

**T7xTBOOK** *pf*

**PEDlAνRlCS**

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**KelSon TableS**

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***Nelson***

**TEXTBOOK** *of*

**EDITION 20**

**PEDIATRICS**

**Tables**

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COnTEnTS

[Growth, Develoment and Behaviour](#_bookmark1) [Nutrition](#_bookmark2)

[Electrolyte and Acid-Base Disorders](#_bookmark3) [Pediatric Drug Therapy](#_bookmark4)

[The Acutely Ill Child](#_bookmark5) [Human Genetics](#_bookmark6) Metabolic Disorders The Newborn Infant Adolescent Development Immunology

Allergic Disorders

Rheumatic Diseases of Childhood Infectious Diseases

The Digestive System Respiratory System

The Cardiovascular System Diseases of the Blood Cancer and Benign Tumors

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The Nervous System Disorders of the Eye The Ear

The Skin

Bone and Joint Disorders Rehabilitation Medicine and others

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Crowth, Develoment and Behaviour

**Chapter 1** ◆ Overview of Pediatrics **17**

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| **Table 1-6** Evidence-based Interventions to Address Newborn | | and Child Health and Undernutrition | |
| **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.

**Pre-pregnancy**

**Pregnancy**

**Birth**

**Neonatal**

**Child**

**Child Health**

Home management Promotion of early care

seeking for illnesses Community case

management of diarrhea, pneumonia, and malaria

**Childbirth**

Promotion of use of skilled care at birth

Referral for emergency obstetric care if needed

Clean delivery kits if delivering at home

**Pre-pregnancy and Adolescent**

Family planning Prevention of

HIV and STIs

**Neonatal/Infant Health**

Essential care of newborn Promotion of hygeine – sanitation

and handwashing

Early and exclusive breastfeeding Complementary feeding

Care of LBW at home

Promotion and provision of vaccine Deworming

Insecticide treated bed nets

**Pregnancy**

Promotion of birth preparedness Promotion and provision of TT Intermittent preventive treatment

of malaria

Insecticide treated bed nets Nutritional supplementation Promotion of PMTCT of HIV

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

**36 Part I** ◆ The Field of Pediatrics

**Diagnosis, evaluation, treatment:** asthma, childhood development, fever

**Workforce:** racial/ethnic diversity, bilingual healthcare providers

**Patient education:** brochures, interpreters, signage

**Services/interventions:** overweight provention and treatment programs; insuring uninsured children; seatbelt use

Practical applications for the office setting: How does one practice cultural competency?

* Patient safety • Patient-physician
* Adherence communication
* Quality • Health outcomes
* Access • Patient satisfaction
* Resource utilization
* Disparities

**Impact: Why it is important**

**Definition:**

What is it?

**Assessment tools:**

How we measure it

**Cultural competency in pediatrics**

Language

Provider practices

Parent/patient beliefs

Folk illnesses

Normative cultural values

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 com- petency in general pediatrics,* Curr Opin Pediatr *20:711–718, 2008, Fig. 1, p. 712.)*

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| --- | --- | --- | --- | --- |
| **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 |
|  | Potatoes or onions in socks† | | 6.5 | 0 |
| Colic | 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

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| --- | --- | --- | --- |
| **Table 10-1** Developmental Milestones in the 1st 2 | Yr | of Life | |
| **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 grammatization, 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 |

**Chapter 10** ◆ The First Year **67**

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| --- | --- |
| **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: Standing: Motor: Adaptive: | Sits up alone and indefinitely without support, with back straight Pulls to standing position; “cruises” or walks holding on to furniture Creeps or crawls  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  Repetitive consonant sounds (“mama,” “dada”)  Responds to sound of name; plays peek-a-boo or pat-a-cake; waves bye-bye |
| Language: Social: |
| 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

Age 1 wk

|  |  |
| --- | --- |
| **Table 10-3** Time of Appearance in X-Rays of Centers of Ossification in Infancy and Childhood | |
| **BOYS—AGE AT BONES AND EPIPHYSEAL** | **GIRLS—AGE AT** |
| **APPEARANCE\* CENTERS** | **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 Scaphoid† | 51 mo ± 12 mo |
| No standards Pisiform† | No standards |
| available | 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 (EPIPHYSES) |  |
| 16 mo ± 4 mo Proximal phalanx, 3rd finger | 10 mo ± 3 mo |
| 16 mo ± 4 mo Proximal phalanx, 2nd | 11 mo ± 3 mo |
| finger |  |
| 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 Femur, distal | Usually present |
| at birth | at birth |
| Usually present Tibia, proximal | Usually present |
| at birth | at birth |
| 4 mo ± 2 mo Femur, head | 4 mo ± 2 mo |
| 46 mo ± 11 mo Patella | 29 mo ± 7 mo |
| FOOT AND ANKLE‡ | |

1. mo

3 mo

6 mo

9 mo

12 mo

18 mo

1. yr
2. yr
3. yr
4. yr
5. yr
6. yr
7. yr
8. yr
9. yr
10. yr
11. yr
12. yr
13. yr
14. yr
15. yr
16. yr
17. yr

Hours of sleep

2 4 6 8 10 12 14 16

Nighttime sleep

Daytime sleep\*

\*Divided into typical number of naps per day. Length of naps may be quite variable.

2 4 6 8

Total hours of sleep

16.5

15.5

15

14.25

14

13.75

13.5

13

12

11.50

11

10.75

10.50

10.25

10

9.75

9.50

9.25

9.25

9

8.75

8.50

8.25

8.25

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.)*

**Chapter 15** ◆ Assessment of Growth **87**

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| **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.*

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **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 Lateral incisors  Cuspids (canines)  First premolars (bicuspids) Second premolars (bicuspids) First molars  Second molars Third molars | | 3-4 mo  Max, 10-12 mo  Mand, 3-4 mo  4-5 mo  18-21 mo  24-30 mo  Birth  30-36 mo  Max, 7-9 yr  Mand, 8-10 yr | 9-10 yr  10-11 yr  12-15 yr   * 1. yr   2. yr   9-10 yr  14-16 yr  18-25 yr | 7-8 yr  8-9 yr  11-12 yr   * 1. yr   2. yr   6-7 yr  12-13 yr  17-22 yr | 6-7 yr  7-8 yr  9-11 yr  10-12 yr  11-13 yr  6-7 yr  12-13 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

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| **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. | |

**Chapter 17** ◆ Childcare **103**

|  |  |
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| **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:   * 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:   * Toxin-producing *Escherichia coli* or *Shigella* infection, until stools are formed and test results of 2 stool cultures obtained from stools produced 24-hr apart do not detect these organisms * *Salmonella* 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

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| **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 *Staphylococcus aureus* (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/*](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/*

**Chapter 19** ◆ Sleep Medicine **113**

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| **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:   * 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 1   16  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 | Behavioral insomnia of childhood, limit setting type |
| Sleep problems may become chronic | Sleepwalking Sleep terrors  Nighttime fears/nightmares Obstructive sleep apnea |
| Middle childhood 9-11 hr (6-12 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 |

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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.

Basic Principles of Healthy Sleep for Adolescents

**Table 19-3**

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| **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) | |

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| **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.

**118 Part II** ◆ Growth, Development, and Behavior

## Algorithm for the Diagnosis and Treatment of Pediatric OSA

**Step 5.** Child is a potential candidate for treatment if at risk for OSA (step 1) and at least one criterion:

**Step 4.** Objective evaluation for OSA severity:

* Overnight polysomnography
* If not available: nocturnal pulse oximetry

**Step 3.** Factors predicting OSA persistence are present (at least one):

* Male gender
* Increasing Body Mass Index percentile, development of obesity

**Step 2b.** Conditions frequently coexisting with OSA are identified (one or more):

* Recurrent otitis media, tympanostomy tubes
* Recurrent wheezing
* Oral-motor dysfunction
* Metabolic syndrome

**Step 2a.** OSA-related morbidity is recognized (one or more):

* Systolic or diastolic blood pressure >95th percentile for gender, age and height, or pulmonary hypertension
* Daytime sleepiness, hyperactivity, inattention, academic difficulties
* Inadequate somatic growth
* Enuresis

**Step 1.** Child is at risk for OSA (one or more):

* Parents report symptoms of OSA
* Physician identifies symptoms of OSA using structured questionnaire
* Conditions predisposing to OSA are present (adenotonsillar hypertrophy- allergic rhinitis, obesity, craniofacial abnormalities, neuromuscular disorders)
* History of prematurity
* Family history of OSA
* AHI >5 episodes/h
* AHI 1–5 and OSA morbidity present (step 2a)
* AHI 1–5 and risk factor for OSA persistence (step 3)
* AHI 1–5 and neuromuscular disorder or craniofacial abnormalities present (step 1)
* ≥3 SpO2 drops <90% and ≥3 clusters of desaturation events or alternatively, desaturation (≥3%) index ≥3.5 episodes/h

## Or if polysomnography or oximetry not available:

* Frequently or almost always loud snoring and male gender
* Frequently or almost always loud snoring and sleepiness
* Frequently or almost always loud snoring and learning problems

## Priority for treatment increases if coexisting OSA-related conditions are present that may also improve with treatment (step 2b)

**Step 6.** Stepwise treatment approach:

1. Weight control for obesity
2. Trial of nasal corticosteroids for adenoidal hypertrophy prior to adenoidectomy
3. Adenotonsillectomy for adenotonsillar hypertrophy
4. Orthodontic devices for mandibular malpositioning, narrow maxilla
5. nCPAP for: i) residual OSA after adenotonsillectomy; ii) OSA related to obesity, neuromuscular disorders or craniofacial abnormalities and unresponsive to other measures
6. Craniofacial surgery or tracheostomy if other treatment modalities fail

**Notes**

1. Information collected in steps 1–4 is used to identify children requiring treatment for OSA (step 5) and to determine the appropriate therapeutic modalities (step 6). Please refer to the text for details.
2. Step 6 represents a hierarchical approach to OSA treatment.

**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.)*

**Chapter 21** ◆ Psychological Treatment of Children and Adolescents **129**

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| **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  Long Acting  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 |
| Intermediate Acting  Methylphenidate (Metadate  CD, Metadate ER, Ritalin LA, Ritalin SR) | ADHD (6 and up) | Inattention Hyperactivity Impulsivity | 10-60 mg | 60 mg |
| Short Acting | | | | |
| Dexmethylphenidate ADHD (6 and up) (Focalin) | | Inattention Hyperactivity Impulsivity | 2.5-20 mg | 20 mg |
| Methylphenidate (Ritalin, Methylin) | 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

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| **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 Not approved for anxiety  (Celexa) & 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 OCD (10-17) (Anafranil) | | Obsessions/compulsions | 25-100 mg | Lesser of 200 mg or 3 mg/kg |
| ATYPICAL ANTIDEPRESSANTS  Bupropion Not approved for  (Wellbutrin depression in children &  XL) 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 Not approved for anxiety (Ativan) | | 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.

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| **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 |

**Chapter 21** ◆ Psychological Treatment of Children and Adolescents **131**

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| **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 Bipolar disorder (10-17)  (Abilify) 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 Psychosis (3-17)  (Haldol) 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 |

1. One or more symptoms or deficits affecting voluntary motor or sensory function.
2. Clinical findings provide evidence of incompatibility between the symptom and recognized neurologic or medical conditions.
3. The symptom or deficit is not better explained by another medical or mental disorder.
4. 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.

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

**Table 22-1**

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

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

Factitious Disorder Imposed on Self

1. Falsification of physical or psychological signs or symptoms, or induction of injury or disease, associated with identified deception.
2. The individual presents himself or herself to others as ill, impaired, or injured.
3. The deceptive behavior is evident even in the absence of obvious external rewards.
4. 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)

1. Falsification of physical or psychological signs or symptoms, or induction of injury or disease, in another, associated with identified deception.
2. The individual presents another individual (victim) to others as ill, impaired or injured.
3. The deceptive behavior is evident even in the absence of obvious external rewards.
4. 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

DSM-5 Diagnostic Criteria for Factitious Disorders

**Table 22-4**

1. One or more somatic symptoms that are distressing or result in significant disruption of daily life.
2. 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.
3. 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).

DSM-5 Diagnostic Criteria for Somatic Symptom Disorder

**Table 22-2**

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

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.

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

**Table 22-5**

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1. A medical symptom or condition (other than a mental disorder) is present.
2. 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.
3. 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).

DSM-5 Diagnostic Criterial for Psychological Factors Affecting Other Medical Conditions

**Table 22-3**

*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   1. Both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently. 2. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset. 3. Onset is before age 18 years. 4. 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   1. Single or multiple motor or vocal tics have been present during the illness, but not both motor and vocal. 2. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset. 3. Onset is before age 18 years. 4. 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). 5. Criteria have never been met for Tourette’s disorder.   *Specify* if:  With motor tics only  With vocal tics only | |
| PROVISIONAL TIC DISORDER   1. Single or multiple motor and/or vocal tics. 2. The tics have been present for less than 1 year since first tic onset. 3. Onset is before age 18 years. 4. 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). 5. 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 | |
| 1. 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):    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.*

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| --- | --- | --- | --- |
| **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.*

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).

1. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
2. 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.
3. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
4. 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.

1. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
2. There has never been a manic episode or a hypomanic episode.

DSM-5 Diagnostic Criteria for Major Depressive Episode

**Table 26-1**

1. 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.

1. 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.
2. 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.
3. Criteria for a major depressive disorder may be continuously present for 2 yr.
4. There has never been a manic episode or a hypomanic episode, and criteria have never been met for cyclothymic disorder.
5. 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.
6. 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).
7. 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.

DSM-5 Diagnostic Criteria for Persistent Depressive Disorder

**Table 26-2**

1. 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.
2. Intense fear of gaining weight or of becoming fat, or persistent behavior that interferes with weight gain, even though at a significantly low weight.
3. 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 ≥ 17 kg/m2 Moderate: BMI 16–16.99 kg/m2 Severe: BMI 15–15.99 kg/m2 Extreme: BMI < 15 kg/m2

DSM-5 Diagnostic Criteria for Anorexia Nervosa

**Table 28-1**

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1. 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).
2. 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.
3. The binge eating and inappropriate compensatory behaviors both occur, on average, at least once a week for 3 mo.
4. Self-evaluation is unduly influenced by body shape and weight.
5. 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.

DSM-5 Diagnostic Criteria for Bulimia Nervosa

**Table 28-2**

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

1. 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.
2. The disturbance is not better explained by lack of available food or by an associated culturally sanctioned practice.
3. 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.
4. 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.

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

**Table 28-3**

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|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Table 28-4** | Eating and Weight Control Habits Commonly Found in Children and Adolescents with | | | an Eating Disorder |
| **HABIT** | **Prominent Feature**  **ANOREXIA NERVOSA BULIMIA NERVOSA** | | **Clinical Comments Regarding Eating Disorder Habits** | |
| **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.

**166 Part III** ◆ Behavioral and Psychiatric Disorders

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| --- | --- | --- |
| **Table 28-5** Symptoms Commonly Reported by Patients with an Eating Disorder | | |
| **SYMPTOMS** | **Diagnosis**  **ANOREXIA NERVOSA BULIMIA NERVOSA** | **CLINICAL COMMENTS REGARDING ED SYMPTOMS** |
| Body image | Feels fat, even with extreme Variable body image distortion emaciation, often with and dissatisfaction, but drive specific body distortions for thinness is less than the (e.g., stomach, thighs); desire to avoid gaining weight Strong drive for thinness,  with self-efficacy closely tied to appraisal of body shape, size, and/or 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 Variable, depending on balance include feeling cold, tired, of intake and output and  and weak and lacking energy hydration May be both bothersome and  reinforcing | 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 No characteristic symptom, bruising, goose flesh self-injurious behavior may be  Orange-yellow skin on hands 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 No characteristic symptom face and upper body  Slow growth and increased loss of scalp hair | 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 Dizziness, fainting, palpitations subtype  Palpitations more common in binge-purge subtype | 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 Discomfort after a binge with eating Cramps and diarrhea with  Constipation laxative abuse Perceives contour as “fat,”  often preferring well-defined abdominal musculature | 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, Depression; PTSD; borderline  obsessive-compulsive personality disorder traits symptoms, alone or in  combination | 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.

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| --- | --- | --- | --- |
| **Table 28-6** Signs | Commonly Found in Patients with Eating Disorders Relative to | | Prominent Feature of Weight Control |
| **PHYSICAL SIGN** | **Prominent Feature**  **RESTRICTIVE INTAKE BINGE EATING/PURGING** | | **CLINICAL COMMENTS RELATED TO EATING DISORDER SIGNS** |
| 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.

**Chapter 30** ◆ Autism Spectrum Disorder **177**

1. 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.
2. 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.
3. 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).
4. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.
5. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay.

DSM-5 Diagnostic Criteria for Autism Spectrum Disorder

**Table 30-1**

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

Medical and Genetic Evaluation of Children with Autism Spectrum Disorder

**Table 30-4**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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** |
| α2-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.*

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| **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   * 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:   + 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 |
| Spoken language   * Language delay (in babble or words—for example, using fewer than 10 words by the age of 2 yr) * Regression in or loss of use of speech * Spoken language (if present) may include unusual features, such as: vocalizations that are not speech-like; odd or flat intonation; frequent repetition of set words and phrases (echolalia); reference to self by name or “you” or “she” or “he” beyond age 3 yr * Reduced and/or infrequent use of language for communication—for example, use of single words, although able to speak in sentences | |
| Responding to others   * 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 | |
| Ideas and imagination   * Reduced or absent imagination and variety of pretend play |
| Unusual or restricted interests and/or rigid and repetitive behaviors   * 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 |
| Interacting with others   * 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 | |

*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.*

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| **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. *For example,* 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. *For example,* 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. *For example,* 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.*

**Chapter 33** ◆ Attention-Deficit/Hyperactivity Disorder **201**

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| **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. 2. 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). 3. Often has difficulty sustaining attention in tasks or play activities (e.g., has difficulty remaining focused during lectures, conversations, or lengthy reading). 4. Often does not seem to listen when spoken to directly (e.g., mind seems elsewhere, even in the absence of any obvious distraction). 5. 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). 6. 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). 7. 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). 8. Often loses things necessary for tasks or activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones). 9. Is often easily distracted by extraneous stimuli (for older adolescents and adults, may include unrelated thoughts). 10. Is often forgetful in daily activities (e.g., doing chores, running errands; for older adolescents and adults, returning calls, paying bills, keeping appointments). 11. 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. 12. Often fidgets with or taps hands or feet or squirms in seat. 13. 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). 14. Often runs about or climbs in situations where it is inappropriate. (Note: In adolescents or adults, may be limited to feeling restless.) 15. Often unable to play or engage in leisure activities quietly. 16. 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). 17. Often talks excessively. 18. Often blurts out an answer before a question has been completed (e.g., completes people’s sentences; cannot wait for turn in conversation). 19. Often has difficulty waiting his or her turn (e.g., while waiting in line). 20. 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). 21. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years. 22. 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). 23. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning. 24. 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. |

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**202 Part IV** ◆ Learning Disorders

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| **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: All of following:  At least 6 of 9 inattentive symptoms At least 6 of 8 inattentive At least 6 of 9 hyperactive or symptoms  impulsive symptoms At least 3 of 5 hyperactive symptoms  At least 1 of 4 impulsive symptoms | |
| PERVASIVENESS  Some impairment from symptoms Criteria are met for >1 setting is present in >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.*

*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

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| **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 | |

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.*

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| **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 ± meningomyelocele, 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.*

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

cap, capsule; tab, tablet.

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

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| **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.) |

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| **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  *p, b,* and *m*  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 *(Come here. Want more?)* | | Babbling has both long and short groups of sounds, such as *tata upup bibibibi.*  Uses speech or noncrying sounds to get and keep attention Imitates different speech sounds  Has 1 or 2 words *(bye-bye, Dada, Mama),* although they might not be clear |
| 1-2 YR  Points to a few body parts when asked  Follows simple commands and understands simple questions  *(Roll the ball. Kiss the baby. Where’s your shoe?)* 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 *(Where kitty? Go bye-bye? What’s that?)*  Puts 2 words together *(more cookie, no juice, mommy book)*  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 *(Get the book and put it on the table.)* | | 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 like to read my books.)*  Tells stories that stick to a topic  Communicates easily with other children and adults  Says most sounds correctly except a few, such as *l, s, r, v, z, ch, sh,* and *th*  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.*](http://www.asha.org/public/speech/development/chart.htm)

|  |  |  |  |
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| **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 |

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| **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 focality 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 (T4, 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; T4, 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.*

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| **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  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:   * Milk letdown * Sense of fullness/emptying * Frequency and duration of feedings * Maternal observation of baby swallowing * Maternal diet and medical problems while breastfeeding Formula feeding: * Type * Method of mixing (concentration) * Frequency and quantity of feedings   Other intake in first few months of life, such as:   * Water * Juice * Tea * Soda * Cereal   Sleep schedule Baby’s temperament  Developmental milestones  Use of alternative or complementary medicines | | PSYCHOSOCIAL SPHERES  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 |

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

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| **Table 41-2** | Diagnostic Classification of Causes and Selected Examples of Failure to Thrive | |
| INADEQUATE INTAKE | | MALABSORPTION |
| Inadequate food offered | | Cystic fibrosis |
| * Food insecurity | | Celiac disease |
| * Poor knowledge of child’s needs | | Hepatobiliary disease |
| * Formula dilution or excessive juice | | Food protein allergy, insensitivity, or intolerance |
| * Breastfeeding difficulties | | Infection (giardiasis) |
| * Medical child abuse/caregiver fabricated illness (Munchausen by | | Short gut syndrome |
| proxy)   * Medical neglect * Food fads including “rice” milk as substitute for formula or cow milk   Child not taking enough food   * Oromotor dysfunction, neurologic disease * Developmental delay * Behavioral feeding problem (altered oromotor sensitivity, pain and conditioned aversion) * Anorexia from systemic causes   Emesis | |
| INCREASED METABOLIC DEMAND  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) |
| * Pyloric stenosis | |  |
| * Gastroesophageal reflux | |  |
| * Eosinophilic esophagitis | |  |
| * Vascular rings | |  |
| * Malrotation with intermittent volvulus | |  |
| * Increased intracranial pressure and other neurologic disorders | |  |
| * Inborn errors of metabolism | |  |
| * Rumination | |  |
| * Cyclic vomiting | |  |

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

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

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| **Table 41-3** | Failure to Thrive: Differential Diagnosis by System | |
| PSYCHOSOCIAL/BEHAVIORAL  Inadequate diet because of poverty/food insufficiency, errors in food preparation  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 | | GASTROINTESTINAL  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 Pseudoobstruction  Hirschsprung disease Food allergy |
| NEUROLOGIC  Cerebral palsy  Hypothalamic and other central nervous system tumors (diencephalic syndrome)  Neuromuscular disorders Neurodegenerative disorders | |
| CARDIAC  Cyanotic heart lesions Congestive heart failure Vascular rings |
| RENAL  Recurrent urinary tract infection Renal tubular acidosis  Renal failure | |
| PULMONARY/RESPIRATORY  Severe asthma  Cystic fibrosis; bronchiectasis Chronic respiratory failure Bronchopulmonary dysplasia Adenoid/tonsillar hypertrophy Obstructive sleep apnea |
| ENDOCRINE  Diabetes mellitus Diabetes insipidus  Hypothyroidism/hyperthyroidism Growth hormone deficiency Adrenal insufficiency | |
| GENETIC/METABOLIC/CONGENITAL  Sickle cell disease  Inborn errors of metabolism (organic acidosis, hyperammonemia, storage disease)  Fetal alcohol syndrome Skeletal dysplasias Chromosomal disorders  Multiple congenital anomaly syndromes (VATER, CHARGE) | | MISCELLANEOUS  Collagen-vascular disease Malignancy  Primary immunodeficiency Transplantation |
| INFECTIONS  Perinatal infection (TORCHES) Occult/chronic infections Parasitic infestation Tuberculosis  HIV |

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.

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| **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 |

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| **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 |

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.

Key Elements of Effective Symptom Management

**Table 43-4**

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.
* Pruritus 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).

Guidelines for Pain Management

**Table 43-5**

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| **Table 43-6** Pharmacologic Approach to Symptoms Commonly Experienced by Children with Life-Threatening Illness | | | |
| **SYMPTOM** | **MEDICATION** | **STARTING DOSE** | **COMMENTS** |
| Pain—mild | Acetaminophen Ibuprofen  Trilisate | 15 mg/kg po q 4 hr, max 4 g/day  10 mg/kg po q 6 hr  10-15 mg/kg po tid | 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 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)  Oxycodone Hydromorphone  Fentanyl Methadone | 0.3 mg/kg po q 4 hr if <50 kg; 5-10 mg po q  4 hr\*†  0.1 mg/kg po q 4 hr if <50 kg; 5-10 mg po q  4 hr if >50 kg\*†  0.05 mg/kg po q 4 hr if <50 kg; 1-2 mg po q  4 hr if >50 kg\*†  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.\*† | Also available in IV/SQ formulation‡§  No injectable formulation‡§  Also available in IV/SQ formulation. Injectable form very concentrated, facilitating subcutaneous delivery‡§  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§ |
| Pain—sustained release | 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  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 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§  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§ |
| Pain—neuropathic | Nortriptyline  Gabapentin  Pregabalin  Methadone | 0.5 mg/kg po at bedtime to maximum of 150 mg/day  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)  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)  See previous listing | 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  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  See previous listing |
| Dyspnea | Morphine, immediate release (i.e., MSIR)  Lorazepam | 0.1 mg/kg po q 4 hr prn\*†  0.025-0.05 mg/kg IV/po q 6 hr, up to 2 mg/ dose | All opioids may relieve dyspnea. For dyspnea, the starting dose is 30% of the dose that would be administered for pain§  See previous listing |

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| **Table 43-6** Pharmacologic Approach to Symptoms Commonly Experienced Illness—cont’d | | | by Children with Life-Threatening |
| **SYMPTOM** | **MEDICATION** | **STARTING DOSE** | **COMMENTS** |
| Respiratory secretions | Scopolamine patch  Glycopyrrolate  Hyoscyamine sulfate  Atropine | 1.5 mg patch, change q 72 hr  0.04-0.1 mg/kg po q 4-8 hr  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 | 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  Powerful antisialagogue. 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  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  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  0.1 mg/kg/dose tid po/IV; max dose 10 mg/ day  See previous listing  2.5-5 mg/m2/dose q 3-4 hr  See previous listing | 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  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, bradyarrhythmias, or in patients on other medications with the potential to cause QT prolongation  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  See previous listing |
|  | Ondansetron |
|  | Dexamethasone |
|  | Lorazepam Dronabinol |
|  | Scopolamine patch |
| Anxiety | 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

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| **Table 43-6** | Pharmacologic Approach to Symptoms Commonly Experienced by Children with Life-Threatening Illness—cont’d | | |
| **SYMPTOM** | **MEDICATION** | **STARTING DOSE** | **COMMENTS** |
| Pruritus | Diphenhydramine  Hydroxyzine | 0.5-1 mg/kg q 6 hr IV/po (100 mg max per day)  0.5-1 mg/kg q 6 hr IV/po (600 mg maximum 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 |
| Constipation | Docusate MiraLAX  Lactulose  Senna Dulcolax  Pediatric Fleets Enema  Methylnaltrexone | 40-150 mg/day po in 1-4 divided doses  <5 yr: 1 scoop (8.5 g) in 4 oz of water daily  2  >5 yr: 1 scoop (17 g) in 8 oz of water daily 5-10 mL po up to q 2 hr until bowel  movement  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  2.5 oz pediatric enema for children 2-11 yr; adult enema for children ≥12 yr  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 | Stool softener available as liquid or capsule Tasteless powder may be mixed in beverage of  choice. Now available nonprescription  Bowel stimulant; dosing q 2 hr may cause cramping  Bowel stimulant; available as granules Available in oral or rectal formulation  May repeat ×1 if needed. Do not use in neutropenic patients  A peripherally acting opioid antagonist for  opioid-induced constipation. Usually works within 30-60 minutes of administration |
| Muscle spasm | Diazepam Baclofen | 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  5 mg po tid, increase by 5 mg/dose as needed | May be irritating if given by peripheral IV  Helpful with neuropathic pain and spasticity; abrupt withdrawal may result in hallucinations and seizures; not for children <10 yr |
| Seizures | Lorazepam Diazepam | 0.1 mg/kg IV/po/SL/PR; repeat q 10 min ×2  0.1 mg/kg q 6 hr (max 5 mg/dose if <5 yr; max  10 mg/dose if >5 yr) | May be given pr as Diastat (0.2 mg/kg/dose q 15 minutes ×3 doses) |
| Neuroirritability | Gabapentin Clonidine  Clonazepam | 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.  <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 | 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 |
| Anorexia | Megestrol acetate  Dronabinol Cyproheptadine | 10 mg/kg/day in 1-4 divided doses, may titrate up to 15 mg/kg/day or 800 mg/day  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 | 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 See previous listing  Potent antihistamine and serotonin antagonist |

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

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

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

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

ECG, electrocardiogram; gtt, drops; hr, hr; 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.

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| **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

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Acute disorders Diarrhea

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

**Table 45-2**

Otitis media

Urinary tract infection Necrotizing enterocolitis Septicemia

Infant botulism

Insulin-dependent diabetes mellitus Celiac disease

Crohn disease Childhood cancer Lymphoma Leukemia

Recurrent otitis media Allergy

Obesity and overweight Hospitalizations

Infant mortality

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

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

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| **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 |

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

1. 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
2. Mother and infant should sleep in proximity to each other to facilitate breastfeeding
3. 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

Recommendations on Breastfeeding Management for Healthy Term Infants

**Table 45-4**

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| **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 |

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| **Table 46-6** | Clinical Signs of Malnutrition | |
| **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.*

no iron

10. Prepare for follow-up

9. Provide loving care and play

8. Rebuild wasted tissue (catch-up growth)

7. Start cautious feeding

with iron

6. Correct deficiencies of micronutrients

5. Treat infections

4. Correct imbalance of electrolytes

3. Treat/prevent dehydration

2. Prevent/treat hypothermia

1. Prevent/treat hypoglycemia

Week 2–6

Day 3–7

Day 1–2

Rehabilitation

Stabilization

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

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| **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 | | 1. Give oxygen 2. Give sterile 10% glucose (5 mL/kg) by IV 3. Give IV fluid at 15 mL/kg over 1 hr, using:    * 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 4. Measure and record pulse and respirations at the start and every 10 minutes   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)  If there are no signs of improvement assume septic shock and:   1. Give maintenance fluid IV (4 mL/kg/hr) while waiting for blood 2. 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 3. 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):   1. 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 2. Give furosemide 1 mL/kg IV at the start of the transfusion |
| Emergency eye care Corneal ulceration | | If corneal ulceration:   1. Give vitamin A immediately (age <6 mo 50,000 IU, 6-12 mo 100,000 IU, >12 mo 200,000 IU) 2. Instill 1 drop atropine (1%) into affected eye to relax the eye and prevent the lens from pushing out |

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| **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:   1. Feed immediately 2. Feed every 3 hr day and night (2 hr if ill) 3. Feed on time 4. Keep warm 5. Treat infections (they compete for glucose)   *Note:* Hypoglycemia and hypothermia often coexist, and are signs of severe infection | If conscious:   1. 10% glucose (50 mL), or a feed (see step 7), or 1 teaspoon sugar under the tongue-whichever is quickest 2. Feed every 2 hr for at least the first day. Initially give 14 of feed every 30 min 3. Keep warm 4. Start broad-spectrum antibiotics If unconscious:    1. Immediately give sterile 10% glucose (5 mL/kg) by IV    2. Feed every 2 hr for at least first day. Initially give 14 of feed every 30 min. Use nasogastric (NG) tube if unable to drink    3. Keep warm.    4. 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   1. Avoid exposure 2. Dress warmly, including head and cover with blanket 3. Keep room hot; avoid draughts 4. Change wet clothes and bedding 5. Do not bathe if very ill 6. Feed frequently day and night 7. Treat infections | Actively rewarm   1. Feed 2. 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) 3. Monitor temperature hourly (or every 30 min if using heater) 4. Stop rewarming when rectal temperature is 36.5°C (97.7°F) |
| 3. Prevent/treat dehydration | | Replace stool losses   1. 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   1. Give ReSoMal 5 mL/kg every 30 min for first 2 hr orally or NG tube 2. 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 3. 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) 4. 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

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| **Table 46-8** | Therapeutic Directives for Stabilization—cont’d | |
| **STEP** | | **PREVENTION TREATMENT** |
| 4. Correct electrolyte imbalance—deficit of potassium and magnesium, excess sodium | | 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 |
| 5. Prevent/treat infections | | Minimize risk of cross-infection Infections are often silent. Starting on the first day, give broad-   1. Avoid overcrowding spectrum antibiotics to all children. 2. Wash hands 1. For antibiotic choices/schedule see Table 46-9 3. Give measles vaccine to 2. Ensure all doses are given, and given on time unimmunized children age >6 mo 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, Do *not* give iron in the stabilization phase  copper, and other trace minerals 1. Give vitamin A on day 1 (under 6 mo 50,000 units; 6-12 mo 100,000 are already added in Nutriset F75 units; >12 mo 200,000 units) if child has any eye signs of vitamin A and F100 packets deficiency or has had recent measles. Repeat this dose on days 2  and 14   1. Folic acid 1 mg (5 mg on day 1) 2. 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 3. 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. |

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| **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, Gentamicin (7.5 mg/kg IV or IM) once daily for 7 days respiratory or urinary tract infections, or lethargy/sickly) *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.

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| **Table 46-10** | Recipes for Milk Formulas F75 and F100 | | | |
|  | | **F75b (STARTER)** | **F75c (STARTER)**  **(CEREAL-BASED)** | **F100d (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.

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| **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).

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

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| **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: MgCl2. 6H2O | | 76.0 | 3 mmol |
| Zinc acetate: Zn acetate.2H2O | | 8.2 | 300 μmol |
| Copper sulfate: CuSO4. 5H2O | | 1.4 | 45 μmol |
| Water: make up to | | 2500 mL |  |

\*Make fresh each month. Use cooled boiled water.

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| **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 | Respiratory | Neurologic | Death | Cardiac compromise | Respiratory |
| volume | Failure | Weakness |  |  | Hypercapnia |
| Respiratory | Neurologic | Tremor |  |  | Failure |
| Impaired diaphragm | Weakness | Tetany |  |  | Other |
| contractility | Paralysis | Seizures |  |  | Ketoacidosis |
| Dyspnea | Gastrointestinal | Altered mental status |  |  | Coma |
| Respiratory failure | Nausea | Coma |  |  | Dehydration |
| Neurologic | Vomiting | Gastrointestinal |  |  | Impaired immune |
| Paresthesia | Constipation | Nausea |  |  | function |
| Weakness | Muscular | Vomiting |  |  |  |
| Confusion | Rhabdomyolysis | Diarrhea |  |  |  |
| Disorientation | Muscle necrosis | Other |  |  |  |
| Lethargy | Other | Refractory |  |  |  |
| Areflexic paralysis | Death | hypokalemia and |  |  |  |
| Seizures |  | hypocalcemia |  |  |  |
| Coma |  | Death |  |  |  |
| 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.*

With complications

Without complications

Severe edema (+++)

Edema (+/++)

OR

OR

MUAC <115 mm AND

any of the following:

MUAC >115 mm

AND

Anorexia

Clinically unwell All of the following: Not alert

Good appetite Clinically well Alert

Inpatient care

Outpatient

therapeutic care

Severe acute malnutrition

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

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| **Table 47-1** Endocrine and Genetic Causes of Obesity | | |
| **DISEASE** | **SYMPTOMS** | **LABORATORY** |
| ENDOCRINE  Cushing syndrome GH deficiency Hyperinsulinism  Hypothyroidism Pseudohypoparathyroidism | Central obesity, hirsutism, moon face, hypertension Short stature, slow linear growth  Nesidioblastosis, pancreatic adenoma, hypoglycemia, Mauriac syndrome  Short stature, weight gain, fatigue, constipation, cold intolerance, myxedema  Short metacarpals, subcutaneous calcifications, dysmorphic facies, mental retardation, short stature, hypocalcemia, hyperphosphatemia | Dexamethasone suppression test Evoked GH response, IGF-1 Insulin level  TSH, FT4  Urine cAMP after synthetic PTH infusion |
| GENETIC  Alstrom syndrome Bardet-Biedl syndrome Biemond syndrome Carpenter syndrome Cohen syndrome  Deletion 9q34  Down syndrome *ENPP1* gene mutations Fröhlich syndrome  *FTO* gene polymorphism  Leptin or leptin receptor gene deficiency  Melanocortin 4 receptor gene mutation  Prader-Willi Syndrome  Proopiomelanocortin deficiency  Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD)  Turner syndrome | Cognitive impairment, retinitis pigmentosa, diabetes mellitus, hearing loss, hypogonadism, retinal degeneration  Retinitis pigmentosa, renal abnormalities, polydactyly, hypogonadism  Cognitive impairment, iris coloboma, hypogonadism, polydactyly  Polydactyly, syndactyly, cranial synostosis, mental retardation  Mid-childhood-onset obesity, short stature, prominent maxillary incisors, hypotonia, mental retardation, microcephaly, decreased visual activity  Early-onset obesity, mental retardation, brachycephaly, synophrys, prognathism, behavior and sleep disturbances  Short stature, dysmorphic facies, mental retardation Insulin resistance, childhood obesity  Hypothalamic tumor  Dysregulation of orexigenic hormone acyl-ghrelin, poor postprandial appetite suppression  Early-onset severe obesity, infertility (hypogonadotropic hypogonadism)  Early-onset severe obesity, increased linear growth, hyperphagia, hyperinsulinemia  Most common known genetic cause of obesity Homozygous worse than heterozygous  Neonatal hypotonia, slow infant growth, small hands and feet, mental retardation, hypogonadism, hyperphagia leading to severe obesity, paradoxically elevated ghrelin  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  Ovarian dysgenesis, lymphedema, web neck, short stature, cognitive impairment | *ALMS1* gene  *BBS1* gene  Mutations in the *RAB23* gene, located on chromosome 6 in humans  Mutations in the *VPS13B* gene (often called the *COH1* gene) at locus 8q22  Deletion 9q34  Trisomy 21  Gene mutation on chromosome 6q Homozygous for *FTO* AA allele Leptin  *MC4R* mutation  Partial deletion of chromosome 15 or loss of paternally expressed genes  Loss-of-function mutations of the  *POMC* gene Unknown genes  May be a paraneoplastic disorder  XO chromosome |

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

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| **Table 47-2** Obesity-Associated Comorbidities | | |
| **DISEASE** | **POSSIBLE SYMPTOMS** | **LABORATORY CRITERIA** |
| CARDIOVASCULAR  Dyslipidemia Hypertension | HDL <40, LDL >130, total cholesterol >200 SBP >95% for sex, age, height | Fasting total cholesterol, HDL, LDL, triglycerides Serial testing, urinalysis, electrolytes, blood urea  nitrogen, creatinine |
| ENDOCRINE  Type 2 diabetes mellitus Metabolic syndrome Polycystic ovary syndrome | Acanthosis nigrans, polyuria, polydipsia  Central adiposity, insulin resistance, dyslipidemia, hypertension, glucose intolerance  Irregular menses, hirsutism, acne, insulin resistance, hyperandrogenemia | Fasting blood glucose >110, hemoglobin A1c, insulin level, C-peptide, oral glucose tolerance test  Fasting glucose, LDL and HDL cholesterol Pelvic ultrasound, free testosterone, LH, FSH |
| GASTROINTESTINAL  Gallbladder disease Nonalcoholic fatty liver disease  (NAFLD) | Abdominal pain, vomiting, jaundice Hepatomegaly, abdominal pain, dependent  edema, ↑ transaminases  Can progress to fibrosis, cirrhosis | Ultrasound  AST, ALT, ultrasound, CT, or MRI |
| NEUROLOGIC  Pseudotumor cerebri Migraines | Headaches, vision changes, papilledema Hemicrania, headaches | Cerebrospinal fluid opening pressure, CT, MRI None |
| ORTHOPEDIC  Blount disease (tibia vara) Musculoskeletal problems  Slipped capital femoral epiphysis | Severe bowing of tibia, knee pain, limp  Back pain, joint pain, frequent strains or sprains, limp, hip pain, groin pain, leg bowing  Hip pain, knee pain, limp, decreased mobility of hip | Knee x-rays X-rays  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  Obstructive sleep apnea | Shortness of breath, wheezing, coughing, exercise intolerance  Snoring, apnea, restless sleep, behavioral problems | Pulmonary function tests, peak flow  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.

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| **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.*

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.”

Anticipatory Guidance: Establishing Healthy Eating Habits in Children

**Table 47-7**

*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.*

**Chapter 49** ◆ Vitamin B Complex Deficiencies and Excess **323**

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| **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 B1) | 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 B2) | 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 B3) | 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 B6) | 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

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| **Table 51-4** | Laboratory Findings in Various Disorders Causing Rickets | | | | | | | | |
| **DISORDER** | | **Ca** | **Pi** | **PTH** | **25-(OH)D** | **1,25-(OH)2D** | **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 hypercalciuria; 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.

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| **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 B5) | 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 B12) | 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 B12 | 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.*](http://fnic.nal.usda.gov/dietary-guidance/dietary-reference-intakes/dri-tables)

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**Chapter 51** ◆ Rickets and Hypervitaminosis D **335**

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| **Table 51-5** Biochemical Changes in Genetic Causes of Rickets | | | | | | | | | | |
| **SERUM BIOCHEMISTRY** | | | | | | | | **URINE BIOCHEMISTRY**  **Phosphate Calcium** | | **OTHER FEATURES** |
|  | **Phosphate** | **Calcium** | **PTH** | **250HD** | **1,250H2D** | **FGF23** | **Alk Phos** |
| HYPOCALCEMIC VITAMIN D PATHWAY DEFECTS  Vitamin D Low Variable High deficiency | | | | Low | Might be increased | NA | Increased | Increased | Low | Variable aminoaciduria |
| VDDR1B | Low | Low | High | Very low | Variable | NA | Increased | Increased | Low | 250HD does not increase after vitamin D dosing |
| VDDR1A | Low | Low | High | Normal or high | Very low or ND | NA | Increased | Increased | Low | 250HD does increase after vitamin D dosing |
| VDDR2A | Low | Low | High | Normal or high | High | NA | Increased | Increased | Low | — |
| VDDR2B | Low | Low | High | Normal or high | High | NA | Increased | Increased | Low | — |
| HYPOPHOSPHATEMIC RICKETS WITH RAISED FGF23  XLH Low Normal Normal or slightly high | | | | Normal | Low | High | Increased | Increased | Variable | Urine calcium : creatinine used in monitoring therapy |
| ADHR | Low | Normal | Normal | Normal | Low | High | Increased | Increased | Variable | — |
| ARHR1 | Low | Normal | Normal | Normal | Low | High | Increased | Increased | Variable | — |
| ARHR2 | Low | Normal | Normal | Normal | Low | High | Increased | Increased | Variable | — |
| HYPOPHOSPHATEMIC RICKETS WITHOUT RAISED FGF23  Dent’s Low Normal Normal disease\* | | | | Normal | Normal | Normal | Increased | Increased | High | Low molecular weight proteinuria |
| HHRH | Low | Normal | Normal | Normal | Normal | Normal | Increased | Increased | High | No loss of low molecular weight protein |
| αKlotho mutation | Low | Normal | Normal | Normal | Normal | Normal | Increased | 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; 250HD, calcidiol; 1,2SOH2D, 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 CYP27Bl encoding 25-hydroxyvitamin D-1alpha hydroxylase; ND, not detected; VDDR2A, vitamin D–dependent rickets due to defects in VDR encoding the vitamin D receptor; VDDR2B, vitamin D–dependent rickets due to defects in *HNRNPC* encoding hnRNPC1 and hnRNPC2; 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 hypercalciuria due to mutations in *SLC34A3*; HPP, hypophosphatasia.

\*Dent’s disease is due to mutations in CLCN5.

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| **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, Vegetables, grains, abdominal pain, coma, and nuts, liver, margarine, hepatic necrosis legumes, corn oil  Chronic toxicity (liver and brain injury) occurs in Wilson disease (see Chapter 357.2) and secondary to excess intake (see Chapter 357.3) |
| Fluoride | Incorporated into bone | Dental caries (see Chapter 312) | Chronic: dental fluorosis Toothpaste,  (see Chapter 307) fluoridated water |
| Iodine | Component of thyroid hormone (see Chapter 564) | Hypothyroidism (see Chapters 566 and 568) | Hypothyroidism and goiter Saltwater fish, iodized (see Chapters 566 and 568); salt  maternal excess can cause congenital hypothyroidism and goiter (see Chapter 568.1) |
| Iron | Component of hemoglobin, myoglobin, cytochromes, and other enzymes | Anemia (see Chapter 456), decreased alertness, impaired learning | Acute (see Chapter 63): nausea, Meat, fortified foods vomiting, diarrhea, abdominal Deficiency can also pain, and hypotension result from blood  Chronic excess usually loss (hookworm  secondary to hereditary infestation, disorders (see Chapters 463.9 menorrhagia) and 357.4); causes organ  dysfunction |
| Manganese | Enzyme cofactor | Hypercholesterolemia, weight loss, decreased clotting proteins\* | Neurologic manifestations, Nuts, meat, grains, tea cholestatic jaundice |
| Molybdenum | Enzyme cofactor (xanthine oxidase and others) | Tachycardia, tachypnea, night blindness, irritability, coma\* | Hyperuricemia and increased Legumes, grains, liver risk of gout |
| Selenium | Enzyme cofactor (prevents oxidative damage) | Cardiomyopathy (Keshan disease), myopathy | Nausea, diarrhea, neurologic Meat, seafood, whole manifestations, nail and hair grains, garlic changes, garlic odor |
| 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, Meat, shellfish, whole vomiting grains, legumes,  Can worsen copper deficiency cheese |

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

# Electrolyte and Acid- Base Disorders

**Chapter 55** ◆ Electrolyte and Acid-Base Disorders **351**

|  |  |
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| **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).](http://www.ncbi.nlm.nih.gov/omim))

\*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.

|  |  |
| --- | --- |
| **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 256100/606966/602088/604387/61 1498)  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) | |

OMIM, database number from the Online Mendelian Inheritance in Man

**Chapter 55** ◆ Electrolyte and Acid-Base Disorders **355**

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| **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 period 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 rental 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) | |

|  |  |
| --- | --- |
| **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) | |

\*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).](http://www.ncbi.nlm.nih.gov/omim))

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

Diagnostic Criteria for Syndrome of Inappropriate Antidiuretic Hormone Secretion

**Table 55-3**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | |  | | |  | | |  |
| High 17-OHP Low cortisol High ACTH | |  | Low / normal 17-OHP Low cortisol  High ACTH | |  | High 17-OHP High cortisol High ACTH | |  | Normal 17-OHP Normal cortisol Normal ACTH | |

**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 circulat- ing levels of glucocorticosteroids often have normal renin activity. 17-OHP, 17-hydroxyprogesterone; ACTH, adrenocorticotropic 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 hyperaldo- steronism 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.)*

Cl— Deficient diet

GI Cl— loss (vomit / NG drainage) Sweat Cl— loss

Post-hypercapnea Post-diuretic effect

Primary aldosteronism

* tumors, hyperplasia
* GRA (FH-I), FH-II

High aldosterone Low / Normal DOC

Drugs (antibiotics, etc.) Polyuric disorders Saline diuresis (K+- free)

Magnesium depletion Congenital K+ wasting Acquired K+ wasting Leukemia

Variable acid-base status

Metabolic alkalosis

Metabolic acidosis

Urine Cl— > 15

Low / normal BP

Urine Cl— ≤ 15

PRA > 0.5 ng/mL/hr; DR > 15 mU/L

PRA ≤ 0.5 ng/mL/hr; DR ≤ 15 mU/L

Renal loss

(Urine K+ > 15 meg/L ; TTKG > 4)

Extra-renal loss

(Urine K+ ≤ 15 mEq/L ; TTKG ≤ 4)

Insufficient K+ intake

Variable aldosterone High DOC

Sweat loss Gi loss

-Pica / geophagia

-K+ binders, fistulas

-Diarrhea, laxatives

Renal tubular acidosis (I and II) Carbonic anhydrase inhibitors Ureterosigmoid diversion Diabetic ketoacidosis

Acute alkalosis Insulin

-adrenergic stimulants Periodic paralysis Barium poisoning

Acute increase in blood cells

Low aldosterone Low / Normal DOC

AME, licorice, Carbenoxolone Chronic grapefruit juice intake Liddle syndrome (PA-I)

MR activating mutation (PA-II) Exogenous mineralocorticoid Excess ACTH / Glucocorticoids\*\*

Renal parenchymal disease Renovascular disease Renal compression

Renal tumors Pheochromocytoma

Excess ACTH / Glucocorticoids\*\*

Recent diuretic effect Bartter syndrome Gitelman syndrome Congenital K+ wasting Hypovolemia

Hypertension

Cellular uptake of K+

Reduced total body K+

Hypokalemia\*

Excessive K+ loss

11- hydroxylase deficiency

DOC-secreting tumors



17- hydroxylase deficiency



GR resistance

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

|  |  |
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| **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 | |

\*This disorder is also associated with renal magnesium wasting. 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).](http://www.ncbi.nlm.nih.gov/omim))

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

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| **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) | |

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| **Table 55-11** | Appropriate Compensation During Simple Acid–Base Disorders |
| **DISORDER EXPECTED COMPENSATION** | |
| Metabolic acidosis PCO2 = 1.5 × [HCO3−] + 8 ± 2  Metabolic alkalosis PCO2 increases by 7 mm Hg for each 10 mEq/L  increase in serum [HCO3−] | |
| RESPIRATORY ACIDOSIS  Acute [HCO3−] increases by 1 for each 10 mm Hg increase in PCO2  Chronic [HCO3−] increases by 3.5 for each 10 mm Hg increase in PCO2 | |
| RESPIRATORY ALKALOSIS  Acute [HCO3−] falls by 2 for each 10 mm Hg decrease in PCO2  Chronic [HCO3−] falls by 4 for each 10 mm Hg decrease  in PCO2 | |

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

|  |  |
| --- | --- |
| **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)†  Hyperkalemic (type IV) RTA (OMIM 201910/264350/177735/145260)‡ 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 | |

|  |  |
| --- | --- |
| **Table 55-12** | Normal Values of Arterial Blood Gases |
| pH 7.35-7.45 | |
| [HCO3−] 20-28 mEq/L | |
| PCO2 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  17β-Hydroxylase deficiency (OMIM 202110) 11β-Hydroxylase deficiency (OMIM 202010) Cushing syndrome  11β-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 | |

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

‡Hyperkalemic 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

EAST, epilepsy, ataxia, sensorineural hearing loss, and tubulopathy; OMIM, database number from the Online Mendelian Inheritance in Man

Step 3 Met.

3 3

HCO3— PCO2 PCO2 PCO2

HCO — HCO —

3 3

HCO —

Acid. and Resp. Alk.

Met.

Acid.

Mixed

Resp. Acid. and Met. Acid.

Simple

Resp. Acid.

Mixed Mixed Simple

PCO2

Mixed

Met. Acid. and Resp. Acid.

Resp.

Acid. and Met. Alk.

Met.

Alk. and Resp. Alk.

Met.

Alk.

Mixed Mixed

Met. Resp.

Alk.

and

Alk.

and

Simple

Resp. Alk.

Resp. Met.

Acid. Acid.

3

Mixed

Resp. Alk. and Met. Alk.

PCO2

Acidemia or Alkalemia

Step 1

Acidemia

Alkalemia

Decreased Increased

Increased

[HCO3 ]

—

Step 2

HCO — HCO —

[HCO3 ]

—

Decreased

PCO2

Metabolic

acidosis

Respiratory

acidosis

Metabolic

alkalosis

Respiratory

alkalosis

Low Expected High Low Expected High Low Expected High Low Expected High

PCO2 PCO2

Mixed Simple

**Figure 55-9** Three-step process for interpreting acid–base disturbances. In step 1, determine whether the pH is low (acidemia) or high (alkale- mia). 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.

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

Treatment of Hypernatremic Dehydration

**Table 57-4**

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

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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

Clinical Evaluation of Dehydration

**Table 57-1**

Restore intravascular volume:

Normal saline: 20 mL/kg over 20 min Repeat as needed

Calculate 24-hr fluid needs: maintenance + deficit volume Subtract isotonic fluid already administered from 24 hr fluid needs Administer remaining volume over 24 hr using 5% dextrose NS +

20 mEq/L KCl

Replace ongoing losses as they occur

Fluid Management of Dehydration

**Table 57-2**

Vital signs:

Pulse

Blood pressure Intake and output:

Fluid balance Urine output

Physical examination:

Weight

Clinical signs of depletion or overload Electrolytes

Monitoring Therapy

**Table 57-3**

**Chapter 56** ◆ Maintenance and Replacement Therapy **385**

Prevent dehydration

Prevent electrolyte disorders Prevent ketoacidosis Prevent protein degradation

Goals of Maintenance Fluids

**Table 56-1**

|  |  |  |
| --- | --- | --- |
| **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.

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)\*

Hourly Maintenance Water Rate

**Table 56-3**

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

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Table 56-4** | Composition of Intravenous Solutions | | | | | |
| **FLUID** | | **[Na]** | **[Cl−]** | **[K+]** | **[Ca2+]** | **[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 |

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| **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 | *Preterm infants (gestational age):*  28 wk: 0.2 mL swabbed into mouth  28-32 wk: 0.2-2 mL, depending on suck/swallow  >32 wk: 2 mL  *Term infants:* 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.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Table 62-4** Pediatric Dosage Guidelines for Opioid Analgesics | | | | | | | | |
| **DRUG** | **EQUIANALGESIC DOSES**  **IV ORAL** | | **PARENTERAL DOSING (WEIGHT)**  **<50 kg >50 kg** | | **IV : PO DOSE RATIO** | **ORAL DOSING (WEIGHT)**  **<50 kg >50 kg** | | **COMMENTS** |
| Fentanyl | 10 μg | 100 μg | 0.5-1 μg/kg q1-2h  0.5-1.5 μg/kg/hr | 0.5-1 μg/kg q1-2h  0.5-1.5 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 | 70-100 times as potent as morphine with rapid onset and shorter duration  With high doses and rapid administration, can cause chest-wall rigidity  Useful for short procedures; transdermal form should be used only in opioid- tolerant patients with chronic pain |
| 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 | * 1. mg q2-4h   2. mg/kg/hr | * 1. mg q2-4h   2. mg/kg/hr | 1 : 3 | 0.04-0.08 mg/kg q3-4h | 2-4 mg q3-4h | 5× 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  When patients who are tolerant to opioids are switched to methadone, they show incomplete cross-tolerance and improved efficacy; because it is associated with prolonged QTc, monitoring is needed for children on high and extended dosing |
| 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 | Immediate release: 15-20 mg q3-4h Sustained release: 30-90 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 |
| Oxycodone | 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 | Strong opioid only available as an oral agent in North America; more potent than and preferable to hydrocodone  Sustained-release form must be swallowed whole; if crushed, becomes immediate- acting, leading to acute overdose |

N/A, not available.

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| **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  Anticholinergics (e.g., antihistamines, TCAs, atropine), sympathomimetics (cocaine, amphetamines, PCP) postanoxic encephalopathy, opiate withdrawal  Anticonvulsants, sedative–hypnotics, alcohols, PCP, ketamine, dextromethorphan Organophosphates, irritant gas or vapors  Methanol |
| Mydriasis |
| Nystagmus Lacrimation Retinal hyperemia |
| 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 Hematemesis Constipation | Antimicrobials, arsenic, iron, boric acid, cholinergics, colchicine, opioid withdrawal Arsenic, iron, caustics, NSAIDs, salicylates  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  β Blockers, calcium channel blockers, digoxin, clonidine, organophosphates, opioids, sedative–hypnotics Sympathomimetics, anticholinergics, monoamine oxidase inhibitors, serotonin syndrome, neuroleptic  malignant syndrome, clonidine withdrawal  β Blockers, calcium channel blockers, cyclic antidepressants, iron, antipsychotics, barbiturates, clonidine, opioids, arsenic, amatoxin mushrooms, cellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide), snake envenomation |
| Bradycardia Hypertension |
| Hypotension |
| RESPIRATORY SIGNS  Depressed respirations Tachypnea | Opioids, sedative-hypnotics, alcohol, clonidine, barbiturates  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.

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| --- | --- | --- | --- |
| **Table 63-4** | Mini-Toxidromes | | |
| **TOXIDROMES** | | **SYMPTOMS AND SIGNS** | **EXAMPLES** |
| α1 Antagonists | | CNS depression, tachycardia, miosis | Chlorpromazine, quetiapine, clozapine, olanzapine, risperidone |
| α2 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, ziprasidone |

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 63-6** | 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 | |

KUB, kidney-ureter-bladder radiograph.

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

SSRI, selective serotonin reuptake inhibitor.

|  |  |
| --- | --- |
| **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 (*Tricholoma equestre*)  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 | |

**Chapter 63** ◆ Poisoning **453**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Table 63-7** Common Antidotes for Poisoning | | | | |
| **POISON** | **ANTIDOTE** | **DOSAGE** | **ROUTE** | **ADVERSE EFFECTS, WARNINGS, COMMENTS** |
| Acetaminophen | *N*-Acetylcysteine (Mucomyst)  *N*-Acetylcysteine (Acetadote) | 140 mg/kg loading, followed by 70 mg/kg q4h  150 mg/kg over 1 hr, followed by 50 mg/kg over 4 hr, followed by 100 mg/kg over 16 hr | PO IV | Vomiting (patient-tailored regimens are the norm)  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% FIO2 via non–rebreather mask (or ET if intubated) | Inhalational | Some patients may benefit from hyperbaric oxygen (see text) |
| Cyanide | Cyanide kit: Amyl nitrate  Sodium nitrate  Sodium thiosulfate  Hydroxocobalamin (Cyanokit) | 1 crushable ampule; inhale 30 sec of each min  0.33 mL/kg of 3% solution if hemoglobin level is not known; otherwise, based on tables with product  1.6 mL/kg of 25% solution; may be repeated q30-60min to max of 50 mL  70 mg/kg (adults: 5 g) given over 15 min | Inhalation IV  IV IV | Methemoglobinemia  Methemoglobinemia Hypotension  If inducing methemoglobinemia is contraindicated; consider only using the thiosulfate component of the kit  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 *Gyromitra*  mushroom ingestions |
| Lead and other heavy metals (e.g., arsenic, inorganic mercury) | BAL (dimercaprol)  Calcium disodium EDTA  Dimercaptosuccinic acid (succimer, DMSA, Chemet) | 3-5 mg/kg/dose q4hr, for the 1st day; subsequent dosing depends on the toxin  35-50 mg/kg/day × 5 days; may be given as a continuous infusion or 2 divided doses/day  10 mg/kg/dose q8h × 5 days, then 10 mg/kg q12h × 14 days | Deep IM  IV  PO | Local injection site pain and sterile abscess, vomiting, fever, salivation, nephrotoxicity  *Caution:* prepared in peanut oil; contraindicated in patients with peanut allergy  Vomiting, fever, hypertension, arthralgias, allergic reactions, local inflammation, nephrotoxicity (maintain adequate hydration, follow UA and renal function)  Vomiting, hepatic transaminase elevation, rash |

### Continued

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|  |  |  |  |  |  |
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| **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 Pralidoxime (2-PAM) | 0.05-0.1 mg/kg repeated q5-10min as needed  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/ET IV/IM | Tachycardia, dry mouth, blurred vision, urinary retention  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 (≥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.

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| **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 |

|  |  |  |
| --- | --- | --- |
| **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) |

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

**T**he **Ac**utel**y I**ll **c**hild

**Chapter 67** ◆ Pediatric Emergencies and Resuscitation **491**

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|  |  |  |
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| **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.*

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| --- | --- | --- |
| **Table 64-1** | Most Commonly Used Dietary Supplements in Pediatrics | |
| **PRODUCT** | | **USES** |
| VITAMINS  B2 (riboflavin) B6 (pyridoxine) | | Migraine headache prophylaxis Pyridoxine-dependent epilepsy;  neuropathy; nausea associated with pregnancy  Prevention of neural tube defects Prevention of rickets; treatment of  deficiencies  General health promotion, ADHD |
| B9 (folate) D | |
| Multivitamins | |
| MINERALS  Iodine (salt) Iron Magnesium | | Prevent goiter and mental retardation Prevent and treat iron deficiency Constipation, asthma, migraine  prevention  Diarrhea in nutrient-poor populations |
| Zinc | |
| HERBS  Aloe vera Chamomile Echinacea | | Mild burns  Mild sedative, dyspepsia Prevention of upper respiratory  infections Nausea  Mild sedative  Irritable bowel syndrome  Anti-bacterial (acne remedies), pediculicide (lice) |
| Ginger  Lavender (aromatherapy) Peppermint  Tea tree oil | |
| OTHER | | Insomnia  ADHD, allergies, inflammation, anxiety and mood disorders  Antibiotic-associated diarrhea; *Clostridium difficile*–associated diarrhea; constipation; irritable bowel syndrome; pouchitis; inflammatory bowel disorders |
| Melatonin | |
| Omega-3 fatty acids (fish | |
| oil) | |
| Probiotics | |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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** | Glasg | ow | Coma Scale | |
| EYE OPENING (TOTAL POSSIBLE POINTS 4)  Spontaneous 4  To voice 3  To pain 2  None 1 | | | | |
| VERBAL RESPONSE (TOTAL POSSIBLE POINTS 5) | | | | |
| **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 | | | | |

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

Life-Threatening Cardiac Causes of Syncope

**Table 69-2**

**490 Part IX** ◆ The Acutely Ill Child 64

#### Pediatric BLS Healthcare Providers

1

**Unresponsive**

**Not breathing or only gasping** Send someone to activate emergency response system, get AED/defibrillator

2

**High-Quality CPR**

* Rate at least 100/min
* Compression depth to at least

1/3 anterior-posterior diameter of chest, about 1 1/2 inches (4 cm) in infants

and 2 inches (5 cm) in children

* Allow complete

chest recoil after each compression

* Minimize interruptions in chest compressions
* Avoid excessive ventilation

#### Lone rescuer: For SUDDEN COLLAPSE,

activate emergency response system get AED/defibrillator

3 Definite 3A

**Check pulse: DEFINITE pulse within 10 seconds?**

* Give 1 breath every 3 seconds
* Add compressions if pulse remains

<60/min with poor perfusion despite adequate oxygenation and ventilation

* Recheck pulse every 2 minutes

pulse

No pulse

4

|  |  |
| --- | --- |
| **One rescuer:** Begin cycles of **30 COMPRESSIONS** and **2 BREATHS** | |
| **Two rescuers:** Begin cycles of **15 COMPRESSIONS** and **2 BREATHS** | |
|  |  |

5

**Resume CPR immediately**

for 2 minutes Check rhythm every

2 minutes; continue until ALS providers take over or victim starts to move

8

Not shockable

**Give 1 shock Resume CPR immediately**

for 2 minutes

7

Shockable

**Check rhythm Shockable rhythm?**

**After about 2 minutes, activate emergency response system and get AED/defibrillator (if not already done).**

**Use AED as soon as available.**

6

*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.)*

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

“Red Flags” in the Evaluation of Patients with Syncope

**Table 69-3**

**Chapter 67** ◆ Pediatric Emergencies and Resuscitation **503**

## Pediatric Cardiac Arrest

**Shock**

**CPR 2 min**

* **Epinephrine every 3-5 min**
* **Consider advanced airway**

6

No

Yes

7

**Shock**

8

**CPR 2 min**

* **Amiodarone**
* **Treat reversible causes**

12

**Rhythm shockable?**

**VF/VT**

5

Yes

No

**Rhythm**

**shockable?**

**Rhythm**

**shockable?**

**Start CPR**

* Give oxygen
* Attach monitor/defibrillator

**Asystole/PEA**

9

**Rhythm shockable?**

* **Asystole/PEA,**  **10 or 11**
* **Organized rhythm**  **check pulse**
* **Pulse present (ROSC)**  **post- cardiac arrest care**

**CPR 2 min**

* **IO/IV access**

**Shout for Help/Activate Emergency Response**

1

##### Doses/Details CPR Quality

* Push hard ≥ 1/3 of anterior- posterior diameter of chest) and fast (at least 100/min) and allow complete chest recoil
* Minimize interruptions in compressions
* Avoid excessive ventilation
* Rotate compressor every 2 minutes
* If no advanced airway, 15:2 compression-ventilation ratio. If

2

3

4

Yes

**Shock**

No

10

advanced airway, 8-10 breaths per minute with continuous chest compressions

##### Shock Energy for Defibrillation

First shock 2 J/kg, second shock

4 J/kg, subsequent shocks ≥ 4 J/kg, maximum 10 J/kg or adult dose.

##### Drug Therapy

* + **Epinephrine IO/IV Dose:**

0.01 mg/kg (0.1 mL/kg of 1:10,000 concentration). Repeat every 3-5 minutes.

If no IO/IV access, may give endotracheal dose: 0.1 mg/kg (0.1 mL/kg of 1:1,000 concentration).

##### Amiodarone IO/IV Dose:

5 mg/kg bolus during cardiac arrest May repeat up to 2 times for refractory VF/pulseless VT.

##### Advanced Airway

* + Endotracheal intubation or supraglottic advanced airway
  + Waveform capnography or capnometry to confirm and monitor ET tube placement.
  + Once advanced airway in

place give 1 breath every

6-8 seconds (8-10 breaths per minute)

**CPR 2 min**

* **IO/IV access**
* **Epinephrine every 3-5 min**
* **Consider advanced airway**

##### Return of Spontaneous Circulation (ROSC)

* + - Pulse and blood pressure
    - Spontaneous arterial pressure waves with intra-

**Rhythm shockable?**

No

11

## CPR 2 min

Yes

arterial monitoring

##### Reversible Causes

* Hypovolemia
* Hypoxia
* Hydrogen ion (acidosis)
* Hypoglycemia
* Hypo-/hyperkalemia
* Hypothermia
* Tension pneumothorax
* Tamponade cardiac
* Toxins
* Thrombosis, pulmonary
* Thrombosis, coronary

## Treat reversible causes

No Yes

**Go to 5 or 7**

**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 2×; 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.*

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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 (atonic, 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

Noncardiac Causes of Syncope

**Table 69-1**

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

|  |  |  |  |  |
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| **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. |

**Chapter 70** ◆ Shock **517**

Recognize decreased mental status and perfusion.

Begin high flow O2. Establish IV/IO access.

**Initial resuscitation:** Push boluses of 20 cc/kg isotonic saline or colloid up to and over 60 cc/kg until perfusion improves or

unless rales or hepatomegaly develop.

Correct hypoglycemia and hypocalcemia. Begin antibiotics.

If 2nd PIV start inotrope.

*Shock not reversed?*

**Fluid refractory shock:** Begin inotrope IV/IO.

Use atropine/ketamine IV/IO/IM

to obtain central access and airway if needed. *Reverse cold shock* by titrating central dopamine or, if resistant, titrate central epinephrine.

*Reverse warm shock* by titrating central norepinephrine.

Dose range: dopamine up to 10 mcg/kg/min, epinephrine

0.05 to 0.3

mcg/kg/min.



0 min

5 min

15 min

60 min

E m e r g e n c y

d e p a r t m e n t

*Shock not reversed?*

**Catecholamine resistant shock:** Begin hydrocortisone if at risk for absolute adrenal insufficiency.

Monitor CVP in PICU, attain normal MAP-CVP and ScvO2 > 70%.

C a r e

U n i t

|  |  |  |  |
| --- | --- | --- | --- |
| **Cold shock with** | **Cold shock with** | | **Warm shock with** |
| **normal blood pressure:** | **low blood pressure:** | | **low blood pressure:** |
| 1. Titrate fluid and epinephrine, | 1. Titrate fluid and epinephrine, | | 1. Titrate fluid and norepinephrine, |
| ScvO2 > 70%, Hgb > 10g/dL | ScvO2 > 70%, Hgb > 10g/dL | | ScvO2 > 70%, |
| 2. If ScvO2 still < 70% Add vasodilator with volume | 2. If still hypotensive consider norepinephrine | | 2. If still hypotensive consider vasopressin, |
| loading (nitrosovasodilators,  milrinone, imrinone, and others) Consider levosimendan | 3. If ScvO2 still < 70% consider dobutamine, milrinone,  enoximone or levosimendan | | terlipressin, or angiotensin  3. If ScvO2 still < 70% consider low dose epinephrine |
|  | |  | |

*Shock not reversed?*

P e d i a t r i c

I n t e n s i v e

**Persistent catecholamine resistant shock:** Rule out and correct pericardial effusion, pneumothorax, and intra-abdominal pressure > 12 mm Hg.

Consider pulmonary artery, PICCO, or FATD catheter, and/or doppler ultrasound to guide fluid, inotrope, vasopressor, vasodilator and hormonal therapies.

Goal C.I > 3.3 and < 6.0 L/min/m2

*Shock not reversed?*

**Refractory shock:** ECMO

**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; FATD, 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.)*

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| --- | --- | --- | --- | --- |
| **Table 70-1** Types of Shock | | | | |
| **HYPOVOLEMIC** | **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 |

**Sepsis or tissue hypoxia with lactic acidosis**

Decreased perfusion

Triggers shock

Initial insult

Body’s compensatory mechanisms

 Nitric oxide

synthase

 Nitric oxide

 ATP,  H+,  lactate

in vascular smooth muscle

 Vasopressin

secretion

Open KCa

Tissue damage

Multisystem

organ failure

**Death**

Decompensated shock

Open KATP

 Vasopressin

stores

 cGMP  Cytoplasmic Ca2+

Compensated shock

 Phosphorylated myosin

 Plasma

vasopressin

**Vasodilation**

**Chapter 70** ◆ Shock **519**

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 completed within 6 hr:

1. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65 mm Hg
2. 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 (ScvO2)\*

1. Remeasure lactate if initial lactate was elevated\*

Surviving Sepsis Campaign Care Bundles

**Table 70-10**

BP, blood pressure; FIO2, fraction of inspired oxygen; GCS, Glasgow Coma Scale; INR, international normalized ratio; PaCO2, arterial partial pressure of carbon dioxide; PaO2, partial pressure arterial oxygen.

\*Targets for quantitative resuscitation included in the guidelines are CVP of

≥8 mm Hg, ScvO2 of ≥70%, and normalization of lactate.

|  |  |
| --- | --- |
| **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 μg/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×  upper limit of normal  Oliguria: urine output <0.5 mL/kg/hr Prolonged capillary refill: >5 sec  Core to peripheral temperature gap >3°C (5.4°F) | |
| Respiratory | PaO2/FIO2 ratio <300 in absence of cyanotic heart disease or preexisting lung disease  *or*  PaCO2 >65 torr or 20 mm Hg over baseline PaCO2  *or*  Need for >50% FIO2 to maintain saturation ≥92%  *or*  Need for nonelective invasive 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/mm3 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, ≥2× 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× upper limit of normal for age |

*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.*

|  |  |
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| **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) | |

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| --- | --- | --- | --- | --- |
| **Table 70-3** | Signs of | Decreased Perfusion | | |
| **ORGAN SYSTEM** | | **↓ PERFUSION** | **↓↓ PERFUSION** | **↓↓↓ PERFUSION** |
| Central nervous system | | — | Restless, apathetic, anxious | Agitated/confused, stuporous, coma |
| Respiration | | — | ↑ Ventilation | ↑↑ Ventilation |
| Metabolism | | — | Compensated metabolic acidemia | Uncompensated metabolic acidemia |
| Gut | | — | ↓ Motility | Ileus |
| Kidney | | ↓ Urine volume  ↑ Urinary specific gravity | Oliguria (<0.5 mL/kg/hr) | Oliguria/anuria |
| Skin | | Delayed capillary refill | Cool extremities | Mottled, cyanotic, cold extremities |
| Cardiovascular system | | ↑ Heart rate | ↑↑ Heart rate  ↓ Peripheral pulses | ↑↑ Heart rate  ↓ Blood pressure, central pulses only |

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| **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 |

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| **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 O2 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  ↑ O2 consumption |

|  |  |
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| **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.*

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| **Table 70-12** Recommendations: Special Considerations in Pediatrics |
| INITIAL RESUSCITATION   1. 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. 2. 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 mL kg−1 hr−1, and normal mental status. ScvO2 saturation ≥70% and cardiac index between 3.3 and 6.0 L/min/m2 should be targeted thereafter. 3. Follow American College of Critical Care Medicine-Pediatric Life Support ( ACCM-PALS) guidelines for the management of septic shock. 4. Evaluate for and reverse pneumothorax, pericardial tamponade, or endocrine emergencies in patients with refractory shock. |
| ANTIBIOTICS AND SOURCE CONTROL   1. 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). 2. Clindamycin and antitoxin therapies for toxic shock syndromes with refractory hypotension. 3. Early and aggressive source control. 4. *Clostridium difficile* colitis should be treated with enteral antibiotics if tolerated. Oral vancomycin is preferred for severe disease. |
| FLUID RESUSCITATION   1. 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   1. Begin peripheral inotropic support until central venous access can be attained in children who are not responsive to fluid resuscitation. 2. 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)   1. Consider ECMO for refractory pediatric septic shock and respiratory failure. |
| CORTICOSTEROIDS   1. 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   1. 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 g/dL) can be considered reasonable. 2. Similar platelet transfusion targets in children as in adults. 3. 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   1. Lung-protective strategies during mechanical ventilation. |
| SEDATION/ANALGESIA/DRUG TOXICITIES   1. We recommend use of sedation with a sedation goal in critically ill mechanically ventilated patients with sepsis. 2. Monitor drug toxicity labs because drug metabolism is reduced during severe sepsis, putting children at greater risk of adverse drug- related events. |
| GLYCEMIC CONTROL   1. Control hyperglycemia using a similar target as in adults (≤180 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   1. 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   1. 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):580-637, 2013, Table 9, p. 614.*

**Chapter 71** ◆ Respiratory Distress and Failure **529**

1. DECREASED LUNG COMPLIANCE
   1. Left-to-Right Shunts
      1. Ventricular septal defect, atrial septal defect, patent ductus arteriosus, atrioventricular canal, truncus arteriosus
      2. Cerebral or hepatic arteriovenous fistula
   2. Ventricular Failure
      1. Left-heart obstructive lesions
         1. aortic stenosis
         2. coarctation of the aorta
         3. mitral stenosis
         4. interrupted aortic arch
         5. hypoplastic left heart syndrome
      2. Myocardial infarction
         1. anomalous left coronary artery arising from the pulmonary artery
      3. Hypertension
         1. acute glomerulonephritis
      4. Inflammatory/Infectious
         1. myocarditis
         2. pericardial effusion
      5. Idiopathic
         1. dilated cardiomyopathy
         2. hypertrophic obstructive cardiomyopathy

C. Pulmonary Venous Obstruction

1. Total anomalous pulmonary venous return with obstruction
2. Cor triatriatum

II. SHOCK RESULTING IN METABOLIC ACIDOSIS

1. Left-Heart Obstructive Lesions
2. Acute Ventricular Failure
   1. Myocarditis, myocardial infarction

Cardiovascular Pathology Manifesting as Respiratory Distress

**Table 71-4**

|  |  |  |  |
| --- | --- | --- | --- |
| **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  α1-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 Poliomyelitis Tumor/abscess |
| NEUROMUSCULAR  Phrenic nerve injury Birth trauma  Infant botulism  Guillain-Barré syndrome Muscular dystrophy Myasthenia gravis Organophosphate poisoning | | |

|  |  |  |
| --- | --- | --- |
| **Table 71-5** | Typical Chronology of Heart Disease Presentation in Children | |
| **AGE** | **MECHANISM** | **DISEASE** |
| Newborn  (1-10 days) | ↑ Arteriovenous pressure difference  Ductal closure  Independent pulmonary and systemic blood flow  Pulmonary venous obstruction | Arteriovenous fistula (brain, liver)  Single ventricle lesions or severe ventricular outflow obstruction  Transposition of the great arteries  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 71-1** | Typical Localizing Signs for Pulmonary Pathology | | | |
| **SITE OF PATHOLOGY** | | **RESPIRATORY RATE** | **RETRACTIONS** | **AUDIBLE SOUNDS** |
| Extrathoracic airway | | ↑ | ↑↑↑↑ | Stridor |
| Intrathoracic extrapulmonary | | ↑ | ↑↑ | Wheezing |
| Intrathoracic intrapulmonary | | ↑↑ | ↑↑ | Wheezing |
| Alveolar interstitial | | ↑↑↑ | ↑↑↑ | Grunting |

**Chapter 71** ◆ Respiratory Distress and Failure **531**

* Acute onset (<7 days)
* Severe hypoxemia (PaO2/FIO2 <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)

Simplified Consensus Definition of Acute Lung Injury

**Table 71-7**

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

|  |  |  |
| --- | --- | --- |
| **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 Acute time frame is specified respiratory symptoms |
| Chest X-rays or tomography scan | | Bilateral opacities not fully explained by effusions, lobar/lung Including illustrative radiographs is important, because collapse, or nodules. (Illustrative clinical cases and chest ARDS appearance may be different in children and in X-rays have been provided) adults |
| Origin of edema | | Respiratory failure not fully explained by cardiac failure Echocardiography widely used, whereas Swan-Ganz  or fluid overload. Need objective assessment (e.g., catheters are rarely used in early childhood. Including echocardiography) to exclude hydrostatic edema, if no risk factors in the ARDS definition is important, because ARDS risk factors are present they may be different in children and in adults |
| Oxygenation\* | | |
| Mild  Moderate Severe | | 200 mm Hg < PaO2/FIO2 ≤ 300 mm Hg with PEEP or CPAP ≥ Noninvasive CPAP is widely used in early childhood. PEEP 5 cm H2O† threshold (5 cm H2O) is a value commonly used during  100 mm Hg < PaO2/FIO2 ≤ 200 mm Hg with PEEP ≥ 5 cm H2O early childhood PaO2/FIO2 < 100 mm Hg with PEEP ≥ 5 cm H2O |

\*If altitude is higher than 1,000 m, the correction factor should be calculated as follows: [PaO2/FIO2 × (barometric pressure/760)].

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

†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 | 2-3 | 10-15 | ↑ HR, BP, and ICP |
|  | |  | 4-6 mg/kg IM |  |  | 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 Morphine | 2-5 μg/kg IV  0.1 mg/kg IV | 3-5  5-15 | 30-90  120-240 | Respiratory depression Chest wall rigidity  ↓ BP  Respiratory depression |
| Neuromuscular | | Vecuronium | 0.1 mg/kg IV | 2-3 | 30-75 | ↑ HR |
| blocking agents | | Rocuronium | 0.6-1.2 mg/kg IV | 5-15 | 15-60 | Renal elimination  ↑ HR |
|  | |  | 1 mg/kg IM |  |  | 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.

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|  |  |
| --- | --- |
| **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:   1. Decreased or muffled heart sounds 2. Distended neck veins from increased venous pressure 3. 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.*

Burns affecting >10% of BSA

Burns >10-20% of BSA in adolescent/adult 3rd-Degree burns

Electrical burns caused by high-tension wires or lightening 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

Indications for Hospitalization for Burns

**Table 75-2**

**Chapter 75** ◆ Burn Injuries **569**

|  |  |
| --- | --- |
| **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.

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

Acute Treatment of Burns

**Table 75-3**

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

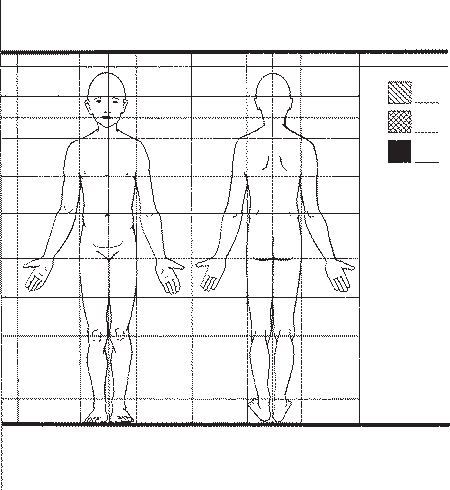
*Adapted from American College of Surgeons Committee on Trauma:* Advanced trauma life support for doctors: student course manual, *Chicago, 2008, American College of Surgeons, p. 234.*

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|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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** | Topica | l 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 *Pseudomonas*  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 | | Bilaminate  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 |



Date Burned

Date of Evaluation

1 2 3 4 5 6 7 8

A

%

1°

B

C

2°

D

3°

E

F

G H

I

J

NEWBORN 3 YR

HEAD 18% 15%

TRUNK 40% 40%

ARMS 16% 16%

LEGS 26% 29%

6 YR 12+ YR

12% 6%

40% 38%

16% 18%

32% 38%

TOTAL

L. LEG

R. LEG

L. ARM

R. ARM

TRUNK

HEAD

POST

ANT

%BURNED

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

**Chapter 75** ◆ Burn Injuries **575**

|  |  |
| --- | --- |
| **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  ≥32°C (89.6°F) in patients who are capable of spontaneous thermogenesis | |
| ACTIVE REWARMING  <32°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°C [89.6°F] for longer than 24 hr): core rewarming Extracorporeal membrane oxygenation  Availability of rapid deployment | |

ABCDE, *a*irway and possibly *a*ntibiotics, *b*reathing, *c*irculation, *d*isability or neurologic and possible *d*extrose, *e*xtracorporeal support if all else fails;

|  |  |
| --- | --- |
| **Table 75-7** | Common Long-Term Disabilities in Patients with Burn Injuries |
| DISABILITIES AFFECTING THE SKIN AND SOFT TISSUE  Hypertrophic 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 polyposis | |
| PREEXISTING DISABILITIES THAT CONTRIBUTED TO THE INJURIES  Risk-taking behavior  Untreated or poorly treated psychiatric disorder | |

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.*

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

Indications for Genetic Counseling

**Table 77-3**

# **)**uman Ceneti**cT**

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Instructions:



Key should contain all information relevant to interpretation of pedigree (e.g., define fill/shading) For clinical (non-published) pedigrees include:

1. name of proband/consultand
2. family names/initials of relatives for identification, as appropriate
3. name and title of person recording pedigree
4. historian (person relaying family history information)
5. date of intake/update
6. reason for taking pedigree (e.g., abnormal ultrasound, familial cancer, developmental delay, etc.)
7. ancestry of both sides of family

Recommended order of information placed below symbol (or to lower right)

1. age; can note year of birth (e.g., b.1978) and/or death (e.g., d. 2007)
2. evaluation (see Figure 75-4)
3. pedigree number (e.g., I-1, I-2, I-3)

Limit identifying information to maintain confidentiality and privacy

1. Individual
2. Affected individual

Male

b.1925

Female

30 y

Gender not specified

4 mo

Comments

Assign gender by phenotype (see text for disorders of sex development, etc.).

Do not write age in symbol.

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.

1. Multiple individuals, number known
2. Multiple individuals, number unknown or unstated
3. Deceased individual
4. Consultand
5. Proband
6. Stillbirth (SB)
7. Pregnancy (P)

5

n

d. 35

P

SB

28 wk

P

5

n

d. 4 mo

P

SB

30 wk

P

5

n

d. 60’s

SB

34 wk

P

Number of siblings written inside symbol. (Affected individuals should not be grouped.)

“n” used in place of “?”.

Indicate cause of death if known. Do not use a cross (†) to indicate death to avoid confusion with evaluation positive (+).

Individual(s) seeking genetic counseling/testing.

An affected family member coming to medical attention independent of other family members.

Include gestational age and karyotype, if known.

Gestational age and karyotype below symbol. Light shading can be used for

LMP: 7/1/2007 47,XY,+21

20 wk

46, XX

affected; define in key/legend.

Pregnancies not carried to term

10. Spontaneous abortion (SAB)

Affected Unaffected

17 wks female cyctic hygroma

<10 wks

If gestational age/gender known, write below

symbol. Key/legend used to define shading.

11. Termination of pregnancy (TOP)

18 wks

47, XY,+18

Other abbreviations (e.g., TAB, VTOP) not

used for sake of consistency.

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.)*

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1. Definitions
   1. relationship line

Comments

If possible, male partner should be to left of female partner on relationship line.

3. sibship line

2. line of descent

Siblings should be listed from left to right in birth order (oldest

to youngest).

4. individual’s line

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
* Infertility

?

?

Indicate reason, if known.

or

vasectomy

tubal

Indicate reason, if known.

or

azoospermia endometriosis

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.)*

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|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Instructions:  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 | D | or |  |  | P | D | 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 | P |  | D |  |  |  |  |  | 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 | S  P | | | | | | | | Couple whose gamets 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 | a) b)  D  or  P | | | | | D  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 |  |  | D |  | D  P |  |  |  | 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.)*

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\*

Eu

Man age 25 with normal physical exam and

uninformative DNA test for Huntington disease (E2).

25 y \*

E1— (physical exam) E2u (36n/18n)

Individual with cystic fibrosis and positive

mutation study; only one mutation has

E+

currently been identified.

E+(F508)

Eu

\*

E+(F508/u)

P

10 wk \* E+(CVS) 47,XY,+18

10 week male fetus with a trisomy

18 karyotype.

5. Affected individual with positive evaluation (E+)

4. Uninformative study (u)

Woman age 25 with negative mammogram and positive BRCA1 DNA test.

25 y \*

E1— (mammogram) E2+ (5385insC BRCA1)

3. Asymptomatic/presymptomatic carrier—clinically unaffected at this time but could later exhibit symptoms

Male carrier of Tay-Sachs disease by patient report (\* not used because results not verified).

2. Carrier—not likely to manifest disease regardless of inheritance pattern

\*

E— (echo)

Woman with negative echocardiogram.

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.

Scenario

Symbol

Definition

Instructions:

E is used for evaluation to represent clinical and/or test information on the pedigree

1. E is to be defined in key/legend
2. If more than one evaluation, use subscript (E1, E2, E3) and define in key
3. 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

**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.)*



7

6

5

4

3

2

III 1

6

5

4

3

2

1

II

2

1

I

**Figure 80-5** Autosomal dominant pedigree. Pedigree showing typical inheritance of a form of achondroplasia *(FGFR3)* inherited as an auto- somal 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.



I

1

2

II

1

2

3

4

III

1

2

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= *GJB2* carrier

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



**Figure 80-8** Pseudodominant inheritance. *Black,* affected (deaf);

*central dot* shows carrier who is asymptomatic (unaffected).



I

II

III

IV

3

2

5

3

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



AA

BB

Aa Aa AA

Bb BB Bb

AA

BB

Aa

Bb

AA

Bb

Aa

BB

AA

BB

AA

Bb

Aa

BB

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



I

II

III

IV

**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 phe-notype 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.



Short stature

Failure to thrive (use Noonan growth curve) Tall forehead

Epicanthal 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 (*KRAS* mutation)

Signs Associated with Noonan Syndrome

**Table 81-17**

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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 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)

Signs Associated with Turner Syndrome

**Table 81-16**

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| **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\* Epicanthal folds  Speckled irises (Brushfield spots) Three fontanels  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.

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| **Table 81-15** | Sex Chromosome Abnormalities | | |
| **DISORDER** | | **KARYOTYPE** | **APPROXIMATE INCIDENCE** |
| Klinefelter syndrome | | 47,XXY  48,XXXY  Other (48,XXYY;  49,XXXYY; 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,XXXXX | 1/1,000 females Rare |
| Other X chromosome abnormalities | |  | 1/3,000 females |
| XY females | | 46,XY | 1/20,000 females |

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| **Table 81-6** | Developmental Milestones | | | | |
| **Milestone** | | **CHILDREN WITH DOWN SYNDROME**  **Average Range**  **(mo) (mo)** | | **UNAFFECTED CHILDREN** | |
| **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.*

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| **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 | |

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| **Table 81-7** | Self-Help Skills | | | | |
|  | | **DOWN SYNDROME CHILDREN** | | **UNAFFECTED CHILDREN** | |
| **Skill** | | **Average (mo)** | **Range (mo)** | **Average (mo)** | **Range (mo)** |
| EATING  Finger feeding Using spoon/fork | | 12  20 | 8-28  12-40 | 8  13 | 6-16  8-20 |
| TOILET TRAINING  Bladder Bowel | | 48  42 | 20-95  28-90 | 32  29 | 18-60  16-48 |
| DRESSING  Undressing Putting clothes on | | 40  58 | 29-72  38-98 | 32  47 | 22-42  34-58 |

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

7

Average intellectual function

Border- line

Mild Moderate

Severe

Profound

6

5

4

Mental Age

2

Mental Retardation

1

1 2 3 4 5 6 7

Chronologic Age (years)

**Figure 81-10** The area shaded in yellow denotes the range of intel- lectual 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.)*

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| **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 seem 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.*

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| **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 Expressed in all molecule regions of the brain and candidate gene for congenital believed to have a role in axonal outgrowth during heart disease 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 |

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| **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] (mosaicism 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 |

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| **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

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| **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.*

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| **Table 83-2** Diagnostic Evaluation of the Neurologically Impaired Child | |
| CONSULTATIONS  Genetics/genetic counseling Neurology  Endocrinology Immunology Rheumatology Dermatology Cardiology Neuropsychology Nutrition  Rehabilitative medicine Physical therapy Occupational therapy Speech therapy | ADDITIONAL TESTING IF CLINICALLY INDICATED  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 |
| RESEARCH SPECIMENS  Cerebrospinal fluid Serum  Plasma  Skin biopsy for fibroblasts and/or melanocytes Isolated DNA/RNA  Urine |
| PROCEDURES  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 |
| 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 biopterin, 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 |
| LABORATORY EVALUATIONS  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  *N*- and *O*-glycans (plasma) Oligosaccharides and free glycans (urine) Glycosaminoglycans (urine) |