mg max	IV	Agitation, seizures; do not use for unknown ingestions
β Blockers	Glucagon	0.15 mg/kg bolus followed by infusion of 0.05-0.15 mg/kg/hr	IV	Hyperglycemia, vomiting
Calcium channel blockers	Insulin	1 unit/kg bolus followed by infusion of 0.5-1 unit/kg/hr	IV	Hypoglycemia Follow serum potassium and glucose closely
	Calcium salts	Dose depends on the specific calcium salt	IV	
Carbon monoxide	Oxygen	100% FIO ₂ via non-rebreather mask (or ET if intubated)	Inhalational	Some patients may benefit from hyperbaric oxygen (see text)
Cyanide	Cyanide kit: Amyl nitrate	1 crushable ampule; inhale 30 sec of each min	Inhalation	Methemoglobinemia
	Sodium nitrate	0.33 mL/kg of 3% solution if hemoglobin level is not known; otherwise, based on tables with product	IV	Methemoglobinemia Hypotension
	Sodium thiosulfate	1.6 mL/kg of 25% solution; may be repeated q30-60min to max of 50 mL	IV	If inducing methemoglobinemia is contraindicated; consider only using the thiosulfate component of the kit
	Hydroxocobalamin (Cyanokit)	70 mg/kg (adults: 5 g) given over 15 min	IV	Flushing/erythema, nausea, rash, chromaturia, hypertension, headache
Digitalis	Digoxin-specific Fab antibodies (Digibind; DigiFab)	1 vial binds 0.6 mg of digitalis glycoside; #vials = digitalis level × weight in kg/100	IV	Allergic reactions (rare), return of condition being treated with digitalis glycoside
Ethylene glycol, methanol	Fomepizole	15 mg/kg load; 10 mg/kg q12h × 4 doses; 15 mg/kg q12h until EG level is <20 mg/dL	IV	Infuse slowly over 30 min; If fomepizole is not available, can treat with oral ethanol (80 proof)
Iron	Deferoxamine	Infusion of 5-15 mg/kg/hr (max: 6 g/24 hr)	IV	Hypotension (minimized by avoiding rapid infusion rates)
Isoniazid (INH)	Pyridoxine	Empirical dosing: 70 mg/kg (max dose = 5 g) If ingested dose is known: 1 g per gram of INH	IV	May also be used for <i>Gyromitra</i> mushroom ingestions
Lead and other heavy metals (e.g., arsenic, inorganic mercury)	BAL (dimercaprol)	3-5 mg/kg/dose q4hr, for the 1st day; subsequent dosing depends on the toxin	Deep IM	Local injection site pain and sterile abscess, vomiting, fever, salivation, nephrotoxicity Caution: prepared in peanut oil; contraindicated in patients with peanut allergy
	Calcium disodium EDTA	35-50 mg/kg/day × 5 days; may be given as a continuous infusion or 2 divided doses/day	IV	Vomiting, fever, hypertension, arthralgias, allergic reactions, local inflammation, nephrotoxicity (maintain adequate hydration, follow UA and renal function)
	Dimercaptosuccinic acid (succimer, DMSA, Chemet)	10 mg/kg/dose q8h × 5 days, then 10 mg/kg q12h × 14 days	PO	Vomiting, hepatic transaminase elevation, rash

Continued

Table 63-7 Common Antidotes for Poisoning—cont'd

POISON	ANTIDOTE	DOSAGE	ROUTE	ADVERSE EFFECTS, WARNINGS, COMMENTS
Methemoglobinemia	Methylene blue, 1% solution	0.1-0.2 mL/kg (1-2 mg/kg) over 5-10 min; may be repeated q30-60min	IV	Vomiting, headache, dizziness, blue discoloration of urine
Opioids	Naloxone	0.01-0.1 mg/kg; adolescents/adults: 0.04-2 mg, repeated as needed; may give continuous infusion	IV	Acute withdrawal symptoms if given to addicted patients May also be useful for clonidine ingestions (inconsistent response)
Organophosphates	Atropine	0.05-0.1 mg/kg repeated q5-10min as needed	IV/ET	Tachycardia, dry mouth, blurred vision, urinary retention
	Pralidoxime (2-PAM)	25-50 mg/kg over 5-10 min (max: 200 mg/min); can be repeated after 1-2 hr, then q10-12hr as needed	IV/IM	Nausea, dizziness, headache, tachycardia, muscle rigidity, bronchospasm (rapid administration)
Salicylates	Sodium bicarbonate	Bolus 1-2 mEq/kg followed by a continuous infusion	IV	Follow potassium closely and replete as necessary Goal urine pH 7.5-8.0
Sulfonylureas	Octreotide and dextrose	1-2 µg/kg/dose (adults 50-100 µg) q6-8hr	IV/SC	
Tricyclic antidepressants	Sodium bicarbonate	Bolus 1-2 mEq/kg; repeated bolus dosing as needed to keep QRS <110 msec	IV	Indications: QRS widening (\geq 110 ms), hemodynamic instability; follow potassium

BAL, British antilewisite; DMSA, dimercaptosuccinic acid; ECG, electrocardiogram; FIO₂, fraction of inspired oxygen; EDTA, ethylenediaminetetraacetic acid; EG, ethylene glycol; ET, endotracheal tube; max, maximum; UA, urinalysis.

Table 63-1 Common Agents Potentially Toxic to Young Children (<6 yr) in Small Doses*

SUBSTANCE	TOXICITY
Aliphatic hydrocarbons (e.g., gasoline, kerosene, lamp oil)	Acute lung injury
Antimalarials (chloroquine, quinine)	Seizures, dysrhythmias
Benzocaine	Methemoglobinemia
β Blockers [lipid-soluble β blockers (e.g., propranolol) are more toxic than water-soluble β blockers (e.g., atenolol)]	Bradycardia, hypotension
Calcium channel blockers	Bradycardia, hypotension, hyperglycemia
Camphor	Seizures
Caustics (pH <2 or >12)	Airway, esophageal and gastric burns
Clonidine	Lethargy, bradycardia, hypotension
Diphenoxylate and atropine (Lomotil)	CNS depression, respiratory depression
Hypoglycemics, oral (sulfonylureas and meglitinides)	Hypoglycemia, seizures
Laundry detergent packets (pods)	Airway issues, respiratory distress, altered mental status
Lindane	Seizures
Monoamine oxidase inhibitors	Hypertension followed by delayed cardiovascular collapse
Methyl salicylate	Tachypnea, metabolic acidosis, seizures
Opioids (especially methadone, buprenorphine)	CNS depression, respiratory depression
Organophosphate pesticides	Cholinergic crisis
Phenothiazines (especially chlorpromazine, thioridazine)	Seizures, dysrhythmias
Theophylline	Seizures, dysrhythmias
Tricyclic antidepressants	CNS depression, seizures, dysrhythmias, hypotension

*"Small dose" typically implies 1 or 2 pills or 5 mL.
CNS, central nervous system.

Table 63-8 Additional Antidotes

ANTIDOTES	TOXIN OR POISON
Latrodectus antivenin	Black widow spider
Botulinum antitoxin	Botulinum toxin
Insulin and glucose	Calcium channel antagonists
Diphenhydramine and/or benztropine	Dystonic reactions
Calcium salts	Fluoride, calcium channel blockers
Protamine	Heparin
Folinic acid	Methotrexate, trimethoprim, pyrimethamine
Crotalidae-specific Fab antibodies	Rattlesnake envenomation
Sodium bicarbonate	Sodium channel blockade (tricyclic antidepressants, type 1 antiarrhythmics)

The Acutely Ill Child

Table 67-2 AVPU Neurologic Assessment

A	The child is awake, alert, and interactive with parents and care providers
V	The child responds only if the care provider or parents call the child's name or speak loudly
P	The child responds only to painful stimuli, such as pinching the nail bed of a toe or finger
U	The child is unresponsive to all stimuli

From Ralston M, Hazinski MF, Zaritsky AL, et al, editors: Pediatric advanced life support course guide and PALS provider manual: provider manual, Dallas, 2007, American Heart Association.

Table 67-1 Normal Vital Signs According to Age

AGE	HEART RATE (beats/min)	BLOOD PRESSURE (mm Hg)	RESPIRATORY RATE (breaths/min)
Premature	120-170*	55-75/35-45 [†]	40-70 [‡]
0-3 mo	100-150*	65-85/45-55	35-55
3-6 mo	90-120	70-90/50-65	30-45
6-12 mo	80-120	80-100/55-65	25-40
1-3 yr	70-110	90-105/55-70	20-30
3-6 yr	65-110	95-110/60-75	20-25
6-12 yr	60-95	100-120/60-75	14-22
12+ yr	55-85	110-135/65-85	12-18

*In sleep, infant heart rates may drop significantly lower, but if perfusion is maintained, no intervention is required.

[†]A blood pressure cuff should cover approximately two-thirds of the arm; too small a cuff yields spuriously high pressure readings, and too large a cuff yields spuriously low pressure readings.

[‡]Many premature infants require mechanical ventilatory support, making their blood pressure. In nonhospital settings, much of the important

Table 67-3 Glasgow Coma Scale

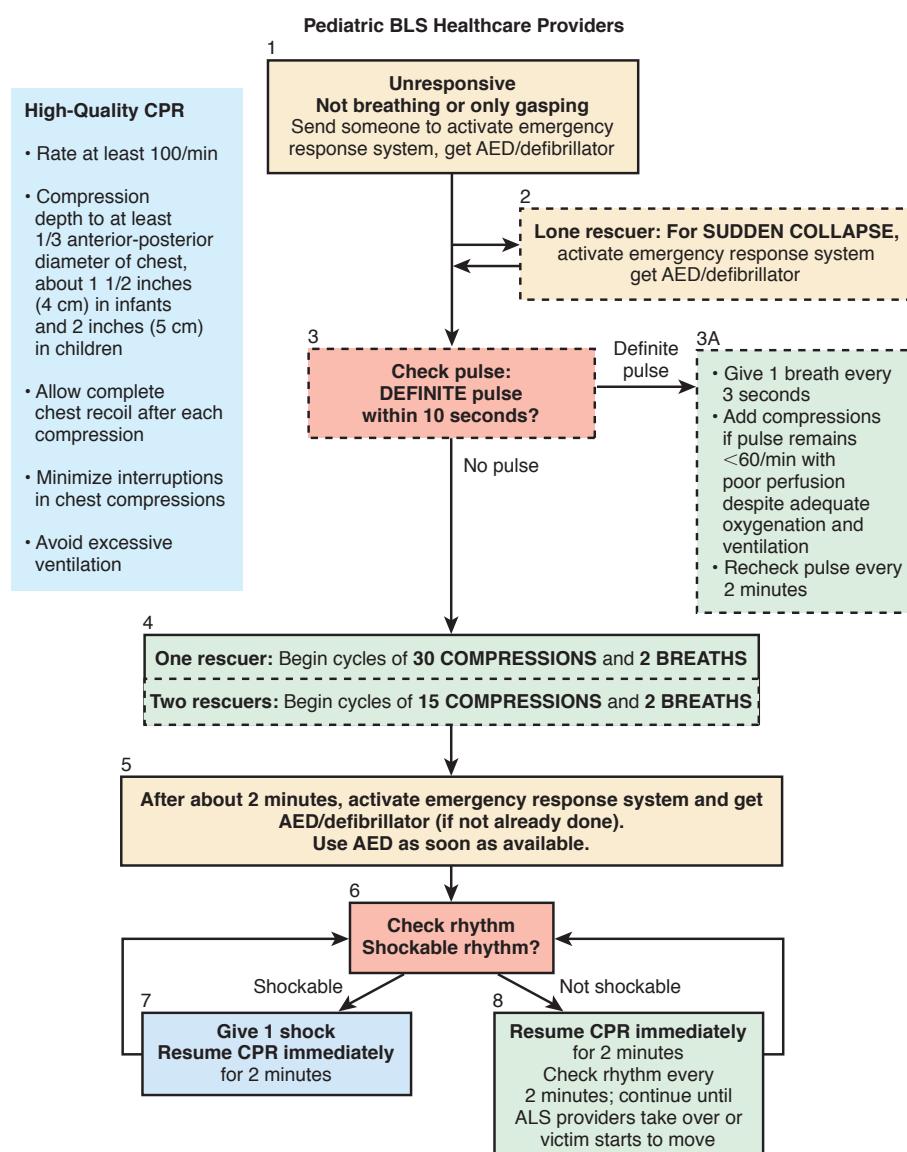
EYE OPENING (TOTAL POSSIBLE POINTS 4)			
OLDER CHILDREN INFANTS AND YOUNG CHILDREN			
Oriented	5	Appropriate words; smiles, fixes, and follows	5
Confused	4	Consolable crying	4
Inappropriate	3	Persistently irritable	3
Incomprehensible	2	Restless, agitated	2
None	1	None	1
MOTOR RESPONSE (TOTAL POSSIBLE POINTS 6)			
Obeys	6		
Localizes pain	5		
Withdraws	4		
Flexion	3		
Extension	2		
None	1		

Table 64-1 Most Commonly Used Dietary Supplements in Pediatrics

PRODUCT	USES
VITAMINS	
B ₂ (riboflavin)	Migraine headache prophylaxis
B ₆ (pyridoxine)	Pyridoxine-dependent epilepsy; neuropathy; nausea associated with pregnancy
B ₉ (folate)	Prevention of neural tube defects
D	Prevention of rickets; treatment of deficiencies
Multivitamins	General health promotion, ADHD
MINERALS	
Iodine (salt)	Prevent goiter and mental retardation
Iron	Prevent and treat iron deficiency
Magnesium	Constipation, asthma, migraine prevention
Zinc	Diarrhea in nutrient-poor populations
HERBS	
Aloe vera	Mild burns
Chamomile	Mild sedative, dyspepsia
Echinacea	Prevention of upper respiratory infections
Ginger	Nausea
Lavender (aromatherapy)	Mild sedative
Peppermint	Irritable bowel syndrome
Tea tree oil	Anti-bacterial (acne remedies), pediculicide (lice)
OTHER	
Melatonin	Insomnia
Omega-3 fatty acids (fish oil)	ADHD, allergies, inflammation, anxiety and mood disorders
Probiotics	Antibiotic-associated diarrhea; <i>Clostridium difficile</i> -associated diarrhea; constipation; irritable bowel syndrome; pouchitis; inflammatory bowel disorders

Table 69-2 Life-Threatening Cardiac Causes of Syncope

Long QT syndromes (congenital and drug induced)
Cardiomyopathies
Hypertrophic cardiomyopathy
Dilated cardiomyopathy
Arrhythmogenic right ventricular dysplasia
Brugada syndrome
Catecholminergic polymorphic ventricular tachycardia
Myocarditis
Wolff-Parkinson-White syndrome
Coronary artery anomalies
Late postoperative arrhythmias
Congenital or acquired complete atrioventricular block
Aortic, mitral, or pulmonic valve stenosis
Primary pulmonary hypertension
Eisenmenger syndrome
Dissecting aortic aneurysm (Marfan syndrome)
Cardiac tumor



Note: The boxes bordered with dashed lines are performed by healthcare providers and not by rescuers

Figure 67-1 Pediatric basic life support algorithm. AED, automated external defibrillator; ALS, advanced life support; CPR, cardiopulmonary resuscitation. (From Berg MD, Schexnayder SM, Chameides L, et al: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care, part 13, Circulation 122[Suppl 3]:S862–S875, 2010, Fig. 3, p. S866.)

Table 69-3 “Red Flags” in the Evaluation of Patients with Syncope

- Syncope with activity or exercise or supine
- Syncope not associated with prolonged standing
- Syncope precipitated by loud noise or extreme emotion
- Absence of presyncope or lightheadedness
- Family history of syncope, drowning, sudden death, familial ventricular arrhythmia syndromes*, cardiomyopathy
- Syncope requiring CPR
- Injury with syncope
- Anemia
- Other cardiac symptoms
- Chest pain
- Dyspnea
- Palpitations
- History of cardiac surgery
- History of Kawasaki disease
- Implanted pacemaker
- Abnormal physical examination
 - Murmur
 - Gallop rhythm
 - Loud and single second heart sound
 - Systolic click
 - Increased apical impulse (tachycardia)
 - Irregular rhythm
 - Hypo- or hypertension
 - Clubbing
 - Cyanosis

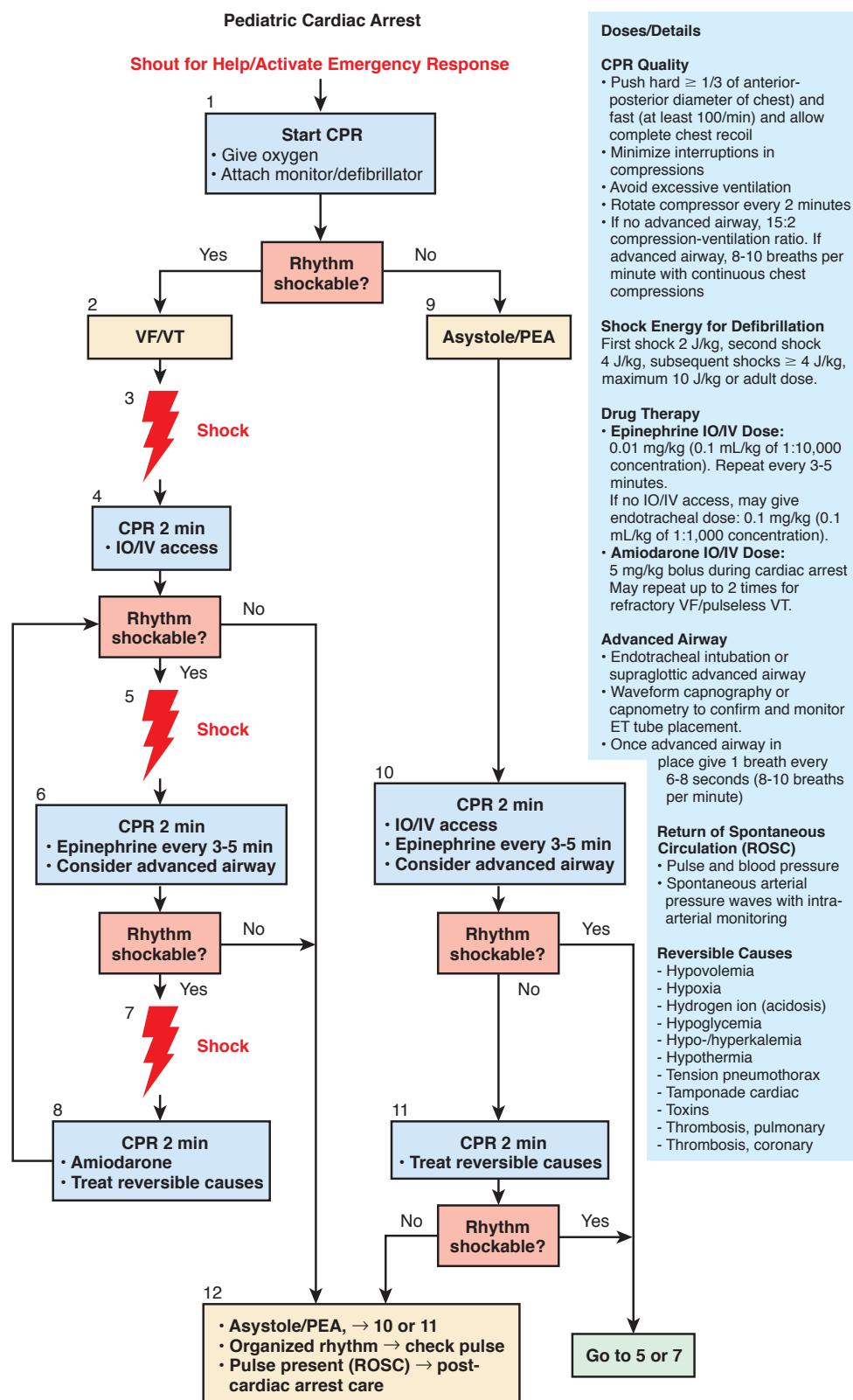


Figure 67-18 Pediatric advanced life support pulseless arrest algorithm. (From Kleinman ME, Chameides L, Schexnayder SM, et al: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care, part 14, Circulation 122[Suppl 3]: S876-S908, 2010, Fig. 1, p. S885.)

504 Part IX ◆ The Acutely Ill Child

Table 67-6 Medications for Pediatric Resuscitation and Arrhythmias

MEDICATION	DOSE	REMARKS
Adenosine	0.1 mg/kg (maximum 6 mg) Repeat: 0.2 mg/kg (maximum 12 mg)	Monitor ECG Rapid IV/IO bolus
Amiodarone	5 mg/kg IV/IO; repeat up to 15 mg/kg Maximum: 300 mg	Monitor ECG and blood pressure Adjust administration rate to urgency (give more slowly when perfusing rhythm is present) Use caution when administering with other drugs that prolong QT interval (consider expert consultation)
Atropine	0.02 mg/kg IV/IO 0.03 mg/kg ET* Repeat once if needed Minimum dose: 0.1 mg Minimum single dose: Child, 0.5 mg Adolescent, 1 mg	Higher doses may be used with organophosphate poisoning
Calcium chloride (10%)	20 mg/kg IV/IO (0.2 mL/kg)	Slowly Adult dose: 5-10 mL
Epinephrine	0.01 mg/kg (0.1 mL/kg 1:10,000) IV/IO 0.1 mg/kg (0.1 mL/kg 1:1,000) ET* Maximum dose: 1 mg IV/IO; 10 mg ET	May repeat q 3-5 min
Glucose	0.5-1 g/kg IV/IO	D10W: 5-10 mL/kg D25W: 2-4 mL/kg D50W: 1-2 mL/kg
Lidocaine	Bolus: 1 mg/kg IV/IO Maximum dose: 100 mg Infusion: 20-50 µg/kg/min ET*: 2-3 mg	
Magnesium sulfate	25-50 mg/kg IV/IO over 10-20 min; faster in torsades de pointes Maximum dose: 2g	
Naloxone	<5 yr or ≤20 kg: 0.1 mg/kg IV/IO/ET* ≥5 yr or >20 kg: 2 mg IV/IO/ET*	Use lower doses to reverse respiratory depression associated with therapeutic opioid use (1-15 µg/kg)
Procainamide	15 mg/kg IV/IO over 30-60 min Adult dose: 20 mg/min IV infusion up to total maximum dose of 17 mg/kg	Monitor EGG and blood pressure Use caution when administering with other drugs that prolong QT interval (consider expert consultation)
Sodium bicarbonate	1 mEq/kg/dose IV/IO slowly	After adequate ventilation

*Flush with 5 mL of normal saline and follow with 5 ventilations.

ECG, electrocardiogram; ET, endotracheal tube; IO, intraosseous; IV, intravenous.

From ECC Committee, Subcommittees and Task Forces of the American Heart Association: 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care, Circulation 112:IV1-203, 2005.

Table 67-7 Medications to Maintain Cardiac Output and for Postresuscitation Stabilization*

MEDICATION	DOSE RANGE	COMMENT
Inamrinone	0.75-1 mg/kg IV/IO over 5 min; may repeat 2x; then: 2-20 µg/kg/min	Inodilator
Dobutamine	2-20 µg/kg/min IV/IO	Inotrope; vasodilator
Dopamine	2-20 µg/kg/min IV/IO in low doses; pressor in higher doses	Inotrope; chronotrope; renal and splanchnic vasodilator
Epinephrine	0.1-1 µg/kg/min IV/IO	Inotrope; chronotrope; vasodilator in low doses; vasopressor in higher doses
Milrinone	50-75 µg/kg IV/IO over 10-60 min then 0.5-0.75 µg/kg/min	Inodilator
Norepinephrine	0.1-2 µg/kg/min	Inotrope; vasopressor
Sodium nitroprusside	1-8 µg/kg/min	Vasodilator; prepare only in D5W

*Alternative formula for calculating an infusion: Infusion rate (mL/hr) = [weight (kg) × dose (µg/kg/min) × 60 (min/hr)]/concentration µg/mL.

D5W, 5% dextrose in water; IO, intraosseous; IV, intravenous.

From ECC Committee, Subcommittees and Task Forces of the American Heart Association: 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care, Circulation 112:IV1-IV203, 2005.

Table 69-1 Noncardiac Causes of Syncope

Reflex vasodepressor syncope
Neurocardiogenic (vasovagal)
Emotion (seeing blood)
Pain (needle phobia)
Miscellaneous situational reflex
Tussive
Sneeze
Exercise/post exercise
Swallowing
Stretching
Defecation
Micturition
Valsalva (increased intrathoracic pressure)
Breath holding spells
Systemic illness
Hypoglycemia
Anemia
Infection
Hypovolemia, dehydration
Adrenal insufficiency
Narcolepsy/cataplexy
Pulmonary embolism
Ruptured ectopic pregnancy
Central nervous system
Seizure (tonic, absence, myoclonic-astatic)
Stroke/transient ischemic attack
Subarachnoid hemorrhage
Dysautonomia
Basilar artery migraine
Drug effects
β-Blocking agents
Vasodilating agents
Opiates
Sedatives
Drugs prolonging QT interval
Diuretics
Anticonvulsant agents
Antihistamines
Antidepressant agents
Anxiolytic agents
Drugs of abuse
Insulin, oral hypoglycemic agents
Carbon monoxide
Other etiologies
Carotid sinus sensitivity
Subclavian steal
Panic attack/anxiety
Conversion disorder

Table 68-1 Commonly Used Coma Scores

GLASGOW COMA SCALE
Eye Opening
1 = does not open eyes
2 = opens eyes in response to noxious stimuli
3 = opens eyes in response to voice
4 = opens eyes spontaneously
Verbal Output
1 = makes no sounds
2 = makes incomprehensible sounds
3 = utters inappropriate words
4 = confused and disoriented
5 = speaks normally and oriented
Motor Response (Best)
1 = makes no movements
2 = extension to painful stimuli
3 = abnormal flexion to painful stimuli
4 = flexion/withdrawal to painful stimuli
5 = localized to painful stimuli
6 = obeys commands
FULL OUTLINE OF UNRESPONSIVENESS (FOUR) SCORE
Eye Response
4 = eyelids open or opened, tracking, or blinking to command
3 = eyelids open but not tracking
2 = eyelids closed but open to loud voice
1 = eyelids closed but open to pain
0 = eyelids remain closed with pain
Motor Response
4 = thumbs-up, fist, or peace sign
3 = localizing to pain
2 = flexion response to pain
1 = extension response to pain
0 = no response to pain or generalized myoclonus status
Brainstem Reflexes
4 = pupil and corneal reflexes present
3 = one pupil wide and fixed
2 = pupil or corneal reflexes absent
1 = pupil and corneal reflexes absent
0 = absent pupil, corneal, and cough reflex
Respiration
4 = not intubated, regular breathing pattern
3 = not intubated, Cheyne-Stokes breathing pattern
2 = not intubated, irregular breathing
1 = breathes above ventilatory rate
0 = breathes at ventilator rate or apnea

Table 68-2 Brainstem Reflex Testing to Determine Brain Death

BRAINSTEM REFLEX	AREA TESTED	HOW TO PERFORM THE EXAM	EXPLANATION OF RESULTS
Pupillary light reflex	CN II and III, midbrain	Shine a light into the eyes while closely observing pupillary size	Midposition (4–6 mm) or fully dilated pupils that are not reactive to light are consistent with brain death. Pinpoint pupils, even if nonreactive, suggest intact function of the Edinger-Westphal nucleus in the midbrain and are therefore not consistent with brain death.
Oculocephalic reflex (doll's-eyes reflex)	CN III, VI, and VIII, midbrain, pons	Manually rotate the patient's head side to side and closely watch the position of the eyes. Should not be performed in a patient with a cervical spine injury.	In an intact patient, the eyes remain fixed on a distant spot, as if maintaining eye contact with that spot. In an exam consistent with brain death, the eyes move in concert with the patient's head movement.
Corneal reflex	CN III, V, and VII, pons	Touch the patient's cornea with a cotton swab.	In the intact patient, the touch results in eyelid closure, and the eye may rotate upward. In an exam consistent with brain death, there is no response.
Oculovestibular reflex	CN III, IV, VI, and VIII, pons, midbrain	Irrigate the tympanic membrane with iced water or saline and look for eye movement.	Absence of eye movement is consistent with brain death.
Gag and cough reflex	CN IX and X, medulla	Touch the posterior pharynx with a tongue depressor or a cotton-tipped swab to stimulate a gag. Advance a suction catheter through the endotracheal tube to the carina to stimulate a cough.	Absence of both a cough and a gag is consistent with brain death.

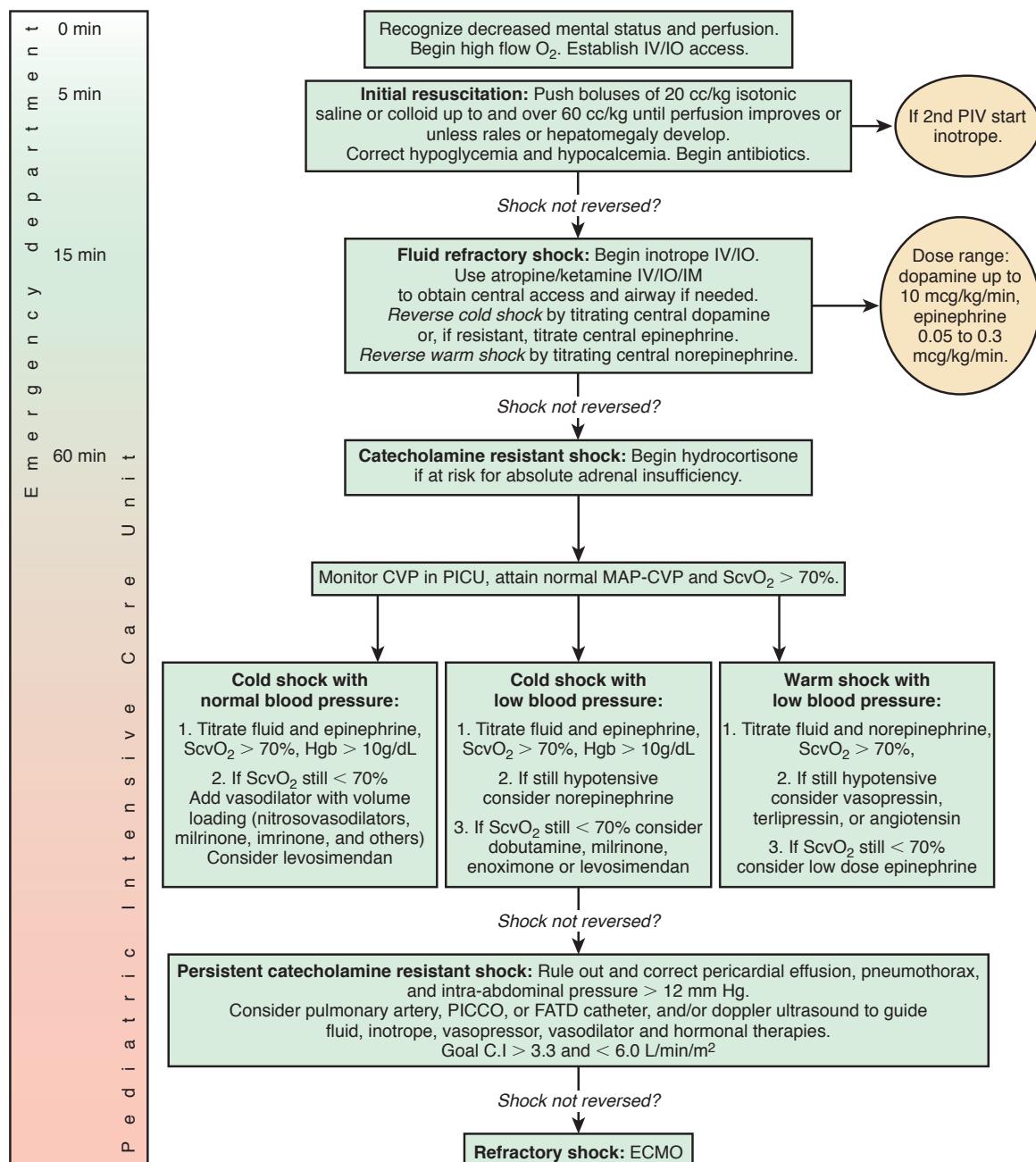


Figure 70-1 Algorithm for time-sensitive, goal-directed, stepwise management of hemodynamic support in infants and children. CI, cardiac index; CRRT, continuous renal replacement therapy; CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; FATT, femoral arterial thermodilution; Hgb, hemoglobin; IM, intramuscular; IO, intraosseous; IV, intravenous; MAP, mean arterial pressure; PICCO, pulse contour cardiac output. (From Brierly J, Carcillo JA, Choong K, et al: Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine, Crit Care Med 37:666-688, 2009. Copyright 2009, Society of Critical Care Medicine and Lippincott Williams & Wilkins.)

518 Part IX ◆ The Acutely Ill Child

Table 70-1 Types of Shock				
HYPVOLEMIC	CARDIOGENIC	DISTRIBUTIVE	SEPTIC	OBSTRUCTIVE
Decreased preload secondary to internal or external losses	Cardiac pump failure secondary to poor myocardial function	Abnormalities of vasomotor tone from loss of venous and arterial capacitance	Encompasses multiple forms of shock Hypovolemic: third spacing of fluids into the extracellular, interstitial space Distributive: early shock with decreased afterload Cardiogenic: depression of myocardial function by endotoxins	Decreased cardiac output secondary to direct impediment to right- or left-heart outflow or restriction of all cardiac chambers
POTENTIAL ETIOLOGIES				
Blood loss: hemorrhage; Plasma loss: burns, nephrotic syndrome; Water/electrolyte loss: vomiting, diarrhea	Congenital heart disease Cardiomyopathies: infectious or acquired, dilated or restrictive Ischemia Arrhythmias	Anaphylaxis Neurologic: loss of sympathetic vascular tone secondary to spinal cord or brainstem injury Drugs	Bacterial Viral Fungal (immunocompromised patients are at increased risk)	Tension pneumothorax Pericardial tamponade Pulmonary embolism Anterior mediastinal masses Critical coarctation of the aorta

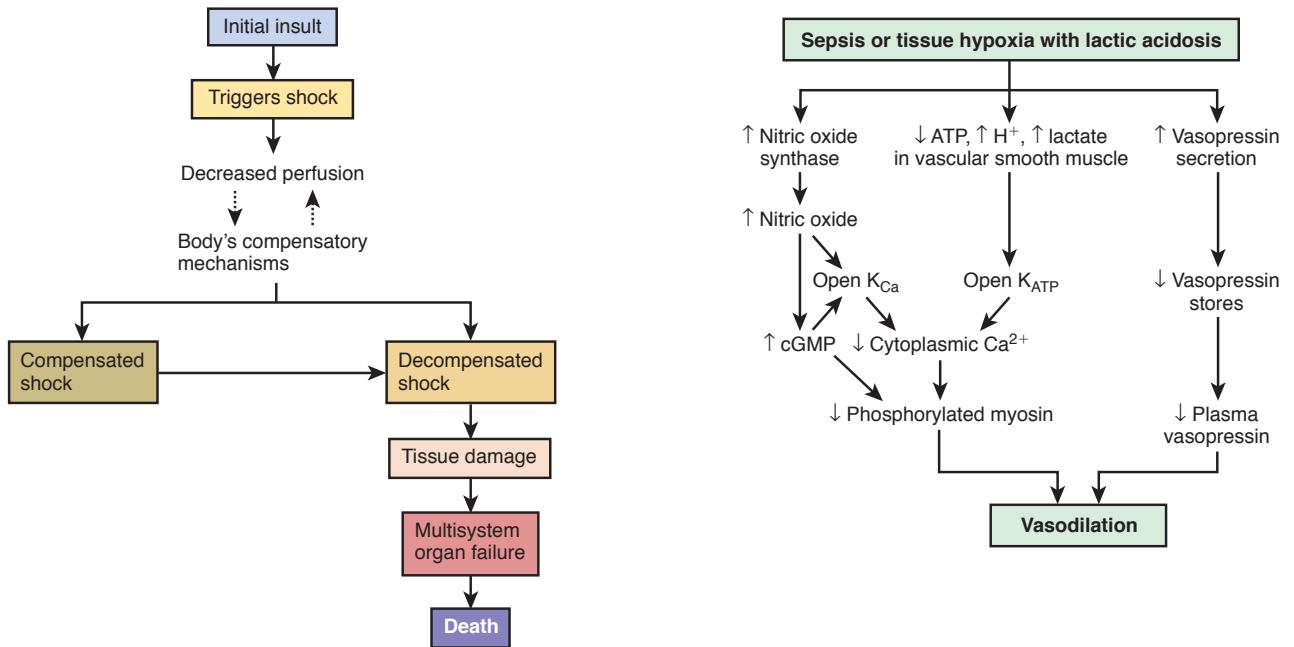


Table 70-2 Criteria for Organ Dysfunction

ORGAN SYSTEM	CRITERIA FOR DYSFUNCTION
Cardiovascular	Despite administration of isotonic intravenous fluid bolus ≥ 60 mL/kg in 1 hr; decrease in BP (hypotension) systolic BP < 90 mm Hg, mean arterial pressure < 70 mm Hg, $<$ 5th percentile for age, or systolic BP < 2 SD below normal for age or Need for vasoactive drug to maintain BP in normal range (dopamine > 5 μ g/kg/min or dobutamine, epinephrine, or norepinephrine at any dose) or Two of the following: Unexplained metabolic acidosis: base deficit > 5.0 mEq/L Increased arterial lactate: > 1 mmol/Liter or $> 2 \times$ upper limit of normal Oliguria: urine output < 0.5 mL/kg/hr Prolonged capillary refill: > 5 sec Core to peripheral temperature gap $> 3^\circ\text{C}$ (5.4°F)
Respiratory	$\text{PaO}_2/\text{FiO}_2$ ratio < 300 in absence of cyanotic heart disease or preexisting lung disease or $\text{PaCO}_2 > 65$ torr or 20 mm Hg over baseline PaCO_2 or Need for $> 50\%$ FiO_2 to maintain saturation $\geq 92\%$ or Need for noninvasive or noninvasive mechanical ventilation
Neurologic	GCS score ≤ 11 or Acute change in mental status with a decrease in GCS score ≥ 3 points from abnormal baseline
Hematologic	Platelet count $< 100,000/\text{mm}^3$ or a decline of 50% in the platelet count from the highest value recorded over the last 3 days (for patients with chronic hematologic or oncologic disorders) or INR > 1.5 or Activated prothrombin time > 60 sec
Renal	Serum creatinine > 0.5 mg/dL, $\geq 2 \times$ upper limit of normal for age, or 2-fold increase in baseline creatinine value
Hepatic	Total bilirubin ≥ 4 mg/dL (not applicable for newborn) Alanine transaminase level $2 \times$ upper limit of normal for age

BP, blood pressure; FiO_2 , fraction of inspired oxygen; GCS, Glasgow Coma Scale; INR, international normalized ratio; PaCO_2 , arterial partial pressure of carbon dioxide; PaO_2 , partial pressure arterial oxygen.

Table 70-3 Signs of Decreased Perfusion

ORGAN SYSTEM	\downarrow PERFUSION	$\downarrow\downarrow$ PERFUSION	$\downarrow\downarrow\downarrow$ PERFUSION
Central nervous system	—	Restless, apathetic, anxious	Agitated/confused, stuporous, coma
Respiration	—	\uparrow Ventilation	$\uparrow\uparrow$ Ventilation
Metabolism	—	Compensated metabolic acidemia	Uncompensated metabolic acidemia
Gut	—	\downarrow Motility	Ileus
Kidney	\downarrow Urine volume \uparrow Urinary specific gravity	Oliguria (< 0.5 mL/kg/hr)	Oliguria/anuria
Skin	Delayed capillary refill	Cool extremities	Mottled, cyanotic, cold extremities
Cardiovascular system	\uparrow Heart rate	$\uparrow\uparrow$ Heart rate \downarrow Peripheral pulses	$\uparrow\uparrow$ Heart rate \downarrow Blood pressure, central pulses only

Table 70-10 Surviving Sepsis Campaign Care Bundles

To be completed within 3 hr:
1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L
To be completed within 6 hr:
5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg
6. In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥ 4 mmol/L (36 mg/dL): Measure central venous pressure (CVP)* Measure central venous oxygen saturation (ScvO_2)*
7. Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥ 8 mm Hg, ScvO_2 of $\geq 70\%$, and normalization of lactate.

Adapted from Dellinger PR, Levy MM, Rhodes A, et al: *Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012*. Crit Care Med 41(2):580-637, 2013, Fig. 1, p. 591.

Table 70-4 Pathophysiology of Shock**EXTRACORPOREAL FLUID LOSS**

Hypovolemic shock may be a result of direct blood loss through hemorrhage or abnormal loss of body fluids (diarrhea, vomiting, burns, diabetes mellitus or insipidus, nephrosis)

LOWERING PLASMA ONCOTIC FORCES

Hypovolemic shock may also result from hypoproteinemia (liver injury, or as a progressive complication of increased capillary permeability)

ABNORMAL VASODILATION

Distributive shock (neurogenic, anaphylaxis, or septic shock) occurs when there is loss of vascular tone—venous, arterial, or both (sympathetic blockade, local substances affecting permeability, acidosis, drug effects, spinal cord transection)

INCREASED VASCULAR PERMEABILITY

Sepsis may change the capillary permeability in the absence of any change in capillary hydrostatic pressure (endotoxins from sepsis, excess histamine release in anaphylaxis)

CARDIAC DYSFUNCTION

Peripheral hypoperfusion may result from any condition that affects the heart's ability to pump blood efficiently (ischemia, acidosis, drugs, constrictive pericarditis, pancreatitis, sepsis)

Table 70-5 Differential Diagnosis of Systemic Inflammatory Response Syndrome

INFECTION

Bacteremia or meningitis (*Streptococcus pneumoniae*, *Haemophilus influenzae* type b, *Neisseria meningitidis*, group A streptococcus, *Staphylococcus aureus*)
 Viral illness (influenza, enteroviruses, hemorrhagic fever group, herpes simplex virus, respiratory syncytial virus, cytomegalovirus, Epstein-Barr virus)
 Encephalitis (arboviruses, enteroviruses, herpes simplex virus)
 Rickettsiae (Rocky Mountain spotted fever, *Ehrlichia*, Q fever)
 Syphilis
 Vaccine reaction (pertussis, influenza, measles)
 Toxin-mediated reaction (toxic shock, staphylococcal scalded skin syndrome)

CARDIOPULMONARY

Pneumonia (bacteria, virus, mycobacteria, fungi, allergic reaction)
 Pulmonary emboli
 Heart failure
 Arrhythmia
 Pericarditis
 Myocarditis

METABOLIC-ENDOCRINE

Adrenal insufficiency (adrenogenital syndrome, Addison disease, corticosteroid withdrawal)
 Electrolyte disturbances (hyponatremia or hypernatremia; hypocalcemia or hypercalcemia)
 Diabetes insipidus
 Diabetes mellitus
 Inborn errors of metabolism (organic acidosis, urea cycle, carnitine deficiency, mitochondrial disorders)
 Hypoglycemia
 Reye syndrome

GASTROINTESTINAL

Gastroenteritis with dehydration
 Volvulus
 Intussusception
 Appendicitis
 Peritonitis (spontaneous, associated with perforation or peritoneal dialysis)
 Necrotizing enterocolitis
 Hepatitis
 Hemorrhage
 Pancreatitis

HEMATOLOGIC

Anemia (sickle cell disease, blood loss, nutritional)
 Methemoglobinemia
 Splenic sequestration crisis
 Leukemia or lymphoma
 Hemophagocytic syndromes

NEUROLOGIC

Intoxication (drugs, carbon monoxide, intentional or accidental overdose)
 Intracranial hemorrhage
 Infant botulism
 Trauma (child abuse, accidental)
 Guillain-Barré syndrome
 Myasthenia gravis

OTHER

Anaphylaxis (food, drug, insect sting)
 Hemolytic-uremic syndrome
 Kawasaki disease
 Erythema multiforme
 Hemorrhagic shock-encephalopathy syndrome
 Poisoning
 Toxic envenomation
 Macrophage activation syndrome

Table 70-13 | Cardiovascular Drug Treatment of Shock

DRUG	EFFECT(S)	DOSING RANGE	COMMENT(S)
Dopamine	↑ Cardiac contractility Significant peripheral vasoconstriction at >10 µg/kg/min	3-20 µg/kg/min	↑ Risk of arrhythmias at high doses
Epinephrine	↑ Heart rate and ↑ cardiac contractility Potent vasoconstrictor	0.05-3.0 µg/kg/min	May ↓ renal perfusion at high doses ↑ Myocardial O ₂ consumption Risk of arrhythmia at high doses
Dobutamine	↑ Cardiac contractility Peripheral vasodilator	1-10 µg/kg/min	—
Norepinephrine	Potent vasoconstriction No significant effect on cardiac contractility	0.05-1.5 µg/kg/min	↑ Blood pressure secondary to ↑ systemic vascular resistance ↑ Left ventricular afterload
Phenylephrine	Potent vasoconstriction	0.5-2.0 µg/kg/min	Can cause sudden hypertension ↑ O ₂ consumption

Table 70-11 | Recommendations: Hemodynamic Support and Adjunctive Therapy—Adults

FLUID THERAPY OF SEVERE SEPSIS
1. Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock.
2. Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock.
3. Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids.
4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients.
5. Fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (e.g., change in pulse pressure, stroke volume variation) or static (e.g., arterial pressure, heart rate) variables.
VASOPRESSORS
1. Vasopressor therapy initially to target a mean arterial pressure (MAP) of 65 mm Hg.
2. Norepinephrine as the first choice vasopressor.
3. Epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure.
4. Vasopressin 0.03 units/min can be added to norepinephrine (NE) with intent of either raising MAP or decreasing NE dosage.
5. Low-dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension and vasopressin doses higher than 0.03-0.04 units/min should be reserved for salvage therapy (failure to achieve adequate MAP with other vasopressor agents).
6. Dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (e.g., patients with low risk of tachyarrhythmias and absolute or relative bradycardia).
7. Phenylephrine is not recommended in the treatment of septic shock except in circumstances where (a) NE is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low, or (c) as salvage therapy when combined inotrope/vasopressor drugs and low-dose vasopressin have failed to achieve MAP target.
8. Low-dose dopamine should not be used for renal protection.
9. All patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available.
INOTROPIC THERAPY
1. A trial of dobutamine infusion up to 20 µg/kg/min be administered or added to vasopressor (if in use) in the presence of (a) myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output, or (b) ongoing signs of hypoperfusion, despite achieving adequate intravascular volume and adequate MAP.
2. Not using a strategy to increase cardiac index to predetermined supranormal levels.
CORTICOSTEROIDS
1. Not using intravenous hydrocortisone to treat adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). In case this is not achievable, we suggest intravenous hydrocortisone alone at a dose of 200 mg per day.
2. Not using the ACTH stimulation test to identify adults with septic shock who should receive hydrocortisone.
3. In treated patients, hydrocortisone tapered when vasopressors are no longer required.
4. Corticosteroids should not be administered for the treatment of sepsis in the absence of shock.
5. When hydrocortisone is given, use continuous flow.

Adapted from Dellinger PR, Levy MM, Rhodes A, et al: Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 41(2):580-637, 2013, Table 6, p. 596.

Table 70-12 Recommendations: Special Considerations in Pediatrics**INITIAL RESUSCITATION**

- For respiratory distress and hypoxemia start with face mask oxygen or if needed and available, high flow nasal cannula oxygen or nasopharyngeal CPAP (NP CPAP). For improved circulation, peripheral intravenous access or intraosseous access can be used for fluid resuscitation and inotrope infusion when a central line is not available. If mechanical ventilation is required then cardiovascular instability during intubation is less likely after appropriate cardiovascular resuscitation.
- Initial therapeutic end points of resuscitation of septic shock: capillary refill of ≤ 2 sec, normal blood pressure for age, normal pulses with no differential between peripheral and central pulses, warm extremities, urine output $> 1 \text{ mL kg}^{-1} \text{ hr}^{-1}$, and normal mental status. ScvO₂ saturation $\geq 70\%$ and cardiac index between 3.3 and 6.0 L/min/m^2 should be targeted thereafter.
- Follow American College of Critical Care Medicine-Pediatric Life Support (ACCM-PALS) guidelines for the management of septic shock.
- Evaluate for and reverse pneumothorax, pericardial tamponade, or endocrine emergencies in patients with refractory shock.

ANTIBIOTICS AND SOURCE CONTROL

- Empiric antibiotics should be administered within 1 hr of the identification of severe sepsis. Blood cultures should be obtained before administering antibiotics when possible but this should not delay administration of antibiotics. The empiric drug choice should be changed as epidemic and endemic ecologies dictate (e.g., H1N1, methicillin-resistant *Staphylococcus aureus* [MRSA], chloroquine-resistant malaria, penicillin-resistant pneumococci, recent ICU stay, neutropenia).
- Clindamycin and antitoxin therapies for toxic shock syndromes with refractory hypotension.
- Early and aggressive source control.
- Clostridium difficile* colitis should be treated with enteral antibiotics if tolerated. Oral vancomycin is preferred for severe disease.

FLUID RESUSCITATION

- In the industrialized world with access to inotropes and mechanical ventilation, initial resuscitation of hypovolemic shock begins with infusion of isotonic crystalloids or albumin with boluses of up to 20 mL/kg crystalloids (or albumin equivalent) over 5-10 minutes, titrated to reversing hypotension, increasing urine output, and attaining normal capillary refill, peripheral pulses, and level of consciousness without inducing hepatomegaly or rales. If hepatomegaly or rales exist then inotropic support should be implemented, not fluid resuscitation. In nonhypotensive children with severe hemolytic anemia (severe malaria or sickle cell crises), blood transfusion is considered superior to crystalloid or albumin bolus.

INOTROPES/VASOPRESSORS/VASODILATORS

- Begin peripheral inotropic support until central venous access can be attained in children who are not responsive to fluid resuscitation.
- Patients with low cardiac output and elevated systemic vascular resistance states with normal blood pressure should be given vasodilator therapies in addition to inotropes.

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

- Consider ECMO for refractory pediatric septic shock and respiratory failure.

CORTICOSTEROIDS

- Timely hydrocortisone therapy in children with fluid refractory, catecholamine resistant shock and suspected or proven absolute (classic) adrenal insufficiency.

PROTEIN C AND ACTIVATED PROTEIN CONCENTRATE

No recommendation as no longer available.

BLOOD PRODUCTS AND PLASMA THERAPIES

- Similar hemoglobin targets in children as in adults. During resuscitation of low superior vena cava oxygen saturation shock ($< 70\%$), hemoglobin levels of 10 g/dL are targeted. After stabilization and recovery from shock and hypoxemia, a lower target ($> 7.0 \text{ g/dL}$) can be considered reasonable.
- Similar platelet transfusion targets in children as in adults.
- Use plasma therapies in children to correct sepsis-induced thrombotic purpura disorders, including progressive disseminated intravascular coagulation, secondary thrombotic microangiopathy, and thrombotic thrombocytopenic purpura.

MECHANICAL VENTILATION

- Lung-protective strategies during mechanical ventilation.

SEDATION/ANALGESIA/DRUG TOXICITIES

- We recommend use of sedation with a sedation goal in critically ill mechanically ventilated patients with sepsis.
- Monitor drug toxicity labs because drug metabolism is reduced during severe sepsis, putting children at greater risk of adverse drug-related events.

GLYCEMIC CONTROL

- Control hyperglycemia using a similar target as in adults ($\leq 180 \text{ mg/dL}$). Glucose infusion should accompany insulin therapy in newborns and children because some hyperglycemic children make no insulin whereas others are insulin resistant.

DIURETICS AND RENAL REPLACEMENT THERAPY

- Use diuretics to reverse fluid overload when shock has resolved, and if unsuccessful then continuous venovenous hemofiltration (CVVH) or intermittent dialysis to prevent $> 10\%$ total body weight fluid overload.

DEEP VEIN THROMBOSIS (DVT) PROPHYLAXIS

No recommendation on the use of DVT prophylaxis in prepubertal children with severe sepsis.

STRESS ULCER (SU) PROPHYLAXIS

No recommendation on the use of SU prophylaxis in prepubertal children with severe sepsis

NUTRITION

- Enteral nutrition given to children who can be fed enterally, and parenteral feeding in those who cannot (grade 2C).

CPAP, continuous positive airway pressure.

Adapted from Dellinger PR, Levy MM, Rhodes A, et al: *Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock: 2012*. Crit Care Med 41(2):680-637, 2013, Table 9, p. 614.

Table 71-1 Typical Localizing Signs for Pulmonary Pathology

SITE OF PATHOLOGY	RESPIRATORY RATE	RETRACTS	AUDIBLE SOUNDS
Extrathoracic airway	↑	↑↑↑↑	Stridor
Intrathoracic extrapulmonary	↑	↑↑	Wheezing
Intrathoracic intrapulmonary	↑↑	↑↑	Wheezing
Alveolar interstitial	↑↑↑	↑↑↑	Grunting

Table 71-3 Nonpulmonary Causes of Respiratory Distress

	EXAMPLE(S)	MECHANISM(S)
Cardiovascular	Left-to-right shunt Congestive heart failure Cardiogenic shock	↑ Pulmonary blood/water content Metabolic acidosis Baroreceptor stimulation
Central nervous system	Increased intracranial pressure Encephalitis Neurogenic pulmonary edema Toxic encephalopathy	Stimulation of brainstem respiratory centers
Metabolic	Diabetic ketoacidosis Organic acidemia Hyperammonemia	Stimulation of central and peripheral chemoreceptors
Renal	Renal tubular acidosis Hypertension	Stimulation of central and peripheral chemoreceptors Left ventricular dysfunction → increased pulmonary blood/water content
Sepsis	Toxic shock syndrome Meningococcemia	Cytokine stimulation of respiratory centers Baroreceptor stimulation from shock Metabolic acidosis

Table 71-2 Examples of Anatomic Sites of Lesions Causing Respiratory Failure

LUNG	RESPIRATORY PUMP
CENTRAL AIRWAY OBSTRUCTION Choanal atresia Tonsilloadenoidal hypertrophy Retropharyngeal/peritonsillar abscess Laryngomalacia Epiglottitis Vocal cord paralysis Laryngotracheitis Subglottic stenosis Vascular ring/pulmonary sling Mediastinal mass Foreign-body aspiration Obstructive sleep apnea	THORACIC CAGE Kyphoscoliosis Diaphragmatic hernia Flail chest Eventration of diaphragm Asphyxiating thoracic dystrophy Prune-belly syndrome Dermatomyositis Abdominal distention
PERIPHERAL AIRWAY OBSTRUCTION Asthma Bronchiolitis Foreign-body aspiration Aspiration pneumonia Cystic fibrosis α ₁ -Antitrypsin deficiency	BRAINSTEM Arnold-Chiari malformation Central hypoventilation syndrome CNS depressants Trauma Increased intracranial pressure CNS infections
ALVEOLAR-INTERSTITIAL DISEASE Lobar pneumonia Acute respiratory distress syndrome/hyaline membrane disease Interstitial pneumonia Hydrocarbon pneumonia Pulmonary hemorrhage/hemosiderosis	SPINAL CORD Trauma Transverse myelitis Spinal muscular atrophy Polioymelitis Tumor/abscess
	NEUROMUSCULAR Phrenic nerve injury Birth trauma Infant botulism Guillain-Barré syndrome Muscular dystrophy Myasthenia gravis Organophosphate poisoning

Table 71-4 Cardiovascular Pathology Manifesting as Respiratory Distress

- I. DECREASED LUNG COMPLIANCE
 - A. Left-to-Right Shunts
 - 1. Ventricular septal defect, atrial septal defect, patent ductus arteriosus, atrioventricular canal, truncus arteriosus
 - 2. Cerebral or hepatic arteriovenous fistula
 - B. Ventricular Failure
 - 1. Left-heart obstructive lesions
 - a) aortic stenosis
 - b) coarctation of the aorta
 - c) mitral stenosis
 - d) interrupted aortic arch
 - e) hypoplastic left heart syndrome
 - 2. Myocardial infarction
 - a) anomalous left coronary artery arising from the pulmonary artery
 - 3. Hypertension
 - a) acute glomerulonephritis
 - 4. Inflammatory/Infectious
 - a) myocarditis
 - b) pericardial effusion
 - 5. Idiopathic
 - a) dilated cardiomyopathy
 - b) hypertrophic obstructive cardiomyopathy
 - C. Pulmonary Venous Obstruction
 - 1. Total anomalous pulmonary venous return with obstruction
 - 2. Cor triatriatum
- II. SHOCK RESULTING IN METABOLIC ACIDOSIS
- A. Left-Heart Obstructive Lesions
 - B. Acute Ventricular Failure
 - 1. Myocarditis, myocardial infarction

Table 71-5 Typical Chronology of Heart Disease Presentation in Children

AGE	MECHANISM	DISEASE
Newborn (1-10 days)	↑ Arteriovenous pressure difference Ductal closure	Arteriovenous fistula (brain, liver) Single ventricle lesions or severe ventricular outflow obstruction
	Independent pulmonary and systemic blood flow	Transposition of the great arteries
	Pulmonary venous obstruction	Total anomalous pulmonary venous return (TAPVR)
Young Infant (1-6 mo)	↓ Pulmonary vascular resistance ↓ Pulmonary artery pressure	Left-to-right shunt Anomalous left coronary artery to the pulmonary artery
Any Age	Rate disturbance Infection Abnormal cardiac myocytes Excess afterload	Tachy- or bradyarrhythmias Myocarditis, pericarditis Cardiomyopathy hypertension

Table 71-7 Simplified Consensus Definition of Acute Lung Injury

- Acute onset (<7 days)
- Severe hypoxemia ($\text{PaO}_2/\text{FiO}_2 < 300$ for acute lung injury, or < 200 for acute respiratory distress syndrome)
- Diffuse bilateral pulmonary infiltrates on frontal radiograph consistent with pulmonary edema (these can be patchy and asymmetric, and pleural effusions can be present)
- Absence of left atrial hypertension (pulmonary artery wedge pressure < 18 mm Hg if measured)

From Wheeler AP, Bernard GR: Acute lung injury and the acute respiratory distress syndrome: a clinical review. Lancet 369:1553-1564, 2007.

Table 71-6 Typical Clinical Manifestations of Respiratory Failure

SITE OF PATHOLOGY	SYMPTOM
Lung and Airways	Nasal flaring, retractions, tachypnea, wheezing stridor, grunting
Chest wall and muscles of respiration	Nasal flaring, tachypnea, paradoxical respirations
Respiratory control	Shallow or slow respirations, abnormal respiratory patterns, apnea

Table 71-8 New Berlin Definition of ARDS in Infancy and Early Childhood

BERLIN DEFINITION CRITERIA			SUITABILITY IN INFANTS
Timing	Within 1 wk of a known clinical insult or new or worsening respiratory symptoms		Acute time frame is specified
Chest X-rays or tomography scan	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules. (Illustrative clinical cases and chest X-rays have been provided)		Including illustrative radiographs is important, because ARDS appearance may be different in children and in adults
Origin of edema	Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g., echocardiography) to exclude hydrostatic edema, if no ARDS risk factors are present		Echocardiography widely used, whereas Swan-Ganz catheters are rarely used in early childhood. Including risk factors in the ARDS definition is important, because they may be different in children and in adults
Oxygenation*			
Mild	200 mm Hg $< \text{PaO}_2/\text{FiO}_2 \leq 300$ mm Hg with PEEP or CPAP ≥ 5 cm H ₂ O [†]		Noninvasive CPAP is widely used in early childhood. PEEP threshold (5 cm H ₂ O) is a value commonly used during early childhood
Moderate	100 mm Hg $< \text{PaO}_2/\text{FiO}_2 \leq 200$ mm Hg with PEEP ≥ 5 cm H ₂ O		
Severe	PaO ₂ /FiO ₂ < 100 mm Hg with PEEP ≥ 5 cm H ₂ O		

*If altitude is higher than 1,000 m, the correction factor should be calculated as follows: [$\text{PaO}_2/\text{FiO}_2 \times (\text{barometric pressure}/760)$].

[†]This may be delivered noninvasively in the mild acute respiratory distress syndrome group.

CPAP, continuous positive airway pressure; FiO₂, fraction of inspired oxygen; PaO₂, partial pressure of arterial oxygen; PEEP, positive end-expiratory pressure.

Table 71-10 Medications Commonly Used for Intubation

	DRUG	DOSE	ONSET (min)	DURATION (min)	COMMENTS
Sedatives/anesthetics	Midazolam	0.1 mg/kg IV	3-5	60-120	Amnesia Respiratory depression
	Lorazepam	0.1 mg/kg IV	3-5	120-240	Amnesia Respiratory depression
	Ketamine	1-2 mg/kg IV 4-6 mg/kg IM	2-3	10-15	↑ HR, BP, and ICP Bronchodilation
	Propofol	1-3 mg/kg IV	0.5-2	10-15	↓ BP Apnea
	Thiopental	4-7 mg/kg IV	0.5-1	5-10	↓ BP Apnea
Analgesics	Fentanyl	2-5 µg/kg IV	3-5	30-90	Respiratory depression Chest wall rigidity
	Morphine	0.1 mg/kg IV	5-15	120-240	↓ BP Respiratory depression
Neuromuscular blocking agents	Vecuronium	0.1 mg/kg IV	2-3	30-75	↑ HR Renal elimination
	Rocuronium	0.6-1.2 mg/kg IV 1 mg/kg IM	5-15	15-60	↑ HR Renal elimination
	Cisatracurium	0.1 mg/kg IV	2-3	25-30	Histamine release Nonrenal elimination

BP, blood pressure; HR, heart rate; ICP, intracranial pressure; IM, intramuscularly; IV, intravenously.

Table 72-4 Life-Threatening Chest Injuries**TENSION PNEUMOTHORAX**

One-way valve leak from the lung parenchyma or tracheobronchial tree
Collapse with mediastinal and tracheal shift to the side opposite the leak
Compromises venous return and decreases ventilation of the other lung
Clinically, manifests as respiratory distress, unilateral absence of breath sounds, tracheal deviation, distended neck veins, tympany to percussion of the involved side, and cyanosis
Relieve first with needle aspiration, then with chest tube drainage

OPEN PNEUMOTHORAX (SUCKING CHEST WOUND)

Effect on ventilation depends on size

MAJOR FLAIL CHEST

Usually caused by blunt injury resulting in multiple rib fractures
Loss of bone stability of the thoracic cage
Major disruption of synchronous chest wall motion
Mechanical ventilation and positive end-expiratory pressure required

MASSIVE HEMOTHORAX

Must be drained with a large-bore tube
Initiate drainage only with concurrent vascular volume replacement

CARDIAC TAMPONADE

- Beck Triad:
- Decreased or muffled heart sounds
 - Distended neck veins from increased venous pressure
 - Hypotension with pulsus paradoxus (decreased pulse pressure during inspiration)
- Must be drained

Modified from Krug SE: The acutely ill or injured child. In Behrman RE, Kliegman RM, editors: Nelson essentials of pediatrics, ed 4, Philadelphia, 2002, WB Saunders, p. 97.

Table 75-3 Acute Treatment of Burns

First aid, including washing of wounds and removal of devitalized tissue
Fluid resuscitation
Provision of energy requirements
Control of pain
Prevention of infection—early excision and grafting
Prevention of excessive metabolic expenditures
Control of bacterial wound flora
Use of biologic and synthetic dressings to close the wound

Table 75-1 Burn Prophylaxis**PREVENT FIRES**

Install and use smoke detectors
Control the hot water thermostat—in public buildings, the maximum water temperature should be 48.9°C (120°F)
Keep fire, matches, and lighters out of the reach of children
Avoid cigarette smoking, especially in bed
Do not leave lit candles unattended
Use flame retardant-treated clothing
Use caution when cooking, especially with oil
Keep cloth items off heaters

PREVENT INJURY

Roll, but do not run, if clothing catches fire; wrap in a blanket
Practice escape procedures
Crawl beneath smoke if a fire occurs indoors
Use educational materials*

*National Fire Protection Association pamphlets and videos.

Table 75-2 Indications for Hospitalization for Burns

Burns affecting >10% of BSA
Burns >10-20% of BSA in adolescent/adult
3rd-Degree burns
Electrical burns caused by high-tension wires or lightning
Chemical burns
Inhalation injury, regardless of the amount of BSA burned
Inadequate home or social environment
Suspected child abuse or neglect
Burns to the face, hands, feet, perineum, genitals, or major joints
Burns in patients with preexisting medical conditions that may complicate the acute recovery phase
Associated injuries (fractures)
Pregnancy

Table 72-5 Differential Diagnosis of Immediately Life-Threatening Cardiopulmonary Injuries

TENSION PNEUMOTHORAX		MASSIVE HEMOTHORAX	CARDIAC TAMPONADE
Breath sounds	Ipsilaterally decreased more than contralaterally	Ipsilaterally decreased	Normal
Percussion note	Hyperresonant	Dull	Normal
Tracheal location	Contralaterally shifted	Midline or shifted	Midline
Neck veins	Distended	Flat	Distended
Heart tones	Normal	Normal	Muffled

Modified from Cooper A, Foltin GL: Thoracic trauma. In Barkin RM, editor: Pediatric emergency medicine, ed 2, St. Louis, 1997, Mosby, p. 325.

Table 72-6 Systemic Responses to Blood Loss in Pediatric Patients

SYSTEM	MILD BLOOD LOSS (<30%)	MODERATE BLOOD LOSS (30-45%)	SEVERE BLOOD LOSS (>45%)
Cardiovascular	Increased heart rate; weak, thready peripheral pulses; normal systolic blood pressure; normal pulse pressure	Markedly increased heart rate; weak, thready central pulses; peripheral pulses absent; low normal systolic blood pressure	Tachycardia followed by bradycardia; central pulses very weak or absent; peripheral pulses absent; hypotension; diastolic blood pressure may be undetectable
Central nervous system	Anxiety; irritability; confusion	Lethargy; dulled response to pain	Coma
Skin	Cool, mottled; capillary refill prolonged	Cyanotic; capillary refill markedly prolonged	Pale and cold
Urine output	Low to very low	Minimal	None

Adapted from American College of Surgeons Committee on Trauma: Advanced trauma life support for doctors: student course manual, Chicago, 2008, American College of Surgeons, p. 234.

Table 75-4 Categories of Burn Depth

	1ST-DEGREE BURN	2ND-DEGREE, OR PARTIAL-THICKNESS, BURN	3RD-DEGREE, OR FULL-THICKNESS, BURN
Surface appearance	Dry, no blisters Minimal or no edema Erythematous Blanches, bleeds	Moist blebs, blisters Underlying tissue is mottled pink and white, with fair capillary refill Bleeds	Dry, leathery eschar Mixed white, waxy, khaki, mahogany, soot-stained No blanching or bleeding
Pain	Very painful	Very painful	Insensate
Histologic depth	Epidermal layers only	Epidermis, papillary, and reticular layers of dermis May include domes of subcutaneous layers	Down to and may include fat, subcutaneous tissue, fascia, muscle, and bone
Healing time	2-5 days with no scarring	Superficial: 5-21 days with no grafting Deep partial: 21-35 days with no infection; if infected, converts to full-thickness burn	Large areas require grafting, but small areas may heal from the edges after wks

Table 75-6 Topical Agents Used for Burns

AGENT	EFFECTIVENESS	EASE OF USE
Silvadene cream (silver sulfadiazine)	Good penetration	Changed once daily Residue must be washed off with each dressing change
Mafenide acetate cream* (Sulfamylon cream)	Broad spectrum, including <i>Pseudomonas</i> Rapid and deep wound penetration	Closed dressings Changed twice daily Residue must be washed off with each dressing changed
0.5% Silver nitrate solution	Bacteriostatic Broad spectrum, including some fungi Superficial penetration	Closed bulky dressing soaked every 2 hr and changed once daily
AQUACEL Ag	Dressing impregnated with silver	Applied directly to 2nd-degree burn; occlusive dressing kept for 10 days

Table 75-5 Partial Listing of Some Commonly Used Wound Membranes—Selected Characteristics

MEMBRANE	CHARACTERISTIC(S)
Porcine xenograft	Adheres to coagulum Excellent pain control
Biobrane	Bilaminar Fibrovascular in growth into inner layer
Acticoat	Nonadherent dressing that delivers silver
AQUACEL-Ag	Absorptive hydrofiber that delivers silver
Various semipermeable membranes	Provide vapor and bacterial barrier
Various hydrocolloid dressings	Provide vapor and bacterial barrier Absorb exudates
Various impregnated gauzes	Provide barrier while allowing drainage

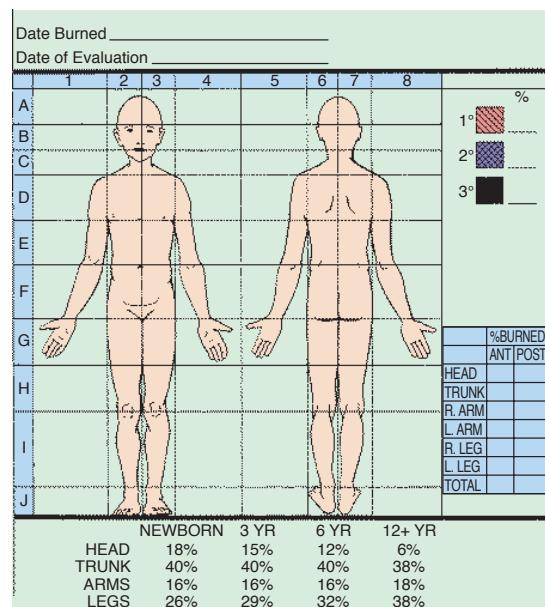


Figure 75-3 Chart to determine the developmentally related percentage of BSA affected by a burn injury. ANT, anterior; POST, posterior; R., right; L., left. (Courtesy of Shriners Hospital for Crippled Children, Burn Institute, Boston Unit.)

Table 76-2 Management of Hypothermia**HISTORY AND PHYSICAL**

Gentle handling of the patient to prevent arrhythmias
ABCDE: cardiopulmonary resuscitation for ventricular fibrillation and asystole
Underlying disease diagnosis and treatment
Vital signs, pulse oximetry, electrocardiogram
Wet or cold clothing removed and patient placed in warm environment

LABORATORY TESTS

Arterial blood gas analysis corrected for temperature
Electrolytes, BUN creatinine, Ca, Mg, P
CBC with differential, PT/PTT, fibrinogen
Glucose, amylase/lipase
LFT

Additional labs, if appropriate, such as toxicology screen

PASSIVE REWARMING

$\geq 32^{\circ}\text{C}$ (89.6°F) in patients who are capable of spontaneous thermogenesis

ACTIVE REWARMING

$<32^{\circ}\text{C}$ (89.6°F), cardiovascular instability, patients at risk for developing hypothermia
Close monitoring for core-temperature afterdrop
Acute: external and/or core rewarming
Chronic ($<32^{\circ}\text{C}$ [89.6°F] for longer than 24 hr): core rewarming
Extracorporeal membrane oxygenation
Availability of rapid deployment

ABCDE, airway and possibly antibiotics, breathing, circulation, disability or neurologic and possible dextrose, extracorporeal support if all else fails; BUN, blood urea nitrogen; Ca, calcium; CDC, complete blood count; LFT liver function test; Mg, magnesium; P, phosphorus; PT, prothrombin time; PTT, partial thromboplastin time.

From Burg FD, Ingelfinger JR, Polin RA, Gershon AA (eds): Current pediatric therapy, ed 18, Philadelphia, 2006, Saunders/Elsevier, Table 4, p. 174.

Table 77-3 Indications for Genetic Counseling

Advanced parental age

- Maternal age ≥ 35 yr
- Paternal age ≥ 50 yr

Previous child with or family history of

- Congenital abnormality
- Dysmorphology
- Intellectual disability
- Isolated birth defect
- Metabolic disorder
- Chromosome abnormality
- Single-gene disorder

Adult-onset genetic disease (presymptomatic testing)

- Cancer
- Huntington disease

Consanguinity

Teratogen exposure (occupational, abuse)

Repeated pregnancy loss or infertility

Pregnancy screening abnormality

- Maternal serum α -fetoprotein
- Maternal triple or quad screen or variant of this test
- Fetal ultrasonography
- Fetal karyotype

Heterozygote screening based on ethnic risk

- Sickle cell anemia
- Tay-Sachs, Canavan, and Gaucher diseases
- Thalassemias

Follow-up to abnormal neonatal genetic testing

Prior to whole genome or exome sequencing

Prior to preimplantation genetic testing

Table 75-7 Common Long-Term Disabilities in Patients with Burn Injuries**DISABILITIES AFFECTING THE SKIN AND SOFT TISSUE**

Hypertrrophic scars
Susceptibility to minor trauma
Dry skin
Contractures
Itching and neuropathic pain
Alopecia
Chronic open wounds
Skin cancers

ORTHOPEDIC DISABILITIES

Amputations
Contractures
Heterotopic ossification
Temporary reduction in bone density

METABOLIC DISABILITIES

Heat sensitivity
Obesity

PSYCHIATRIC AND NEUROLOGIC DISABILITIES

Sleep disorders
Adjustment disorders
Posttraumatic stress syndrome
Depression
Body image issues
Neuropathy and neuropathic pain
Long-term neurologic effects of carbon monoxide poisoning
Anoxic brain injury

LONG-TERM COMPLICATIONS OF CRITICAL CARE

Deep-vein thrombosis, venous insufficiency, or varicose veins
Tracheal stenosis, vocal cord disorders, or swallowing disorders
Renal or adrenal dysfunction
Hepatobiliary or pancreatic disease
Cardiovascular disease
Reactive airway disease or bronchial polypsis

PREEXISTING DISABILITIES THAT CONTRIBUTED TO THE INJURIES

Risk-taking behavior
Untreated or poorly treated psychiatric disorder

Human Genetics

Instructions:				
—Key should contain all information relevant to interpretation of pedigree (e.g., define fill/shading)				
—For clinical (non-published) pedigrees include:				
a) name of proband/consultant b) family names/initials of relatives for identification, as appropriate c) name and title of person recording pedigree d) historian (person relaying family history information) e) date of intake/update f) reason for taking pedigree (e.g., abnormal ultrasound, familial cancer, developmental delay, etc.) g) ancestry of both sides of family				
—Recommended order of information placed below symbol (or to lower right)				
a) age; can note year of birth (e.g., b.1978) and/or death (e.g., d. 2007) b) evaluation (see Figure 75-4) c) pedigree number (e.g., I-1, I-2, I-3)				
—Limit identifying information to maintain confidentiality and privacy				
	Male	Female	Gender not specified	Comments
1. Individual				Assign gender by phenotype (see text for disorders of sex development, etc.). Do not write age in symbol.
	b.1925	30 y	4 mo	
2. Affected individual				Key/legend used to define shading or other fill (e.g., hatches, dots, etc.). Use only when individual is clinically affected.
				With ≥2 conditions, the individual's symbol can be partitioned accordingly, each segment shaded with a different fill and defined in legend.
3. Multiple individuals, number known				Number of siblings written inside symbol. (Affected individuals should not be grouped.)
4. Multiple individuals, number unknown or unstated				"n" used in place of "?".
5. Deceased individual				Indicate cause of death if known. Do not use a cross (+) to indicate death to avoid confusion with evaluation positive (+).
d. 35	d. 4 mo	d. 60's		
6. Consultand				Individual(s) seeking genetic counseling/testing.
7. Proband				An affected family member coming to medical attention independent of other family members.
P	P			
8. Stillbirth (SB)				Include gestational age and karyotype, if known.
LMP: 7/1/2007 47,XY,+21	20 wk 46, XX			
9. Pregnancy (P)				Gestational age and karyotype below symbol. Light shading can be used for affected; define in key/legend.
LMP: 7/1/2007 47,XY,+21	20 wk 46, XX			
Pregnancies not carried to term	Affected	Unaffected		
10. Spontaneous abortion (SAB)			If gestational age/gender known, write below symbol. Key/legend used to define shading.	
	17 wks female cystic hygroma	<10 wks		
11. Termination of pregnancy (TOP)			Other abbreviations (e.g., TAB, VTOP) not used for sake of consistency.	
	18 wks 47, XY,+18			
12. Ectopic pregnancy (ECT)			Write ECT below symbol.	
	ECT			

Figure 80-1 Common pedigree symbols, definitions, and abbreviations. (From Bennett RL, French KS, Resta RG, et al: Standardized human pedigree nomenclature: update and assessment of the recommendations of the National Society of Genetic Counselors, J Genet Couns 17:424–433, 2008.)

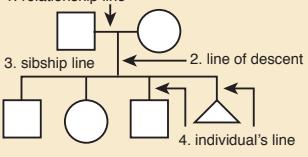
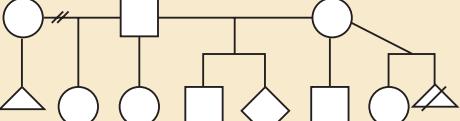
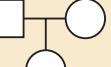
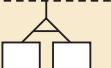
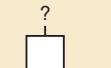
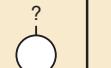
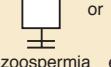
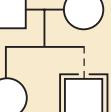
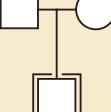
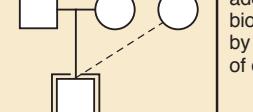
1. Definitions		Comments		
 1. relationship line 2. line of descent 3. sibship line 4. individual's line		If possible, male partner should be to left of female partner on relationship line. Siblings should be listed from left to right in birth order (oldest to youngest).		
2. Relationship line (horizontal)				
a. Relationships 		A break in a relationship line indicates the relationship no longer exists. Multiple previous partners do not need to be shown if they do not affect genetic assessment.		
b. Consanguinity 		If degree of relationship not obvious from pedigree, it should be stated (e.g., third cousins) above relationship line.		
3. Line of descent (vertical or diagonal)				
a. Genetic 		Biologic parents shown.		
- Multiple gestation	Monozygotic 	Dizygotic 	Unknown 	
	Trizygotic 	The horizontal line indicating monozygosity is placed between the individual's line and not between each symbol. An asterisk (*) can be used if zygosity proven.		
- Family history not available/ known for individual				
- No children by choice or reason unknown		 or 	Indicate reason, if known.	
- Infertility		 or 	Indicate reason, if known.	
b. Adoption in 		out 	by relative 	Brackets used for all adoptions. Adoptive and biological parents denoted by dashed and solid lines of descent, respectively.

Figure 80-2 Pedigree line definitions. (From Bennett RL, French KS, Resta RG, et al: Standardized human pedigree nomenclature: update and assessment of the recommendations of the National Society of Genetic Counselors, *J Genet Couns* 17:424–433, 2008.)

596 Part X ◇ Human Genetics

Instructions:		
<ul style="list-style-type: none"> — D represents egg or sperm donor — S represents surrogate (gestational carrier) — If the woman is both the ovum donor and a surrogate, in the interest of genetic assessment, she will only be referred to as a donor (e.g., 4 and 5); the pregnancy symbol and its line of descent are positioned below the woman who is carrying the pregnancy — Available family history should be noted on the gamete donor and/or gestational carrier 		
Possible Reproductive Scenarios		Comments
1. Sperm donor	<p>or</p>	Couple in which woman is carrying pregnancy using donor sperm. No relationship line is shown between the woman carrying the pregnancy and the sperm donor.
2. Ovum donor		Couple in which woman is carrying pregnancy using a donor egg and partner's sperm. The line of descent from the birth mother is solid because there is a biologic relationship that may affect the fetus (e.g., teratogens).
3. Surrogate only		Couple whose gametes are used to impregnate a woman (surrogate) who carries the pregnancy. The line of descent from the surrogate is solid because there is a biological relationship that may affect the fetus (e.g., teratogens).
4. Surrogate ovum donor	<p>a)</p> <p>b)</p> <p>or</p>	Couple in which male partner's sperm is used to inseminate (a) an unrelated woman or (b) a sister who is carrying the pregnancy for the couple.
5. Planned adoption		Couple contracts with a woman to carry a pregnancy using ovum of the woman carrying the pregnancy and donor sperm.

Figure 80-3 Assisted reproductive technology symbols and definitions. (From Bennett RL, French KS, Resta RG, et al: Standardized human pedigree nomenclature: update and assessment of the recommendations of the National Society of Genetic Counselors, J Genet Couns 17:424–433, 2008.)

Instructions:

- E is used for evaluation to represent clinical and/or test information on the pedigree
 - a. E is to be defined in key/legend
 - b. If more than one evaluation, use subscript (E₁, E₂, E₃) and define in key
 - c. Test results should be put in parentheses or defined in key/legend
- A symbol is shaded only when an individual is clinically symptomatic
- For linkage studies, haplotype information is written below the individual. The haplotype of interest should be on left and appropriately highlighted
- Repetitive sequences, trinucleotides, and expansion numbers are written with affected allele first and placed in parentheses
- If mutation known, identify in parentheses

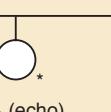
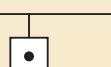
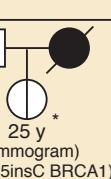
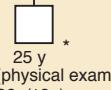
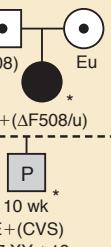
Definition	Symbol	Scenario
1. Documented evaluation (*) Use only if examined/evaluated by you or your research/clinical team or if the outside evaluation has been reviewed and verified.	○*	Woman with negative echocardiogram.  E ₋ (echo)
2. Carrier—not likely to manifest disease regardless of inheritance pattern	●	Male carrier of Tay-Sachs disease by patient report (* not used because results not verified). 
3. Asymptomatic/presymptomatic carrier—clinically unaffected at this time but could later exhibit symptoms	○	Woman age 25 with negative mammogram and positive BRCA1 DNA test. 
4. Uninformative study (u)	□ Eu	Man age 25 with normal physical exam and uninformative DNA test for Huntington disease (E ₂). 
5. Affected individual with positive evaluation (E+)	■ E+	Individual with cystic fibrosis and positive mutation study; only one mutation has currently been identified. 

Figure 80-4 Pedigree symbols of genetic evaluation and testing information. (From Bennett RL, French KS, Resta RG, et al: Standardized human pedigree nomenclature: update and assessment of the recommendations of the National Society of Genetic Counselors, J Genet Couns 17:424-433, 2008.)

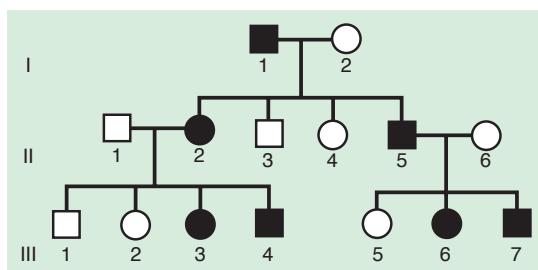


Figure 80-5 Autosomal dominant pedigree. Pedigree showing typical inheritance of a form of achondroplasia (FGFR3) inherited as an autosomal dominant trait. Black, affected patients.

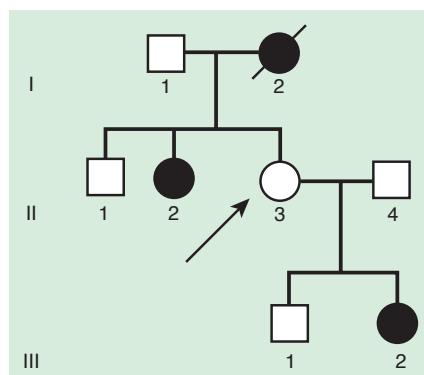


Figure 80-6 Incomplete penetrance. This family segregates a familial cancer syndrome, familial adenomatous polyposis. Individual II-3 is an obligate carrier, but there are no findings to suggest the disorder. This disorder is nonpenetrant in this individual.

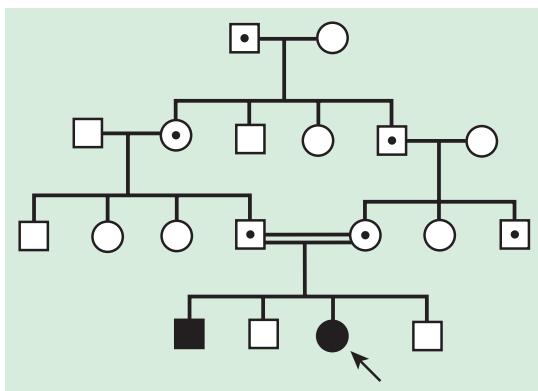


Figure 80-7 Autosomal recessive pedigree with parental consanguinity. Central dot, carriers; black, affected patients.

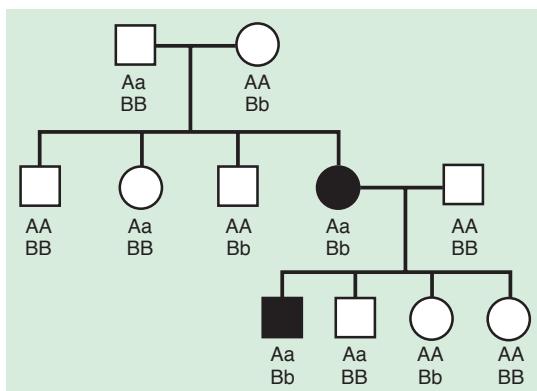


Figure 80-14 Digenic pedigree. Here, the disease alleles are *a* and *b* and they reside on distinct genetic loci or genes. For a person to have the disease, heterozygosity for mutant alleles in both genes (*A/a;B/b*) is required.

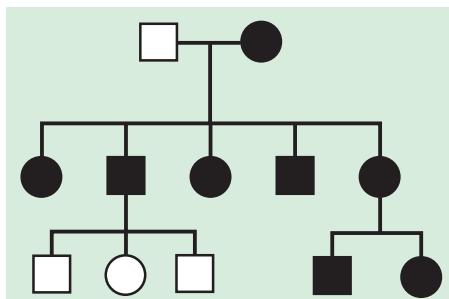


Figure 80-15 Pedigree of a mitochondrial disorder, exhibiting maternal inheritance. Black, affected patient.

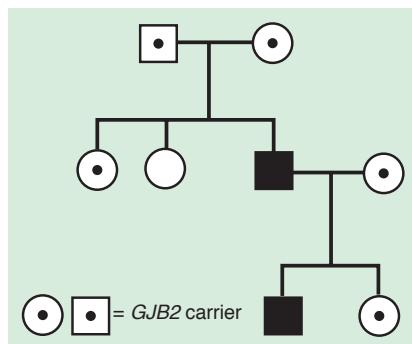


Figure 80-8 Pseudodominant inheritance. Black, affected (deaf); central dot shows carrier who is asymptomatic (unaffected).

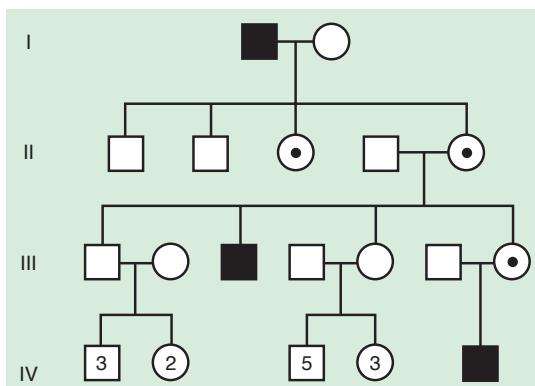


Figure 80-9 Pedigree demonstrating X-linked recessive inheritance.

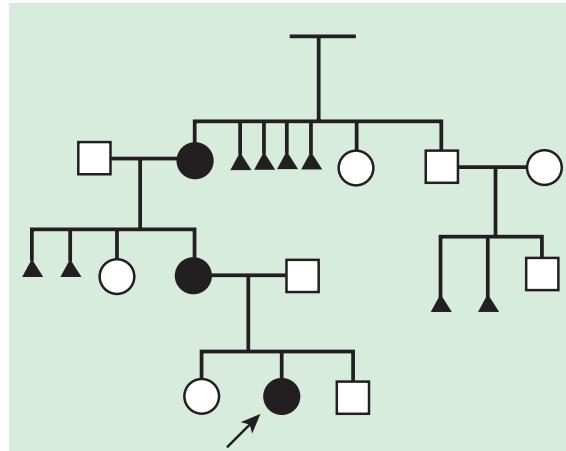


Figure 80-12 Pedigree of an X-linked dominant disorder with male lethality, such as incontinentia pigmenti.

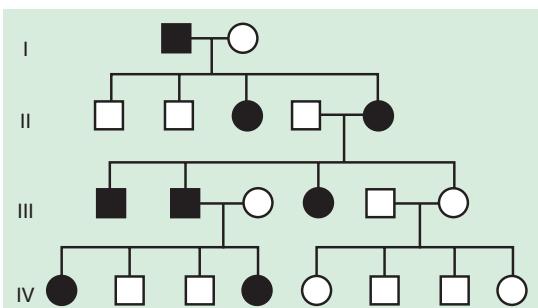


Figure 80-11 Pedigree pattern demonstrating X-linked dominant inheritance. Note there is no father-to-son transmission in this situation, and hemizygosity (i.e., X-linked gene in a male) is not lethal. In some X-linked dominant conditions, X-linked males have a more severe phenotype and might not survive. In that case, only females manifest the disease (see Fig. 80-12).

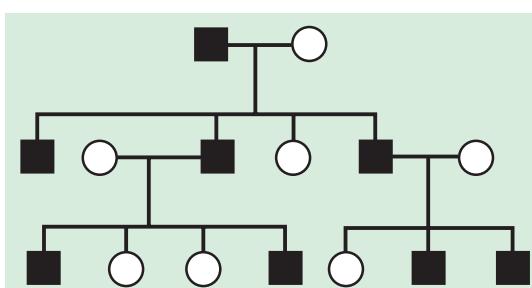


Figure 80-13 Y-linked inheritance. Black, affected patient.

612 Part X ◇ Human Genetics

Table 81-16 Signs Associated with Turner Syndrome

Short stature
Congenital lymphedema
Horseshoe kidneys
Patella dislocation
Increased carrying angle of elbow (cubitus valgus)
Madelung deformity (chondrodysplasia of distal radial epiphysis)
Congenital hip dislocation
Scoliosis
Scoliosis
Widespread nipples
Shield chest
Redundant nuchal skin (in utero cystic hygroma)
Low posterior hairline
Coarctation of aorta
Bicuspid aortic valve
Cardiac conduction abnormalities
Hypoplastic left-heart syndrome and other left-heart abnormalities
Gonadal dysgenesis (infertility, primary amenorrhea)
Gonadoblastoma (increased risk if Y chromosome material is present)
Learning disabilities (nonverbal perceptual motor and visuospatial skills) (in 70%)
Developmental delay (in 10%)
Social awkwardness
Hypothyroidism (acquired in 15-30%)
Type 2 diabetes mellitus (insulin resistance)
Strabismus
Cataracts
Red-green color blindness (as in males)
Recurrent otitis media
Sensorineural hearing loss
Inflammatory bowel disease
Celiac disease (increased incidence)

Table 81-17 Signs Associated with Noonan Syndrome

Short stature
Failure to thrive (use Noonan growth curve)
Tall forehead
Epicantal folds
Ptosis
Blue-green irises
Hypertelorism
Low nasal bridge, upturned nose
Downward-slanting palpebral fissures
Myopia
Nystagmus
Low-set auricles
Dental malocclusion
Low posterior hairline
Short webbed neck (excessive nuchal skin), cystic hygroma
Shield chest
Pectus carinatum superiorly
Scoliosis
Pigmented villonodular synovitis (polyarticular)
Cubitus valgus
Pulmonary valve stenosis (dysplastic valve)
Hypertrophic cardiomyopathy
Atrial septal defect, ventricular septal defect
Lymphedema
Nevi, lentigines, café-au-lait spots
Cryptorchidism
Small penis
Delayed puberty
Bleeding disorders, including thrombocytopenia and factor deficiencies
Leukemia, myeloproliferative disorders, other malignancies
Cognitive delay (<i>KRAS</i> mutation)

Table 81-4 Clinical Features of Down Syndrome in the Neonatal Period

CENTRAL NERVOUS SYSTEM
Hypotonia*
Developmental delay
Poor Moro reflex*
CRANIOFACIAL
Brachycephaly with flat occiput
Flat face*
Upward slanted palpebral fissures*
Epicantal folds
Speckled irises (Brushfield spots)
Three fontanelles
Delayed fontanel closure
Frontal sinus and midfacial hypoplasia
Mild microcephaly
Short hard palate
Small nose, flat nasal bridge
Protruding tongue, open mouth
Small dysplastic ears*
CARDIOVASCULAR
Endocardial Cushing defects
Ventricular septal defect
Atrial septal defect
Patent ductus arteriosus
Aberrant subclavian artery
Pulmonary hypertension
MUSCULOSKELETAL
Joint hyperflexibility*
Short neck, redundant skin*
Short metacarpals and phalanges
Short 5th digit with clinodactyly*
Single transverse palmar creases*
Wide gap between 1st and 2nd toes
Pelvic dysplasia*
Short sternum
Two sternal manubrium ossification centers
GASTROINTESTINAL
Duodenal atresia
Annular pancreas
Tracheoesophageal fistula
Hirschsprung disease
Imperforate anus
Neonatal cholestasis
CUTANEOUS
Cutis marmorata

*Hall's criteria to aid in diagnosis.

Table 81-15 Sex Chromosome Abnormalities

DISORDER	KARYOTYPE	APPROXIMATE INCIDENCE
Klinefelter syndrome	47,XXY 48,XXXYY Other (48,XXYY; 49,XXXXYY; mosaics)	1/575-1/1,000 males 1/50,000-1/80,000 male births
XYY syndrome	47,XYY	1/800-1,000 males
Other X or Y chromosome abnormalities		1/1,500 males
XX males	46,XX	1/20,000 males
Turner syndrome	45,X Variants and mosaics	1/2,500-1/5,000 females
Trisomy X	47,XXX 48,XXXX and 49,XXXXXX	1/1,000 females Rare
Other X chromosome abnormalities		1/3,000 females
XY females	46,XY	1/20,000 females

Table 81-5 Additional Features of Down Syndrome That Can Develop or Become Symptomatic with Time

NEUROPSYCHIATRIC	
Developmental delay	
Seizures	
Autism spectrum disorders	
Behavioral disorders (disruptive)	
Depression	
Alzheimer disease	
SENSORY	
Congenital or acquired hearing loss	
Serous otitis media	
Refractive errors (myopia)	
Congenital or acquired cataracts	
Nystagmus	
Strabismus	
Glaucoma	
Blocked tear ducts	
CARDIOPULMONARY	
Acquired mitral, tricuspid, or aortic valve regurgitation	
Endocarditis	
Obstructive sleep apnea	
MUSCULOSKELETAL	
Atlantoaxial instability	
Hip dysplasia	
Slipped capital femoral epiphyses	
Avascular hip necrosis	
Recurrent joint dislocations (shoulder, knee, elbow, thumb)	
ENDOCRINE	
Congenital or acquired hypothyroidism	
Diabetes mellitus	
Infertility	
Obesity	
Hyperthyroidism	
HEMATOLOGIC	
Transient myeloproliferative syndrome	
Acute lymphocytic leukemia	
Acute myelogenous leukemia	
GASTROINTESTINAL	
Celiac disease	
Delayed tooth eruption	
Respiratory	
Obstructed sleep apnea	
Frequent infections (sinusitis, nasopharyngitis, pneumonia)	
CUTANEOUS	
Hyperkeratosis	
Seborrhea	
Xerosis	
Perigenital folliculitis	

Table 81-6 Developmental Milestones

Milestone	CHILDREN WITH DOWN SYNDROME		UNAFFECTED CHILDREN	
	Average (mo)	Range (mo)	Average (mo)	Range (mo)
Smiling	2	1.5-3	1	1.5-3
Rolling over	6	2-12	5	2-10
Sitting	9	6-18	7	5-9
Crawling	11	7-21	8	6-11
Creeping	13	8-25	10	7-13
Standing	10	10-32	11	8-16
Walking	20	12-45	13	8-18
Talking, words	14	9-30	10	6-14
Talking, sentences	24	18-46	21	14-32

From Levine MD, Carey WB, Crocker AC, editors: Developmental-behavioral pediatrics, ed 2, Philadelphia, 1992, Saunders.

Table 81-7 Self-Help Skills

Skill	DOWN SYNDROME CHILDREN		UNAFFECTED CHILDREN	
	Average (mo)	Range (mo)	Average (mo)	Range (mo)
EATING				
Finger feeding	12	8-28	8	6-16
Using spoon/fork	20	12-40	13	8-20
TOILET TRAINING				
Bladder	48	20-95	32	18-60
Bowel	42	28-90	29	16-48
DRESSING				
Undressing	40	29-72	32	22-42
Putting clothes on	58	38-98	47	34-58

From Levine MD, Carey WB, Crocker AC, editors: Developmental-behavioral pediatrics, ed 2, Philadelphia, 1992, Saunders.

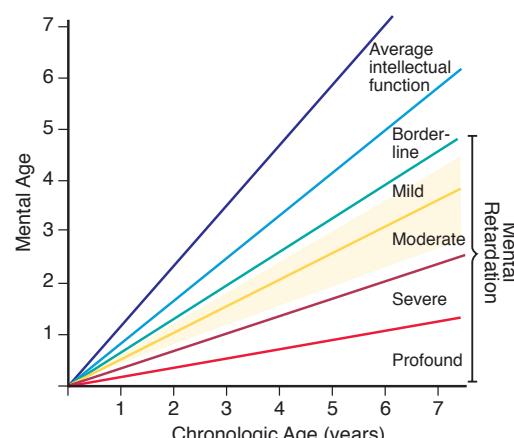


Figure 81-10 The area shaded in yellow denotes the range of intellectual function of the majority of children with Down syndrome. (From Levine MD, Carey WB, Crocker AC, editors: Developmental-behavioral pediatrics, ed 2, Philadelphia, 1992, WB Saunders, p. 226.)

614 Part X ◇ Human Genetics

Table 81-8 | Health Supervision for Children with Down Syndrome

CONDITION	TIME TO SCREEN	COMMENT
Congenital heart disease	Birth; by pediatric cardiologist Young adult for acquired valve disease	50% risk of congenital heart disease; increased risk for pulmonary hypertension
Strabismus, cataracts, nystagmus	Birth or by 6 mo; by pediatric ophthalmologist Check vision annually	Cataracts occur in 15%, refractive errors in 50%
Hearing impairment or loss	Birth or by 3 mo with auditory brainstem response or otoacoustic emission testing; check hearing q6mo up to 3 yr if tympanic membrane is not visualized; annually thereafter	Risk for congenital hearing loss plus 50-70% risk of serous otitis media
Constipation	Birth	Increased risk for Hirschsprung disease
Celiac disease	At 2 yr or with symptoms	Screen with IgA and tissue transglutaminase antibodies
Hematologic disease	At birth and in adolescence or if symptoms develop	Increased risk for neonatal polycythemia (18%), leukemoid reaction, leukemia (<1%)
Hypothyroidism	Birth; repeat at 6-12 mo and annually	Congenital (1%) and acquired (5%)
Growth and development	At each visit Use Down syndrome growth curves	Discuss school placement options Proper diet to avoid obesity
Obstructive sleep apnea	Start at ~1 yr and at each visit	Monitor for snoring, restless sleep
Atlantoaxial subluxation or instability (incidence 10-30%)	At each visit by history and physical exam Radiographs at 3-5 yr or when planning to participate in contact sports Radiographs indicated wherever neurologic symptoms are present even if transient (neck pain, torticollis, gait disturbances, weakness) Many are asymptomatic	Special Olympics recommendations are to screen for high-risk sports, e.g., diving, swimming, contact sports
Gynecologic care	Adolescent girls	Menstruation and contraception issues
Recurrent infections	When present	Check IgG subclass and IgA levels
Psychiatric, behavioral disorders	At each visit	Depression, anxiety, obsessive-compulsive disorder, schizophrenia seen in 10-17% Autism spectrum disorder in 5-10% Early-onset Alzheimer disease

IgA, immunoglobulin A; IgG, immunoglobulin G.

Data from Committee on Genetics: Health supervision for children with Down syndrome, Pediatrics 107:442-449, 2001; and Baum RA, Spader M, Nash PL, et al: Primary care of children and adolescents with Down syndrome: an update, Curr Probl Pediatr Adolesc Health Care 38:235-268, 2008.

Table 81-9 | Genes Localized to Chromosome 21 That Possibly Affect Brain Development, Neuronal Loss, and Alzheimer Type Neuropathology

SYMBOL	NAME	POSSIBLE EFFECT IN DOWN SYNDROME	
			FUNCTION
SIM2	Single-minded homolog 2	Brain development	Required for synchronized cell division and establishment of proper cell lineage
DYRK1A	Dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 1A	Brain development	Expressed during neuroblast proliferation Believed important homolog in regulating cell-cycle kinetics during cell division
GART	Phosphoribosylglycinamide formyltransferase Phosphoribosylglycinamide synthetase Phosphoribosylaminoimidazole synthetase	Brain development	Expressed during prenatal development of the cerebellum
PCP4	Purkinje cell protein 4	Brain development	Function unknown but found exclusively in the brain and most abundantly in the cerebellum
DSCAM	Down syndrome cell adhesion molecule	Brain development and possible candidate gene for congenital heart disease	Expressed in all molecule regions of the brain and believed to have a role in axonal outgrowth during development of the nervous system
GRIK1	Glutamate receptor, ionotropic kainite1	Neuronal loss	Function unknown, found in the cortex in fetal and early postnatal life and in adult primates, most concentrated in pyramidal cells in the cortex
APP	Amyloid beta (A4) precursor protein (protease nexin-II, Alzheimer disease)	Alzheimer type neuropathy	Seems to be involved in plasticity, neurite outgrowth, and neuroprotection
S100B	S100 calcium binding protein β (neural)	Alzheimer type neuropathy	Stimulates glial formation
SOD1	Superoxide dismutase 1, soluble (amyotrophic lateral sclerosis, adult)	Accelerated aging?	Scavenges free superoxide molecules in the cell and might accelerate aging by producing hydrogen peroxide and oxygen

Table 81-10 Other Rare Aneuploidies and Partial Autosomal Aneuploidies

DISORDER	KARYOTYPE	CLINICAL MANIFESTATIONS
Trisomy 8	47,XX/XY,+8	Growth and mental deficiency are variable The majority of patients are mosaics Deep palmar and plantar furrows are characteristic
Trisomy 9	47,XX/XY,+9	The majority of patients are mosaics Clinical features include craniofacial (high forehead, microphthalmia, low-set malformed ears, bulbous nose) and skeletal (joint contractures) malformations and heart defects (60%)
Trisomy 16	47,XX/XY,+16	The most commonly observed autosomal aneuploidy in spontaneous abortion; the recurrence risk is negligible
Tetrasomy 12p	46,XX[12]/46,XX, +i(12p)[8] (mosicism for an isochromosome 12p)	Known as Pallister-Killian syndrome. Sparse anterior scalp hair, eyebrows, and eyelashes, prominent forehead, chubby cheeks, long philtrum with thin upper lip and cupid-bow configuration, polydactyly, and streaks of hyper- and hypopigmentation

Table 81-11 Findings That May Be Present in Trisomy 13 and Trisomy 18

TRISOMY 13	TRISOMY 18
HEAD AND FACE	
Scalp defects (e.g., cutis aplasia) Microphthalmia, corneal abnormalities Cleft lip and palate in 60%-80% of cases Microcephaly Microphthalmia Sloping forehead Holoprosencephaly (arhinencephaly) Capillary hemangiomas Deafness	Small and premature appearance Tight palpebral fissures Narrow nose and hypoplastic nasal alae Narrow bifrontal diameter Prominent occiput Micrognathia Cleft lip or palate Microcephaly
CHEST	
Congenital heart disease (e.g., VSD, PDA, and ASD) in 80% of cases Thin posterior ribs (missing ribs)	Congenital heart disease (e.g., VSD, PDA, ASD) Short sternum, small nipples

Continued

Table 81-11 Findings That May Be Present in Trisomy 13 and Trisomy 18—cont'd

TRISOMY 13	TRISOMY 18
EXTREMITIES	
Overlapping of fingers and toes (clinodactyly) Polydactyly Hypoplastic nails, hyperconvex nails	Limited hip abduction Clinodactyly and overlapping fingers; index over 3rd, 5th over 4th; closed fist Rocker-bottom feet Hypoplastic nails
GENERAL	
Severe developmental delays and prenatal and postnatal growth restriction Renal abnormalities Only 5% live >6 mo	Severe developmental delays and prenatal and postnatal growth restriction Premature birth, polyhydramnios Inguinal or abdominal hernias Only 5% live >1 yr

ASD, atrial septal defect; PDA, patent ductus arteriosus; VSD, ventricular septal defect.

From Behrman RE, Kliegman RM: Nelson essentials of pediatrics, ed 4, Philadelphia, 2002, WB Saunders, p. 142.

Table 83-2 Diagnostic Evaluation of the Neurologically Impaired Child

		ADDITIONAL TESTING IF CLINICALLY INDICATED
CONSULTATIONS		Electron microscopy of white blood cell buffy coat for inclusion bodies Electron microscopy of skin biopsy for evidence of storage Stool for ova and parasites, occult blood, fecal fat, or fecal calprotectin Autoimmune antibodies Vaccine response titers C3/C4 Quantitative immunoglobulins T-cell subsets Conjunctival or salivary gland biopsy
PROCEDURES		RESEARCH SPECIMENS Cerebrospinal fluid Serum Plasma Skin biopsy for fibroblasts and/or melanocytes Isolated DNA/RNA Urine
LABORATORY EVALUATIONS		STUDIES UNDER SEDATION 3T MRI/magnetic resonance spectroscopy of brain (and spine if indicated) Skin biopsy Ophthalmologic exam Brainstem auditory evoked response Electroretinogram Lumbar puncture for bipterin, neopterin, neurotransmitters, folate, and inflammatory markers Dental exam Large blood draws Catheterization for urine Any part of the physical exam difficult to do in an awake child, including dysmorphology measurements and genital and rectal exam Electromyography and nerve conduction studies
Genetics/genetic counseling Neurology Endocrinology Immunology Rheumatology Dermatology Cardiology Neuropsychology Nutrition Rehabilitative medicine Physical therapy Occupational therapy Speech therapy		
Swallow study for aspiration Abdominal ultrasound (hepatosplenomegaly) Skeletal survey (dysostosis) Bone density scan (nonambulatory or growth-failure patients) Bone age Electroencephalogram Muscle biopsy for electron transport chain function and histology Nerve biopsy		
Complete blood count with differential and peripheral smear Comprehensive metabolic panel Prothrombin time/partial thromboplastin time (for anesthesia sedation) Thyroid-stimulating hormone, thyroxine Vitamins A, E, 1,25-dihydroxyvitamin D Lactate/pyruvate Ammonia Amino acids (plasma and urine) Organic acids (urine) Acylcarnitine profile Total and free carnitine Lysosomal enzyme analysis in leukocytes and/or fibroblasts White blood cell coenzyme Q Purines and pyrimidines (urine) α -Glucosidase (plasma and urine) Peroxisomal panel Oxysterols Methylmalonic acid and homocystine (plasma) Copper/ceruloplasmin Vitamins A and E Transferrin isoelectric focusing <i>N</i> - and <i>O</i> -glycans (plasma) Oligosaccharides and free glycans (urine) Glycosaminoglycans (urine)		