26

Integrative Pediatric Primary Care

LAWRENCE D. ROSEN

KEY CONCEPTS

- Primary care is collaboration between healthcare providers and families. Communication is key to success.
- The medical home paradigm provides a framework for integrative primary care.
- Primary care should focus on the promotion of wellness.
- Common problems during infancy, like colic, atopy, and ear infections, are best addressed from an evidence-guided integrative perspective and offer opportunities to promote wellness and healing concepts.
- Immunizations should be discussed openly and honestly by all parties. Families have many concerns and questions which are best answered through respectful dialogue.
- The "primary care" of a child is shared by many: pediatricians or other healthcare practitioners, the child[1]s family and community, and the child herself.
- It is not so much the use of any specific CAM therapy that defines someone as an integrative pediatrician but the belief that healing is inexorably bound to the connection between practitioner and patient. In no area of healing practice is this more evident and needed than in primary care.
- Individualizing a treatment plan is extremely important in the management of colic, as some approaches work quite well for some families and not at all for others.
- 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 7 years postnatally.

- Given the links between immune dysregulation and the development of atopic phenomena, a growing number of practitioners are concerned about the potential contribution of vaccines in a subset of children to disease expression.
- Primary care practitioners, in ideal position to adopt and advocate the medical home paradigm, should engage their patients and families in respectful, collaborative dialogue regarding the use of CAM therapies. As the number of children with special healthcare needs grows, and as more families develop an interest in a holistic model of care for prevention and treatment, integrative primary care is poised to become the standard of healthcare.

Introduction

Primary care, in the world of medicine, is conventionally defined as "the activity of a healthcare provider who acts as a first point of consultation for all patients."(Primary Care—Wikipidia, 2007) Historically, many types of healthcare practitioners have served as primary care providers for children, including pediatricians, family practice doctors, nurses, and alternative healthcare practitioners. In truth, the "primary care" of a child is shared by many: pediatricians or other healthcare 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, 2002). 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 in her Presidential Address to the Ambulatory Pediatric Association (Kemper, 2000).

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 healthcare practitioners, including open discussions about CAM therapies, environmental health concerns, nutrition, immunization, and parenting practices. Integrative pediatric practitioners view lifestyle issues (nutrition, fitness,

mind-body-spirit connections) as cornerstones of optimal health. Perhaps most importantly, one of the central tenets of integrative primary care—the one that serves as the core—is the belief that the relationship between practitioner and patient/family is what truly provides the power in holistic practice. It is not so much the use of any specific CAM therapy that defines someone as an integrative pediatrician but the belief that healing is inexorably bound to the connection between practitioner and patient. In no area of healing practice is this more evident and needed than in primary care.

The appeal of the integrative model for pediatric primary care is indeed growing, witnessed by the anecdotal growth in office- and hospital-based integrative practices, and by the documented increased use of CAM therapies for both well and chronically-ill children (Loman, 2003; Sanders, 2003; Sawni-Sikand, 2002; Spigelblatt, 1994) Adolescent use of CAM in particular is rising (Braun, 2005; Wilson, 2002), and primary care practitioners need to engage teens in discussions about safety and efficacy concerns, as they would with any therapies. Children with special healthcare needs—those with chronic or serious acute illnesses (e.g., autism, cancer)—are seen in increasing numbers in primary care offices and a majority are likely to use CAM therapies (Cohen, 2006; Harrington, 2006; Sanders, 2003).

Pediatricians are more interested than ever in learning about CAM therapies so that they can more effectively communicate and connect with their patients and families (AAP, 2001). In order to increase awareness and knowledge of commonly used CAM therapies, this chapter will feature clinical scenarios that illustrate the potential for evidence-based integrative care as a new paradigm for primary care pediatric practice.

General Approach to the Newborn

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 in order to assess growth and development but also to establish a relationship so that we can, together, create a foundation for optimal health for each and every child. This nonjudgmental, two-way relationship is one of the keys to the success for pediatric primary care, especially with families of children with special healthcare needs. Liptak et al. (2006) reported that families of children with developmental disabilities were unsatisfied with their current primary care practitioners, in part because of pediatricians' perceived lack of knowledge about and unwillingness to discuss CAM therapies.

In the scope of daily practice, primary care pediatricians encounter a variety of common conditions requiring 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. The following case discussion, emphasizing prevention and evidence-guided integration of CAM and conventional therapies, will be threaded throughout this chapter to serve as a window into the actual practice of integrative primary care.

CASE (Part 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 "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 quite 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 they are wondering if you can help them.

Colic

When the typical baby cries an average of 2.25 hours per day (Brazelton, 1962), others are excessively irritable and are said to have "colic." Surveys indicate that over one-quarter of infants are diagnosed with colic (Fireman, 2006), making the condition one of the most common reasons for infant visits to primary care practitioners today. Dr. Morris Wessel (1954), 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 (2004) 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 with 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, as will be discussed in more detail, have been associated with colic, perhaps through an immunomodulatory mechanism involving gastroesophageal (GE) reflux (Heine, 2006). 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 (Savino, 2005). In this prospective study of one hundred 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 theoretical impetus for colic intervention is strengthened by the trial's findings.

CONVENTIONAL APPROACH

It is often difficult to distinguish conventional from CAM approaches for managing colic, as culture and geography play such a large role in what is "conventional." The typical

conventional pediatric approach to colic might include psychological support for caregivers with reassurance that the baby is physically well and that the colic will resolve by 12 weeks or so. This approach is distinguishable by intent and by intensity from the mind-body methods described below. Additionally, many parents comment that fussiness is often accompanied by "gas" or other gastrointestinal concerns, and practitioners frequently advise the use of simethicone-containing infant drops. This therapy has been shown to be no more effective than placebo (Garrison, 2000), and most simethicone-containing over-the-counter products contain artificial sweeteners and dyes.

CAM THERAPIES

Individualizing a treatment plan is extremely important in the management of colic, as some approaches work quite well for some families and not at all for others. Common CAM approaches for colic include the use of mind-body methods, biologically based therapies, and manipulative and body-based methods, and whole medical systems.

Mind-Body Methods

Mind-body medicine "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" (Mind-Body Medicine, NCCAM, 2007), Stress can indeed modulate neurological 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 both parental stress and infant colic exacerbate each other. There are established links between maternal mood states, including post-partum depression, and the development of colic in infants (Akman, 2006). Reducing parenting stress is a proven method of helping families cope with irritable infants (Keefe, 2006), and there are many strategies to do so. This study by Keefe et al. utilized 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 (Dihigo, 1998; Wolke, 1994). 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.

BIOLOGICALLY BASED THERAPIES

Surveys of CAM use in culturally diverse populations indicate that colic is a common reason for use of biologically based therapies (Lohse, 2006; Smitherman, 2005). The largest systematic review to date of treatments for colic found little evidence to support many routinely advocated therapies while noting that several nutritional and botanically based approaches were quite safe and effective (Garrison, 2000).

Botanicals

Biologically 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 (Blumental, 2000). 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 with "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 in order to determine which herbs are being ingested.

One natural health product database lists five separate products labeled as "gripe water," all with different constituents (Natural Medicines Comprehensive Database, 2007). 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 et al. (1993) evaluated an herbal tea preparation containing chamomile, vervain, licorice, fennel, and lemon balm. In this trial, 68 colicky infants aged 2–8 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 et al. (2003) 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 2 to 3 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 et al. (2005) 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 per day twice daily prior to 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. While breastfeeding exclusively does not seem to prevent colic (Clifford, 2002), nursing mothers may have success in reducing infant irritability by altering their nutritional intake. Hill et al. (2005) 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. Both cruciferous vegetables (e.g., broccoli, cauliflower) and chocolate in the maternal diet have been linked to colic in breastfed babies (Lust, 1996). Some food constituents, like essential fatty acids, may actually be desirable in higher amounts; though not directly connected to colic, maternal docosahexaenoic acid (DHA) levels have been associated with positive infant sleep patterning (Cheruku, 2002).

Certain formulas have been shown to reduce colic symptoms though no prospective studies evaluating prevention of colic have been published. Extensively hydrolyzed casein and whey formulas are both more effective than non-hydrolyzed cow's milk formulas in reducing crying times in colicky babies (Jakobsson, 2000; Lucassen, 2000) Studies do not support either soy and partially hydrolyzed formulas as options for colic reduction (AAP, 1998, 2000)

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" (Schrezenmeier, 2001). Prebiotics are biological 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 with colic versus those without (Savino, 2004, 2005).

Savino et al. (2007) 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 non-prescription medication, has been previously shown to be ineffective for colic treatment (Garrison, 2000). 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 (Savino, 2006). 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.

MANIPULATIVE AND BODY-BASED METHODS

Infant Massage

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" (Underdown, 2006). Infant massage is effective in reducing excessive crying in even the most vulnerable of infants, including premature babies and cocaine-exposed neonates (Field, 1995; Wheeden, 1993). Self-care is a 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 (Huhtala, 2000) and may be enhanced by the use of essential oils such as sesame seed oil (Agarwal, 2000). Whether this latter effect is related to the oil as aromatherapy or simply adds to the physical massage technique, or both, is unknown.

Osteopathy

Hayden and Mullinger (2006) evaluated cranial osteopathy for the treatment of infant colic in an open, controlled, prospective study. Twenty-eight infants received weekly OMT for 4 weeks, and parents reported a significant reduction in crying time and improvement in sleeping time in treated infants versus controls (no intervention). Authors concluded that "this preliminary study suggests that cranial osteopathic treatment can benefit infants with colic; a larger, double-blind study is warranted."

Chiropractic

Hewitt, in a 2004 publication, notes that the rationale for chiropractic treatment in colic is "that an 'infant irritability continuum' exists with contentment on one end and colic on the other. In between are various degrees of irritability, many of which may be the result of discomfort secondary to mechanical lesions in the infant's spine and cranium… the fussiness may be due to discomfort arising from mechanical lesions, also termed subluxations, in the infant's spine and/or cranium. Subluxations may arise from in utero malposi-tion or from subtle trauma to the spine or cranium during the birth process" (Hewitt, 2004). A review of the chiropractic literature with respect to colic treatment includes two controlled single-blinded clinical trials, one uncontrolled prospective study and several case studies (Klougart, 1989; Wiberg, 1999). All but one published study suggest that there seems to be a positive effect of chiropractic spinal manipulation for infantile colic. The one negative trial (Olaffsdottir, 2001) was a randomized, single-blinded, controlled study with a tremendous intention response. While nearly 70% of the treatment group improved, 60% of the control group similarly improved; this difference was not statistically significant.

WHOLE MEDICAL SYSTEMS

Homeopathy

According to a general practice homeopathy survey from Scotland, "The most frequently prescribed medicines were for common self-limiting infantile conditions such as colic…" (Ekins-Daukes, 2005). There are multiple homeopathic remedies used for newborn colic, including single remedies and pre-packaged combinations, and while frequently used by parents, there are no published research trials regarding the safety or efficacy of homeopathy for colic treatment available for review at the present time.

Case (Part 2): 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 as well. While he is less fussy, he is now spitting up most of his feedings, though 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 rising in prevalence at epidemic rates (Asher, 2006). Practitioners report they are seeing many more infants today suffering from early atopic signs (dermatitis, gastroesophageal reflux, chronic rhinorrhea, and recurrent wheezing) than ever before. Some infants with 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(Heine, 2006), although infants with colic do not necessarily develop atopy at higher rates than other babies later in life (Castro-Rodriguez, 2001). The atopic march, as it has come to be known, represents the natural tendency of children with early signs of allergic reaction to environmental stimuli (e.g., atopic dermatitis) to progress to more severe manifestations of allergic disease (e.g., asthma) (Spergel, 2003).

What predisposes certain infants to develop atopic symptoms? While 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 (SNP's, 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 (Negoro, 2006). A baby with a given genomic predisposition,

under certain environmental conditions, will manifest immune dysregulation, resulting in an imbalance between Th1 dominant and Th2 dominant responses (Kidd, 2003). Th2 dominance leads to immune dysregulation marked by a proliferation of inflammatory cellular mediators (e.g., 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 (Noverr, 2005). According to this theory, our environments are now too "clean"—we are not exposed to as many antigens (bacteria, 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 (Duramad, 2006). Numerous studies also have supported a correlation between early life antibiotic exposure and atopy (particularly wheezing) in children (Johnson, 2005; Kozyrskyj, 2007; Kummeling, 2007; Marra, 2006; Noverr, 2004; Thomas, 2006) 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 (Bornehag, 2004; Chalubinski, 2006; Sherriff, 2005).

CONVENTIONAL APPROACHES

The assessment of atopy in conventional pediatric practice may include measuring blood IgE response to common dietary allergens or prick skin testing. If testing reveals documented allergy, parents are advised to avoid the offending food(s). Environmental modulation including household control of dust mites and discussion of pet exposure is sometimes employed. Classically, pharmaceutical agents including immunomodulators (e.g., steroids) and antihistamines are used for symptom management of atopic conditions.

CAM THERAPIES

Many families turn to CAM therapies for their children suffering atopic disorders (Bielroy, 2004; Braganza, 2003; Johnston, 2003; Ko, 2006; Reznick, 2002). Parents may be wary of potential adverse effects of conventional pharmaceuticals or may be interested in a more preventative approach. The most well studied CAM therapies for both prevention and treatment of infant atopy are those that are biologically based. Other CAM approaches integrated include mind-body methods, manipulative and body-based methods, and whole medical systems.

Mind-Body Methods

The stress connection to atopic expression is well documented. On a clinical level, psychological stress has been demonstrated to exacerbate asthma in children (Bloomberg, 2005; Wright, 2005). On a molecular level, anxiety is associated with an acceleration of

the pro-atopic Th2 response in patients with atopic dermatitis (Hashizume, 2005). These findings provide a rationale for the use of mind-body medicine therapies for atopic disorders. Self-hypnosis has been demonstrated by Anbar (2001, 2005) to be effective for the management of pulmonary conditions such as asthma, probably through the reduction of stress mechanisms. Similar results have been shown for children with eczema as well (Mantle, 1999).

BIOLOGICALLY BASED THERAPIES

Nutritional Modulation

For those infants at risk, exposure to certain foods in- and ex-utero may contribute to the development of atopy. We will focus on the following key areas: maternal pre- and post-natal antigen avoidance, breastfeeding, choice of infant formula supplementation, timing of solid food introduction, and fatty acid intake (both 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 (Kramer, 2006). In families at highest risk (parents and/or siblings with 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 (Zeiger, 2003). 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 of developing atopic dermatitis, food allergy, allergic rhinitis, and asthma (Friedman, 2005; Kull, 2005a, 2005b) If exclusive breastfeeding is not possible, the AAP recommends hydrolyzed protein formulas for high-risk babies (Zeiger, 2003). A Cochrane database systematic review supports this recommendation (Osborn, 2006a). These formulas may contain extensively or partially hydrolyzed cow's milk proteins (casein or whey), and there is debate about whether they are both equivalently effective in preventing atopic expression (Hays, 2005). 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 (Zeiger, 2003); again, this contention is supported by a Cochrane database systematic review (Osborn, 2006b).

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 both 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 delayed 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 until 36 months. (80) These guidelines are supported by other major US and European groups, but only for infants at high risk (Zeiger, 2003). Early solid feeding (prior to 4 months of age), particularly of gluten-containing products, is associated with atopic disease as well as celiac disease (Norris, 2005; Tarini, 2006). There have also been several encouraging studies looking at the treatment of atopic disorders with nutritional modulation (avoiding specific food allergens) (Fiocchi, 2004; Johnston, 2004; Lothian, 2006).

Recent studies have looked at the role of essential fatty acids in both preventing and reducing allergic disease. Atopy can be prevented when mothers ingest higher amounts of omega-3 polyunsaturated fatty acids (Puffs) (Denburg, 2005). It also appears that babies who ingest breast milk relatively rich in omega-3 are less likely to develop allergic symptoms (Oddly, 2006; Wigan, 2006). 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-3s PUFAs in children at high risk demonstrated reduction in atopy (Mihrshahi, 2004; Peat, 2004), and another study showed improvement with supplementation of evening primrose oil, an omega-6 PUFA (Biagi, 1988). Perhaps it is the balance of the two that is most important, and one must also take into account pre-existing 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 7 years postnatally (Kalliomaki, 2001, 2003, 2007). Prebiotics have also been shown to prevent eczema in a vulnerable infant population (Moro, 2006). Several randomized controlled trials have pointed towards a positive effect of probiotics and prebiotics on the course of atopic dermatitis (Passeron, 2006; Rosenfeldt, 2003; Viljanen, 2005; Weston, 2005), though one publication reported no such effect (Brouwer, 2006). More research is needed to determine the ideal doses and types of pre- and probiotics for atopy prevention and treatment.

MANIPULATIVE AND BODY-BASED METHODS

Most of the studies of manual therapies for atopic disorders are for the treatment of asthma. A 2005 Cochrane Database Systematic Review of all manual therapies for asthma identified only three trials with acceptable methodology for review, including two on chiropractic and one on massage (Hondras, 2005). The authors concluded that "there is insufficient evidence to support or refute the use of manual therapy for patients with asthma."

Therapeutic Massage

One published trial of massage for asthma demonstrated that children in the intervention group had less anxiety and improved pulmonary function testing compared with a relaxation therapy control group (Field, 1998). A small, controlled trial of massage for atopic dermatitis yielded positive results, too, as treated children's clinical skin measures, affect and activity level significantly improved (Schachner, 1998).

Osteopathy

Guiney, Chou, Vianna, and Lovenheim (2005) conducted a randomized controlled trial demonstrating the effect of OMT for pediatric asthma. The treatment group showed a statistically significant improvement in peak expiratory flow rates. In another small controlled trial of OMT for childhood asthma, Bockenhauer, Julliard, Lo, Huang, and Sheth (2002) found that some measures of pulmonary function in the intervention group (compared with control) improved while others did not.

Chiropractic

Published trials of chiropractic for pediatric asthma treatment are few and generally negative. One study reported that children in the intervention group noted improved quality of life and decreased asthma severity but also demonstrated "no important changes in lung function or hyperresponsiveness at any time" (Bronfort, 2002). Two other randomized trials of chiropractic for asthma demonstrated no statistically or clinically relevant effect compared with control measures (Balon, 1998; Nilsson, 1995).

WHOLE MEDICAL SYSTEMS

Homeopathy

According to Colin (2006), "Allergies, especially respiratory allergies, are one of the indications for which homeopathic treatment is most frequently sought." The author presents a summary of 147 cases of respiratory allergy treated in a private homeopathic practice as evidence of success with the treatment. He notes that only seven patients did not improve with treatment in this case series. He comments that "Lycopodium, Pulsatilla and Sulphur were most frequently prescribed for ENT allergies and that there was no predominantly prescribed remedy in the pulmonary allergy group." White et al. (2003) published a randomized, double-blinded, placebo-controlled study of individualized homeopathy combined with conventional therapy for the treatment of childhood asthma. The authors concluded that there was no evidence in this group of a superior effect of homeopathy versus placebo in the integrative treatment of asthma.

Case (Part 3): With the careful elimination of dairy from Mom's diet and the introduction of probiotics and essential fatty acids, the baby returns for his four-month visit with reduced eczema and GE reflux, no coughing, and only occasional rhinorrhea. However, given his continued symptoms and a reportedly "bad reaction" (high fever, severe irritability, poor feeding) after his first set of immunizations, his parents wonder whether it's prudent to delay further vaccination at this point in time.

IMMUNIZATION

Perhaps no subject in primary care practice today draws more attention and debate than vaccination. Historically, some holistic groups have always questioned immunization, but public health agencies and conventional pediatric associations in many countries today include the development of herd immunity as a cornerstone of preventative health policies. Almost all public educational institutions (based on state laws) require specific immunizations for entry, though all states allow for medical exemption, most (48) allow for religious exemption, and some (20) allow for philosophical exemption (parent and patient choice) (VaccineEthics.org, 2007). Furthermore, third-party payors (health insurers) are starting to expand "pay-for-performance" models based in part by a practice's vaccine coverage (percent of patients "appropriately" vaccinated).

There are several issues informing the vaccine debate. There are biological questions about the influence of immunization on infant immune/neuroimmune regulation. These questions center on both particular vaccine antigens and other biological substances used as preservatives (Offit, 2003). Vaccine antigens and their additional components do in fact induce immune modulation. This is, of course, the intended effect of immunization—to stimulate a strong enough immune response to a given antigen to induce immunity so the child does not develop the targeted infectious disease upon exposure. Following logically, given a specific genomic predisposition and environmental circumstances, vaccine antigens can also induce undesirable immune and other biological effects. All studies used for vaccine licensing include lists of adverse effects, though rare, and noted adverse reactions include seizures (Geier, 2004), wheezing (Belshe, 2007), and arthritis (Asakawa, 2005). Vaccine additives, which include 2-phenoxyethanol, phenol, thimerosal (ethyl mercury), various aluminum compounds, formaldehyde, antibiotics, egg and yeast proteins, gelatin and albumin, are included to either enhance immune response or preserve the product from contamination (Offit, 2003). Some of the preservative compounds also stimulate the immune response in animal models, including heavy metal-based compounds such as thimerosal and aluminum that have known immune and neuroimmune dysregulation properties (Havarinasab, 2006; Hornig, 2005; Petrovsky, 2004). The difficulty has been in conclusively demonstrating

these effects in children. Given the links between immune dysregulation and the development of atopic phenomena, a growing number of practitioners are concerned about the potential contribution of vaccines in a subset of children to disease expression. Clearly, much more research is needed in this area.

Ethically, the immunization issue involves the principles of human rights and the common good (individual rights versus state/societal rights) and of informed consent (risk-benefit decisions, exemptions, and waivers). Integrative practice is in part grounded in the tenets of individualizing care and in supporting a relationship-centered, open approach to child wellness care. Practitioners even in conventional circles are urged not to dismiss families who wish to alter standard vaccine practice and are encouraged to discuss risk and benefits in an open-minded manner (Diekema, 2005). But prevention is a key concept, too, and most integrative pediatricians concur that vaccines effectively prevent disease. In fact, it is in part the near-disappearance of vaccine-preventable diseases like polio and measles that have led some parents to conclude that the risks of their children developing the disease are outweighed by the perceived risks of developing vaccine-related illnesses. How does one reconcile the scientific and ethical principles noted above when there is so much uncertainty? In the "real-world" practice of integrative primary care, parents and practitioners communicate and debate risks and benefits, and we develop a plan that best serves each individual child.

Case (Part 4): The now 6-month-old baby has developed a series of acute ear infections with persistent middle ear fluid, which seem to be associated with the onset of teething and frequent upper respiratory infections. Both you and his parents would like to avoid antibiotic use and surgical intervention if possible. What are your other options?

Otitis Media

One of the most common reasons parents visit pediatricians is for the evaluation and treatment of ear infections (acute otitis media or AOM). AOM is the most common infection for which antibacterial agents are prescribed for children in the United States. There are billions of dollars spent yearly on prescriptions medications for AOM, and there is great concern about the appropriate use of antibiotics for the condition in an age when we are witnessing increasing rates of microbial resistance to anti-infectives (AAP, 2004).

There is a known association of AOM with URIs; less certain is the connection to teething. Anecdotally, many parents will report that teething seems to trigger ear infections in their infants. It is unclear whether teething simply causes ear pain or actually predisposes to Eustachian tube dysfunction. The main concern in these families regarding AOM is the need, regardless of cause, for quick and effective pain relief as well as

prevention of chronic serous otitis media (CSOM), or persistent middle ear fluid. The latter is the most common reason for elective surgery in children (other than circumcision) in the United States (Kogan, 2000).

CONVENTIONAL APPROACH

Although widely debated, the use of antibiotics for AOM is currently the standard of care for children under 2 years old in the United States. Indeed, for many older children, antibiotics are often prescribed for acute otitis media. These practices are less certain in other parts of the world. Concern regarding the development of antibiotic resistance has led more practitioners to develop an interest in integrating CAM therapies for the treatment of AOM (MacKay, 2003). Additionally, many parents use and practitioners recommend over-the-counter remedies for URI and teething symptoms. The use of these products in infants is not recommended due to concerns about lack of efficacy and potential for harm (Public Health Advisory, 2007), so that safe and effective alternatives for pain management are desirable. The conventional management of CSOM includes a wait-and-see approach, and if fluid persists for some length of time, myringotomy and pressure-equalizing tube placement is advised (American Academy of Family Physicians, 2004). Even this approach, however, is under scrutiny as to when and whether benefits outweigh risks (Lous, 2005).

CAM THERAPIES

In integrative care, the goal is primarily prevention of otitis media, and secondarily the use of naturally based methods for symptom management to optimize children's inherent healing mechanisms. Effective preventative measures include breastfeeding (Duncan, 1993) and avoiding environmental triggers like second-hand smoke and air pollution (Adair-Bischoff, 1998; Brauer, 2006). Regarding symptom management, we encourage parents to view URI and AOM symptoms (fever, congestion, rhinorrhea, cough) as the body's way of fighting infection. Natural viral infections theoretically allow for natural immune system development. Of course, one must consider the degree of symptoms and the possibility of overwhelming bacterial infection requiring the use of pharmaceutical agents including antibiotics. Pain relief—alleviating the suffering of children with AOM—is paramount as well and not to be dismissed lightly. Commonly used CAM therapies for otitis media management include biologically-based therapies, manipulative and body-based methods, and whole medical systems.

BIOLOGICAL-BASED THERAPIES

Botanical

Botanically based naturopathic topical ear drops have been shown to be effective and safe in prospective, randomized and controlled trials (Sarrell 2001, 2003). The specific

product tested included the following extracts: allium sativum, verbascum thapsus, calendula flores, hypericum perfoliatum, lavender and vitamin E, in an olive oil base. These components have anti-viral, anti-bacterial, anti-fungal, and anti-inflammatory properties. This topical botanical combination appears to be as effective for acute otitis media pain relief as prescription anesthetic ear drops with or without concurrent antibiotic use. No adverse effects were reported in these two trials. This approach seems to be a reasonable complement for AOM management during a time of observation without antibiotic use if clinically warranted.

Nutritional

Cod liver oil, which contains omega-3 essentially fatty acids as well as vitamins A and D, was studied in combination with selenium (an antioxidant mineral), in a small pilot trial for prevention of AOM (Linday, 2002). Eight children, serving as their own historical controls, received this combination of nutritional supplements for one "OM season" and were noted to receive antibiotics for significantly fewer days than in the prior "OM season." Larger, controlled trials are needed before general recommendations can be made.

Larch arabinogalactans, polysaccharides made up of galactan backbones with side-chains of galactose and arabinose sugars, have been linked in one report to decreased frequency and severity of pediatric AOM (D'Adamo, 1996). Larch arabinogalactan is a source of dietary fiber and also serves as a prebiotic, or substrate for growth of probiotic organisms. Whether its immune stimulating effects are via this mechanism or others is unclear.

Probiotics

When used, antibiotics cause significant gastrointestinal morbidity in children. Antibiotic-associated diarrhea (AAD) has been clearly demonstrated to be lessened by the preventive use of probiotics (Johnston, 2007). Whether this is particularly true or not with respect to AOM treatment has not been studied, but there is no reason to believe probiotics would not be helpful in this scenario. Which strain(s) and what dose(s) are safe and effective for AAD in children is debatable and worthy of further research.

MANIPULATIVE AND BODY-BASED METHODS

Osteopathy

Osteopathic manipulative treatment (OMT) has been studied in two published trials for preventing recurrent otitis media, with the goal of decreasing the need for surgical intervention for CSOM and recurrent AOM. Degenhardt and Kuchera (2006) treated eight children with recurrent AOM in an uncontrolled, pilot study. Patients received

weekly OMT for 3 weeks; intervention was performed in a complementary manner, concurrently with traditional medical management. Five children had no recurrence of symptoms, and only one required myringotomy and tube placement surgery at 1-year follow-up.

Mills, Henley, Barnes, Carreiro, and Degenhardt (2003) performed a prospective, controlled trial of OMT in 57 children with recurrent AOM. The control group received routine pediatric care and the intervention group OMT plus routine care for nine visits over a 6 month study period. Children receiving OMT has significantly fewer episodes of AOM, surgical procedures and "surgery-free months." No adverse reactions were reported.

Chiropractic

Although prevention of recurrent AOM and treatment of CSOM are both frequent reasons for pediatric chiropractic visits, there is little published data regarding the safety and efficacy of this practice. Most reported trials demonstrating success are uncontrolled, non-randomized case-studies (Froehle, 1996; Fysh, 1996). Sawyer, Evans, Boline, Branson, and Spicer (1999) demonstrated the feasibility of performing a randomized study of active chiropractic spinal manipulative therapy (SMT) or placebo chiropractic SMT. There are no RCT trials of chiropractic SMT for otitis media available for review on NCBI PubMed.

WHOLE MEDICAL SYSTEMS

Homeopathy

Two published studies evaluated the use of individualized homeopathic remedies for treatment of AOM in children. A group from Switzerland found that pain resolution was significantly faster in homeopathically-treated children than in controls (Frei, 2001). A US study reported that children receiving individualized homeopathic remedies had more significant reductions in symptoms (pain) at 24 and 64 hours than in placebo-controls (Jacobs, 2001). There is difficulty, of course, in extrapolating the importance of these positive findings of individualized treatments to a larger, generalized pediatric population. However, the study design mechanism does take into account the actual practice of homeopathy, which is based on individualizing remedies.

Case (Part 5/Conclusion): Now approaching his first birthday, our young patient and his family are thriving. With continued dietary vigilance and judicious use of topical herbals, homeopathy and manipulative therapy, the baby is growing and developing as expected, and everyone is looking forward to an exciting second year.

Conclusion

The integration of CAM therapies into primary care pediatric practice is well illustrated by the case discussion threaded throughout this chapter. CAM therapies are being more frequently utilized 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 pediatric conditions has steadily increased in volume and improved in quality. While 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, in ideal position to adopt and advocate the medical home paradigm, should engage their patients and families in respectful, collaborative dialogue regarding the use of CAM therapies. As the number of children with special healthcare needs grows, and as more families develop an interest in a holistic model of care for prevention and treatment, integrative primary care is poised to become the standard of children's healthcare.

Internet Resources

AAP Provisional Section on Complementary, Holistic and Integrative Medicine: http://www.aap.org/sections/CHIM

AAP National Center of Medical Home Initiatives for Children with Special Needs: http://www.medicalhomeinfo.org

Center for Medical Home Improvement: http://www.medicalhomeimprovement.org

The Collaborative on Health and the Environment: http://healthandenvironment.org

Commonweal: http://www.commonweal.org

Environmental Working Group: http://www.ewg.org

Environmental Health News: http://www.environmentalhealthnews.org

The Green Guide (National Geographic): http://www.thegreenguide.com

Healthy Child Healthy World: http://healthychild.org

Institute for Children's Environmental Health: http://www.iceh.org

Integrative Pediatrics Council:
http://www.integrativepeds.org

The National Environmental Education & Training Foundation: http://www.neetf.org

Teleosis Institute: Green Health Care—Ecologically Sustainable Medicine: http://www.teleosis.org

The Whole Child Center
http://www.wholechildcenter.org

REFERENCES

Adair-Bischoff, C. E., & Sauve, R. S. (1998). Environmental tobacco smoke and middle ear disease in preschool-age children. *Archives of Pediatrics & Adolescent Medicine*, *152*(2), 127–133.

American Academy of Family Physicians; American Academy of Otolaryngology-Head and Neck Surgery; American Academy of Pediatrics Subcommittee on Otitis Media With Effusion. (2004). Otitis media with effusion. *Pediatrics, 113*(5), 1412–1429.

AAP Committee on Nutrition. (1998). Soy protein-based formulas: recommendations for use in infant feeding. *Pediatrics, 101*, 148–153.

AAP Committee on Nutrition. (2000). Hypoallergenic infant formulas. *Pediatrics, 106*, 346–349.

AAP Division of Health Policy Research. Periodic Survey of Fellows #49: Complementary and Alternative Medicine (CAM) Therapies in Pediatric Practices (2001). Retrieved November 6, 2007, from http://www.aap.org/research/periodicsurvey/ps49bexs.htm

AAP Medical Home Initiatives for Children with Special Needs Project Advisory Committee. (2002). The medical home. *Pediatrics, 110*(1), 184–186.

AAP Subcommittee on Management of Acute Otitis Media. (2004). Diagnosis and management of acute otitis media. *Pediatrics, 113*(5), 1451–1465.

Agawam, K. N., Gupta, A., Pushkin, R., et al. (2000). Effects of massage & use of oil on growth, blood flow & sleep pattern in infants. *The Indian Journal of Medical Research*, *112,* 212–217.

Kaman, I., Kusch, K., Ozdemir, N., et al. (2006). Mothers' postpartum psychological adjustment and infantile colic. *Archives of Disease in Childhood*, *91*, 417–419.

Alexandrovich, I., Rakovitskaya, O., Kolmo, E., et al. (2003). The effect of fennel (foeniculum vulgare) seed oil emulsion in infantile colic: A randomized, placebo-controlled study. *Alternative Therapies in Health and Medicine, 9*, 58–61.

Anbar. R. D. (2001). Self-hypnosis for management of chronic dyspnea in pediatric patients. *Pediatrics*, *107*, e21.

Anbar, R. D., & Geisler, S. C. (2005). Identification of children who may benefit from self-hypnosis at a pediatric pulmonary center. *BMC Pediatrics*, *5*, 6.

Asakawa, J., Kobayashi, S., Kaneda, K., Ogasawara, H., Sugawara, M., Yasuda, M., et al. (2005). Reactive arthritis after influenza vaccination: Report of a case. *Modern Rheumatology, 15*(4), 283–285.

Asher, M. I., Montefort, S., Bjorksten, B., et al. (2006). Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet, 368*, 733–743.

Balon, J., Aker, P. D., Crowther, E. R., Danielson, C., Cox, P. G., O'Shaugnessy, D., et al. (1998). A comparison of active and simulated chiropractic manipulation as adjunctive treatment for childhood asthma. *New England Journal of Medicine*, *339*(15), 1013–1020.

Belshe, R. B., Edwards, K.M., Vesikari, T., Black, S. V., Walker, R. E., Hultquist, M, et al. (2007). CAIV-T Comparative Efficacy Study Group. Live attenuated versus inactivated influenza vaccine in infants and young children. *The New England Journal of Medicine*, *356*(7), 685–696.

Biagi, P. L., Bordoni, A., Masi, M., et al. (1988). A long-term study on the use of evening primrose oil (Efamol) in atopic children. *Drugs Under Experimental and Clinical Research*, *14*, 285–290.

Bielroy, L. (2004). Complementary and alternative interventions in asthma, allergy, and immunology. *Annals of allergy, Asthma and Immunology, 93*(Suppl 1), S45–S54.

Bloomberg, G. R., & Chen, E. (2005).The relationship of psychological stress with childhood asthma. *Immunology and Allergy Clinics of North America*, *25*, 83–105.

Blumental, I. (2000). The gripe water story. *Journal of the Royal Society of Medicine, 93*, 172–174.

Bockenhauer, Se., Julliard, K. N., Lo, K. S., Huang, K. E., & Sheth, A. M. (2002). Quantifiable effects of osteopathic manipulative techniques on patients with chronic asthma. *Journal of the American Osteopathic Association*, *102*(7), 371–375.

Bornehag, C. G., Sundell, J., Weschler, C. J., et al. (2004). The association between asthma and allergic symptoms in children and phthalates in house dust: A nested case-control study. *Environmental Health Perspectives*, *112*, 1393–1397.

Braganza, S., Ozuah, P. O., & Sharif, I. (2003). The use of complementary therapies in inner-city asthmatic children. *The Journal of Asthma*, *40*, 823–827.

Brauer, M., Gehring, U., Brunekreef, B., de Jongste, J., Gerritsen, J., Rovers, M., et al. (2006). Traffic-related air pollution and otitis media. *Environmental Health Perspectives*, *114*(9), 1414–1418.

Braun, C. A., Bearinger, L. H., Halcon, L. L., et al. (2005). Adolescent use of complementary therapies. *The Journal of Adolescent Health*, *37*, 76e.1–76e.9.

Brazelton, T. B. (1962).Crying in infancy. *Pediatrics, 29*, 579–588.

Bronfort, G., Evans, R. L., Kubic, P., & Filkin, P. (2002). Chronic pediatric asthma and chiropractic spinal manipulation: A prospective clinical series and randomized clinical pilot study. *Journal of Manipulative and Physiological Therapeutics*, *24*(6), 369–377.

Brouwer, M. L., Wolt-Plompen, S. A., Dubois, S. E., et al. (2006). No effects of probiotics on atopic dermatitis in infancy: A randomized placebo-controlled trial. *Clinical and Experimental Allergy*, *36,* 899–906.

Castro-Rodriguez, J, A., Stern, D.A,, Halonen, M., Wright, A. L., Holberg, C. J., Taussig, L. M., et al. (2001). Relation between infantile colic and asthma/atopy: a prospective study in an unselected population. *Pediatrics*, *108*(4), 878–882.

Chalubinski, M., & Kowalski, M. L. (2006). Endocrine disrupters—potential modulators of the immune system and allergic response. *Allergy, 61*, 1326–1335.

Cheruku, S. R., Montgomery-Downs, H. E., Farkas, S. L., et al. (2002). Higher maternal plasma docosahexanoic acid during pregnancy is associated with more mature neonatal sleep-state patterning. *The American Journal of Clinical Nutrition, 76*, 608–613.

Clifford, T. J., Campbell, M. K., Speechley, K. N., et al. (2002). Infant colic: empirical evidence of the absence of an association with source of early infant nutrition. *Archives of Pediatrics & Adolescent Medicine, 156*, 1123–1128.

Cohen, M. H. (2006). Legal and ethical issues relating to use of complementary therapies in pediatric hematology/oncology. *Journal of Pediatric Hematology/Oncology, 28*, 190–193.

Colin, P. (2006). Homeopathy and respiratory allergies. *Homeopathy*, *95*, 68–72.

D'Adamo, P. (1996). Larch arabinogalactan. *Journal of Naturopathic Medicine, 6*, 33–37.

Degenhardt, B. F., & Kuchera M. L. (2006). Osteopathic evaluation and manipulative treatment in reducing the morbidity of otitis media: A pilot study. *The Journal of the American Osteopathic Association*, *106*(6), 327–334.

Denburg, J. A., Hatfield, H. M., Cyr, M. M., et al. (2005). Fish oil supplementation in pregnancy modifies neonatal progenitors at birth in infants at risk of atopy. *The Journal of the American Osteopathic Association, 57*, 276–281.

Diekema, D. S.; American Academy of Pediatrics Committee on Bioethics. (2005). Responding to parental refusals of immunization of children. *Pediatrics, 115*(5), 1428–1431.

Dihigo, S. K. (1998). New strategies for the treatment of colic: Modifying the parent/infant interaction. *Environmental Health Perspectives, 12*, 256–262.

Duncan, B., Ey, J., Holberg, C. J., Wright, A. L., Martinez, F. D., & Taussig L. M. (1993). Exclusive breast-feeding for at least 4 months protects against otitis media. *Pediatrics, 91*(5), 867–872.

Duramad, P., Harley, K., Lipsett, M., et al. (2006). Early environmental exposures and intracellular Th1/Th2 cytokine profiles in 24-month-old children living in an agricultural area. *Environmental Health Perspectives, 114*, 1916–1922.

Ekins-Daukes, S., Helms, P. J., Taylor, M. W., Simpson, C. R., & McLay J. S. (2005). Paediatric homoeopathy in general practice: Where, when and why? *British Journal of Clinical Pharmacology, 59*(6), 743–749.

Fallon J. M. (1997). The role of the chiropractic adjustment in the care and treatment of 332 children with otitis media. *Journal of Clinical Chiropractic Pediatrics*, *2*(2), 167–183.

Field, T. (1995). Massage therapy for infants and children. *Journal of Developmental & Behavioral Pediatrics*, 105–111.

Field, T., Henteleff, T., Hernandez-Reif, M., Martinez, E., Mavunda, K., Kuhn, C., et al. (1998). Children with asthma have improved pulmonary function after massage. *The Journal of Pediatrics, 132*(5), 854–858.

Fiocchi, A., Bouygue, G. R., Martelli, A., et al. (2004). Dietary treatment of childhood atopic eczema/dermatitis syndrome (AEDS). *Allergy, 59*(Suppl. 78), 78–85.

Fiocchi, A., Assa'ad, A, Bahna, S., et al. (2006). Food allergy and the introduction of solid foods to infants: A consensus document. Adverse Reactions to Foods Committee, American College of Allergy, Asthma and Immunology. *Annals of Allergy, Asthma and Immunology, 97*, 10–20.

Fireman, L. (2006). Colic. *Pediatr Review, 27*, 357–358.

Frei, H., & Thurneysen, A. (2001). Homeopathy in acute otitis media in children: Treatment effect or spontaneous resolution? *The British Homoeopathic Journal, 90*, 178–179.

Friedman, N. J., & Zieger, R. S. (2005). The role of breast-feeding in the development of allergies and asthma. The *Journal of Allergy and Clinical Immunology, 115*, 1238–1248.

Froehle R. M. (1996). Ear infection: A retrospective study examining improvement from chiropractic care and analyzing for influencing factors. *Journal of Manipulative and Physiological Therapeutics, 19*(3), 169–177.

Fysh P. N. (1996). Chronic recurrent otitis media: Case series of five patients with recommendations for case management. *Journal of Clinical Chiropractic Pediatrics*, *1*, 66–178.

Garrison, M. M., & Christakis, D. A. (2000). A systematic review of treatments for infant colic. *Pediatrics, 106*, 184–190.

Geier, D. A., & Geier M. R. (2004). An evaluation of serious neurological disorders following immunization: A comparison of whole-cell pertussis and acellular pertussis vaccines. *Brain and Development, 26*(5), 296–300.

Guiney, P. A., Chou, R., Vianna, A., & Lovenheim, J. (2005). Effects of osteopathic manipulative treatment on pediatric patients with asthma: A randomized controlled trial. *Journal of the American Osteopathic Association, 105*, 7–12.

Harrington, J. W., Rosen, L., Garnecho, A., & Patrick, P. A. (2006). Parental perceptions and use of complementary and alternative medicine practices for children with autistic spectrum disorders in private practice. *Journal of Developmental and Behavioral Pediatrics, 27*(2 Suppl), S156–S161.

Hashizume, H., et al. (2005). Anxiety accelerates T-helper 2-tilted immune responses in patients with atopic dermatitis. *The British Journal of Dermatology, 152*, 1161–1164.

Havarinasab, S., & Hultman, P. (2006). Alteration of the spontaneous systemic autoimmune disease in (NZB x NZW)F1 mice by treatment with thimerosal (ethyl mercury). *Toxicology and Applied Pharmacology,* 214(1), 43–54.

Hayden, C., Mullinger, B. (2006). A preliminary assessment of the impact of cranial osteopathy for the relief of infantile colic. *Complementary Therapies in Clinical Practice, 12*(2), 83–90.

Hays, T., & Wood, R. A. (2005). A systematic review of the role of hydrolyzed infant formulas in allergy prevention. *Archives of Pediatrics & Adolescent Medicine*, *159*, 810–816.

Heine, R. G. (2006). Gastroesophageal reflux disease, colic and constipation in infants with food allergy. *Current Opinion in Allergy and Clinical Immunology, 6*, 220–225.

Hewitt, E. G. (2004). Chiropractic care and the irritable infant. *Journal of Clinical Chiropractic Pediatrics*, *6*(2), 394–397.

Hill, D. J., Roy, N., Heine, R. G., et al. (2005). Effect of a low-allergen maternal diet on colic among breastfed infants: a randomized, controlled trial. *Pediatrics, 116*, e709–e715.

Hondras, M. A., Linde, K., & Jones, A. P. (2005). Manual therapy for asthma. *Cochrane Database of Systematic Reviews, 18*(2), CD001002.

Hornig, M., Chian, D., & Lipkin W. I. (2004). Neurotoxic effects of postnatal thimerosal are mouse strain dependent. *Molecular Psychiatry, 9*(9), 833–845.

Huhtala, V., Lehtonen, L., Heinonen, R., et al. (2000). Infant massage compared with crib vibrator in the treatment of colicky infants. *Pediatrics, 105*, e84–e89.

Jacobs, J., et al. (2001). Homeopathic treatment of acute otitis media in children: A preliminary randomized placebo-controlled trial. *The Pediatric Infectious Disease Journal, 20*, 177–183.

Jakobsson, I., Lothe, L., Ley, D., et al. (2000). Effectiveness of casein hydrolysate feedings in infants with colic. *Acta Paediatrica, 89*, 18–21.

Johnson, C. C., Ownby, D. R., Alford, S. H., et al. (2005). Antibiotic exposure in early infancy and risk for childhood atopy. *The Journal of Allergy and Clinical Immunology, 115*, 1218–1224.

Johnston, G. A., Bilbao, R. M., & Graham-Brown, R. A. (2003). The use of complementary medicine in children with atopic dermatitis in secondary care in Leicester. *British Journal of Dermatology, 149*, 566–571.

Johnston, G. A., Bilbao, R. M., & Graham-Brown, R. A. (2004). The use of dietary manipulation by parents of children with atopic dermatitis. British Journal of Dermatology, *150*, 1186–1189.

Johnston, B. C., Supina, A. L., Ospina, M., & Vohra, S. (2007). Probiotics for the prevention of pediatric antibiotic-associated diarrhea. *Cochrane Database of Systematic Reviews*, *18*(2), CD004827.

Kalliomaki, M., Salminen, S., Arvilommi, H., et al. (2001). Probiotics in primary prevention of atopic disease: A randomized placebo-controlled trial. *Lancet, 357*, 1076–1079.

Kalliomaki, M., Salminen, S., Poussa, T., et al. (2003). Probiotics and prevention of atopic disease: 4-year follow-up of randomised placebo-controlled trial. *Lancet, 361*, 1869–1871.

Kalliomaki, M., Salminen, S., Poussa, T., & Isolauri, E. (2007). Probiotics during the first 7 years of life: A cumulative risk reduction of eczema in a randomized, placebo-controlled trial. *The Journal of Allergy and Clinical Immunology, 119*(4), 1019–1021.

Karp, H. (2004). The "fourth trimester": A framework and strategy for understanding and resolving colic. *Contemporary Pediatrics, 21*, 94–116.

Keefe, M. R., Kajrlsen, K. A., Lobo, M. L., et al. (2006). Reducing parenting stress in families with irritable infants. *Nursing Research, 55*, 198–205.

Kemper K. J. (2000). Holistic pediatrics = good medicine. *Pediatrics,* 105(1 Pt 3), 214–218.

Kidd, P. (2003). Th1/Th2 balance: The hypothesis, its limitations, and implications for health and disease. *Alternative Medicine Review, 8*, 223–246.

Klougart, N., Nilsson, N., & Jacobsen, J. (1989). Infantile colic treated by chiropractors: A prospective study of 316 cases. *Journal of Manipulative and Physiological Therapeutics, 12*(4), 281–288.

Ko, J., Lee, J. I., Munoz-Furlong, A., et al. (2006). Use of complementary and alternative medicine by food-allergic patients. *Annals of Allergy, Asthma and Immunology,, 97*, 365–369.

Kogan, M. D., Overpeck, M. D., Hoffman, H. J., & Casselbrant, M. L. (2000). Factors associated with tympanostomy tube insertion among preschool-aged children in the United States. *American Journal of Public Health*, *90*(2), 245–250.

Kozyrskyj, A. L., Ernst, P., & Becker, A. B. (2007). Increased risk of childhood asthma from antibiotic use in early life. *Chest, 131*(6), 1753–1759

Kramer, M. S., & Kakuma, R. (2006). Maternal antigen avoidance during pregnancy or lactation, or both, for preventing or treating atopic disease in the child. *Cochrane Database of Systematic Reviews, 19,* 3, CD000133.

Kull, I., Wickman, M., Lilja, G., et al. (2002). Breast feeding and allergic disease in infants—a prospective birth cohort study. *Archives of Disease in Childhood, 87*, 478–481.

Kull, I., Almqvist, C., Lilja, G., et al. (2005a). Breast-feeding reduces the risk of asthma during the first 4 years of life. *The Journal of Allergy and Clinical Immunology, 114*, 755–760.

Kull, I., Bohme, M., Wahlgren, C. F., et al. (2005b). Breast-feeding reduces the risk for childhood eczema. *The Journal of Allergy and Clinical Immunology, 116*, 657–661.

Kummeling, I., Stelma, F. F., Dagnelie, P. C., Snijders, B. E., Penders, J., Huber, M., et al. (2007). Early life exposure to antibiotics and the subsequent development of eczema, wheeze, and allergic sensitization in the first 2 years of life: The KOALA Birth Cohort Study. *Pediatrics, 119*(1), e225–231.

Linday, L. A., Dolitsky, J. N., Shindledecker, R. D., & Pippenger C. E. (2002). Lemon-flavored cod liver oil and a multivitamin-mineral supplement for the secondary prevention of otitis media in young children: Pilot research. *The Annals of Otology, Rhinology, and Laryngology, 111*(7 Pt 1), 642–652.

Liptak, G. S., Orlando, M., Yingling, J. T., Theurer-Kaufman, K. L., Malay, D. P., Tompkins, L. A., et al. (2006). Satisfaction with primary healthcare received by families of children with developmental disabilities. *Journal of Pediatric Health Care, 20*(4), 245–252.

Lohse, B., Stotts, J. L., & Priebe, J. R. (2006). Survey of herbal use by Kansas and Wisconsin WIC participants reveals moderate, appropriate use and identifies herbal education needs. *Journal of the American Dietetic Association, 106*, 227–237.

Loman, D. G. (2003). The use of complementary and alternative healthcare practices among children. *Journal of Pediatric Health Care, 17*, 58–63.

Lothian, J. B., Grey, V., & Lands, L. C. (2006). Effect of whey protein to modulate immune response in children with atopic asthma. *International Journal of Food Sciences and Nutrition, 57*, 204–211.

Lous, J., Burton, M. J., Felding, J. U., Ovesen, T., Rovers, M. M., & Williamson I. (2005). Grommets (ventilation tubes) for hearing loss associated with otitis media with effusion in children. *Cochrane Database of Systematic Reviews*, *25*(1), CD001801.

Lucassen, P. L., Assendelft, W. J., Gubbels, J. W., et al. (2000). Infantile colic: Crying time reduction with a whey hydrolysate: A double-blind, randomized, placebo-controlled trial. *Pediatrics, 106*, 1349–1354.

Lust, K. D., Brown, J. E., & Thomas, W. (1996). Maternal intake of cruciferous vegetables and other foods and colic symptoms in exclusively breast-fed infants. *Journal of the American Dietetic Association, 96*, 46–48.

Mantle, F. (1999). Hypnosis in the management of eczema in children. *Paediatric Nursing, 11*, 24–26.

Marra, F., Lynd, L., Coombes, M., et al. (2006). Does antibiotic exposure during infancy lead to development of asthma? A systematic review and metaanalysis. *Chest, 129*, 610–618.

Mihrshahi, S., Peat, J. K., Webb, K., et al. (2004). Effect of omega-3 fatty acid concentrations in plasma on symptoms of asthma at 18 months of age. *Pediatric Allergy and Immunology, 15*, 517–522.

Mills, M. V., Henley, C. E., Barnes, L. L. B., Carreiro, J. E., & Degenhardt B. F. (2003). The use of osteopathic manipulative treatment as adjuvant therapy in children with recurrent acute otitis media. *Archives of Pediatrics and Adolescent Medicine, 157*(9), 861–866.

Mind-Body Medicine: An Overview (NCCAM). Retrieved November 6, 2007, from http://nccam.nih.gov/health/backgrounds/mindbody.htm#intro

Moro, G., Arslanaglu, S., Stahl, B., et al. (2006). A mixture of prebiotic oligosaccharides reduces the incidence of atopic dermatitis during the first six months of age. *Archives of Disease in Childhood, 91*, 814–819.

Natural Medicines Comprehensive Database. Retrieved November 6, 2007, from http://www.naturaldatabase.com

Negoro, T., Orihara, K., Irahara, T., et al. (2006). Influence of SNP's in cytokine-related genes on the severity of food allergy and atopic eczema in children. *Pediatric Allergy and Immunology, 17*, 583–590.

Nilsson, N. H., Bronfort, G., Bendix, T., Madsen, F., & Weeke, B. (1995). Chronic asthma and chiropractic spinal manipulation: A randomized clinical trial. *Journal of Clinical and Experimental Allergy, 25*(1), 80–88.

Norris, J. M., Barriga, K., Hoffenberg, E. J., et al. (2005). Risk of celiac disease autoimmunity and timing of gluten introduction in the diet of infants at increased risk of disease. *The Journal of the American Medical Association, 293*, 2343–2351.

Noverr, M. C., Noggle, R. M., Toews, G. B., et al. (2004). Role of antibiotics and fungal microbiota in driving pulmonary allergic responses. *Infection and Immunity, 72*, 4996–5003.

Noverr, M. C., & Huffnagle, G. B. (2005). The 'microflora hypothesis' of allergic diseases. *Clinical and Experimental Allergy, 35*, 1511–1520.

Oddy, W. H., Pal, S., Kusel, M. M., et al. (2006). Atopy, eczema and breast milk fatty acids in a high-risk cohort of children followed from birth to 5 yr. *Pediatric Allergy and Immunology, 17*, 4–10.

Offit, P. A., & Jew, R. K. (2003). Addressing parents' concerns: Do vaccines contain harmful preservatives, adjuvants, additives, or residuals? *Pediatrics, 112*(6 Pt 1), 1394–1397.

Olafsdottir, E., Forshei, S., Fluge, G., & Markestad, T. (2001). Randomised controlled trial of infantile colic treated with chiropractic spinal manipulation. *Archives of Disease in Childhood, 84*(2), 138–141.

Osborn, D. A., & Sinn, J. (2006a). Formulas containing hydrolysed protein for prevention of allergy and foodx intolerance in infants. *Cochrane Database of Systematic Reviews, 18*(4), CD003664.

Osborn, D. A., & Sinn, J. (2006b). Soy formula for prevention of allergy and food intolerance in infants. *Cochrane Database of Systematic Reviews, 18*(4), CD003741.

Passeron, T., Lacour, J. P., Fontas, E., et al. (2006). Probiotics and synbiotics: Two promising approaches for the treatment of atopic dermatitis in children above 2 years. *Allergy, 61*, 431–437.

Peat, J. K., Mihrshahi, S., Kemp, A. S., et al. (2004). Three-year outcomes of dietary fatty acid modification and house dust mite reduction in the Childhood Asthma Prevention Study. *The Journal of Allergy and Clinical Immunology, 114*, 807–813.

Petrovsky, N., & Aguilar J. C. (2004). Vaccine adjuvants: Current state and future trends. *Immunology and Cell Biology*, *82*(5), 488–496.

Primary Care—Wikipedia. Retrieved November 6, 2007, from http://en.wikipedia.org/wiki/Primary_care

Public Health Advisory: Nonprescription Cough and Cold Medicine Use in Children. Retrieved November 6, 2007, from http://www.fda.gov/cder/drug/advisory/cough_cold.htm

Reznick, M., Ozuah, P. O., Franco, K., et al. (2002). Use of complementary therapy by adolescents with asthma. *Archives of Pediatrics & Adolescent Medicine, 156*, 1042–1044.

Rosenfeldt, V., Benfeldt, E., Nielsen, S. D., et al. (2003). Effect of probiotic Lactobacillus strains in children with atopic dermatitis. *The Journal of Allergy and Clinical Immunology, 111*, 389–395.

Sanders, H., Davis, M. F., Duncan, B., et al. (2003). Use of complementary and alternative medical therapies among children with special healthcare needs in southern Arizona. *Pediatrics, 111*, 584–587.

Sarrell, E. M., Mandelberg, A., Cohen, H. A. (2001). Efficacy of naturopathic extracts in the management of ear pain associated with acute otitis media. *Archives of Pediatrics & Adolescent Medicine, 155*(7), 796–799.

Sarrell, E. M., Cohen, H. A., & Kahan, E. (2003). Naturopathic treatment for ear pain in children. *Pediatrics, 111*(5 Pt 1), e574–e579.

Savino, F., Cresi, F., Pautasso, S., et al. (2004). Intestinal microflora in breastfed colicky and non-colicky infants. *Acta Paediatrica, 93*, 825–829.

Savino, F., Castagno, E., Bretto, R., et al. (2005). A prospective 10-year study on children who had severe infantile colic. *Acta Paediatrica, 94*(Suppl), 129–132.

Savino, F., Cresi, F., Castagno, E., et al. (2005). A randomized double-blind placebo-controlled trial of a standardized extract of Matricariae recutita, Foeniculum vulgare and Melissa officinalis (ColiMil) in the treatment of breastfed colicky infants. *Phytotherapy Research, 19*, 335–340.

Savino, F., Bailo, E., Oggero, R., et al. (2005). Bacterial counts of intestinal Lactobacillus species in infants with colic. *Pediatric Allergy and Immunology, 16*, 72–75.

Savino, F., Palumeri, E., Castagno, E., et al. (2006). Reduction of crying episodes owing to infantile colic: A randomized controlled study on the efficacy of a new infant formula. *European Journal of Clinical Nutrition, 60*, 1304–1310.

Savino, F., Pelle, E., Palumeri, E., et al. (2007). *Lactobacillus reuteri* (American Type Culture Collection Strain 55730) versus simethicone in the treatment of infantile colic: A prospective randomized study. *Pediatrics, 119*, e124–e130.

Sawni-Sikand, A., Schubiner, H., & Thomas, R. L. (2002). Use of complementary/alternative therapies among children in primary care pediatrics. *Ambulatory Pediatrics, 2*, 99–103.

Sawyer, C. E., Evans, R. L., Boline, P. D., Branson, R., & Spicer, A. (1999). A feasibility study of chiropractic spinal manipulation versus sham spinal manipulation for chronic otitis media with effusion in children. *Journal of Manipulative and Physiological Therapeutics, 22*(5), 292–298.

Schachner, L., Field, T., Hernandez-Reif, M., Duarte, A. M., & Krasnegor, J. (1998). Atopic dermatitis symptoms decreased in children following massage therapy. *Pediatric Dermatology, 15*(5), 390–395.

Schrezenmeir, J., & de Vrese, M. (2001). Probiotics, prebiotics, and synbiotics—approaching a definition. *The American Journal of Clinical Nutrition, 73*, 361S–364S.

Sherriff, A., Farrow, A., Golding, J., et al. (2005). Frequent use of chemical household products is associated with persistent wheezing in pre-school age children. *Thorax, 60*, 45–49.

Smitherman, L. C., Janisse, J., & Mathur, A. (2005). The use of folk remedies among children in an urban black community: Remedies for fever, colic, and teething. *Pediatrics, 115*, e297–e304.

Spergel, J. M., & Palier, A. S. (2003). Atopic dermatitis and the atopic march. *The Journal of Allergy and Clinical Immunology, 112,* 118–127.

Spigelblatt, L., Laine-Ammara, G., Pless, I. B., et al. (1994). The use of alternative medicine by children. *Pediatrics, 94*, 811–814.

Tarini, B. A., Carroll, A. E., Sox, C. M., et al. (2006). Systematic review of the relationship between early introduction of solid foods to infants and the development of allergic disease. *Archives of Pediatrics & Adolescent Medicine, 160*, 502–507.

Thomas, M., Custovic, A., Woodcock, A., et al. (2006). Atopic wheezing and early life antibiotic exposure: A nested case-control study. *Pediatric Allergy and Immunology, 17*, 184–188.

Underdown, A., Barlow, J., Chung, V., et al. (2006). Massage intervention for promoting mental and physical health in infants aged under six months. *Cochrane Database of Systematic Reviews, 18*(4), CD005038.

VaccineEthics.org: Vaccination Requirements and Exemptions. Retrieved November 6, 2007, from http://www.vaccineethics.org/issue_briefs/requirements.php

Viljanen, M., Savilahti, E., Haahtela, T., et al. (2005). Probiotics in the treatment of atopic eczema/dermatitis syndrome in infants: a double-blind placebo-controlled trial. *Allergy, 60*, 494–500.

Weizman, Z., Alkrinawi, S., Goldfard, D., et al. (1993). Efficacy of herbal tea preparation in infantile colic. *The Journal of Pediatrics, 122*, 650–652.

Wessel, M. A., Cobb, J. C., Jackson, E. B., et al. (1954). Paroxysmal fussing in infancy, sometimes called "colic." *Pediatrics, 14*, 421–435.

Weston, S., Halbert, A., Richmond, P., et al. (2005). Effects of probiotics on atopic dermatitis: A randomized controlled trial. *Archives of Disease in Childhood, 90*, 892–897

Wheeden, A. (1993). Massage effects on cocaine-exposed preterm neonates. *Journal of Developmental and Behavioral Pediatric, 14*(5), 318–322.

White, A., Slade, P., Hunt, C., Hart, A., & Ernst. E. (2003). Individualized homeopathy as an adjunct in the treatment of childhood asthma: A randomised placebo controlled trial. *Thorax, 58*(4), 317–321.

Wiberg, J. M. M., Nordsteen, J., Nilsson, N. (1999). The short-term effect of spinal manipulation in the treatment of infantile colic: A randomized controlled trial with a blinded observer. *Journal of Manipulative and Physiological Therapeutics, 22*(8), 517–522.

Wijga, A. H., van Houwelingen, A. C., Kerkhof, M., et al. (2006). Breast milk fatty acids and allergic disease in preschool children: The Prevention and Incidence of Asthma and Mite Allergy birth cohort study. *The Journal of Allergy and Clinical Immunology, 117*, 440–447.

Wilson, K. M., & Klein, J. D. (2002). Adolescents' use of complementary and alternative medicine. *Ambulatory Pediatrics, 2*, 104–110.

Wolke, D., Gray, P., & Meyer, R. (1994). Excessive infant crying: A controlled study of mothers helping mothers. *Pediatrics, 94*, 322–332.

Wright, R. J., Cohen, R. T., & Cohen, S. (2005). The impact of stress on the development and expression of atopy. *Current Opinion in Allergy and Clinical Immunology, 5*(1), 23–29.

Zeiger, R. S. (2003). Food allergen avoidance in the prevention of food allergy in infants and children. *Pediatrics, 111*, 1662–1671.