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CHAPTER 11

Select Populations: Children

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CAM Therapy Usage in Children

Users of complementary and alternative medicine (CAM) in the general population increased from 34% in 1990 to 42% in 1997.[96] A comprehensive survey in 1994 indicates that the number of children receiving CAM rose rapidly from approximately 2% in 1992 to 11% in 1994.[386] Four recent surveys focused on specific groups rather than the general pediatric population; two surveys revealed a high rate of CAM usage in children with cancer,[123,205] and two others focused on CAM usage in Hispanics, who often combine Western treatment with folk remedies.[312,346] There is growing evidence that the use of CAM has dramatically increased in the pediatric population in the United States, Canada, and western Europe,[25,71,104,130,290] although more recent statistics are not currently available.

Multiple factors influence parents to seek CAM for their children: word-of-mouth recommendations, fear of the side effects of medications, persistence of chronic conditions not well alleviated with conventional treatment, and preference for CAM philosophies and health beliefs.[46,386,425,427] Although most evidence indicates CAM usage in chronic disorders, increasing evidence indicates that CAM therapy also is used as adjunctive treatment for acute pediatric illnesses, from the common cold[312] to hospitalized illnesses,[13] and even for children in the pediatric intensive care unit (PICU).[285] CAM therapy is also given to a wide range of ages, from preterm infants in neonatal intensive care unit (NICU)[154] to adolescents[12,130] and even homeless youths.[40] A review conducted by Tufts University in 2000 indicated that more adolescents are turning to CAM for various conditions, including headaches, asthma, and dietary supplements for athletic events.[130] The autonomy of being able to obtain unregulated products and services is particularly attractive to the teenager.

There is no specific socioeconomic characteristic of CAM therapy patients, who range from affluent, well-educated populations[450] to ethnic, low-income groups.[39,331,445] In a 2001 prospective review of patients seeking consultations from the Center for Holistic Pediatric Education and Research in Boston, children with cancer constitute

the majority, usually seeking CAM therapy as an adjunctive management for pain and other discomforts related to the oncologic illness or to medications.[207]

In the general pediatric population, *chiropractic* is the most common form of CAM treatment used by children. Reports indicate that children made up 1% of chiropractic patients in 1977 and 8% in 1985.[303] A survey of the Boston metropolitan area revealed that an estimated 420,000 chiropractic visits were made by children in 1998.[237] Childhood disorders being treated include pain, respiratory and gastrointestinal tract problems, ear infection, enuresis, and hyperactivity.[303] *Homeopathy* was the second most popular form of CAM therapy used by children in Spiegelblatt's 1994 report.[386] In 2001, however, the University of Pittsburgh found that homeopathy was the most common CAM therapy used by children who visited an emergency department (ED).[329] Also, in a 2000 survey of homeopathic practitioners in Massachusetts, children constituted one third of patient visits.[236]

Homeopathic remedies are highly diluted substances that induce self-healing. These remedies are readily available from a variety of sources, including some grocery stores. Although homeopathy may be safe and effective in many childhood conditions, many practitioners believe that homeopathic remedies are best used as adjunctive therapy to conventional medicine in chronic conditions and in acute disorders that respond poorly to conventional therapy.[197,198]

Acupuncture is the third most common therapeutic method used in children[386] but has the largest body of scientific data compared with other CAM therapies.[248] A Harvard survey of 47 patients with a median age of 16 years who received acupuncture treatment, which included needle insertion, moxa/heat, cupping, and magnets, reported that 67% of patients rated the therapy as pleasant and 70% thought treatment helped their symptoms.[209] Electrical stimulation, laser, heat, magnet methods, and acupressure or acumassage[324] are effective alternatives to needles for treating children with needle phobia. Acupuncture and *traditional Chinese medicine* (TCM) have been used in Asia and Europe to treat a wide spectrum of childhood illnesses. Their use in the United States has been recent but is growing rapidly in popularity.

Naturopathy ranks with acupuncture as the third most common complementary therapy used by children,[385] although scientific data are sparse. Currently, evidence-based information is limited about safety and efficacy of herbal remedies, especially in terms of dosage and application in infants and children, who may be more susceptible to some of the adverse effects and toxicities because of differences in physiology and immature metabolic enzyme systems.[293,412]

Other CAM treatments used in children include touch therapy (therapeutic touch), osteopathy, oligotherapy, and hypnosis. Religious practices such as prayer have also become prevalent in the pediatric population.[22] Children have reported the ability to readily feel energy field from touch therapy.[118] The increasing support for *therapeutic touch* (TT)[223,226] has been anecdotal with little scientific data. Approximately 9% of children receiving treatment with CAM therapies seek *osteopaths,*[386] who claim success in treating many common childhood conditions, including colic and otitis.[19] Approximately 4% of pediatric CAM visits are to *oligotherapists,*[386] who administer poorly absorbed trace elements such as copper, manganese, and zinc to improve

TABLE 11–1. **CAM THERAPIES FOR PEDIATRIC CONDITIONS**

Condition	Most Common Therapies	Supportive/Other Data
ADHD	Biofeedback	Improved attention, behavior, and cognition; effects last as long as 10 years[49,246,253,407]
	Acupuncture (laser)	Improved behavior and cognition, but ineffective in severe ADHD (pilot data)[249]
	TCM	Increased urinary neurotransmitter metabolites[464]
	Magnesium supplement	Decreased hyperactivity (200 mg/day)[390]
Allergies	Nutrition	Breast-feeding decreased atopy[451]
	Acupuncture	More effective (greater desensitization) in older teenagers[228]
Asthma	Hypnosis	Asthmatic children were more hypnotizable; reduced physician visits[68,217]
	TCM (oral)	Improved symptoms[170]
	TCM (patch)	Effective in acute atacks; antitussive/antiasthmatic herbal external preventive[400]
Colic	Chiropractic	Controlled colic[215]
	Massage (TT)	Empirically decreased colic[111]
Diarrhea (acute)	Homeopathy	Significant decrease in duration[182]
	Shallow acupuncture	Higher therapeutic effect than drugs[244]
Diarrhea (chronic)	TCM (individualized)	Eliminated symptoms; normalized stools[109]
Enuresis	Hypnotherapy	High success in uncontrolled studies[24,67,74,.308-310]
		Longer dry period than with imipramine[21]
	Acupuncture	Effective alone; more effective with DDAVP[52]
	Chiropractic	Decreased enuretic symptoms[341]
	Oligoantigenic diet	Relapse with reintroduction of foods[281]
Immunization	Homeopathy	Parental preference over vaccination[379]
Otitis media	Homeopathy	Reduced pain; prevented relapses[124]
	Chiropractic	Decreased symptoms (1 chiropractor)[124]
Skin rashes	TCM	Widespread nonexudative eczema[373]
	Acupuncture	Effective for acne[456]
URI	Nutrition	Breast-feeding: less frequent, shorter bouts[251]
	Homeopathy	Ineffective in reducing symptoms[78]
	TCM	Effective in infants[465]

ADHD, Attention deficit–hyperactivity disorder; *TCM*, traditional Chinese medicine, Chinese herbs; *TT*, therapeutic touch; *URI*, upper respiratory tract infection; *DDAVP*, 1-deamino-8-D-arginine vasopressin.

health. *Relaxation training* and *imagery* are forms of hypnosis that have also been effective in children.[309] In fact, children seem to be able to learn relaxation training better and faster than adults.[122] Table 11-1 summarizes the CAM therapies most often used to treat various pediatric conditions. Box 11-1 lists additional and recent surveys and reviews of CAM therapies used to treat pediatric conditions.

Immunizations

Vaccination is an essential component of pediatric well-child care and has both public health and educational ramifications because up-to-date vaccination is required for

BOX 11–1. Additional and Recent Surveys, Systematic Reviews, and Cochrane Reviews of CAM and Pediatrics

Fong DP, Fong LK: Usage of complementary medicine among children, *Australian Family Physician* Apr 31(4):388, 2002.
Survey data taken from public hospital indicated 33% of parents used CAM for their children. Vitamins were more popular than acupuncture and positive correlations existed between CAM use and inadequate vaccination. No correlation exists with age, complaint, duration of hospital stay, or previous number of admissions.

Glazener CMA, Evans JHC: Simple behavior: physical interventions for nocturnal enuresis in children, Cochrane Library 3, 2002 (Online: Update software).
Reward systems produce fewer wet nights and higher cure rates along with lower relapse rates when compared with controls. Importance of a medication comparison group is noteworthy.

Glazener CMA, Evans JHC: Alarm interventions for nocturnal enuresis in children, Cochrane Library 3, 2002 (Online: Update software).
Most of the studies were poorly done (22 trials selected; n = 1125). The groups using the alarm maintained dry condition although tricyclic medication was as effective.

Heuschkel R et al: Complementary medicine use in children and young adults with inflammatory bowel disease, *American Journal of Gastroenterology* 97(2):382, 2002.
Of children with inflammatory bowel disease, 40% use CAM. Parental use and adverse effects from conventional therapies were best predictors of CAM use.

Moher D et al: Assessing the quality of reports of systematic reviews in pediatric complementary and alternative medicine, *Biomedical Central Pediatrics* 2(1):3, 2002.
Evaluated quality of reviews (n = 36; 17 CAM pediatrics systematic reviews with 19 systematic reviews taken from conventional pediatrics evaluating the same disease.) It was reported that eligibility criteria and evaluation of CAM data were "good," but there was little description of how bias in the selections of major studies was avoided or how "validity" parameters could best be described. Many individual CAM studies failed to randomize subjects, so they were not included in the overall analysis. There seemed to be a disparity between individual CAM trials and their "combined" subsequent integration into any type of review and evaluation. Importantly, the Oxman and Guyatt validated scale was used to evaluate individual aspects of the systematic review, i.e., types of search methods used.[311a]

entering school.[50] As with all pharmaceutical products, however, vaccines have risks and can cause rare but serious adverse effects.[99] Controversy is ongoing regarding pediatric immunization schedules[347,375] and effectiveness of multiple-antigen vaccines.[85,105,321] At present, vaccine-preventable disease rates are at their lowest level ever. In 1999 in the United States there were only 86 reported cases of measles, 238 cases of rubella, one case of diphtheria, 33 cases of tetanus, and no wild polio.[103,421]

Vaccine safety is monitored closely. Adverse events are reported to the *Vaccine Adverse Event Reporting System* (VAERS), administered by the Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA). Approximately 10,000 adverse cases are reported each year. Data are shared internationally by independent scientific experts on the Joint Committee on Vaccination and Immunization and committees of the Medicines Control Agency. Surveillance results in product withdrawal when there is clear evidence of a safety issue.[300] Currently, several serious pediatric conditions are controversially attributed to vaccination: immune compromise,[377] neurologic sequelae, autism, and Crohn's disease.

The medical community has expressed concern about the effects of vaccination on an immature immune system, especially in neonates.[419] Controversial debates are ongoing regarding the possible connection between vaccination and autoimmune illnesses, such as the association between measles and anti–hepatitis B virus (HBV) vaccines with multiple sclerosis. Tetanus toxoid, influenza vaccines, polio vaccine, and others have been related to autoimmune phenomena ranging from autoantibody production to full-blown illness, such as rheumatoid arthritis and Guillain-Barré syndrome. Recent evidence suggests that autism may be related to the immune system.[273]

The mechanism of autoimmune reactions after immunization has not yet been elucidated. One possibility is molecular similarity between some viral antigen (or other component of the vaccine) and a self-antigen. This similarity may be the trigger to the autoimmune reaction.[16,374]

Before 1991, whole-cell pertussis vaccine was used, composed of a suspension of formalin-inactivated *Bordetella pertussis* B cells. Convulsions occurred in 1 case to 1750 doses administered, and acute encephalopathy occurred rarely, at 10.5 cases per million doses administered. Sudden infant death syndrome (SIDS) and infantile spasms have also been suggested to be associated with diphtheria-pertussis-tetanus (DPT) vaccination.[103] In the 1970s, reports linking pertussis vaccine with infant brain damage attracted media attention,[227] which in turn caused great parental and professional anxiety; the immunization rate fell from 80% to 30%. Between 1976 and 1988, three major pertussis epidemics occurred in the United States, resulting in more than 300,000 hospitalizations and at least 70 deaths.[300] In countries such as Sweden, Japan, United Kingdom, Ireland, Italy, and Australia, antivaccine movements targeted pertussis whole-cell vaccines.[129]

Opponents to the pertussis vaccine have argued that the risks of vaccination outweigh the benefits.[103] The largest study to date conducted by the National Institute of Child Health and Human Development at the National Institutes of Health (NIH) revealed that SIDS was actually less likely to occur in recently vaccinated infants.[165] Another large study showed that the permanent neurologic sequelae due to pertussis vaccine are so rare as to be unquantifiable.[280]

Nevertheless, concerns about brain damage led to the development of *acellular* pertussis vaccine (DTaP) that contains purified, inactivated components of *B. pertussis* cells. This form is associated with a lower frequency of adverse events and is more effective in preventing pertussis disease. DTaP was first licensed for the fourth and fifth doses of the pertussis series in 1991 and for the primary series in 1996. Several studies conducted in Europe and Africa revealed that U.S.-licensed DTaP vaccines

have efficacy ranging from 71% to 84%. Currently, only acellular pertussis vaccine is used.[103]

No encephalopathy has been reported. *Hypotonic hyporesponsive episode* (HHE) is the sudden onset of hypotonia, hyporesponsiveness, and pallor or cyanosis that occurs within 48 hours of vaccination, usually after pertussis vaccine administered to children under 2 years of age. HHE occurred in approximately 1 of every 1750 DTa vaccinations. The largest published report of 40,000 cases concluded that although HHE does occur after the administration of DTaP and other non–pertussis-containing vaccines, it is generally benign, self-limited, and nonrecurrent.[92]

The connection of encephalopathy with pertussis vaccine was biologically more plausible than the proposed link between pertussis, measles vaccines, and autism.[300] The incidence of autism has increased from 1 in 10,000 in 1978 to 1 in 300 in 1999 in some U.S. communities. A study of 60 autistic children suggests that autism may be caused by a pertussis toxin found in the DPT vaccine. The toxin separates the G-alpha protein from retinoid receptors, which are critical for vision, sensory perception, language processing, and attention—characteristic problems of autism. Those children most at risk have at least one parent with a preexisting G-alpha protein defect, presenting clinically with night blindness, pseudohypoparathyroidism, or adenoma of the thyroid or pituitary gland. Natural vitamin A may reconnect the retinoid receptors.[273] In recent years, discussion has increasingly centered on the controversy concerning the possible association of the measles-mumps-rubella (MMR) vaccine with autism and Crohn's disease.*

The Chinese were among the first populations to vaccinate, beginning with smallpox vaccine, which was injected intranasally. TCM considers most childhood illnesses to occur at superficial levels, and vaccination actually introduces pathogens, still considered energetically active, into deeper blood levels of the body. In addition, TCM also posits that the body can usually effectively handle only one process at a given time. When two separate processes occur at the same time, the human system could become overwhelmed, especially the tender system of an infant or a young child. Therefore, although multiple vaccines given at the same time are less traumatic for children and save nursing time, they can easily overwhelm an immature immune system and make the child weak and deficient.[352] Although the fear of epidemics motivates the Chinese to vaccinate all their children, TCM practitioners in the West often advise against immunization.[320]

There is discrepancy among the homeopaths regarding recommendation of conventional vaccines. A German questionnaire survey reported that homeopathic physicians generally do not refuse vaccinations but show a preference for the DPT vaccines.[239] A British survey conducted between 1987 and 1993 reported that preference for homeopathic remedies for illnesses and religion were the most common reasons parents refused immunization; 21% believed the risk of diseases to be less than the risk of vaccination and would seek homeopathic treatment if any illness developed in their children, and 17% believed that children "are protected by God and

*References 8, 33, 51, 59, 80, 81, 97, 98, 117, 279, 314, 409, 410, 430, 431.

not by vaccines."[379] A U.S. cross-sectional descriptive survey of 42 homeopathic practitioners and 23 naturopathic practitioners in Massachusetts revealed that the majority of the practitioners did not actively recommend immunizations.[236] Many homeopaths recommend homeopathic vaccines, which are not yet supported by scientific data.[399]

A random sample survey by mail of 1% of American chiropractors revealed that one third believe there is no scientific proof that immunization prevents disease, that vaccinations cause more disease than they prevent, and that contracting an infectious disease is safer than immunization.[66] A reported 81% believed that immunization should be voluntary and that spinal adjustment is a viable alternative. A cross-sectional, descriptive survey of 90 chiropractics in the Boston metropolitan area reported that only 30% actively recommended childhood immunization.[237]

The decision of whether or not to immunize a child is difficult for both parents and practitioners. The advantages of vaccination are difficult to refute, but the temporal relationship between immunization and side effects and the controversies surrounding potential risks are disconcerting. Although data are insufficient on CAM approaches to vaccination today, practitioners should be aware of the slow yet steady trend toward alternatives and should properly address parental concerns and questions regarding immunization.[348] Each practitioner needs to inform parents of the most up-to-date pros and cons of vaccination, be as objective as possible, put aside personal belief systems, and be supportive and understanding of whichever decision the parents make. Parents need to become as informed as possible, consider all the pros and cons, weigh the risks and benefits, and realize that ultimately they must live with the outcome of their decision.

Upper Respiratory Tract Infections

The common cold is the most frequent infection in children in the United States and throughout the industrialized world.[394] A preschool-aged child has an average of 4 to 10 colds per year.

The clinical symptoms vary greatly without any correlation with specific viruses.[94,121] The majority of the symptoms are mild, consisting of rhinorrhea, sneezing, nasal congestion and obstruction, postnasal drip, and cough. There may often be additional symptoms of low-grade fever, sore throat, clear eye discharge, digestive discomfort, and general malaise.[180,213,276] Some common viruses that cause upper repiratory tract infections (URIs) include rhinovirus, coronavirus, adenovirus, respiratory syncytial virus (RSV), influenza virus, and parainfluenza virus.[101,121,139] Transmission varies with different viruses. For example, RSV spreads primarily through contact with symptomatic children and contaminated objects, whereas influenza spreads mainly through airborne droplets. The precise route of transmission for rhinovirus remains controversial.[139] The virulence of rhinovirus is maximum in infants before 1 year of age (median age 6.5 months)[327] and in immunocompromised children.[330] Wheezing is associated with RSV in children younger than 2 years of age and with rhinovirus in those over age 2.[338]

Simultaneous infection by more than one virus, such as RSV and adenovirus together, can also occur frequently in the pediatric population. Many children may also have associated bacterial infection, such as *Haemophilus influenzae* conjunctivitis.[327]

The viruses gain entry into host cells through specific viral surface proteins, which cause tissue injury and result in clinical disease.[432] Recent studies suggest that the host's response to the virus, not the virus itself, determines the pathogenesis and severity of the common cold. Proinflammatory mediators, especially the cytokines, appear to be the central component of the response by infected epithelial cells.[158,417] Specific viral diagnosis is not necessary because of the benign, self-limiting nature of the disease[294] and the prevalence of different viruses overlapping from fall to spring, which makes it difficult to determine precisely which virus or viruses are causing the symptoms.[121]

Current medical management of URI remains symptomatic, controversial, and in most cases, ineffective. Fluid, rest, humidifier, and saline nose drops constitute the mainstay of nonpharmacologic treatment. Topical adrenergic agents do not have systemic side effects, but overuse can result in rebound congestion.[84,114] Antihistamine and combinations of antihistamine with decongestants are the ingredients in at least 800 over-the-counter (OTC) cold remedies. The majority of studies have concluded that antihistamines are of marginal or no benefit in treating cold symptoms.[47,110,153,254,383] Dextromethorphan is an antitussive that is abundant in OTC formulations. Although this medication is reportedly safe when taken in the recommended dosages, there have been cases of "recreational" use by teenagers, and deaths by overdose have been reported.[291] Codeine is ineffective in controlling URI cough.[95]

Medications are often overprescribed, leading to higher health care costs[102] and dangerous side effects, such as greater antibiotic resistance.[257] More steroids are prescribed, which leads to a myriad of complications.[274] Although interferon has been shown to produce good protection against infection, the high doses necessary to produce a prophylactic effect are often associated with serious undesirable side effects, including nasal stuffiness, bloody mucus, and mucosal erosions,[213] and the trauma of daily intramuscular injection makes it an unlikely remedy for children.[169]

Research for new medical therapies for the common cold is directed toward increasing resistance to or immunity against the viruses. Histamine antagonists are not indicated in the common cold.[369] Antiinflammatory mediators[417] and specific antiviral agents[361] may be promising. Development of an effective vaccine against the common cold is unlikely because of the large number of viral serotypes.[213] *Rhinovirus,* for example, has at least 100 different immunotypes.[158] Although viral URI is a benign illness of short duration, it can lead to bacterial complications such as otitis media, sinusitis, lower respiratory tract infections, mastoiditis, and even meningitis.[330]

Scientific data on CAM treatment for the common cold are surprisingly sparse. In 1971, Linus Pauling carried out a meta-analysis of four placebo-controlled trials and concluded that vitamin C alleviates cold symptoms, but subsequent reviews indicated that the role of vitamin C in URI is still controversial.[146-148,199]

Although *breast-feeding* has been believed to protect against infection in infants, studies have been inconsistent in demonstrating its efficacy. In a 4-year prospective

study that actively tracked breast-feeding and respiratory illnesses in 1202 healthy infants, breast-feeding was found to reduce significantly the duration of respiratory illnesses during the first 6 months of life.[75] A retrospective review from Saudi Arabia of randomly selected charts revealed that a direct correlation exists between duration of breast-feeding and frequency of URI in the first 2 years of life.[1] A hospital-based descriptive recall study from Sri Lanka examined the relationship between breast-feeding and morbidity from respiratory illnesses in infants. Of the 343 infants, 285 were admitted and 58 were controls. An inverse relationship was found between the length of breast-feeding and incidence of respiratory illnesses.[319] A nutritional study of 170 healthy newborns followed for 6 months demonstrated that breast-feeding lowers frequency and duration of acute respiratory tract infection compared with formula feeding.[251] A more recent Japanese study examined the incidence of pathogenic bacteria isolated from the throat of 113 healthy infants fed with different methods.[166] No pathogens were detected in breast-fed and mixed-fed infants, while *H. influenzae* and *Moraxella catarrhalis* were isolated from the oropharynx of formula-fed infants. The investigators suggest that breast milk may inhibit the colonization by respiratory bacterial pathogens of the throat of infants. The mechanism was thought to be enhancement of mucosal immunity against respiratory tract infection.

In addition to the presence of secretory immunoglobulin A (IgA), another mechanism may be the presence of complex carbohydrates in human milk. These glycoconjugates may exert various antipathogenic effects, such as inhibiting the binding of pathogens to the receptors and reducing the production of bacterial toxins.[299] However, a U.S. study that examined nasopharyngeal swabs from 211 infants at 1 month of age and swabs from 173 of these infants at 2 months of age (keeping environmental parameters similar, e.g., number of children in household, number of siblings in day care, proportion with recent URI) revealed that the exclusively breast-fed ($n = 84$) and exclusively formula-fed ($n = 76$) infants did not differ significantly in the number of pathogens.[196] A multicenter randomized trial was conducted in 31 hospitals in the Republic of Belarus.[228] Evaluation within the first year revealed that breast-feeding had no significant reduction in respiratory tract infection compared with the control group. A survey from Singapore of breast-feeding mothers at 6 months postpartum revealed no significant differences in the rates of URI between breast-fed and non–breast-fed infants.[64]

Data are sparse on acupuncture, herbal, and homeopathic remedies for treatment of URI, especially in children. Most data are uncontrolled, clinical reports. Current information on adults supports efficacy of acupuncture for treating the common cold.[172,311,454,462] *Acupuncture* has been shown to increase the velocity of the nasal mucociliary transport in chronic rhinitis patients.[454] One possible use of acupuncture in URI is its potential effect on the immune system.[322] When Chinese herbs were pasted onto acupoints for treating rhinitis and bronchitis in infant, serum immunoglobulin M (IgM), IgG, complement C3, and especially IgA levels increased.[461] Acupuncture has also been shown to increase T lymphocytes.[404] Even massaging local acupoints was effective in relieving symptoms and in enhancing immune functions, with increases in immune indices that persisted for at least 6 months.[466] One report of acu massage of only one point for just 30 seconds resulted

in clinical relief from nasal congestion, even though there was no change in nasal airway resistance or airflow.[403] These reports are encouraging for parents because acupressure can be easily learned by nonprofessionals, is well tolerated by children of all ages (including infants), has no side effects, and costs nothing.

A clinical trial administering a nontoxic Chinese herbal mixture to 305 infants demonstrated more than 95.1% effectiveness in treatment of URI.[465] In a single-blind trial using a Chinese herb for acute bronchiolitis with serologic evidence of RSV, 96 hospitalized children were randomized into three treatment groups: herbs, herbs with antibiotics, and antibiotics alone. Herbal treatment was found to decrease symptoms and duration of illness without adverse effects.[218] In a randomized, controlled trial using an herbal mixture, 89 children in the treatment group demonstrated 92% efficacy versus 67% of 61 children in the control group.[255] There was no description in the abstract (original article in Chinese) of what constituted control (e.g., placebo herb, no treatment, conventional drugs) or what constituted efficacy (e.g., improvement in symptoms, duration, of illness). Further rigorous studies are needed to demonstrate safety and efficacy of herbal treatment.

A recent clinical trial that included children over age 12 years and used a fixed-combination homeopathic remedy for a mean 4.1 days of treatment reported that 81.5% reported subjective feelings of being symptom free or significantly improved without complaint of any adverse side effects.[4] A randomized, double-blind, placebo-controlled study from Great Britain of 170 children with a starting median age of 4.2 years in the experimental group and 3.6 years in the placebo group concluded that individually prescribed homeopathic remedies seem to be ineffective in reducing symptoms or decreasing the use of antibiotics in pediatric patients with URI.[78]

Otitis Media

Otitis media (OM) represents a continuum of conditions that include acute OM, chronic OM with persistent effusion, chronic suppurative OM, recurrent OM, unresponsive OM, and OM with complications.[28]

Acute otitis media (AOM) is most prevalent in young children 8 to 24 months of age. Approximately two thirds of all children will have had at least one episode of AOM before age 3 years, and half of them will have recurrences or chronic serous OM with effusion into early elementary school years.[132] By the time the child reaches adolescence, AOM occurs infrequently.[443] Almost one third of pediatric office visits are for treatment of AOM.[109] The most common etiologic factors are allergic rhinitis[72,336] and ascending bacterial or viral agents from the nasopharynx attributable to eustachian tube dysfunction. The most common viral culprits are RSV,[10] influenza virus,[153] and adenovirus.[108] Two thirds of middle ear infections are caused by bacteria.[109] The predominant organisms are pneumococci, *H. influenzae, M. catarrhalis,*[53,305,358,388] and group B streptococcus.[325] Bacterial pathogens adhere to mucous membranes, and colonization ensues.

The severity of infection or the response to the invading bacteria depends on the health of the child's immune system.[53] The humoral system is especially significant in

protecting the middle ear cavity from disease, and the nasopharyngeal lymphoid tissues are the first line of defense against bacterial colonization.[335,359] The sterility of the eustachian tube and tympanic cavity depends on the mucociliary system and on secretion of antimicrobial molecules, such as lysozyme, lactoferrin, and beta-defensins.[313] Evidence indicates that a number of children with recurrent episodes of AOM have minor immunologic defects.[359] *Pneumococcus* is by far the most virulent of AOM bacteria. It causes approximately 6 million cases of OM annually in the United States.[468] Uncontrolled pneumococcal otitis can lead to meningitis.[416] The incidence of AOM is higher in winter and early spring.

Clinically, the child with AOM presents with earache and fever, usually accompanied by upper respiratory symptoms such as rhinorrhea. On otoscopic examination the tympanic membrane varies from hyperemia with preservation of landmarks to a bright-red, tense, bulging, distorted appearance. In advanced stages of suppuration the tympanic membrane ruptures with a gush of purulent or blood-tinged fluid from the ear.[108] Because viral or bacterial OM usually cannot be distinguished by otoscopic examination, AOM is usually treated empirically, using antibiotics such as amoxicillin that have a high concentration in the middle ear fluid.[214,224]

However, the widespread use of antibiotics has resulted in increasing resistance to the more common medications.[53,358] Currently, 10% of children with AOM are recalcitrant to antibiotic therapy.[277] The prevalence of resistant organisms tends to increase in the winter months.[43] Economically, treatment failure due to drug resistance has been responsible for further escalating the billions of dollars spent treating AOM.[287] In addition, antimicrobials suppress normal flora, which is beneficial to the host because the antibiotic can interfere with and therefore prevent pathogenic infections and may enhance recovery from URIs.[43] On the other hand, since the advent of antibiotics, complications such as mastoiditis and intracranial infections have significantly decreased.[297]

The current focus is on prevention of AOM. Breast-feeding confers lifesaving protection against infectious illness, including otitis.[134,156] *Pneumococcal conjugate vaccine* (PCV), approved in 2000 for use in the United States, covers the seven serotypes that account for about 80% of invasive infections in children younger than age 6 years. PCV was demonstrated to have more than 90% efficacy[468] and has resulted in a modest reduction of total episodes of AOM.[317] The goal of PCV is to prevent symptomatic infections in the middle ear and prevent colonization of the pneumococci that can cause subsequent middle ear infections.[41] PCV may eliminate nasopharyngeal carriage of pneumococci.[235] However, because PCV only prevents disease caused by the most common serotypes, there is concern that the nonvaccine serotypes will become more common, especially in children less than 2 years of age.[317]

An effective RSV vaccine for the infant and young child could greatly decrease OM disease.[10] Intranasal spray of attenuated viruses is currently under investigation, in the hope that early antiviral therapy would reduce the risk of OM after URI.[137,153]

Chronic otitis media with effusion (OME) is one of the most common diseases in childhood.[91] OME is associated with infection, eustachian tube obstruction, allergic or immunologic disorders, and enlarged adenoids.[108] The serous fluid still contains bacteria, such as *H. influenzae* and pneumococci.[48] OME has been implicated to be an

immune-mediated disease[91] because immune complexes have been demonstrated in the middle ear effusion,[268] and highly organized lymphatic tissue has been found in the middle ear mucosa.[422]

The rationale for treating OME is prevention of recurrence of AOM. Currently, a once-daily antibiotic regimen is the recommended prophylaxis. The benefit is also weighed against the increasing risk of emergence of resistant bacteria.[134] When antibiotics fail to control recurrent OM, a short trial of prednisone may be prescribed. Surgery is recommended when medical treatment fails,[277] especially when the child has hearing loss.[305] Tympanostomy tubes appear to be beneficial in OME but are of less value in chronic suppurative otitis.[134] Increase in hearing loss has been reported with insertion of ventilation tubes.[144] Adenoidectomy is sometimes recommended,[193] especially after tympanostomy tube failure.[134]

Any safe and effective CAM therapy for OM would be an important contribution to the pediatric population. Large-scale, randomized, controlled studies for CAM treatment would need medical collaboration, especially for otoscopic examination and tympanometry.[366] In addition, since AOM has a high rate of spontaneous resolution, any clinical study must also prove that treatment effect is faster than natural improvement.

Although breast-feeding has been found to reduce URI, data concerning its association with frequency or duration of OM have been conflicting. Epidemiologic reports consistently provide evidence of protection of young children from chronic otitis with prolonged breast-feeding.[138] A U.S. study that followed 306 infants at well-baby visits in two suburban pediatric practices reported that the cumulative incidence of first OM episodes increased from 25% to 51% between 6 and 12 months of age in infants exclusively breast-fed versus 54% to 76% in infants formula-fed from birth.[89] There was a two-fold risk of first episodes of AOM or OME in formula-fed babies in the first 6 months. A Danish study that evaluated 500 infants using monthly questionnaires reported no statistical difference in the breast-fed versus formula-fed infants in incidence of OM.[355] An earlier Jewish study comparing 480 infants visiting a pediatric ED with 502 healthy infants found that breast-feeding significantly reduced infectious diseases, including OM in infants under 5 months of age.[76]

A study from Switzerland evaluated 230 children with AOM by administering individualized homeopathic medicine in the pediatric office.[119] If there was insufficient pain reduction after 6 hours, a second (different) homeopathic medicine was given. Antibiotics were given if there was lack of response to the second dose. Pain control was achieved in 39% of the patients after 6 hours, with another 33% after 12 hours. The resolution rate was 2.4 times faster than in placebo controls. No complications were observed in the study group.[119] In a U.S. double-blind, placebo-controlled pilot study, 75 children ages 18 months to 6 years with OME and ear pain and/or fever for more than 36 hours were randomized into individualized homeopathic medicine or placebo group.[181] No statistically significant results were noted. A British nonblinded, randomized pilot study was done with 33 children ages 18 months to 8 years who had OME and hearing loss greater than 20 dB and an abnormal tympanogram.[150] The results revealed that the homeopathy group had more children with

a normal tympanogram, fewer referrals to specialists, lower antibiotic consumption, and a higher proportion with a hearing loss less than 20 dB at follow-up. However, the differences were not statistically significant. Further research with larger groups is needed for a definitive trial.

In a prospective, observational study carried out by one homeopath and four conventional ear-nose-throat (ENT) physicians, a single (nonindividualized) homeopathic remedy was compared with nasal drops, antibiotics, and antipyretics.[125] Children between 6 months and 11 years of age were included in the study. Homeopathic treatment was given to 103 children and conventional treatment to 28 children. Homeopathic remedies were found to be significantly more effective in reducing duration of pain and in preventing relapses. Because OM tends to affect predominantly young children, it would be more appropriate for studies to compare results in children of similar age rather than a wide range of ages, from infancy to preadolescence.

A retrospective, nonrandomized study of 46 children under 5 years of age receiving 3 weeks of treatment from a single chiropractor reported a decrease in OM symptoms. The limitations to this study included retrospection and a lack of comparison with the natural course of ear infections.[124]

An Israeli controlled clinical trial examined the efficacy and tolerance of ear drops made with naturopathic extracts in the management of AOM pain.[362] Ranging in age from 6 to 18 years, 103 children were randomized into the treatment group and control group using a conventional anesthetic ear drop. There was statistically significant improvement in both groups, indicating that the naturopathic ear drops were as effective as the anesthetic ear drops. The University of Arizona has initiated a study of the use of *echinacea,* a dietary supplement, in the prevention of recurrent OM.[261] Acupuncture data are lacking on treatment of OM in children.[411] The theoretical potential benefit of acupuncture would appear to be its effect on the immune system, as discussed in the section on URI.

Allergies

Allergic rhinitis affects 5% to 9% of children.[113] *Perennial rhinitis* is related to allergens that children are exposed to continuously, such as animal dander, house dust mites, mold, and feathers. *Seasonal rhinitis* is related to seasonal pollenosis and rarely affects children under age 4 or 5 years.[100] Allergic diseases are major causes of morbidity in children of all ages,[437,447,448] and allergic rhinitis is a significant cause of middle ear effusions.[72,267,336,452] Conventional therapy usually consists of avoidance of allergens, use of air-clearing devices, desensitization shots, and medication with antihistamines and at times steroids, both of which are frequently abused.[179,200] Antihistamines may be beneficial when sneezing and itching are present.[114]

CAM therapy is common among children with allergic diseases in Sweden[155] and is becoming more popular in the United States, although scientific data specifically on children are still lacking. Physicians have become more aware of the importance of nutrition[384,424] and environmental factors in the development of allergic

symptomatology in childhood.[289,396,446] A prospective, longitudinal study of healthy infants followed from birth to 6 years of age concluded that recurrent wheezing is less common in nonatopic children who were breast-fed as infants.[450] Hypnosis has been reported anecdotally to be effective in hay fever.[439]

Homeopathic efficacy has received increasing attention in recent years,[342] but data consist of adult studies. An international multicenter study involving 30 investigators in four countries and 500 patients with three diagnoses, including upper and lower respiratory tract allergies, concluded that homeopathy appeared to be at least as effective as conventional medicine.[345] Another multicenter study using a randomized, double-blind, placebo-controlled parallel group design also demonstrated that homeopathic preparations differ from placebo for allergic rhinitis.[408] Homeopathic remedies for allergic children are unsupported by scientific studies at this time.

An adult study using changes in conductance of specific acupuncture points for diagnosis and treatment demonstrated statistically significant changes that correlated with clinical improvement.[195] In a randomized study of 143 patients that included older teenagers, desensitization was compared with specific acupuncture treatment for allergic asthma, allergic rhinitis, or chronic urticaria. The study was ridden with multiple, tedious variables. The conclusion that acupuncture was significantly more effective than desensitization in improving symptoms and in reducing recurrence in all three conditions did not give a breakdown in age groups.[228] In a clinical report of 75 chronic allergic rhinitis cases that included three cases in children 6 to 10 years of age and 17 cases in 11- to 20-year-olds, two different acupuncture treatments were administered according to TCM diagnoses. There was a cumulative 40% cure rate without age differentiation.[454]

Asthma

Asthma is the most common cause of chronic illness in childhood, with approximately 10% of children in the United States carrying the diagnosis.[259,297,442] A significant number of school days are lost because of asthma. A wide variation of incidence is found in different countries, with the highest rates in the United Kingdom, Australia, and New Zealand and the lowest rates in Eastern Europe, China, and India.[296,442] In recent years, prevalence of asthma is increasing worldwide, especially in children under 12 years of age.[17,382]

Although asthma can have onset at any age, 80% to 90% of asthmatic children have their first symptoms before 4 to 5 years of age.[297] Children up to age 4 years have distinct symptoms and require special consideration.[36] They have increased health service utilization, including a higher annual rate of hospitalization,[298] which has almost doubled in the United States from 1980 to 1992 for children 1 to 4 years of age.[17] The same trend is observed by other nations worldwide.[9,18] Among American children ages 5 to 14 years, asthma death rates almost doubled from 1980 to 1995.[17] New Zealand and Canada have observed a similar increase in severity and mortality.[73,387]

Asthma is a diffuse, reversible, obstructive lung disease with three major features: bronchial smooth-muscle spasm, edema and inflammation of the mucous membrane lining the airways, and intraluminal mucus plugs.[442] During the last two decades, chronic airway *inflammation,* rather than smooth muscle contraction alone, has been recognized as playing the key role in the pathogenesis of asthma in adults.[63,131] Although this association is less well established in children, recent guidelines for managing asthma in the pediatric population still have emphasized that treatment be directed toward the inflammatory aspects of the disease.[206,402,440] Chronic inflammation is caused by the local production of inflammatory mediators and an increase in recruitment of inflammatory cells, predominantly eosinophils and mast cells. Studies in young adults suggest that the chronic inflammation may be responsible for long-term pulmonary changes, including bronchial hyperresponsiveness, airway remodeling, and irreversible airflow obstruction. Because of difficulties in conducting studies in infants and young children, pediatric information is incomplete.[230] Limited studies have detected increases in inflammatory cells and thickening of the lung basement membrane in infants and young children and have found that asthmatic children have significantly lower lung function at 6 years of age compared with nonwheezers when both groups of children began with the same baseline at age 6 months. These data support the possible presence of an asthmalike inflammation at a very early age that is associated with nonreversible impairment of lung function.[263]

The excessive inflammatory changes indicate that asthma is caused by a poorly regulated "immunologic runaway response" that, instead of protecting the host, destroys normal structure. Increased concentrations of proinflammatory mediators, such as histamine and leukotrienes, are found in the airways as well as the blood and urine of asthmatic patients[131] during an acute attack and after allergen and exercise challenge.[34] Strong evidence correlates asthma with RSV infection; children who enter day nursery before age 12 months and who are exposed to viruses early in life have built up immunity, with decreased development of allergies.[88] In most children, whose asthma is triggered mainly by respiratory infections at a younger age, asthma symptoms appear to remit by the adolescent years.[263] In older children and teenagers, emotions play a significant role both as the cause of symptoms and as the result of interplay of a chronic illness affecting the child's self-image and family dynamics.[297]

The latest asthma management guidelines classify pediatric asthma into four groups of severity: mild intermittent, mild persistent, moderate persistent, and severe.[206] Mild intermittent asthma can be typified by *exercise-induced asthma,* a common pediatric condition. *Status asthmaticus,* defined as progressive respiratory failure that does not respond to conventional management, is becoming more prevalent in American children.[442]

Conventional treatments for pediatric asthma vary from allergen avoidance to state-of-the-art biochemical therapy. Avoiding allergens has been a successful management of asthma since the sixteenth century. Asthma is a much more complex problem today because of the increasing number of pollutants and chemicals in the environment that are potential allergens for children.[157] Parental education, especially in regard to smoking, can reduce hospital admissions.[449] Because infections that trigger asthma attacks are mostly viral,[31] antibiotics are not routinely indicated.

Medication consists primarily of bronchodilators and inhaled steroids, which are now justified as first-line therapy,[191] both as long-term management[402] and for acute attacks.[231] Because growth suppression due to inhaled corticosteroids has been well documented,[61] it is important to distinguish infants with early-onset asthma from those with transient wheezing.[469]

Recently, the FDA has also approved leukotriene receptor antagonists for use in asthmatic children under 4 years of age.[380] These agents counteract the hyperimmune response, resulting in diminished airway inflammation and decreased eosinophilia in the airway mucosa and peripheral blood.[34]

Parents turn to CAM for their asthmatic children because of drug side effects or fear of taking long-term medication, especially steroids.[11,62] A recent survey from Texas of 48 multicultural parents of children with asthma reported the usage of a variety of CAM therapies, including homeopathy, herbal therapy, vitamins, and massages. Hispanic parents were more likely to use herbal and massage therapies, whereas African-American parents often turned to prayers.[269] The relatively abundant studies on CAM therapy in asthma are on adults and often have flaws in methodology.

Significant improvement[15,308,310] and even complete cure[83] have been demonstrated with hypnosis, although most studies had weak designs. Hypnosis was recommended for children because they were found to be more hypnotizable,[68] but it is unclear whether the efficacy of hypnosis in asthmatic children is a reflection of children's greater suggestibility or a result of a more reversible disease process.[439] In a recent preschool program, 25 children ages 2 to 5 years received treatment with seven hypnotherapy sessions. The number of physician visits was reduced, and parental confidence in self-management skills increased.[217]

TCM has been used to treat asthma for centuries. Asthma epitomizes the Chinese medicine concept of "winter disease, summer cure," which means the best treatment for asthma should be given during the summer, when the child is symptom free. In China, many asthmatic children who were treated with herbal patches applied to acupoints during the summer had minimal or no symptoms during asthmatic seasons.[37,58,320]

Although several recent adult studies used herbs for asthma,[107] only two involved children. A controlled study comparing herbal treatment of 30 children with penicillin and aminophylline treatment of another 30 children revealed no significant difference in the response from the two groups.[242] A multicenter double-blind, placebo-controlled clinical herbal study from Taiwan evaluated 303 asthmatic children using TCM diagnoses.[170] The children were randomized into three different herbal and placebo groups. Although both groups showed improvement, the herbal groups showed greater improvement in symptomatology and in biochemical changes, such as increase in total T cells and decrease in histamine. An animal experiment using a 13-herb concoction revealed 99.1% efficacy in easing bronchial spasm.[170] Another animal study with an herbal preparation demonstrated strong smooth muscle relaxation through inhibition of histamine and acetylcholine.[242]

From the pediatric standpoint, it would be worthwhile to follow the development of external TCM approaches and noninvasive acupuncture. One clinical obser-

vation of pasting Chinese herbs to acupuncture points in 72 infants with acute bronchitis showed high cure and improvement rate, especially in infants.[461] Humoral immune substances, especially IgA, were found to be increased after treatment. Another clinical observation reported 78% efficacy in 46 children treated with external application of plasters made of herbal mixtures with antitussive and antiasthmatic properties and 88% efficacy in 17 children treated with antiasthmatic herbal patches. Success was also reported with a different herbal patch for acute attacks. The patches were well received by the children.[401]

Improvement from acupuncture treatment has been reported in asthmatic adults.[392,406,428,463] Despite methodologic weaknesses, it still seems that acupuncture may help asthma, especially drug-induced or allergic asthma.[439] In some European countries, almost a fourth of general practitioners believe in the efficacy of acupuncture in the treatment of asthma.[216] Its role in the United States is still controversial; some physicians accept acupuncture's effectiveness,[426] whereas others criticize data based on poorly conducted studies.[5]

The few current studies and clinical reports on acupuncture treatment of children with asthma are generally favorable.[168,457] A German practitioner reported good results treating asthmatic children using a simple acupuncture regimen in uncontrolled clinical experience.[145] One study demonstrated that although acupuncture did not affect the basal bronchomotor tone, when administered 20 minutes before exercise, acupuncture was shown to be effective in attenuating exercise-induced asthma,[128] which is common in children. One possible mechanism of acupuncture is in reducing the reflex component of bronchoconstriction, but not in influencing direct smooth muscle constriction caused by histamine.[460] For children who are fearful of or who cannot tolerate needles, safe and painless treatments such as cupping and auricular press pellets,[457] laser acupuncture,[288,292] and massage of acupuncture points[168] have also been found to be effective.

The most interesting future role for acupuncture in asthma lies in its potential both in stimulating an immune response and, more importantly, in regulating or modulating a hyperimmune response. At this time, ample biochemical data in the literature support the theory that acupuncture activates both the humoral and the cellular immune systems to protect the host.* Studies have also demonstrated that acupuncture can modulate the synthesis and release of proinflammatory mediators.[192,256,458] Current hypotheses suggest that this is most likely mediated through a common pathway connecting the immune system and the opioids,[30,321,363] which has been well known to be associated with analgesic effects of acupuncture.

Homeopathic remedies have been reported to be remarkably effective in asthma in adults,[120,345,427] and homeopathic doses of allergens have been shown to alleviate allergic symptoms and desensitize patients to allergens.[433] However, there is paucity of scientific data on homeopathy in both children and adults, as well as a lack of consensus among homeopaths as to the appropriate treatment, administration regimen, or

*References 86, 192, 306, 349, 360, 363.

potency for asthma.[439] Homeopathic practitioners believe that in chronic conditions such as asthma, homeopathic remedies can stimulate the child's innate healing ability, thereby leading to improvement.[197,198] Two recent large reviews on the role of homeopathy in clinical medicine concluded that, except for the occasionally demonstrated benefit, little scientific evidence exists to support the use of homeopathy in most clinical settings.[159,439] The availability of homeopathic, nutritional, and herbal remedies without a prescription is appealing to the asthmatic adolescent's desire for independence.[12]

In a number of European countries, chiropractic is often used for treatment of asthma.[186] One of the many difficulties in evaluating chiropractic efficacy lies in the varying abilities of the manual therapy practitioners. Natural human differences exist in manual applications and techniques. The practitioners have various training backgrounds, including physiotherapy, respiratory therapy, chiropractic, and osteopathy. A Danish questionnaire survey of 115 families with children up to age 7 years reported that 92% of parents who sought chiropractic help considered the treatment beneficial for their children.[77,423] An Australian survey reported that the most common CAM visits were to chiropractors.[87] A U.S. prospective, observer-blinded, clinical pilot evaluated 36 children from 6 to 17 years of age with mild to moderate persistent asthma for chiropractic treatment in addition to optimal medical management.[42] Children were randomized into treatment and sham spinal manipulative therapy (SMT) for 3 months. The children with combined SMT and medical treatment rated their quality of life substantially higher and their asthma severity substantially lower, and their improvements were maintained at 1-year follow-up. However, there were no significant changes in lung function or hyperresponsiveness. Further research is needed to determine which components of the chiropractic encounter are responsible for the improvements.

A controlled, patient-blinded trial of chiropractic manipulation for 91 children with mild or moderate asthma randomized the children into an active or a simulated chiropractic manipulation for 4 months.[20] Each subject was treated by 1 of 11 participating chiropractors, selected by the family according to location. No significant benefit was observed in the treatment group. A few studies in adults generated statistically insignificant data.[176] One study found subjective but not objective improvements in individuals with asthma who received treatment in a chiropractic clinic.[186] A 2001 systematic review revealed that the majority of the studies on SMT had poor methodology; the two good studies did not demonstrate significant differences between chiropractic SMT and sham maneuver.[167] The reviewers concluded that the evidence is still insufficient at this time to support the use of manual therapies for patients with asthma.

A German pilot study of 15 children ages 5 to 11 years with bronchial asthma combined relaxation using various techniques, including progressive muscle relaxation, autogenic training, fantasy travels, mantras, and periodic music, and demonstrated significant improvement in a number of pulmonary function parameters.[142] However, it is difficult to interpret the results because of the variety of techniques used.[143] A U.S. review of anecdotal reports indicated that massage therapy can improve asthmatic symptoms.[110–112]

Diarrhea

Acute diarrhea is a common occurrence in the pediatric population and a significant cause of pediatric morbidity and mortality in both developed and underdeveloped countries.[79,302,354] Each year an estimated 54,000 to 55,000 U.S. children are hospitalized for diarrhea,[136] and more than 4 million infants and young children worldwide die of acute infectious diarrhea.[354] Infants under 3 months of age have the highest risk for hospitalization and mortality.[304] Children under age 3 years have an average of approximately 2.5 episodes of gastroenteritis per year in the United States.[143,302] Internationally, the average is approximately 3.3 episodes annually.[354] Both diagnosis and treatment continue to be problematic in the pediatric population.[260]

The infectious pathogens that cause acute diarrheal episodes in children include viruses, bacteria, and parasites.[229] Transmission is most likely through the fecal-oral route, from ingesting contaminated food or water,[434] or in infants and toddlers, by mouthing contaminated toys. The nature of food-borne diseases is changing as more mass-produced, minimally processed, and widely distributed foods result in nationwide and international outbreaks of diarrheal disease instead of just a few individuals who shared a meal.[143] A majority of the cases are caused by viral infections. Rotavirus is the most prevalent,[264] and human astrovirus (HAstV) is a significant cause of diarrheal outbreaks.[434] Frequently, children are co-infected by several viruses. Viral diarrhea tends to involve the small bowel, producing large, watery, but relatively infrequent stools.[82] These illnesses usually have short, self-limiting courses,[6] typically lasting 3 to 7 days.[264] However, the diarrheal bouts can be devastating to children with compromised immune systems or structural abnormalities of the gastrointestinal tract.[143]

The most common bacterial agents are enteropathogenic *Escherichia coli, Shigella/Salmonella,* and *Campylobacter*.[82,264] These are much more virulent pathogens that usually cause mucocal injury in the small and large intestines, producing frequent, often bloody stools containing leukocytes.[82] *E. coli* has become an important public health problem in recent years, causing more than 20,000 cases of infection and up to 250 deaths per year in the United States.[220,381]

Transmission of infection is most often linked to consumption of contaminated meat, water, unpasteurized milk, leafy lettuce, alfalfa sprouts, and goat's milk,[220,413] and exposure to contaminated water in recreational swimming sites.[413] The most common parasitic infection is *Giardia lamblia,* which often causes secretory diarrhea without blood[264] and frequently leads to chronic diarrhea.[161]

Diagnosis and treatment are still inconsistent. Because most acute diarrheal conditions are self-limited, physicians often do not obtain stool cultures or examination for ova and parasites because the results are not available sometimes for several days. Stool culture can identify different types of bacteria, but detection of specific enteropathogenic strains of *E. coli* requires specific serotyping that is not performed in routine stool cultures.[220] It is expensive, time-consuming, and often not sufficiently specific or sensitive and therefore is not recommended for routine diagnosis.[151]

The primary treatment focus is on correction of *dehydration,*[275] which is the most important cause of morbidity and mortality in acute diarrhea.[243] Oral rehydration treatment (ORT) with solutions containing appropriate concentrations of electrolytes and carbohydrates is recommended by the World Health Organization (WHO) and has significantly reduced mortality.[82,140,367] After rehydration, early refeeding with a lactose-free[82] or normal, age-appropriate diet[229] is important for reducing diarrheal duration, severity, and nutritional impact. Supplementation with specific dietary ingredients that are lost in diarrhea, such as vitamin A, zinc, and folate, is also recommended.[140]

Because most of the acute infectious diarrheal conditions are viral, patients do not require antimicrobial therapy.[326,333] The rotavirus vaccine was put on the market in the United States in October 1998. This vaccine, as the natural infection, decreases the risk of acute rotavirus diarrhea by 50% and the risk of severe diarrhea with dehydration by more than 70%.[367] Improving hygiene such as handwashing is also important, especially in day care.

Breast-feeding is one of the most important preventive measures.[351] Continuation of breast-feeding has been found to control acute diarrheal episodes[140] and lower the frequency and duration of acute diarrhea, especially in infants under 6 months of age.[251] A large-scale randomized trial was conducted in 31 hospitals in the Republic of Belarus. Evaluation within the first year revealed that breast-feeding significantly reduced the risk of gastrointestinal tract infection compared with the control group.[228] However, a survey from Singapore of breast-feeding mothers at 6 months postpartum revealed no significant differences in the rates of diarrheal diseases between breast-fed and non–breast-fed infants.[64]

Treatment with antimicrobial therapy must be instituted carefully and only with specific identification of pathogen and drug sensitivity. With the increasing frequency of antibiotic resistance, common antibiotics may be ineffective in patients with acute diarrhea.[143,351,367] Treatment of salmonellosis with antibiotics can prolong the carrier state and lead to a higher clinical relapse rate.[143] Injudicious antimicrobial therapy may also lead to susceptibility to other infections, enhance colonization of resistant organisms,[29,143] and disrupt the normal intestinal flora, the body's natural defense against infection.[270]

Homeopathy has the most convincing evidence of efficacy in treating diarrhea in children. A randomized, double-blind clinical trial comparing homeopathic medicine with placebo in the treatment of acute childhood diarrhea was conducted in Nicaragua in 1991. Eighty-one children 6 months to 5 years of age were given treatment with individualized homeopathic medicine. Standard ORT was also given. There was a statistically significant decrease in the duration of diarrhea in the treatment group.[182] Although criticisms of the study include homeopathic theory being inconsistent with scientific belief[378] and possible toxicity of the dilute homeopathic remedies,[210] the report was also praised for being an impressive,[54] well-designed[44] study that paves the way for future research into the efficacy of homeopathy and other CAM therapies.[115] Using the predefined measures based on the 1991 study, the same group of researchers more recently carried out a similar study and replicated the same findings of decrease in the duration of diar-

rhea and number of stools in 126 children in Nepal, ranging in age from 6 months to 5 years.[183]

A few studies have demonstrated effectiveness of *acupuncture* in pediatric diarrhea. The treatment protocols in point selections generally depend on TCM diagnoses, with the majority of points chosen on the two major digestive channels.[109,190,245,398,455] Acupuncture has also been shown to induce favorable anatomic and biochemical changes in improving intestinal peristaltic function and in enhancing both humoral and cellular immunity.[244]

A randomized study comparing *shallow* acupuncture treatment (needles inserted superficially and withdrawn swiftly) with drugs in 761 children ages 1 to 35 months reported significantly higher therapeutic effect in the acupuncture group.[244] The diagnosis and subsequent choice of points were based on TCM principles, not on stool culture results. Unlike the homeopathy study, this investigation grouped together patients with acute and chronic diarrhea. In a clinical trial using one Chinese herbal formula for treatment of acute diarrhea, there was significant reduction of symptoms and duration of diarrhea.[38] A clinical report of 20 years' application of a seven-herb concoction in 419 children demonstrated 96.4% improvement and 90% cure rate.[241] This nonrandomized, nonblinded report used TCM diagnoses that encompassed a variety of diarrheal conditions, including acute, chronic, infectious, and noninfectious diarrhea. The mechanisms were hypothesized as eliminating pathogenicity, improving immunity, accelerating intestinal digestion, and inhibiting intestinal peristalsis. In a clinical report comparing Chinese herbs to Western medicine in 158 children with diarrhea due to rotavirus, the herbs were reported to be superior and had a viral inhibitory rate of 71.43%, but no mention was made of the efficacy of conventional medicine.[435]

Chronic nonspecific diarrhea of childhood differs from acute diarrhea in that it is not associated with significant morbidity. Once potentially serious causes are excluded, appropriate diet can be instituted to minimize complications, and reasonable time is then allowed for spontaneous resolution.[414] In a nonrandomized clinical trial involving 30 children ages 3 months to 8 years with chronic diarrhea of 2 to 4 months' duration that was unresponsive to Western medicine and TCM, individualized acupuncture treatment eliminated symptoms and normalized stools.[109]

Colic

Infantile colic is estimated to affect 20% to 30% of all infants under 4 months of age and remains a medical enigma of nature versus nurture. Colic may represent a heterogeneous expression of developmental variance, unmet biologic needs, psychologic or emotional distress from poor parent-infant interaction, intrinsic temperamental predisposition, colonic hypermotility,[278] or milk allergy.* Although colic is self-limiting by 3 to 4 months of age, treatment is mandated because the psychologic

*References 69, 133, 184, 185, 188, 204, 356.

consequences may result in a disturbed mother-infant relationship.[174,355] Evidence suggests that uncontrollable crying is the precipitating factor in many cases of infant abuse.[178,441]

Because the precise etiology is not understood, the therapeutic goal of Western medicine is not aimed at "curing" colic but at containment of the crying.[328] Removing cow's milk protein from the mother's diet, changing formula, and prescribing antispasmodic medications are the mainstays of conventional treatment and may be helpful.[69] Treatment is often directed toward behavioral changes in mothers. Parents may be referred for therapy to learn parenting and coping skills.

CAM treatments yield inconsistent results. Herbs have not yet been proven to be efficacious,[265] although a survey of 51 Hispanic mothers in an urban neighborhood in Texas revealed that herbal teas were commonly used for colic.[346] Evidence is controversial for chiropractic treatment of colic. A multicenter prospective, uncontrolled study of 316 colicky infants involving 73 chiropractors in 50 clinics in the United Kingdom for 3 months demonstrated efficacy with chiropractic SMT in controlling colic, as reported by mothers in 94% of cases.[215] A retrospective questionnaire study in 1985 revealed satisfactory results of chiropractic treatment in 90% of infants.[301] A randomized, blinded, placebo-controlled clinical trial of 100 infants with typical colic reported that chiropractic manipulation was no more effective than placebo.[307] However, a randomized, controlled, 2-week trial comparing SMT with the drug dimethicone demonstrated significantly better results in the chiropractic treatment group.[444]

Craniosacral therapists empirically claim success in treatment of colic.[19] Massage therapists have also found empirically that touch therapy can decrease severity of colic.[111] In a Finnish clinical trial, 58 infants less than 7 weeks of age perceived as colicky by their parents were randomized into an infant massage group ($n = 28$) and a crib vibrator group ($n = 30$).[173] Over 4 weeks there was no difference in the reduction of colicky crying between infants receiving massage and those with a crib vibrator, leading the investigators to conclude that the decrease of crying reflects more the natural course of early infant crying and colic than a specific effect of intervention. Therefore infant massage is not recommended as treatment for colic.

Enuresis

Enuresis is defined as inappropriate or involuntary voiding during the night at an age when urinary control should be achieved.[7] Enuresis is a complex disorder with poorly understood pathogenicity and pathophysiology. It affects children worldwide,[297] with about 5 to 7 million children affected in the United States[281] and as many as 30% of school-age children in Italy.[48]

The condition is classified as *primary nocturnal enuresis* (PNE) when the child has never been dry at night or *secondary nocturnal enuresis* (SNE) when wetting follows a dry period, usually after an identifiable stress.[203,297] By age 8 years, 87% to 90% of children should have nighttime dryness.[65] In 85% of PNE patients, bedwetting is monosymptomatic, with a spontaneous remission rate of 15% per year of age. Both the etiology and the pathophysiology of enuresis are still not well understood.

Multiple factors may interplay: genetic and psychologic predispositions, delayed maturation of the central nervous system, sleep disorders, urinary reservoir abnormalities, detrusor-sphincter incoordination, and urine production disorders.[48]

Although enuresis is benign, treatment is warranted because of adverse personal, family, and psychosocial effects.[281,282] Nocturnal enuresis delays early autonomy and socialization because of a decrease in self-esteem and self-confidence and a fear of detection by peers. The child may be at increased risk for emotional or even physical abuse from family members.[368,438]

The conventional treatment modalities are still controversial. Because the vast majority of PNE cases resolve spontaneously with time, treatment should carry minimal or no risk. The *moisture alarm* is both safe and inexpensive and should be the treatment of choice in most cases[65,286,357] but is often the one least prescribed.[15,258] The medications imipramine and DDAVP were frequently chosen as first-line treatment choices. Adjunctive therapy may include bladder-stretching exercises, which have a success rate of 30%, and behavioral conditioning.[357]

Numerous CAM therapies are available for childhood enuresis; the most common are hypnosis, acupuncture, and biofeedback. Less common CAM therapies are chiropractic and nutrition management.

Hypnotherapy has been recognized by conventional practitioners as a potentially effective therapy.[262,286] Uncontrolled studies have reported high rates of success.[24,67,74,308,310] In one comparative study of imipramine and direct hypnotic suggestion with imagery for functional nocturnal enuresis in 5- to 16-year-old patients, 76% of the imipramine group and 72% of the hypnosis group had positive response.[21] After termination of treatment, the hypnosis group continued practicing self-hypnosis. At 9-month follow-up, 64% of the hypnosis group maintained dryness compared with only 24% of the imipramine group. Hypnosis and self-hypnosis were found to be less effective in younger children (ages 5 to 7 years) compared with imipramine treatment.

Hypnotherapy has the added advantage that nonphysician health care professionals, such as nurse practitioners, can easily learn the technique to help children.[163] A recent review of controlled studies reported promising findings for hypnosis in children with enuresis, but none of the interventions can currently qualify as efficacious. A major limitation is the lack of treatment specification via a manual of its equivalent.[283] The requirement that the child practice the self-hypnosis technique several times a day limits compliance with the program.[286]

Acupuncture has been used as an effective treatment for enuresis since at least the 1950s.[459] Current worldwide literature in general demonstrates its viability as either a primary or an adjunctive therapy for the enuretic child.* A Turkish clinical study on 162 subjects treated with electroacupuncture therapy reported a success rate of 98.2%.[418] Acupuncture has been found to be successful both in decreasing the occurrence of enuresis during treatment and in exerting a long-term effect after treatment.[35,48,370] Parents also report a decrease in sleep arousal threshold.[35] Although the

*References 23, 35, 48, 52, 61, 172, 175, 194, 281, 284, 370, 415, 453, 459.

precise mechanism of acupuncture is still unknown, a multidisciplinary approach that included acupuncture demonstrated on electroencephalography (EEG) that treatment normalized activities of the cerebral cortex.[415]

Data from China usually consist of clinical reports of large sample populations. Results in one study of 500 patients treated with acupuncture on only two body points demonstrated cure in 476 patients (98%), improvement in 14, and no response in 10 patients.[459] Number of treatments ranged from one to three in 453 patients and four to six in 23. Another study of 302 enuretic children ages 3 to 15 years (10 over 15 years; oldest 23 years) used TCM diagnosis of organ imbalance and different combinations of acupuncture points, with 10 treatments constituting one course.[453] The results showed that 221 patients were cured, 71 showed marked improvement, and 10 were "effectively" treated. Treatment using scalp acupuncture has also been reported to be successful. In one clinical study, 59 children ages 4 to 17 years were treated for 10 to 15 sessions, and some needed a second course.[61] Cure was obtained in 9 children, marked improvement in 27, improvement in 19, and no response in 4 children.

In all these clinical reports, subjects of a wide range of ages were included in the same study; the discussions were short and generalized, giving very few or no details about the children (e.g., types of enuresis, duration of enuresis, number of wet nights, types of improvement); the methods of treatment were laden with numerous variables (e.g., number of points, treatment courses).

A clinical study from Italy of 20 children with bladder instability due to uninhibited contractions of the detrusor muscle reported that acupuncture treatment was successful in gradual elimination of enuresis in 11 and improvement of symptoms in 7 children. The mechanism was not clarified.[284] A Russian clinical trial of using acupuncture specifically for enuresis due to neurogenic bladder dysfunction demonstrated that acupuncture was beneficial in 17 of 25 children.[194] In a clinical report of 54 enuretic children, short-term success in reducing wet nights was 55% with acupuncture versus 79% with DDAVP, whereas long-term success rates were 40% and 50%, respectively.[48] A Zagreb report of a clinical trial of acupuncture treatment on 37 children with mean age of 8 years who failed psychotherapy demonstrated a statistically significant decrease in enuresis even at 6 months after treatment.[350] A self-controlled regulating device operating on the principles of acupuncture was found to be effective in the treatment of nocturnal enuresis attributable to neurogenic bladder dysfunction.[233] A controlled clinical study of 40 children between 5 and 14 years of age randomly selected into four groups of 10: treatment with DDAVP alone, acupuncture alone, combined DDAVP with acupuncture, and placebo. Efficacy of treatment, expressed as a percentage of dry nights, was high in both DDAVP and acupuncture groups, but the combined-treatment group had the best results.[52]

A Scandinavian clinical trial used traditional Chinese acupuncture for treatment of primary persistent PNE in 50 children ranging in age from 9 to 18 years. The response rate was monitored at 2-week, 4-week, and 3-month intervals.[370] Within 6 months, 43 (86%) of children were completely dry and 2 (10%) were dry on at least 80% of nights, leading the clinicians to conclude that acupuncture is effective, with

stable results. Another Scandinavian study investigated the efficacy of electroacupuncture in treating 25 children ranging in age from 7 to 16 years.[35] Twenty treatments were administered over 8 weeks. The number of dry nights consistently increased when the children were reevaluated at 3 weeks, 3 months, and 6 months after treatment. Five children had more than 90% reduction of wet nights at 6 months, and 65% had more dry nights at the 6-month follow-up.

A recent teaching round at the China Academy of Traditional Chinese Medicine in Beijing discussed successful acupuncture treatment of a complicated case of enuresis in a 16-year-old student who had previously failed both Western and Chinese medicines for his physical and emotional sequelae.[171] Using TCM diagnosis of organ imbalances, the treatment combined body acupuncture, scalp acupuncture, and auricular acupressure seed. The patient began improving after three treatments in the first week. He received 3 more weeks of treatment, with no recurrence of enuresis at 6-month follow-up.

Children are often unwilling to undergo needle acupuncture because of fear of pain,[61] prompting researchers to use noninvasive forms of acupuncture. Simple acumassage has been previously reported to be beneficial to the enuretic child.[21] An Austrian prospective, randomized trial evaluated efficacy of laser acupuncture versus desmopressin in 40 children over age 5 years with PNE.[337] At 6-month follow-up, the desmopressin-treated group had 75% success rate with complete resolution of symptoms, an additional 10% had a more than 50% reduction in wet nights, and 20% did not respond. The laser acupuncture group had 65%, 10%, and 15% rates, respectively. The results were not statistically significant. Therefore laser acupuncture should be considered as an alternative, noninvasive, painless, cost-effective, and short-term therapy in children with normal bladder function and high nighttime urine production.

Worldwide reports have demonstrated efficacy in treating enuresis with *biofeedback*,[164,250,318,332] which aims at learning or relearning of influence of involuntary functions.[266] A clinical study from Italy treated 16 boys and 27 girls ages 4 to 14 years with detrusor-sphincter dyssynergy. Biofeedback was successful in all the children, with SNE resolving significantly sooner than PNE and girls responding better than boys. Two-year follow-up still revealed an 87.18% success rate, with 80% at 4 years.[332] In a French study, 120 children with three predominant urinary disorders that included nocturnal enuresis were treated with biofeedback. Detrusor-sphincter discoordination was diagnosed in 33 children. Pelvic floor biofeedback produced excellent results in these children.[323]

Belgian investigators reported a clinical biofeedback study of 24 children with median age of 10.4 years who did not respond to anticholinergics.[164] Seventeen subjects had complete resolution of enuresis, six had a decrease in symptoms, and one child did not respond. At 6-month follow-up, two children in the cured group had recurrence of enuresis. Another study from Belgium also reported success in using biofeedback in 26 children with pseudo-detrusor-sphincter dyssynergy; 17 were completely cured, and 5 improved considerably.[266] A Spanish study used biofeedback to treat unstable detrusor in 65 enuretic children; complete disappearance of symptoms was seen in 70.5%, with improvement in 78.2%.[318]

In a U.S. report of 8 boys and 33 girls ages 5 to 11 years who underwent an average of 6 hours of biofeedback for nocturnal and diurnal enuresis, improvement was noted in 90% of nocturnal enuresis and 89% of diurnal enuresis.[272] Another U.S. clinical study used biofeedback for 21 children with dysfunctional voiding; 17 (81%) had an excellent response, 3 (14%) had a fair response, and 1 (5%) was too inconsistent to rate.[70] The average number of sessions to achieve a consistent urodynamic response was 3.7 (range 2 to 14). Average follow-up was 34 months (range 14 to 51 months). The investigators recommended biofeedback as an effective method that requires only a short period for treating dysfunctional voiding.[70]

All these worldwide studies were clinical reports, not randomized, controlled, blinded studies.

The efficacy of chiropractic manipulation in enuresis has been inconsistent. One clinical report identified an 8-year-old boy with functional enuresis who had successful treatment with manipulation.[37] In an uncontrolled study of 175 children ages 4 to 15 years, with responses monitored by parents, chiropractic manipulation resulted in only 15.5% success.[234] However, a randomized, controlled clinical trial of 57 children demonstrated that 25% of the treatment group had 50% or more reduction in enuretic symptoms, although the pretreatment to posttreatment change in wet night frequency was not statistically significant, and there was no long-term follow-up.[341] A comprehensive review of the literature revealed that SMT was no more effective than the natural regression of enuresis with age.[225]

Food allergy as a cause of enuresis has been in the literature for several decades.[106] A recent study of children with severe migraine or attention deficit disorder (ADD) included 21 children with enuresis. Oligoantigenic diets were successful in curing 12 children and improving enuresis in 4 other children. Relapse of wetting occurred when foods were reintroduced; the substances implicated most often were chocolate, citrus, fruits, and milk from cows.[281] Although no studies are available on naturopathic approaches, which focus on natural remedies (e.g., corn silk and tea, tea and honey), physicians should not dismiss parental opinion that these remedies may be safe and effective.

The future of treatment for enuresis should combine various methods to increase the probability of treatment success and minimize risk to the child.[281]

Skin Rashes

Atopic dermatitis affects almost 10% of all children[56] and 20% of children ages 3 to 11 years.[201,202] It accounts for more than 30% of outpatient pediatric visits.[95] Most children with atopic dermatitis typically come to medical attention with cradle cap and facial and extremity rashes by age 2 to 3 months.[95]

Despite considerable research, the etiology of allergic disease remains poorly understood.[16] Allergic dermatitis can be thought of as an inherited skin "sensitivity" that reacts to various external allergens and changes in psychologic states.[357] Food causes atopic dermatitis in 50% of infants, 20% to 30% of young children, and 10% to 15% of children after puberty.[395] Topical steroids remain the main therapeutic

method. Dermatologists tend to prescribe antibiotics and use potent topical steroids,[343] which are more readily absorbed in children and can result in hypothalamic-pituitary-adrenal axis suppression.[179] New immune modulators have shown promise in severe atopic dermatitis.[149,212]

CAM therapies are increasingly used for dermatitis,[127] although most of the information is in clinical reports, and research data are limited. A database review of 272 randomized clinical trials of atopic eczema covering at least 47 different interventions revealed that evidence is still insufficient to make recommendations on maternal allergen avoidance for disease prevention, herbs, dietary restrictions, homeopathy, massage therapy, hypnotherapy, or various topical CAM therapies.[162] A multicenter randomized clinical trial conducted in 31 hospitals in the Republic of Belarus reported that breast-feeding significantly reduced the risk of atopic eczema compared with the control group in the first year of life.[228]

Psoriasis was found to worsen with CAM treatments such as herbs, dietary manipulation, and vitamins.[116] Dietary management with evening primrose oil, rich in gamma-linolenic acid, has been found to be inconsistently effective in small studies. Fish oil supplements (enriched in n-3 polyunsaturated fatty acids) have also been used.[357]

Various herbs offer relief for eczema.[127] A placebo-controlled, double-blind trial used a Chinese herbal prescription specifically formulated for widespread nonexudative atopic eczema. Thirty-seven children were randomly assigned to 8-week active treatment and placebo, with an intervening 4-week "washout" period. The response to active treatment was significantly superior to placebo, without evidence of hematologic, renal, or hepatic toxicity.[373] The same investigators monitored the children over the following 12 months. Eighteen children had at least a 90% reduction in eczema, and five showed lesser degrees of improvement.[374] Two randomized, double-blind placebo-controlled trials from Singapore revealed that a concoction of 10 Chinese herbs was efficacious in the treatment of atopic dermatitis in both children and adults, and that the mechanism may be through the beneficial immunosuppressive effects. Toxicity is a concern, however, because exact dosing of the active derivatives is difficult to achieve.[339]

Acupuncture treatment of acne has been reported to be successful[247] in as many as 91.3% of adolescents given treatment.[456] Other TCM techniques have also been reported to be helpful.[57] A clinical trial treated 20 children with severe, resistant atopic dermatitis with hypnosis.[393] Nineteen showed immediate improvement, 10 maintained improvement in itching, and 9 maintained improvement in sleep disturbance 18 months after treatment.

Homeopathy is frequently used to treat dermatitis. In one homeopathic clinic in Israel, more than 80% of the patients expressed satisfaction with treatment. However, the authors of the survey believed that homeopathic medicine complements conventional medicine and is not an alternative.[316] Chiropractic treatment has also been sought by children for allergic problems.[303]

A small British study tested the hypothesis that massage with essential oils *(aromatherapy)* used as a complementary therapy in conjunction with normal medical treatment would help to alleviate the symptoms of childhood atopic eczema.[9] Eight

children were randomized into the treatment group, who were massaged with oil, and the control group, massaged without essential oil. No significant difference was found between the two groups. There was a later deterioration of eczema in the oil massage group, suggesting allergic contact dermatitis provoked by the essential oils themselves.

Attention Deficit–Hyperactivity Disorder

Attention deficit–hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder of childhood, with a prevalence rate between 2% and 11%,[373] averaging about 5%.[14,371,405] The road constellation of hyperactive, inattentive, and impulsive symptoms combined with the multiple comorbid conditions makes the definition and ADHD controversial and the diagnosis flawed.[405] ADHD is a chronic, heterogeneous condition with academic, social, and emotional ramifications for the school-age child.[371] The disabling symptoms persist into adolescence in approximately 85% of children and into adulthood in approximately 50%.[14,32] There is a developmental pattern in the primary symptoms of the disorder; hyperactivity diminishes while attentional deficits persist or increase with age.[371]

The precise etiology of ADHD is still unknown, and assessment and management remain diverse. Medication continues to be the mainstay of treatment, with methylphenidate (Ritalin) the treatment of choice.[141] The tricyclic antidepressants were added as an alternative medication in the 1970s,[32] with clonidine, buspirone (Buspar), and other antidepressants and neuroleptics added to the list in the 1980s.[55,60] Although it is generally agreed that drugs are beneficial on a short-term basis, there is a paucity of data on the long-term efficacy and safety of medications, especially in children younger than 3 years of age. These drugs have not been shown to produce long-term gains academically or socially.[90]

Besides pharmacotherapy, a multimodal approach using a combination of drugs and other methods, such as *cognitive-behavioral therapy* (CBT), psychotherapy, social skills training, and school interventions, is frequently prescribed for ADHD. CBT represents the most widely used alternative to pharmacotherapy, although previous studies have shown disappointing results.[2,3,45,177] In 1992 the National Institutes of Mental Health (NIMH) began a 14-month, multisite clinical trial, the Multimodal Treatment Study of ADHD (MTA).[160,189] The results indicated that high-quality medication management (with careful titration and follow-up) and a combination of medication and intensive behavioral therapy were substantially superior to behavioral therapy and community medication management. There is slight advantage of combination of medication and behavioral therapy over medication alone. *Psychotherapy* can be an effective adjunct to medication[364,365] but usually requires a long-term commitment to several years of treatment.

Concerns about side effects of medication,[232,391] treatment acceptability,[27,334] and compliance are additional factors that complicate management of the ADHD child. Clearly, there is room to explore safe, acceptable, and relatively easy alternatives. Interest is increasing in more natural, holistic integrative approaches to ADHD.

Studies using CAM therapy for treating ADHD encompass more than the usual research difficulties because of the complexity and heterogeneity of the disorder, as well as subjective evaluation by parents and teachers of a wide range of 18 characteristics that may qualify for several different diagnoses. A majority of the CAM therapies to date continue to have mostly anecdotal and empiric evidence. The few well-designed studies include biofeedback, herbal medicines, dietary modifications or supplements, and acupuncture.[46]

Studies have demonstrated that there is a significant difference in baseline EEG measurements in children with attention deficit disorder (ADD) compared with normal-achieving preadolescent males. These differences occur mainly in the parietal region for on-task conditions[187] and in the cortex and corticothalamic excitatory and inhibitory interactions.[252,255] *Biofeedback* or *neurofeedback* is a technique for modifying neurophysiology for learning.[252] In 1991 a critical review of 36 studies in which biofeedback was used as a treatment for hyperactivity indicated that biofeedback alone had not been effectively evaluated, and methodologic problems limit generalizations that it may be applicable to the entire hyperactive population.[238] A 2001 review continues to indicate that although anecdotal and case reports cite promising evidence, methodologic problems coupled with a paucity of research preclude any definitive conclusions as to the efficacy of enhanced alpha and hemisphere-specific EEG biofeedback training.[340] Some recent studies using more sophisticated technology claim that neurofeedback can improve attention, behavior, and intellectual function in the child with ADD,[49,246,253] with measurable EEG improvement in the frontal/central cortex.[295] Its stabilizing effect has also been found to last as long as 10 years after treatment.[407]

Hypnotherapy and biofeedback do not appear to alter the core symptoms of ADHD but may be helpful in controlling secondary symptoms. These methods allow children to become active agents of their own coping strategies.[26]

DIET THERAPY

A mailed questionnaire survey of 381 children with ADHD with a 76% response rate reported that 69% were using stimulant medication and that 64% of the respondents used or were using a nonprescription therapy. Diet therapies constitute the most common CAM therapy (60%).[397] One review of CAM therapy lends support to individualized dietary management and specific trace element supplementation in some children with ADHD.[26]

Nutritional management of ADD includes elimination diet, megavitamins,[26,372] supplements, and trace element replacement. Simple sugar restriction seems ineffective.[14] The well-known Feingold diet eliminates natural salicylates, food colors, and artificial flavors. Studies have demonstrated mixed results.[211] Megavitamins were demonstrated to be ineffective in the management of ADD in a two-stage study with clinical trial and double-blind crossover. Potential hepatotoxicity is a major concern with use of megavitamins.[152]

In a recent longitudinal, nonrandomized clinical trial, 17 ADHD children were given a glyconutritional product containing saccharides known to be important in

healthy functioning and a phytonutritional product containing flash-dried fruits and vegetables.[93] Five children were not receiving methylphenidate (Ritalin), six children were taking prescribed doses of methylphenidate, and the remaining six children had their medications reduced by half after 2 weeks. The glyconutritional supplement was administered for the entire 6 weeks, and the phytonutritional supplement was added after 3 weeks. The teachers and parents rated behavioral items for ADHD, oppositional defiant disorder, and conduct disorder. The conclusion was that the glyconutritional supplement decreased the number and severity of ADHD, associated ODD and CD symptoms, and side effects of medications during the first 2 weeks of the study; there was little further reduction with the addition of the phytonutritional supplement. The three groups did not differ statistically in degree or reduction of symptoms.[93] This 6-week study had too many variables and too few subjects without control for a definitive conclusion, although the concept of simple nutritional supplement is important to explore.

There is increasing interest in abnormality of fatty acid metabolism as the etiology of at least some features of ADHD.[344] These abnormalities can range from genetic abnormalities in the enzymes involved in phospholipid metabolism to symptoms that were reportedly improved after dietary supplementation with long-chain fatty acids.[436] In a randomized, double-blind, placebo-controlled trial of docosahexaenoic acid (DHA) supplementation, 63 children ages 6 to 12 years receiving stimulant medication were randomly assigned to receive DHA supplementation or placebo for 4 months. There was no significant improvement in the treatment group.[429]

Oligotherapy focuses on deficiency of trace elements in children with ADD.[221,389] In a Polish controlled clinical trial, magnesium deficiency was found in blood and in hair of hyperactive children.[390] Fifty 7- to 12-year-old ADD children were given a magnesium supplement of 200 mg/day for 6 months while the control group of 25 children continued on their medical regimen. Increase in magnesium contents in hair correlated with a significant decrease of hyperactivity in the treatment group, whereas hyperactivity actually intensified in the control group. The same investigators also found deficiencies of copper, zinc, calcium, and iron, with magnesium being the most common deficiency, in 116 children with ADHD.[389]

CHINESE HERBAL THERAPY

A thorough literature review of alternative treatments for ADHD identified 24 CAM therapies and reported that Chinese herbal treatment has promising pilot data.[14] A clinical trial using Chinese herbs in the treatment of 66 children with a diagnosis of hyperkinesia based on the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders,* ed 3 revised (*DSM*-IIIR) criteria demonstrated 84.8% effectiveness in ameliorating hyperactivity and improved attention and school performance.[401] The herbal remedy was prepared according to the TCM diagnosis of common energetic (qi) imbalance found in these children. Clinical observations were substantiated by laboratory findings of significant increase in urinary content of norepinephrine, dopamine, dihydroxyphenylacetic acid, cyclic adenosine monophosphate, and creatinine.[401] In a randomized study, Chinese herbal treatment was found

to be comparable to methylphenidate but had fewer side effects.[464] Research is currently being conducted to investigate the efficacy of herbal and homeopathic remedies because current evidence is inconsistent or lacking.[26]

In a prospective, randomized, double-blind pilot study funded by NIH that integrated *DSM*-IV diagnostic criteria, conventional theories of frontal lobe dysfunction, and neurotransmitter abnormalities with traditional Chinese theories of energetic imbalances, laser acupuncture was used in the treatment of ADHD in 7- to 9-year-old children.[249] Preliminary data on the six children in the treatment group showed promise in reducing signs and symptoms of ADHD. Using Conners scale as a weekly follow-up measure, improvement in classroom behavior was reflected by substantial drops in the teachers' scores before and after treatment in five of six children. The parents' scores dropped in three children but did not change in the other three children (Figures 11-1 and 11-2). One child was promoted to the gifted program, and another demonstrated marked improvement in learning disabilities.

HOMEOPATHY AND CHIROPRACTIC

There are no data at this time on homeopathic or chiropractic treatment of ADHD, although many practitioners claim anecdotal success with the use of homeopathic desipramine (Norpramin) and manipulation.

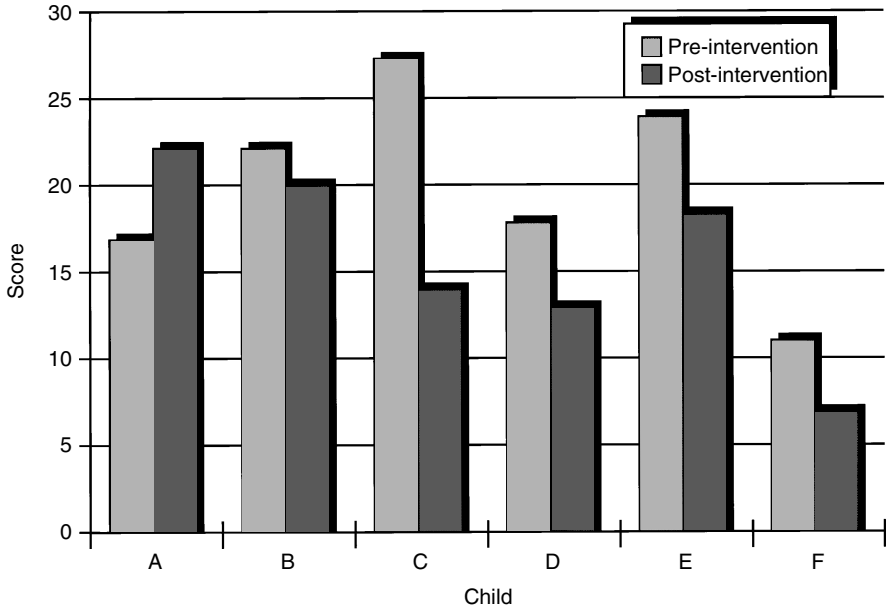

FIGURE 11-1. Teachers' scores (Conners scale) for each of six children before and after treatment of attention deficit–hyperactivity disorder (ADHD) by laser acupuncture.

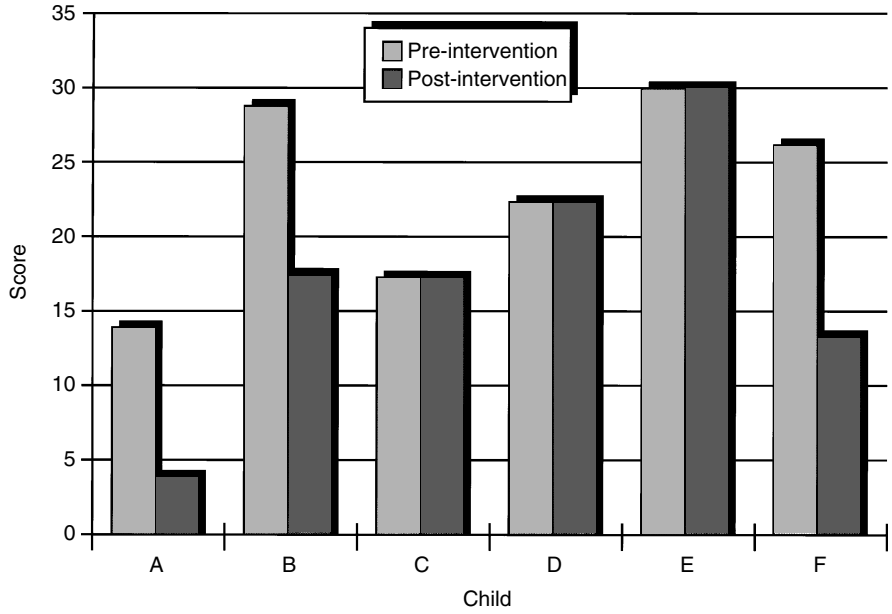

FIGURE 11–2. Parents' scores (Conners scale) for each of six children before and after treatment of ADHD by laser acupuncture.

Physicians and CAM Therapy in Children

Pediatric use of CAM therapies continues to increase.[385] It is therefore advisable for physicians who treat children to take a thorough history of CAM use, especially in those with chronic disorders, to become knowledgeable about the various alternative therapies that can complement conventional care. This allows practitioners to consider possible adverse effects or interactions of CAM with conventional therapy, to open lines of communication with CAM providers, and even to consider integrating effective CAM therapy into their medical regimen. Although CAM therapy is in general considered safe, there have been a few reports of significant side effects.[219,271] Continuous research is needed to investigate the safety and efficacy of CAM therapies for children; to address explicitly the tremendous heterogeneity between and among the practices, beliefs, and providers of professional and lay services; and to study how CAM may enhance the quality of mainstream health services.[208]

Although children are entitled to new therapies, pediatric research in CAM is further complicated by children's vulnerability to violation of their personal rights and to risk exposure.[420] In children of the same age, varying cognitive capacity can be required for informed consent.[315,353] Differences in physiologic maturation can change the kinetics, end-organ responses, and toxicity of therapy, so data from adult studies cannot be extrapolated for children.[240] Even in conventional medicine, children are

often rendered "therapeutic orphans"[376] because of history of abuses in pediatric research, a heightened sensitivity to risks in children—especially since the thalidomide disaster—and a limited market potential.[353] In the United States, 80% of drugs have age limits or contain disclaimers for pediatric use.[135] Therefore protecting children by giving them only scientifically proven therapies is counterbalanced by denying them access to possible safe and effective treatment that may not be proven for many years to come.

A frequently expressed concern is that visits to CAM practitioners may cause delay in diagnosis.[467] A more serious concern is the lack of formal pediatric training in many CAM therapists so that they may fail to recognize potentially serious illnesses, especially in infants.[236] Conventional medicine is endowed with superb technologic support for making physical diagnoses, whereas some CAM practitioners may claim the ability to diagnose a discomfort on an "energetic level" that is not yet defined biomedically. An integration of these disciplines should provide a better understanding of human health and disease. Currently, many medical centers are incorporating courses in CAM. When the gap between conventional medicine and CAM is bridged, delay in diagnosis can be minimized, and the common goal of finding safe and effective treatment for children can be achieved.

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