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Primary Care from Infancy to Adolescence

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What is primary care? And who is this primary care practitioner/pediatrician or ''PCP'' to whom we so often refer? How limited or wide is our role? Primary care, in the world of medicine, is conventionally defined as ''the activity of a health care provider who acts as a first point of consultation for all patients'' [1]. Historically, many types of health care practitioners have served as primary care providers for children, including pediatricians, family practice doctors, nurses, and alternative health care practitioners. In truth, the primary care of a child is shared by many: pediatricians or other health care practitioners, the child's family and community, and the child herself. The scope of primary care includes a focus on prevention and well care, and implies a comprehensive, collaborative, and coordinated approach exemplified by the medical home model developed by the American Academy of Pediatrics (AAP) [2]. The medical home model is holistic in the sense that it views the health of a child as intricately connected to the child's environment—her family, her community, and the world around her. And holistic pediatrics—the concept of nurturing the whole child toward optimal wellness—is simply ''good medicine,'' as noted by Dr. Kathi Kemper [3] in her Presidential Address to the Ambulatory Pediatric Association.

Integrative pediatrics, a holistic practice that includes an examined integration of complementary and alternative medicine (CAM) and conventional therapies, is ideally suited for primary care. In addition to supporting medical home tenets, integrative pediatrics emphasizes a collaborative and individualized approach to working with families and other health care

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practitioners, including open discussions about CAM therapies, environmental health concerns, nutrition, immunization, and parenting practices. The appeal of integrative pediatrics for pediatric primary care is indeed growing, as evidenced by the increased use of CAM therapies for well children and those who have special health care needs [4–7]. Adolescent use of CAM in particular is rising [8,9], and primary care practitioners need to engage teens in discussions about safety and efficacy concerns, as they would with any therapies. Pediatricians are in fact more interested than ever in learning about CAM therapies so that they can more effectively communicate and connect with their patients and families [10]. To increase awareness and knowledge of commonly used CAM therapies in primary care practice, we describe three cases that illustrate the potential for evidence-based integrative care from infancy through adolescence.

Infancy

Ideally, primary care is grounded in the concept of prevention and emphasizes regular well care visits to provide anticipatory guidance for families. We meet with families most frequently in the first months of a child's life to assess growth and development and also to establish a relationship so that together we can create a foundation for optimal health for each and every child. In the scope of daily practice, however, primary care pediatricians encounter various common conditions requiring an acute intervention. These acute problems offer us opportunities not simply to treat the presenting problem but to modulate the course of an infant's health for the future.

Case I

A 6-week-old baby, new to your practice, is brought in by his parents for a well visit. The family is interested in more holistic care and has heard in the community that you are open minded to "natural approaches." The baby was full term and has been generally healthy; he is breastfed with occasional supplemental bottles of a cow's milk–based formula. The parents are concerned about how fussy their baby has become over the past month, and are wondering if you can help them.

Colic

The typical baby cries an average of 2.25 hours per day [11]; others are excessively irritable and are said to have colic. Surveys indicate that more than one quarter of infants are diagnosed with colic [12], making the condition one of the most common reasons for infant visits to primary care practitioners today. Dr. Morris Wessel [13], who studied infant crying behavior as part of the Yale Rooming-In Project, defined colic as paroxysmal fussing in infancy for more than 3 hours per day, at least 3 days per week, for at least 3 weeks' duration. Colic is currently best understood as an extreme variant of infant

irritability, perhaps related to neural regulation differences. Pediatrician Harvey Karp [14] speculates that some babies have a more difficult time adjusting to what he terms the ''fourth trimester,'' a 3-month period of time in which infants must cope with potentially overwhelming sensory stimuli. Just like adults, babies vary in how well they integrate external stimuli, and colic may well represent an adjustment disorder, the far end of an infant irritability syndrome, or perhaps an early sensory integration disorder. Most parents who have colicky babies believe that there is some component of abdominal pain; in fact, the gastrointestinal tract may be involved in colic through neuro-gut-immune pathways. Atopic disorders (discussed in more detail later) have been associated with colic, perhaps through an immunomodulatory mechanism involving gastroesophageal reflux [15]. Of greatest concern, a recently published 10-year prospective study challenges the commonly held view that there are no long-term health-related issues in children who had colic in infancy [16]. In this prospective study of 100 children, there was an association noted between infantile colic and later recurrent abdominal pain, atopic disease, and sleep disorders. This association does not prove causation, but suggests that processes involved in the development of colic may also predispose children to subsequent health concerns. Larger prospective studies are needed for confirmation, but the theoretic impetus for colic intervention is strengthened by the trial's findings.

Complementary and alternative medicine therapies for colic

It is often difficult to distinguish conventional from CAM approaches for managing colic because culture and geography play such a large role in what is considered conventional. Surveys of CAM use in culturally diverse populations indicate that colic is a common reason for use of herbal and nutritional therapies [17,18]. The largest systematic review to date of treatments for colic found little evidence to support many routinely advocated therapies, including simethicone, while noting that several nutritional and botanically based approaches were safe and effective [19]. Individualizing a treatment plan is extremely important in the management of colic because some approaches work well for some families and not at all for others. Common CAM approaches for colic include the use of mind–body therapies, infant massage, botanically based therapies, nutritional modulation, and probiotics.

Mind–body medicine

Mind–body medicine, according the National Center for Complementary and Alternative Medicine (NCCAM), ''focuses on the interactions among the brain, mind, body, and behavior, and on the powerful ways in which emotional, mental, social, spiritual, and behavioral factors can directly affect health'' [20]. Stress can indeed modulate neurologic responses, supporting the need to promote parental stress-coping mechanisms in the face of excessive infant irritability. In a chicken–egg analogy, it is likely that

parental stress and infant colic exacerbate each other. There are established links between maternal mood states, including postpartum depression, and the development of colic in infants [21]. Reducing parenting stress is a proven method of helping families cope with irritable infants, and there are many strategies to do so. A study by Keefe and colleagues [22] used a home-based nursing intervention for stress reduction, but teaching families other mind–body therapies may be equally helpful. Other parenting interventions, included parent-to-parent guidance, have been demonstrated to reduce crying time in colicky babies [23,24]. Despite the lack of randomized controlled trials proving efficacy or cost effectiveness in colic management, practices such as guided imagery, self-hypnosis, mindfulness-based stress reduction, or yoga might be equally helpful in reducing parental distress.

Infant massage

Infant massage is a specific therapeutic massage technique developed for soothing babies and for facilitating bonding between parent and child. A Cochrane Database Systematic Review of infant massage acknowledged "evidence of benefits on mother–infant interaction, sleeping and crying, and on hormones influencing stress levels" [25]. Infant massage is effective in reducing excessive crying in even the most vulnerable of infants, including premature babies and cocaine-exposed neonates [26,27]. Self-care is an important part of the healing power for many CAM modalities, including massage, and families can learn infant massage techniques for safe and effective use at home. This positive effect for soothing infants seems to be superior to simple vibration devices [28] and may be enhanced by the use of essential oils, such as sesame seed oil [29]. Whether this latter effect is related to the oil as aromatherapy or simply adds to the physical massage technique, or both, is unknown.

Botanically based therapies

Botanically based therapies for colic have been used historically in many cultures. One of the more widely known in recent times, gripe water, dates back to the 1800s, when it was developed by William Woodward, a British pharmacy apprentice [30]. Woodward's formula, a mixture of dill seed oil, sodium bicarbonate, and alcohol, among other substances, derived from a solution used at the time to treat babies who had "fen fever," related to malaria. Babies soothed by the concoction reportedly found relief from gastrointestinal troubles ("watery gripes"). Over the years, the gripe water formula has changed and commercially available solutions may contain any number of botanicals, though alcohol has been removed from many of these products. One must ask families specifically about the use of gripe water and other herbal blends for colic treatment to determine which herbs are being ingested.

One natural health product database lists five separate products labeled as gripe water, all with different constituents [31]. Herbs most commonly found in these preparations include dill (*Anethum graveolens*), fennel (*Foeniculum*

vulgare), ginger (*Zingiber officinale*), and German chamomile (*Matricaria recutita*). There have been several published studies of herbal remedies for colic. Weizman and colleagues [32] evaluated an herbal tea preparation containing chamomile, vervain, licorice, fennel, and lemon balm. In this trial, 68 colicky infants aged 2 to 8 weeks were randomized to receive either tea or placebo for 7 days. Infants were allowed drink up to 5 ounces up to three times per day, but the average actual intake per baby was approximately 3 ounces per day. Significantly more babies in the treatment group (57%) improved than in the placebo group (26%). No significant adverse effects were reported. Unfortunately, many unknown variables in the study design make it difficult to base recommendations on the results. The amounts and types of each herb and the exact nature of the placebo are unspecified and may have had an impact on resolution of colic. Alexandrovich and colleagues [33] examined the effect on colic of an emulsion of fennel seed oil in a randomized controlled trial of 125 infants. The babies were allowed 5 to 20 mL of either fennel seed oil emulsion or placebo up to four times per day for 1 week, but actually ingested an average of two to three doses per day, for a total of less than 2 ounces per day. Colic was eliminated in 65% of the treatment group versus 23.7% of the placebo group. There were no reported adverse effects in this trial. Savino and colleagues [34] compared a standardized extract of three herbs (chamomile, fennel, and lemon balm) with a placebo in 93 breastfed colicky infants. Each infant received a standardized dose of extract or placebo at 2 mL/kg/d twice daily before breastfeeding for a 7-day trial period. A significant reduction in crying time was observed in 85.4% of patients receiving the treatment extract and in 48.9% of infants receiving the placebo. Interestingly, crying time was still reduced 2 weeks after the end of the trial in the intervention group. There were no reported adverse side effects in either group.

Nutritional modulation

Modulating the diets of babies, whether breastfed or formula-fed, is often attempted to reduce infant fussiness. Although breastfeeding exclusively does not seem to prevent colic [35], nursing mothers may have success in reducing infant irritability by altering their nutritional intake. Hill and colleagues [36] found that elimination from maternal diet of common allergenic foods (cow's milk, soy, wheat, eggs, peanuts, tree nuts, and fish) was associated with a reduction in colic in breastfed infants. Cruciferous vegetables (eg, broccoli, cauliflower) and chocolate in the maternal diet have been linked to colic in breastfed babies [37,38]. Some food constituents, like essential fatty acids, may actually be desirable in higher amounts; although not directly connected to colic, maternal docosahexaenoic acid levels have been associated with positive infant sleep patterning [39].

Certain formulas have been shown to reduce colic symptoms, although no prospective studies evaluating prevention of colic have been published. Extensively hydrolyzed casein and whey formulas are more effective than nonhydrolyzed cow's milk formulas in reducing crying times in colicky

babies [40,41]. Studies do not support either soy or partially hydrolyzed formulas as options for colic reduction [42,43].

Probiotics and prebiotics

Probiotics are "viable, defined microorganisms in sufficient numbers, which alter the microflora (by implantation or colonization) in a compartment of the host and by that exert beneficial health effects in this host" [44]. Prebiotics are biologic substances that increase the growth and activity of probiotic organisms. There are differences in the types and number of probiotic microorganisms colonizing the intestinal tracts of infants who have colic versus those who do not [45,46].

Savino and colleagues [47] have evaluated the effect of probiotics and prebiotics on colic. In one trial, they compared a probiotic (*Lactobacillus reuteri*) with simethicone in a randomized controlled trial in 90 exclusively breastfed colicky infants. Simethicone, a conventional nonprescription medication, has been previously shown to be ineffective for colic treatment [19]. After the 1-month trial, 95% of the probiotic treatment group responded (no longer met Wessel criteria for colic) versus only 7% of the simethicone group. The second study randomized 267 formula-fed infants to one of two arms [48]. The treatment group was fed a novel partially hydrolyzed whey protein formula supplemented with prebiotic oligosaccharides and the control group received the standard formula (without prebiotics) and simethicone. The treatment group, after both 1 and 2 weeks, had a significant reduction in crying episodes when compared with the control group.

Case I, continued

The parents return for a visit several weeks later. They have been using chamomile tea and gripe water with some success, and find that the infant massage lessons they took are helping to calm their baby also. Although he is less fussy, he is now spitting up most of his feedings, although his mother is trying to avoid dairy and other common food allergens in her diet; they are still occasionally supplementing with an "easier-to-digest" cow's milk formula. Furthermore, he is covered by a patchy, dry, red rash and has noticeable nasal congestion with a frequent nighttime cough.

Atopic disorders

Atopic disorders, including asthma and food allergies, are widely considered to be increasing in prevalence at epidemic rates [49]. In primary care pediatric practice, we are seeing many more infants suffering from early atopic signs (dermatitis, gastroesophageal reflux, chronic rhinorrhea, and recurrent wheezing). Some infants who have colic develop signs and symptoms of atopy, including eczema, chronic rhinitis, and gastroesophageal reflux. Research supports the finding that atopy may be responsible for symptoms of colic [15], although infants who have colic do not necessarily

develop atopy at higher rates than other babies later in life [50]. The atopic march, as it has come to be known, represents the natural tendency of children who have early signs of allergic reaction to environmental stimuli (eg, atopic dermatitis) to progress to more severe manifestations of allergic disease (eg, asthma) [51].

What predisposes certain infants to develop atopic symptoms? Although it has long been appreciated that some are at higher risk for atopic disorders based on family history, we are only now recognizing how complicated the nature–nurture equation might be. Even single nucleotide polymorphisms (SNPs, or very small DNA shifts) may not only account for the presence or absence of atopy in a given person but may also affect the severity of disease, the likelihood of other atopic conditions developing, and the success of various therapies [52]. A baby who has a given genomic predisposition, under certain environmental conditions, manifests immune dysregulation, resulting in an imbalance between Th1-dominant and Th2-dominant responses [53]. Th2 dominance leads to immune dysregulation marked by a proliferation of inflammatory cellular mediators (eg, cytokines, interleukins, leukotrienes). Inflammation involves excess mucous production and other clinically observable phenomena we call allergies.

The ''hygiene hypothesis'' is a popular current theory to explain why we are experiencing a surge in atopic disease prevalence [54]. According to this theory, our environments are now too clean—we are not exposed to as many antigens (bacterial, fungal, viral) as previous generations. With a reduction in infectious exposure, certain individuals over time may produce altered gastrointestinal, immunologically active microorganisms, leading to a Th2 immune shift [55]. Numerous studies also have supported a correlation between early life antibiotic exposure and atopy (particularly wheezing) in children [56–61]. Other environmental factors, too, have been implicated in triggering allergic responses. These include immune and endocrine disrupting agents in air, water, food, and industrial products [62–64].

Complementary and alternative medicine therapies for atopy

Many families turn to CAM therapies for their children suffering atopic disorders [65–69]. Among the most well studied for prevention and treatment of infant atopy are nutritional modulation and probiotics.

Nutritional modulation

For those infants at risk, exposure to certain foods in and ex utero may contribute to the development of atopy. We focus on the following key areas: maternal pre- and postnatal antigen avoidance, breastfeeding, choice of infant formula supplementation, timing of solid food introduction, and fatty acid intake (in breastfeeding mothers and in infants).

General antigen avoidance (milk, soy, eggs, tree nuts, peanuts, shellfish) for the population as a whole is not supported by current data [70]. In families at highest risk (parents or siblings who have significant atopic history),

avoidance of most highly allergenic foods, especially peanuts and tree nuts, should be considered during pregnancy and during duration of breastfeeding. The AAP advises avoiding peanuts and tree nuts for nursing mothers for maximal atopy prevention [71]. If avoiding specific food groups, one must take great care to ensure proper compensatory intake of vitamins, minerals, and amino acids.

The AAP also supports breastfeeding as a means to reduce allergic disorders. Exclusive breastfeeding for 4 to 6 months is associated with a lower risk for developing atopic dermatitis, food allergy, allergic rhinitis, and asthma [72–75]. If exclusive breastfeeding is not possible, the AAP recommends hydrolyzed protein formulas for high-risk babies [71]. A Cochrane Database Systematic Review supports this recommendation [76]. These formulas may contain extensively or partially hydrolyzed cow's milk proteins (casein or whey), and there is debate about whether they are equivalently effective in preventing atopic expression [77]. Most experts currently recommend extensively hydrolyzed products, but cost and availability issues are factors. The AAP recommends against using soy formulas for atopic prevention in high-risk infants [71]; again, this recommendation is supported by a Cochrane Database Systematic Review [78].

There is no clear consensus guideline for treating infants who develop atopic symptoms, even in the absence of family history. Common practice includes advising exclusive breastfeeding with maternal antigen avoidance, or, if not possible, using extensively hydrolyzed formulas.

When is the optimal time to introduce solid foods to infants for the general population and those at high risk? Prevention of atopy seems to be the key focus in published trials. With increasing prevalence of allergic disorders, some experts are advocating for delaying solid food introduction in all babies until 6 months, with the introduction of highly allergenic foods as follows: dairy products at 12 months, eggs at 24 months, and peanuts, tree nuts, and shellfish at 36 months [79]. These guidelines are supported by other major United States and European groups, but only for infants at high risk [71]. Early solid feeding (before 4 months of age), particularly of gluten-containing products, is associated with atopic disease and celiac disease [80,81]. There have also been several encouraging studies looking at the treatment of atopic disorders with nutritional modulation (avoiding specific food allergens) [82–84].

Recent studies have examined the role of essential fatty acids in preventing and reducing allergic disease. Atopy can be prevented when mothers ingest higher amounts of omega-3 polyunsaturated fatty acids (PUFAs) [85]. It also seems that babies who ingest breast milk relatively rich in omega-3 are less likely to develop allergic symptoms [86,87]. This effect is most evident in those babies at highest risk genetically. The results of directly feeding infants PUFAs are not as clear. Some studies of dietary modification with omega-3 PUFAs in children at high risk demonstrated reduction in atopy [88,89], and another study showed improvement with supplementation

of evening primrose oil, an omega-6 PUFA [90]. Perhaps it is the balance of the two that is most important, and one must also take into account preexisting dietary deficiencies and genomic factors. More research is clearly needed in this realm before universal recommendations can be made.

Probiotics

Randomized controlled trials have demonstrated that probiotics (*Lactobacillus* GG) given prenatally to women and then postnatally to either breastfeeding mothers or directly to formula-fed infants can reduce the incidence of atopic dermatitis by half in those infants at high risk for up to 4 years postnatally [91,92]. Prebiotics have also been shown to prevent eczema in a vulnerable infant population [93]. Several randomized controlled trials have pointed toward a positive effect of probiotics and prebiotics on the course of atopic dermatitis [94–97], although one publication reported no such effect [98]. More research is needed to determine the ideal doses and types of pre- and probiotics for atopy prevention and treatment.

Adolescence

Adolescence is a time full of changes and a particularly challenging period of life not only for the patients and their families but also for the primary care practitioner. In adolescence there is a recapitulation of many of the stages of infantile emotional development, including the oral, anal, and genital, where the fires of conflict are rekindled. During early adolescence (11–13 years) teens are preoccupied with body image and peer group identity. Middle adolescence (14–16 years) is characterized by desire for separation from the family and development of individual identity. In late adolescence (16–20 years), the young adult begins to foster long-term relationships and plan for his or her future. The physical and psychosocial transitions of adolescence are challenging in healthy teens and even more so in those who have chronic illnesses requiring frequent medical interventions and hospitalizations. It is important to recognize that the psychosocial issues faced by an adolescent can be different from a child or older adult, although the medical treatment may be similar. The tasks of adolescence include winning the acceptance of peers, achieving independence from families, developing the capacity to love a person of the opposite or same sex, and achieving an effective ego (a sense of self; an individuality inclusive of sexual and vocational identities) and an effective superego (eg, a conscience, a value system, a sense of right and wrong).

Integrative care—complementary and alternative medicine and adolescents

Holistic care in the adolescent population is exciting territory that resonates with many avenues for improving outcomes in this population. An

integrative approach can be helpful in discussing pregnancy prevention, sexually transmitted diseases, the effects of smoking, the need for immunizations, substance use, and health education regarding improved efforts at compliance in those who have specific health care needs.

CAM has a large range of use in children and adolescents and is more common in certain geographic areas of North America and in those young people who have chronic illnesses [99–106]. CAM use is considerably higher in specific groups of children and adolescents, such as in those who have cystic fibrosis, cancer, or arthritis, and in those undergoing surgery [103–108]. Other frequent users of CAM in adolescence include homeless youth, who have a 70% use rate [107]. Why teens and their families turn to CAM in the face of chronic illness is a subject of much conjecture but may be because conventional medical approaches may only target specific aspects of the illness. The integrative and alternative interventions may support the child and the family as the illness becomes more physically and psychologically pervasive.

Case study II

D' Andree is a 12-year-old who has been on stimulant medication twice daily for his attention-deficit/hyperactivity disorder (ADHD). His teacher thinks he is not focused enough and needs more medication. Mom is concerned about his weight and self esteem. He eats voraciously when the medication wears off and has been battling obesity for many of his school years. His mom has been seeing a nutritionist for her own weight issues and has used some nutritional supplements and herbals with good results. It turns out that D'Andree already had been taking some herbs and supplements. He tells you he has been drinking two or three cans of energy drink daily to "lower my appetite." He also thinks it is helping him pay better attention at school. Mom and D'Andree come to the follow-up appointment with a bag of many different herbs and supplements, including yerba mate, guaraná, green tea, ginseng, and hoodia, recommended by the nutritionist, and they are wondering whether you think they might help him.

Herbal therapies and nutritional supplements

Among adolescents, it is common to find the use of herbal therapies for several conditions: weight loss, depression and anxiety, upper respiratory tract infections, and the enhancement of athletic performance. Outlined here is a brief review of a few commonly used herbal therapies pertinent to the above case.

Caffeine is the only stimulating supplement that can be easily and abundantly consumed and even purchased by children and adolescents. Caffeine is found in pain relievers, diuretics, cold remedies, weight control products, and sport supplements. A U.S. Department of Agriculture survey showed that for children (6 to 9 years old), the mean daily caffeine intake was 20 mg compared with adults in whom the average is 200 mg per day [108]. A survey of 8- to 11-year-olds in Massachusetts found the average

daily caffeine intake was 18.9 mg, or 0.6 mg/kg, and that greater than 50% of the caffeine consumed was from carbonated beverages [109].

Caffeine, a member of the methylxanthine drug class, increases norepinephrine and epinephrine secretion and blocks central adenosine receptors. It increases the heart rate and basal metabolic rate, promotes secretion of acid in the stomach, is a diuretic, and acts as a vasoconstrictor and vasodilator. Caffeine enhances alertness and gives a person a jolt by peaking in the blood plasma within 30 minutes after ingestion. The half-life of caffeine varies from several hours to days; the average in adults is 3 to 7 hours. In one clinical study, school-aged boys who consumed caffeine showed a greater increase in motor activity and in rate of speech and decrease in reaction time compared with adults. There was also improvement in attention with less nervousness and jitteriness and fewer omission errors on a continuous performance test [110]. For ADHD, caffeine has been shown to have mixed results [111]. Studies have demonstrated that caffeine is not more effective than placebo and is less effective than stimulant medication in treating ADHD symptoms [112].

Caffeine withdrawal symptoms in the child or adolescent can occur after only 2 weeks of daily caffeine use and include irritability, depression, anxiety, fatigue, and headache. In one study, during caffeine withdrawal children had a worse performance reaction time on a task requiring sustained attention; this deterioration may persist for a week [113]. Importantly, caffeine can interact with stimulant, analgesic, and other over-the-counter medications. Its use is not recommended in those who take prescribed stimulant medications. Caffeine has been believed to cause decreased bone mineral density because of its propensity to increase urinary calcium excretion in adults. In a study in adolescent women, however, dietary caffeine consumed by American white, adolescent girls was not correlated with a decrease in total bone mineral gain or hip bone density at age 18 [114]. This remains an ongoing area of concern and there is a need for further research.

Ephedra, also known by its Chinese name *Ma huang*, is a naturally occurring substance derived from plants. Its principal active ingredient is ephedrine. Although it was not recommended in the above case study many teens know about its propensity to assist in weight loss. Ephedra products have been used to suppress appetite, enhance sports performance, and increase energy. Ephedra acts by increasing the levels of norepinephrine, epinephrine, and dopamine, and stimulating alpha and beta adrenoreceptors. This stimulation leads to anorectic and thermogenic effects by speeding up metabolism, which leads to increased alertness, less fatigue, and a decreased perceived need for sleep. Ultimately there is increased anxiety, jitteriness, and insomnia. In a meta- analysis of 52 controlled trials and 65 case reports, ephedrine and ephedra were shown to promote modest short-term weight loss ($\sim$0.9 kg/mo compared with placebo) [115].

It is well known that ephedra has the potential to cause serious side effects that have led to several reported deaths. In 2004, the FDA banned

the sale of dietary supplements containing ephedra because of reported serious adverse effects; although the ban has been contested legally, the medical concerns remain. Based on known side effects and minimal benefit, this product should not be recommended for use. Combining caffeine and ephedra may lead to psychiatric symptoms, such as euphoria, neurotic behavior, agitation, depressed mood, giddiness, and extreme irritability. Other side effects may include elevated blood pressure, palpitations, tachycardia, chest pain, coronary vasospasm, and possibly cardiomyopathy.

Guaraná (*Paullinia cupana*) is a small shrub native to Venezuela and northern Brazil, known for the high stimulant content of the fruit. The dried paste made from the crushed seeds of guaraná is used to enhance athletic performance, as an appetite suppressant, and as an aphrodisiac. Guaraná seeds contain the caffeine-like product guaranine, along with theobromine, theophylline, xanthine, and other xanthine derivatives. There are several energy drinks containing guaraná equivalent to 3.6% to 5.8% caffeine (compared with 1% to 2% in coffee). One study of overweight adults reported that the combination of guaraná, yerba mate (see later discussion), and damiana (*Turnera diffusa*, a purported aphrodisiac) significantly delayed gastric emptying, causing prolonged perceived gastric fullness with an associated weight loss over 45 days [116]. The side effects are similar to those of ephedra and caffeine.

Yerba mate (*Ilex paraguariensis*), a member of the holly family, is a widely cultivated medium-sized evergreen tree native to South American countries. Yerba mate tea leaves are used as a diuretic, for weight loss, and for fatigue and depression. The primary active chemical constituents are caffeine (0.3%–2.0%), theobromine, theophylline, saponins, tannins, and chlorogenic acid. Yerba mate may cause insomnia, gastric irritation, nervousness, diuresis, and arrhythmias. Side effects are similar to those herbs that contain caffeine [117].

Hoodia gordonii is a succulent from the Kalahari Desert in southern Africa. Bushmen from the area have been using hoodia for centuries to help ward off hunger during long trips in the desert. A steroidal glycoside termed P57AS3 (P57) has been isolated from *H gordonii* and may increase the content of ATP causing a decrease in hunger [118]. Preliminary data suggest that overweight men who consume P57 have significantly lower calorie intake than those taking a placebo. No side effects have been reported to date [119].

Green tea (*Camellia sinensis*) is a popular drink among adolescents and has been advertised as a weight loss aid and a treatment for fatigue, gastrointestinal disorders, and headaches. It can be found everywhere, including in grocery stores, in energy drinks, and at ever-present fancy chain coffee shops. Green tea leaves are steamed and heated, rather than rolled and exposed to air as in black tea, to remove the enzyme that promotes oxidation. The caffeine in green tea is believed to be milder than that in black tea because of its combination with catechin in the steaming process. The active ingredients include caffeine, 2-amino-5-(N-ethylcarboxyamido)-pentanoic

acid, catechins, and polyphenolic compounds. In vitro studies show green tea to be antibacterial, antimutagenic, and anticarcinogenic [120]. Thermogenesis, fat oxidation, or both may be affected by green tea; a cup may contain 22 to 46 mg of caffeine [121].

Side effects of green tea include those similar to caffeine and include withdrawal after 2 weeks of consumption if ingestion is abruptly discontinued. As with any caffeine product, excessive green tea consumption should be avoided in pregnant or breastfeeding women, in those who have cardiac arrhythmias, hypertension, gastrointestinal ulcers, anxiety, or renal disease, and in those taking antifungal medications or aminophylline. There is a precautionary use in infants and young children. A retrospective trial noted that microcytic anemia can occur in infants consuming daily green tea [122].

Ginseng (*Panax ginseng*) has been used for more than 2000 years to strengthen mental and physical capacity. Recently, ginseng has become popular as an "adaptogenic" (stress-protective) agent. Ginseng is believed to have effects on nitric oxide synthesis in endothelial tissue of lung, heart, and kidney. In addition, effects on serotonin and dopamine may also be responsible for its actions. Other effects may be related to activity on the hypothalamic-pituitary-adrenal system. To date, seven trials investigating ginseng's effects on physical performance in young, active volunteers during cycle ergometer exercises have been reported. Four studies found no significant difference between ginseng and placebo, whereas three studies found a significant decrease in heart rate and increase in maximal oxygen uptake with ginseng [123]. Adverse effects may include nervousness, insomnia, and gastrointestinal disturbance associated with prolonged use. Because of the estrogen-like effect, ginseng has been reported to cause mastalgia and vaginal bleeding in women. Importantly, ginseng may interact with oral anticoagulants, antiplatelet agents, corticosteroids, and hypoglycemic agents [124].

Case III

Alicia is a 17-year-old referred to the clinic by her naturopathic physician with a history of a 15-pound weight loss over the past 6 months. Her weight has decreased from 100 to 85 pounds; her height is 5 ft 1 in, putting her at 80% of her ideal body weight. She has had no menses for 3 months. Alicia's parents and her naturopathic physician are concerned about her increasing anxiety and insomnia. The family would like to avoid conventional medications at all costs and ask you about alternative therapies to help Alicia. They were wondering about interventions such as meditation, yoga, and massage. They describe Alicia as extremely anxious. She obsesses about her grades and relationships with friends and has considerable difficulty falling asleep.

Eating disorders represent a devastating condition that primarily affects adolescent women. Although the lifetime prevalence rates according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revised are listed as 1% to 3%, more recent research suggests it is much

higher, with a range of 3% to 6% in young women [125]. Adolescents who have eating disorders experience various symptoms, including food preoccupation, anxiety, and depression. They may also face low body weight, loss of menses, biochemical imbalances in the brain, family difficulties, financial hardship, poor adaptation, disruption of academic progress, prolonged care in hospital settings, and ultimately death. Conventional treatments for these eating disorders include psychopharmacologic interventions, nutritional interventions, and psychologic treatments. CAM therapies integrated in the management of eating disorders often include mind–body therapies (eg, meditation and yoga), natural health products, and therapeutic massage.

Mind–body therapies

The use of relaxation psychotherapies for the treatment of physical and mental ailments is an old practice. Historically, various relaxation psychotherapies have been used to alleviate symptoms associated with psychologic and medical conditions, including stuttering, cancer treatment, insomnia, diabetic care, affective disorders, irritable bowel syndrome, and eating disorders [126]. One important benefit has been the reduction of problematic symptomatology (eg, anxiety, sleep disorders) by way of relatively low-risk and cost effective methods of care.

The use of *meditation* in the treatment of eating disorders originates from various sources. Mindfulness meditation can be defined as "intentional self-regulation of attention from moment to moment [127]. It is neither contemplation nor rumination, as in thinking about a conceptual theme." In mindfulness meditation, the individual observes thoughts and experiences from a detached perspective thus allowing thoughts and experiences to come into awareness, be noticed, and dissipate from consciousness. Mindfulness meditation has been used in the treatment of pain amplification disorders, depression, and various other chronic conditions. Success with this approach has spurred researchers to examine the impact of mindfulness meditation on individuals who have eating disorders.

A meditation intervention for the treatment of binge eating disorder was studied and results indicated that the number of binges dropped significantly over the course of treatment, with nine participants binging less than once a week and five participants bingeing less than once or twice a week post-treatment. Participants who spent time using eating meditation were subsequently able to change their bingeing behaviors with an increased sense of eating control, sense of mindfulness, and awareness of hunger cues and satiety cues [128]. Results were comparable to cognitive-behavioral therapy (CBT) interventions, which suggest that meditation may be an alternative to CBT in cases in which CBT is not feasible because of financial or geographic concerns [129].

Another mind–body therapy integrated in the treatment of eating disorders is *yoga*. Because yoga is viewed as form of exercise by some practitioners, the use of yoga to treat eating disorders is controversial. Most clinics advise

against strenuous exercise because of the possibility of increasing weight loss. There are known negative effects of long-term abstinence from exercise, however, such as decreased bone mass and an increased risk for atherosclerosis. In a study examining the positive effects of yoga, eating disorder patients who completed yoga trended toward experiencing an improved quality of life and did not lose weight compared with those who did not receive yoga [130]. Although these results suggest a preliminary positive use for yoga, controlled clinical trials are needed to support these results.

The use of yoga to treat anxiety is mostly theoretic. Although several articles have attempted to examine the impact of yoga on anxiety or other affective states, the lack of controlled clinical trials or adequate statistical analysis makes it difficult to interpret the results. In a multifaceted treatment approach for individuals who have eating disorders yoga may help reduce severe physical discomfort and feelings of guilt after eating [131]. In another study, yoga was noted to decrease food preoccupation in adolescents who had eating disorders [132]. Scheduling yoga sessions before and after meals helps reduce many typical anxiety responses that occur in patients who have eating disorders and alleviates some of the problems of after-meal supervision.

Natural health products

Kava is an important cultural product in the South Pacific, particularly in the Fiji Islands, where it is used as a ceremonial drink. It is also used for its calming effects. More recently, it has been used as a natural alternative to sedatives and anxiolytics.

It is believed to work by inhibiting γ-aminobutyric acid (GABA) receptor binding. A Cochrane Systematic Review found that kava does have an antianxiety effect compared with placebo [133]. Adverse effects include kava dermopathy, a yellowing and flaking of the skin associated with excessive use of kava, which resolves with discontinuation of the herb. There is a potential risk for liver injury associated with the use of kava-containing dietary supplements, although some speculate the liver toxicity is reversible on discontinuation of the herb [134].

Valerian has been used for centuries as a sedative agent and sleep aid. Valerian root has effects on GABA receptors, leading to its sedative effects. Several human trials confirm a mild sedative effect. Few studies exist regarding the anxiolytic effects of valerian root in vivo. A Cochrane Systematic Review concluded that ''there is insufficient evidence to draw any conclusions about the efficacy or safety of valerian'' [135]. Side effects include headache, excitability, uneasiness, and cardiac disturbances.

Chamomile has been used for gastrointestinal discomfort, peptic ulcer disease, infantile colic, and mild anxiety. Chamomile may act by binding to central benzodiazepine receptors [136]. Several small human trials have noted chamomile to have hypnotic-sedative properties. None of these trials have been randomized or controlled, however. The FDA regards chamomile

as safe when used as a spice, seasoning, or flavoring agent. Although several cases of allergic reactions to chamomile have been reported, no significant toxicity or herb–drug interactions have been noted.

Melatonin is a hormone produced nocturnally by the pineal gland and functions as a biologic and circadian cue to promote sleep. Melatonin also has a direct radical scavenging and antioxidant action. It has been used to successfully alleviate jet lag [137]. Reports are conflicting for those who have chronic sleep disorders, however. A retrospective study in adolescents who had delayed sleep phase syndrome revealed that those treated with 3 to 5 mg/d of melatonin for an average of 6 months reported quicker sleep onset, longer sleep duration, and a decrease in school difficulties. No adverse effects of melatonin were noted [138].

Therapeutic massage

It is important to briefly mention therapeutic massage as a CAM therapy commonly used by patients who have eating disorders. In a small placebo controlled study, massage therapy was shown to decrease body dissatisfaction. Massage may help those who have eating disorders by decreasing levels of cortisol and increasing levels of serotonin and dopamine [139]. Risk for adverse effects is theoretically low, but more research is necessary before routine recommendations can be made.

Summary

The integration of CAM therapies into primary care pediatric practice is well illustrated by these case discussions. From infancy to adolescence, CAM therapies are being used more frequently in the pediatric population, and primary care pediatricians are in an ideal position to work with families to explore all safe and effective remedies. Evidence supporting the use of CAM therapies for common conditions, such as colic, atopy, ADHD, eating disorders, and anxiety, has steadily increased in volume and improved in quality. Although we clearly need additional research examining the safety and efficacy of all therapies for these common childhood conditions, evidence to date supports the judicious use of specific CAM therapies. Primary care practitioners should routinely discuss the use of CAM therapies with their patients and their families.

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