
State of the Art —

Complementary and Alternative Therapies: Use in Pediatric Pulmonary Medicine

Youngran Chung, MD^{1*} and Robert C. Dumont, MD²

Summary. With increased awareness of complementary/alternative medicine (CAM) and concern of potential adverse effects or limited effectiveness of conventional medications, patients and parents are looking to CAM approaches as either an alternative or as adjunct therapy, especially for chronic diseases such as asthma or cystic fibrosis. It is important that practitioners have adequate information so that patients and parents receive balanced and accurate information, especially regarding safety and potential efficacy. This review provides an overview of some of the more frequently used CAM therapies for children with chronic pulmonary disorders and summarizes the basic principles of each modality, along with efficacy and safety data. *Pediatr Pulmonol.* 2011; 46:530–544. © 2011 Wiley-Liss, Inc.

Key words: complementary medicine; alternative medicine; integrative medicine; children; pulmonary disorders.

Funding source: none reported.

INTRODUCTION

Complementary and alternative medicine (CAM), “defined as those interventions neither taught widely in medical schools nor generally available in US hospitals”,¹ has shown a continued rise in the past few decades. In the US, more than 50% of children with chronic medical conditions use CAM almost always in conjunction with conventional care.² One of the most commonly treated chronic diseases of our time, asthma, has a variable prevalence rate of CAM use (33–89% in children).³ In one study, 71% of caregivers said they would consider using CAM for their child in the future.⁴ We have seen a parallel increase in the use of CAM among cystic fibrosis patients. Many patients with cystic fibrosis who are followed at accredited CF centers use CAM therapies in conjunction with their standard conventional therapies. In one of the earliest studies on the use of CAM therapies by CF patients at one center, at least one type of nonconventional treatment was used by 66% of their patients.⁵ There is a rising parallel interest among healthcare providers to acquire more knowledge regarding these therapies. This is reflected in the inclusion of CAM topics or workshops and symposiums at the North American Cystic Fibrosis Conference, pediatric pulmonology conferences, as well as the American Academy of Pediatrics in the last 10 years.

There are several reasons we should familiarize ourselves with the various CAM modalities: (1) Respond to patients who seek CAM, and assist in monitoring for safety in a reasonable manner. (2) Find other options for patients who cannot tolerate or cannot find adequate relief from conventional medicines. (3) Promote better understanding and communication among CAM practitioners and physicians, thereby encouraging more well-designed clinical studies.

There are very few active clinical studies on the efficacy of various CAM modalities for specific pulmonary

¹Division of Pulmonary Medicine, Children’s Memorial Hospital, Northwestern University Feinberg School of Medicine, Chicago, Illinois.

²Raby Institute for Integrative Medicine at Northwestern, LLC, Chicago, Illinois.

*Correspondence to: Youngran Chung, MD, Division of Pulmonary Medicine, Children’s Memorial Hospital, 2300 Children’s Plaza, Box 43, Chicago, IL 60614-3394. E-mail: ychung@childrensmemorial.org

Received 10 August 2010; Revised 15 December 2010; Accepted 16 December 2010.

DOI 10.1002/ppul.21426

Published online 18 February 2011 in Wiley Online Library
(wileyonlinelibrary.com).

disorders such as cystic fibrosis or asthma. However, from the existing studies, historical use, and current experience with various CAM therapies, we can gain insight into potential benefits for other pulmonary disorders. Due to the vast array of CAM therapies, this review will only focus on some of the more common therapies in use in the US, addressing (1) underlying principles, (2) efficacy, (3) safety, and (4) practicality. These include Acupuncture, Herbs/supplements, Homeopathy, Mind–Body Medicine (MBM), and Bodywork therapies (e.g., chiropractics, massage).

ACUPUNCTURE AND CHINESE MEDICINE (CM)

Background and Basic Theory

Acupuncture's first "text" was compiled over 2000 years ago and news of acupuncture was reported in Europe in the sixteenth and seventeenth centuries from missionaries returning from China with stories of "miraculous healing" with needles. Acupuncture is part of an ancient and comprehensive Chinese medical system with a complex theory of pathophysiology distinctly different from our Western view of human physiology and medicine. It is often complemented by other therapeutic modalities such as herbal combinations, massage, dietary therapy, and lifestyle modification. A basic concept of acupuncture is the flow of Qi through the body. The definition of Qi is elusive, but it could be defined as life force or vital energy that is the driving force behind bodily animation and function. Qi "flows through the body" via channels (meridians), and it is thought that disease occurs when this flow is disrupted. Acupuncture needles access these channels to re-establish the flow of Qi. In present day, there are multiple styles and techniques of acupuncture including microsystems such as hand, ear, or scalp acupuncture. The National Center for Complementary and Alternative Medicine defines acupuncture as a family of procedures involving stimulation of specific anatomic locations on the skin by a variety of techniques. Among these are needle-free acupuncture techniques using laser, magnetic or non-magnetic pellets, and other devices.

Acupressure is a technique stimulating acupuncture points using manual pressure. In the US, the National Institute of Health Consensus Development Conference on Acupuncture endorsed acupuncture in 1997 for many

medical conditions, including asthma.⁶ The World Health Organization also lists many conditions treatable by acupuncture. Some of the conditions often treated by pulmonologists include allergic rhinitis (proved through controlled trials to be an effective treatment); asthma, whooping cough, insomnia (therapeutic effect exist but further proof is needed), and small airway obstruction (only individual controlled trials reporting some therapeutic effects).⁷

Efficacy

Literature on acupuncture treatment for medical disorders is extensive, and there are a number of clinical studies on asthma. Since asthma is a disease of chronic airway inflammation, some of these results may be applicable to other respiratory diseases with similar symptoms and airway pathology. A 1996 comprehensive review of acupuncture studies in pulmonary disorders showed a number of positive results for asthma as well as for chronic bronchitis and chronic obstructive pulmonary disease.⁸ However, in the same year, a systematic review of 11 studies for acupuncture and asthma, authors concluded that there was insufficient evidence to support acupuncture for asthma, but acknowledged the need for further research because of the variability of acupuncture treatments in these studies.⁹ Many of these studies are inconclusive due to methodological problems such as difficulty in blinding, standardization of acupuncture points, and use of "sham" points for control (sham points can be active and adequate inert placebo is almost impossible to obtain). Another caveat is that isolating acupuncture from other Chinese medicine (CM) therapies may be less effective because in the practice of CM, Chinese herbs and other CM therapies (energy movement therapies such as Tai Chi, QiGong) are used synergistically along with needle acupuncture. It is also important to know that acupuncture and other CM therapies require a regimen that is specifically tailored for an individual for optimal results.

Acupuncture is used extensively in China to treat a variety of pulmonary diseases in addition to asthma (e.g., viral pneumonia, pleural effusion, etc.). In cystic fibrosis, there are no controlled clinical trials using acupuncture. There is a single case report using acupuncture and Chinese herbs to treat a 10-year-old boy with cystic fibrosis with lingering pulmonary exacerbation symptoms.¹⁰ Acupuncture and Chinese herbal treatment for several weeks was associated with noticeable clinical improvement, including a chest CT which revealed no mucus plugs 2 weeks following treatment. He remained healthy at 1 year follow-up.

A randomized-controlled trial involving patients with non-CF bronchiectasis in adults who received standard treatment (control) or standard treatment plus self-administered acupressure or sham acupressure was done to look

ABBREVIATIONS

CAM	complementary and alternative medicine
CF	cystic fibrosis
CM	Chinese medicine
FDA	Food & Drug Administration
MBM	mind–body medicine
NIH	National Institute of Health

at effects on symptoms that limited daily activity. The acupressure group resulted in better quality of life score ($P = 0.01$) compare to the control group but there was no difference in other parameters (6-min walk, sputum, dyspnea). The sham acupressure group showed improvement ($P = 0.03$) only in the sputum self-assessment score (subject's sensation of effort to clear sputum).¹¹ In a prospective randomized study of chronic obstructive asthma patients, there was improvement in quality of life measures when acupuncture or acupressure was added to standard therapy.¹²

While acupuncture may not reverse the basic disorder of a disease such as CF, it has the potential to alleviate symptoms and can be effective for treating associated chronic pain. Though not consistent in their findings, recent systematic reviews suggest a possible positive effect of acupuncture for specific pain conditions^{13–19} which may also be seen in cystic fibrosis (e.g., low back pain, postoperative pain, osteoarthritis, and headache). A single pilot study on cystic fibrosis patients showed effectiveness of acupuncture for diminishing pain with no side effects or complications.²⁰

There is obviously a need for more studies on the use of acupuncture for specific pulmonary conditions. However, based on some of the positive results seen in asthma, we can see the potential applicability to other pulmonary conditions characterized by chronic airway obstruction and inflammation. Acupuncture is also routinely used to maintain general health and support the immune system and could be a useful adjunct to treating any chronic pulmonary disease.

Safety and Practical Issues

In skilled hands acupuncture is a very safe procedure. The needles are applied using a clean needle technique and are almost always single use/disposable so infection is extremely rare. Mild side effects can include minor bleeding and nausea. Syncope may occur in about 1% of patients, especially in the first treatment session and is preventable by treating the patient in a supine position.²¹ An analysis by White which included 12 prospective studies that surveyed more than a million treatments showed the estimated risk of a serious adverse event with acupuncture to be 0.05 per 10,000 treatments, and 0.55 per 10,000 individual patients.²² While there are no absolute contraindications to acupuncture, relative contraindications would include extreme frailty with concurrent febrile illness, early pregnancy, and bleeding disorders. Potentially, deep needling of points on the thorax could cause a pneumothorax in a very emaciated patient, but this serious adverse effect is exceedingly rare. Acupuncture needles, are generally painless as they are nonbeveled, therefore noncutting thin needles and are well tolerated by all ages. Nevertheless, the use of many noninvasive acupuncture

techniques (e.g., laser acupuncture or pellets used on hands or ears) make this even more acceptable especially in young children, though efficacy studies using these techniques are lacking. To derive benefit from acupuncture, a patient generally requires several or more treatments over a period. The time required for visits to the acupuncturists and insurance coverage may be an issue for some patients.

HERBAL MEDICINE

Background and Basic Theory

Herbs have been widely popularized and are particularly likely to be used by patients with chronic medical conditions such as asthma or cystic fibrosis. Unfortunately, in the US herbal medicines do not go through the same rigorous process as pharmaceuticals. Thus, there are legitimate questions regarding the safety of herbal products. Otherwise, many herbal supplements have a written history spanning hundreds of years and some have been in use for thousands of years. This historical information gives important clues about safety and effectiveness. Of course, each herbal product must be judged on its own merit, based on documented historical information and existing clinical studies. The amount of information available varies significantly from herb to herb. There are four major herbal healing traditions: Chinese, Ayurvedic (India), European, and Native American. The use of herbal medicines may vary according to the principles of pathophysiology practiced in a particular tradition. Chinese Medicine practitioners use multiple herbs in combinations based on a CM diagnosis and the individualized need of the patient. Two patients with the same Western diagnosis would not necessarily receive the same herbal preparation. Earlier use of Western herbs was somewhat similar to CM with a goal to re-establish physiological balance and some "herbalist" still practice with this goal. However, today Western herbs are mostly practiced within the framework of a conventional biomedical model based on their pharmacologically active components. It is important to realize that herbal medicines differ from pharmaceuticals in several ways: First, they are poly-pharmaceuticals often containing a complex mixture of chemicals (e.g. >100 chemicals have been identified in tea tree oil mixture²³) thus they may have more than one pharmacological effect. This could produce an independent effect (therapeutic or harmful), a synergistic effect or a quenching effect (one ingredient canceling out the adverse effect of another). Second, the quality of herbal products (active ingredients) can be influenced by growing factors such as soil composition, weather, and time of harvest.

Efficacy

While herbs may be one of the more commonly used therapies by CF patients, there are very few clinical trials

of herbs for CF lung disease. Most interventions that might be used to treat CF are extrapolated from treatment of other similar disease processes such as bronchitis or asthma. Two systematic reviews, one of 17 randomized clinical trials²⁴ and a more recent review of 26 trials,²⁵ evaluated the use of herbal medicines for the treatment of asthma. Both reviews included CM and Ayurvedic herbs. The first review concluded that there was no definitive evidence for any of the herbal preparations in the treatment of asthma, but several products showed promise: Three of the CM herbal products resulted in significant improvement in forced expiratory volume (FEV1) ($P < 0.05$), and several traditional Indian (Ayurvedic) herbal products similarly showed either an increase in FEV1 ($P < 0.05$) or symptom relief. In the second review, *Boswellia*, *Pycongenol®*, *Mai-men*, *Jia-Wei*, and *Tylophora* were considered to have promise, improving lung function (FEV1 and/or peak flow rates) based on few studies; in the same review, a single study showed Eucalyptol resulted in statistically significant decrease in daily oral steroid intake. Both reviews noted that variation in formulations of CM herbal preparations, poor reporting, and the quality of studies made it difficult to draw conclusions to strongly support use of these herbs for asthma.

Several individual herbs with relevance to pulmonary disease are of particular interest.

Boswellia serrata (frankincense), an Ayurvedic herb has traditionally been used for its anti-inflammatory effects. Its pharmacologically active ingredients have been shown to inhibit pro-inflammatory processes by their effects on 5-lipoxygenase and cyclo-oxygenase and on the complement system. It has shown promise, though not yet compelling evidence, for clinical effects in other inflammatory processes (inflammatory bowel disease, arthritis) in past reviews.^{26–28} No significant adverse effects were noted. In a double-blind, placebo-controlled clinical trial of 40 adult asthmatic patients given *B. serrata* gum resin for a period of 6 weeks, 70% of patients had decrease in dyspnea, rhonchi, number of attacks, and increase in FEV1 ($P < 0.0001$), FVC, and PEFR as well as a decrease in eosinophilic count and ESR.²⁹ *Tylophora indica* (Indian ipecac) is another Ayurvedic herb traditionally used to treat asthma conditions. It is thought to have anti-inflammatory activity.^{30,31} Crude extract of the leaves of *Tylophora* inhibited delayed hypersensitivity reaction to sheep red blood cells in rats, and suppressed cellular immune responses when administered at any stage during the immune response.³² It may also increase endogenous steroid production.³³ Of the five randomized clinical trials on *Tylophora* in the 1960s and 1970s, two showed improvement in asthma symptom scores,^{34,35} one had significant improvement in FEV1 as well as symptoms,³⁶ another had improvement only in nocturnal dyspnea,³⁷ and one study showed no change in symptom score or

lung function.³⁸ *Curcumin*, a yellow pigment in the spice turmeric (curry powder), is probably the most recognized of herbs with potential use in CF, largely due to studies showing that it can open cystic fibrosis transmembrane conductance regulator chloride channels.³⁹ Over the centuries its traditional use has emphasized its anti-inflammatory effects, which have recently been documented. These immunomodulatory effects include down regulation of various proinflammatory cytokines.⁴⁰ One factor that may limit its use is its poor bioavailability as demonstrated in both animal and human studies.⁴¹ There is ongoing investigation in this area⁴² but clinical trials in humans are lacking. In general curcumin is regarded as safe. *Butterbur* (*Petasites hybridus*), another herb mentioned for treatment of asthma appears to possess anti-allergic properties reducing histamine and leukotriene levels in nasal fluids.⁴³ There are two studies that show promise. In an 8-week nonrandomized, open trial of adults and children with mild to moderate asthma, the group that took butterbur had decreased number, duration, and severity of asthma attacks while peak flow, FEV1, and all symptoms improved. More than 40% of patients reduced intake of their asthma medications.⁴⁴ This study appears promising although limited by its lack of blinding and small sample size. In the second small randomized placebo cross-over study, Butterbur as add-on therapy to asthmatic patients maintained on inhaled corticosteroids showed improvements in inflammatory markers over the placebo group.⁴⁵ *Garlic* (*Allium sativum*), commonly used as a natural “broad spectrum antibiotic” may have useful effects on biofilm with in vitro studies demonstrating a quorum sensing inhibition of *Pseudomonas aeruginosa* biofilm.⁴⁶ When introduced into a murine pulmonary infection model there was clearing of the pseudomonas organism.⁴⁷ A recent randomized-controlled pilot study in cystic fibrosis patients subjects assessed potential clinical effects of garlic capsules versus olive oil placebo capsules taken for 8 weeks. Only a suggestion of improvement was noted with no significant change in pulmonary function or clinical parameters.⁴⁸ Generally regarded as safe, there are cautions for garlic in large amounts due to inhibition of platelet aggregation and enhanced fibrinolytic activity. Garlic may also cause gastrointestinal disturbance in some people.

Other Herbs traditionally used for asthma, including *Lobelia*, *Sanguinaria*, *Grindelia camporum*, *Ginko biloba*, have little supportive evidence for efficacy. *Ma Huang* (*ephedra sinica*), a classic Asian herbal remedy for asthma contains ephedra and may be present in other herbal remedies for asthma. Serious side adverse effects reported include dysrhythmias, hypertension, seizures, death, and for this reason the Food and Drug Administration (FDA) recommends against its use in asthma. These warnings come from the use of ephedra in doses that are much larger

than those used for treatment of asthma in Traditional Chinese Medicine.³

Safety and Practical Issues

Herbal medications are not regulated by the FDA in the US, but legal protection is provided under the DSHEA (Dietary Supplement Health and Education Act, 1994). This places the burden of proof of safety on the FDA, as the manufacturer does not have to provide evidence for safety or efficacy, so care must be taken when choosing an herbal product. In general, many herbs are safe when used in appropriate dosages. However, herbal products could potentially contain contaminants in the form of other herbs, heavy metals, or undesirable organic compounds and they may contain unknown amounts of the active ingredient. As pharmacologically active substances, there can be herb–drug interactions. Some herbs can induce or inhibit cytochrome p450 and can affect blood concentrations of other herbs or drugs concurrently taken. Reputable companies follow strict standardized protocols (good manufacturing practice) ensuring quantifiable amounts of active ingredients and assurance of no contamination. Some companies submit their herbal products to independent labs for certification of product quality. The Natural Standard (Cambridge, Mass) evaluates evidence using the criteria of Jadad et al.⁴⁹ to indicate methodological quality of information. When using herbal medicines, side effects, contraindications, and known drug interactions should be examined. Children can be more susceptible than adults to the adverse effects of herbs due to the difference in their absorption, distribution, metabolism, and excretion of some substances. For example, some herbs can be cathartic, or have powerful diuretic properties and may cause dehydration and electrolytes disturbances more quickly in young children or infants. There can also be allergic cross-reactivity such as ragweed allergy with Echinacea or Chamomile. Since self-administration is common with herbs, inappropriate use of herbs such as excessive doses or using inappropriate combinations could cause toxicity and is more often the cause of adverse effects. Long-term use may be required for some herbs to achieve expected clinical effect before clinical benefit might be achieved. Raw herbs are sometimes recommended and preparation can be time consuming. Most are available in liquid, tablets and concentrated drops, making them easier to consume. In traditional Chinese Medicine approach, diet, acupuncture, and Chinese therapeutic massage are commonly used along with Chinese herbal medicines. This whole system multimodality approach may be important to achieve the greatest beneficial effect. CF patients who already take multiple drugs and do other therapies may find it difficult to add herbs to their regimen.

NUTRITIONAL SUPPLEMENTS

Background and Basic Theory

The widespread use of Nutritional supplements has long generated concerns, which was best expressed over 12 years ago when Jane Brody of the New York Times wrote “Consumers are, in effect, volunteering for a vast largely unregulated experiment with substances that may be helpful, harmful, or simply ineffective.”⁵⁰ The situation is slowly changing as use of some supplements such as probiotics and Omega 3 fatty acids have been incorporated into conventional medicine practice based on mainstream epidemiologic studies. The use of supplements by integrative medicine practitioners is based on the framework of functional medicine, an approach designed to reestablish balance to the various systems of the body (digestive, immune, inflammatory, oxidation-reduction, hormonal, etc.) that have been thrown into imbalance brought about by inappropriate diet, lifestyle, exposure to pollutants, and (genetic and acquired) disease. Integral to the functional medicine approach is lifestyle and dietary modification.

There is lowered antioxidant activity and increased oxidative stress present in CF patients despite normal dietary antioxidant intake, suggesting that the immune response might be a key factor causing oxidative stress.^{51,52} These antioxidant levels decrease with age in the CF patient suggesting ongoing antioxidant depletion.⁵³ Chronically stimulated immune cells as well as invading pathogens are able to produce free radicals, thus increasing the free radical load. Nutritional supplements with anti-inflammatory and antioxidant properties would thus seem beneficial for chronic inflammatory disorders such as asthma or CF. Several studies suggest that intervention with antioxidant supplementation may improve pulmonary status. *Whey*, a supplement commonly thought to improve muscle mass for athletic performance, may also enhance the antioxidant effect in CF. Rich in sulfated amino acids (primarily cysteine), important components in the synthesis of glutathione (GSH), whey is a potent intracellular antioxidant. Studies have shown increase in lymphocyte glutathione levels (46.6% increase) when whey protein isolate was administered to CF patients for 3 months.⁵⁴ Though no clinical changes were seen in that study, a more recent study showed improvement in FEV1 in children and a tendency to decreasing inflammatory marker in the majority of adults with CF. Both children and adults had enhanced nutritional status based on body mass index.⁵⁵ The later study utilized hyperbaric pressure-treated whey protein which is thought to enhance availability of cysteine, increasing lymphocytic glutathione.⁵⁶ There may also be a relationship between asthma and low levels of antioxidants such as *Vitamin C*, which was found to be low in sputum levels of asthmatic patients.⁵⁷ A systematic review and meta-

analysis showed that dietary vitamin C intake was significantly lower in people with asthma compared to those without asthma (mean differences $-182 \mu\text{g/day}$, 95% confidence interval -288 to -75 ; three studies) and in people with severe asthma versus mild asthma (mean differences $-344 \mu\text{g/day}$; two studies). Lower quantile dietary intakes (odds ratio 1.12, 95% confidence interval 1.04–1.21; nine studies) and serum levels of vitamin C were also associated with an increased odds of asthma.⁵⁸ Whether or not supplementation can improve lung function is uncertain. One systematic review revealed no significant relationship between dietary antioxidant intake (vitamins C, E, and Beta-carotene) and lung function except for a positive association between vitamin C and increase in FEV1.⁵⁹ A Cochrane review of vitamin C supplementation and asthma could not recommend a specific role for vitamin C in the treatment of asthma as larger randomized control trials were needed.⁶⁰ *Selenium* is well known as a component of GSH antioxidation. With low selenium levels in both CF and asthma populations, supplementation would arguably make sense. In an 8-week randomized study of CF patients given antioxidant supplement cocktail, there was a correlation between selenium and improvement in FEV1.⁶¹ In asthma, effects of selenium supplementation are not clear. In two randomized studies, one showed no significant improvement in quality of life scores⁶² and the second study showed subjective clinical improvement.⁶³ In neither study was there any objective improvement in lung status. A Cochrane Database review in 2004 concluded that selenium supplementation could be a useful adjunct for chronic asthma but the data is limited.⁶⁴ Aside from its role as an antioxidant selenium may have a role as a modulator of immune function. Through its actions via a family of selenoproteins selenium may modulate the nuclear factor kappa-B (NF-kappaB) signaling pathway affecting the inflammatory response (interleukin-6 and TNF-alpha production).⁶⁵ Though considered safe if supplemented within dietary guidelines, continued work is needed to unravel the relationship of selenium and airway disease. *Pycnogenol*® (Horphag Research, Cointrin/GENEVA, Switzerland) is a proprietary extract of mixed bioflavonoids containing antioxidant and anti-inflammatory properties extracted from the French maritime pine (*Pinus pinaster*). Generally considered to be safe, it appears to have very potent antioxidant properties, and has been studied in two asthma clinical trials. Both were placebo-controlled, one lasting 3 months in patients with mild to moderate asthma⁶⁶ and the other a blinded cross-over design for patients with varying degrees of severity with 4 weeks for each limb of the trial.⁶⁷ Both studies demonstrated a significant reduction in leukotrienes and improvement in symptoms. Pulmonary function and asthma scores were significantly improved in the first study. It has not been studied in CF. *Omega 3 Fatty Acids*.

Of the radical change in our diets for over the past 100 years, one of the most significant is the tremendous increase in omega 6 fatty acids with a decrease in omega 3 fatty acids.⁶⁸ This alteration of the Omega 3 to Omega 6 ratio has pushed the western diet toward a pro-inflammatory tendency. Correcting this imbalance by increasing omega-3 fatty acids may act to decrease the inflammatory response by competitive inhibition of the proinflammatory effects of omega-6 dietary fats. Fish oils with their high levels of the anti-inflammatory fatty acids (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) have been the most used in clinical trials. So far there is evidence for its benefit in cancer, as well as in several chronic inflammatory diseases including cardiovascular diseases, inflammatory bowel disease and rheumatoid arthritis.⁶⁹ For respiratory disease the evidence is not clear. A 2007 Cochrane Database review of Omega 3 fatty acids and CF came to the conclusion of promising effects but not enough evidence to suggest a definitive beneficial effect.⁷⁰ Similarly, there is yet no conclusive evidence for asthma.^{71,72} All three reviews call for larger and better controlled randomized studies. A recent clinical trial of adult CF patients who receive low-dose supplements of omega-3 and gammalinolenic fatty acids over 1 year appeared to improve pulmonary status and anthropometric measures with a decrease in inflammatory parameters.⁷³ *Magnesium* is known to relax smooth muscle, and low magnesium levels have been shown to be associated with airway hyper-reactivity and wheezing.⁷⁴ It also reduces inflammation through stabilization of T cells and inhibition of mast cell degranulation. It has been used intravenously for acute treatment of asthma⁷⁵ but it is unknown whether there is any benefit from routine oral Mg supplementation for treatment of chronic asthma. Several studies suggest that it may be beneficial with a reduction in exacerbations and albuterol use in children; though no change in pulmonary function measurements were found.⁷⁶ *Probiotics*, long a mainstay in the alternative medicine field are increasingly used in conventional medicine as therapeutic evidence accumulates for a variety of medical problems such as antibiotic and viral-induced diarrhea, atopy, irritable bowel syndrome, necrotizing enterocolitis, and a number of other acute and chronic inflammatory and infectious gastrointestinal disorders. Probiotics are packaged as either individual strains or as a mix of different species and strains usually composed of various strains of lactobacilli and bifidobacteria. Individual strains can have different metabolic effects, so the selection of appropriate strains is important. Intestinal flora is responsible for the production of specific nutrients, antioxidants, inhibition of potential pathogens, and enhancement of the immune system. There are several CF studies supporting a beneficial effect. Both reduction of intestinal inflammatory markers⁷⁷ and improvement in bacterial overgrowth symptoms⁷⁸ in CF children have

been demonstrated. Whether probiotics can positively influence pulmonary function was investigated. The first, a placebo-controlled, cross-over study of 19 children receiving lactobacillus or placebo (each arm for 6 months). During treatment phase there was a reduction of pulmonary exacerbations and hospital admissions and an improvement in FEV1 and body weight.⁷⁹ In a smaller 6-month study using a (mixed) probiotic in 10 children with CF, pulmonary exacerbation rates were reduced though PFT values were not changed.⁸⁰ Probiotics have a status of "Generally Regarded As Safe" (GRAS) status by the FDA in the US, but should not be given to critically ill and immune compromised patients. Probiotics appear to be safe.⁸¹⁻⁸⁴

Safety and Practical Issues

Many nutritional supplements are considered generally safe in the short-term but long-term effects are unknown in many supplements. Caution is especially important for chronic use in young children. Preparations mostly come in the form of tablets and capsules, and some liquids. Many dietitians emphasize the use of foods containing specific nutrients as an alternative to preparations. Similarly, like herbal medicines, supplements are not FDA regulated in the US.

HOMEOPATHY

Background and Theory

Although homeopathy is one of the most widely used form of complementary medicines worldwide, it is probably one of the most controversial. Developed in the early 19th century by the German Physician Samuel Hahnemann, homeopathy competed with orthodox medicine in the 19th century only to decline in the early part of the 20th century. It has since undergone a revival in the past 30 years. It is based on the principle of "like cures like," a concept which dates back to Hippocrates. The premise is that a substance which may produce a particular constellation of symptoms at a pharmacologic/toxic dose, will "cure" the same symptoms present in a patient when administered in an ultra-diluted form. Since homeopathic medicines are often diluted beyond Avogadro's number (6.02×10^{-23}) they may not even contain a molecule of the original substance. Therefore, it would seem implausible that homeopathic therapy could have any effect over placebo. However, the hypotheses for mechanism of action is not thought to be pharmacological but biophysical; that some form of information is transferred from the substance to the water, possibly resulting in rearrangement of the molecular structure of the water. An explanation of the mechanism behind homeopathy is not understood; the effect is thought to be biophysical rather than pharmacological. The theory that changes in

the physical properties but not chemical structure of water by homeopathic dilutions has been suggested via studies utilizing thermoluminescence,⁸⁵ calorimetry,⁸⁶ and spectroscopy.^{87,88} Further research is obviously needed in this area. Physiologic effects induced by such ultramolecular dilutions have been demonstrated at the cellular level such as the inhibition of human basophil degranulation by homeopathic dilution of histamine.⁸⁹ In a systematic review of 67 in vitro homeopathic studies,⁹⁰ 75% of the studies were positive, including studies with a high methodological standard. Most recently, an in vitro study showed preferential cytotoxic effect induced by homeopathic medicines against two breast cancer lines while not affecting the normal breast cell line.⁹¹

Efficacy

There are a considerable number of clinical studies in homeopathy. Independent systematic reviews that examined whether the effects of homeopathic medicines are due to placebo showed a surprising number of positive studies and conclusion that there was an effect beyond placebo.⁹² An analysis of studies that met the criteria of double blind randomized, placebo-controlled, concluded that homeopathy can be efficacious for a number of conditions.^{93,94} Though one systematic review concluded no difference between homeopathy and placebo,⁹⁵ reanalysis of the postpublication data did not support the conclusion that homeopathy is a placebo effect.⁹⁶ One study on allergic rhinitis and another on allergic asthma (designed by homeopathic physicians but implemented by pulmonologists) led the authors to conclude that "homeopathy differs from placebo in an inexplicable but reproducible way."^{97,98} There is evidence from randomized, controlled trials that homeopathy may be more effective than placebo for the treatment of influenza,⁹⁹ postoperative ileus,¹⁰⁰ and childhood diarrhea.^{101,102} While there are systematic reviews showing questionable results for asthma,¹⁰³ this appeared to be due in part to variability of study design and form of homeopathy used. A prospective, randomized, double-blind, placebo-controlled study on intubated chronic obstructive pulmonary disease patients to assess the influence of homeopathic potassium dichromate on tenacious tracheal secretions showed significant decrease in the amount of stringy tracheal secretions and earlier extubation in the treated group.¹⁰⁴ There are no published studies for homeopathy in CF.

Safety and Practical Issues

Unlike herbal and supplemental products, homeopathics have been FDA regulated in the US since 1939 and are available over-the-counter. The preparation process inherent to homeopathy eliminates any risk of pharmacological side effects and there are no interactions with conventional drugs. Rarely, there are reports of

“aggravation,” which is a phenomenon of transient worsening of symptoms before improvement.¹⁰⁵ Based on world literature search 1975–1995, the incidence of adverse effects are very low, mostly minor and transient.¹⁰⁵ Caution must be taken as some products are sold as “homeopathic” but may be combined with an herbal product. The homeopathic medicines are very convenient and easy to take as liquid, or more often in the form of small tablets/beads (sugar beads that have been impregnated with homeopathic dilutions, a manufacturing process that creates a stable reliable vehicle for sublingual absorption of the homeopathic solution). Although they are available over the counter, homeopathic practitioners feel that self-directed use is generally only effective for treating acute and minor symptoms, as chronic conditions require more in depth evaluation for selection of the appropriate medicine.

MIND/BODY MEDICINE

Background and Theory

MBM includes a number of related techniques such as hypnosis, biofeedback, relaxation techniques, meditation, breathing exercises, and may also include yoga, tai chi, qi gong which involve some bodywork. These approaches are based on the premise of a bidirectional influential communication between mind and body. MBM is typically used for symptom relief, preparation of surgery, and as adjunctive treatment for a variety of medical conditions, particularly those which have a strong stress-related component. It is well documented that stress can enhance airway inflammation in asthma by modulating immune cell function through neural and hormonal pathways.^{106–108} In general, there exists a substantial body of clinical evidence, demonstrating the effectiveness of mind/body techniques in many areas of medicine. However, most of these studies are small and there are obvious obstacles to developing well-controlled studies. In patients with asthma and CF, there are studies which have shown that these therapies, specifically relaxation and self-hypnosis may minimize symptoms. Efficacy for several techniques is examined below. *Hypnosis* is the process of producing an alternate state of awareness and alertness in which an individual is selectively focused, absorbed, and concentrating upon a particular idea or image (with or without relaxation), with a specific purpose of achieving some goal or realizing some potential.¹⁰⁹ All clinical hypnosis is considered self-hypnosis, and the clinician’s role is as a facilitator. In North America, clinical application of hypnosis emerged in the late 1950s, and has been shown to be efficacious for a wide spectrum of conditions from asthma, enuresis, encopresis to substance abuse.¹⁰⁹ The NIH Technology Assessment Conference Panel in 1995 found very strong evidence for the efficacy of hypnosis in relieving pain associated with cancer and moderate evidence for the

treatment of irritable bowel syndrome, oral mucositis, temporomandibular disorders, and tension headaches.¹¹⁰ Self-hypnosis taught to children in one pulmonary center showed improvement or resolution of symptoms such as dyspnea, asthma, chest pain, and anxiety.^{111,112} There are two studies utilizing self-hypnosis for cystic fibrosis. One study in 1994 showed a significant increase in peak expiratory flow rates immediately after self-hypnosis along with improved aspects of psychological state.¹¹³ Forty-nine cystic fibrosis patients successfully used self-hypnosis techniques for a variety of purposes including pain relief associated with medical procedures, headache, changing the taste of medications to make them more palatable and control of other symptoms associated with CF. Subjectively, success was achieved 86% of the time in subjects with no worsening of symptoms from hypnotherapy.¹¹⁴ A review of hypnosis and asthma concluded that hypnosis likely helps with the behavioral/emotional component of asthma and shows promise decreasing severity and relieving airway hyper-responsiveness.¹¹⁵

Other frequently used forms of MBM include various relaxation techniques, guided imagery, biofeedback, and music therapy. The 1995 NIH Technology Assessment Conference Panel on Relaxation and Behavioral Approaches for Chronic pain and Insomnia concluded that: “relaxation techniques” (e.g., deep and brief autogenic training, meditation, progressive muscle relaxation) are effective for the treatment of a variety medical conditions.¹¹⁰ Guided imagery or relaxation techniques have shown benefit in asthma.¹¹⁶ In CF patients, a positive influence on lung function was observed after 4 months of biofeedback assisted breathing retraining.¹¹⁷ A controlled study looking at benefits of music therapy for CF patients as an adjunct to chest physiotherapy showed that music compiled by music therapist can be an aid when doing chest physiotherapy for young children and their parents.¹¹⁸

It is known that psychosocial stress may enhance airway inflammation in asthma by modulating immune cell function through neural and hormonal pathways.¹⁰⁷ There is growing evidence that mind–body techniques such as meditation, yoga, and other mind–body exercises when practiced over time can reduce anxiety and may even help with lung expansion. Some of these exercises incorporate regular breathing exercises. A Cochrane review concluded that yoga as well as other forms of breathing exercises (Buteyko, diaphragmatic breathing) resulted in decreased use of beta-agonist medication and trend toward improvement in quality of life although no improvement in lung function.¹¹⁹ Subsequently though, a number of studies on the effect of yoga breathing and asthma or chronic obstructive pulmonary disease showed benefit with some demonstrating improvement in pulmonary function, decreased airway hyper-responsiveness in addition to subjective measures.^{120–123} While most of these studies are on adults,

a systematic review of studies on yoga for children also showed physiological benefits.¹²⁴ However, not all studies showed these benefits,^{125,126} and further investigative studies are needed to determine circumstances under which yoga could benefit in asthma or other chronic lung disease and to elucidate the mechanism by which this observed effect occurs.

Safety and Practical Issues

Used appropriately, hypnosis is safe¹⁰⁹ but it is important to recognize psycho-emotional issues such as anxiety or depression which may require psychotherapy or medication. Promising long-term benefits of mind–body medicine techniques is the modification of behavioral patterns of the child (and family); giving children effective tools to maintain health and deal with stress in a healthy and effective manner. Used adjunctively with conventional therapies, mind–body modalities have the potential to benefit patients with a variety of disorders seen by pulmonologists including asthma, cystic fibrosis, and sleep disorders. However, these techniques require active participation and a commitment by the patient, so each method must be evaluated with consideration of patient age and ability.

CHIROPRACTIC THERAPY

Background and Theory

Chiropractic care is one of the largest healthcare profession in the US and is one of the most utilized CAM modalities. While it is primarily used to treat chronic musculoskeletal disorders and pain, it is also used by some chiropractors for general well-being and treatment of a wide variety of conditions such as asthma, GERD, chronic constipation, sleep apnea, chronic otitis media, and enuresis. Chiropractics is based on the premise that proper alignment of the spine is important for the nervous system to work properly. It is thought that subluxation of the spine causes irritation of related neurological structures, affects resting muscle tone, and disrupts blood flow to affected structures leading to inflammation, pain, and organ dysfunction. The chiropractor employs various techniques to restore normal biomechanics to the articulations of the spine, cranium, and sometimes extremities to modulate neurological and physiological function.¹²⁷ Patients with CF and other respiratory disorders may turn to chiropractic care for chronic pain related to kyphosis and hypertrophic osteoarthropathy as well as specific respiratory problems, immune health, and general health maintenance.

Efficacy

While there are some studies showing benefits of chiropractic for management of pain syndromes, studies on chiropractic for asthma have so far shown no objective

improvement.¹²⁸ In a recent systematic review of chiropractic therapy for asthma, chiropractic care showed improvements in subjective measures and to a lesser degree objective measures, none of which were statistically significant.¹²⁹ In one CF center survey where 14% of patients sought chiropractic care, 69% of users perceived improvement in their pain, again showing only subjective benefits.¹³⁰

Safety and Practical Issues

The issue of safety has always been a particular concern of chiropractic manipulation. The major concerns have been for (vertebral) arterial dissection or clot formation with a resultant cerebrovascular event, myelopathy, vertebral disc extrusion, epidural hematoma, and cauda equine syndrome. From past safety review complications range from 1 in 500,000 to 1 in 10,000,000 manipulations with most agreeing on a complication rate of 1 CVAs per 1–3 million manipulations.^{131,132} A systematic review of adverse events examining the literature of the past 110 years revealed 11 cases of adverse events following spine manipulation in children, 4 of which did not involve a chiropractor. A more recent systematic review concluded no robust data concerning the incidence or prevalence of adverse reactions after chiropractic manipulation.¹³² Modifications are made by chiropractors when treating pediatric patients¹³³ and caution must be taken in cystic fibrosis patients as there is a high prevalence of osteopenia and osteoporosis.¹³⁴

Patients who choose to seek chiropractic treatment as an alternative to conventional medicine especially for non-musculoskeletal disorders such as asthma should be monitored closely to avoid any delay in allopathic treatment, although chiropractic care for asthma is generally used for chronic maintenance.

BODYWORK

Background and Theory

This is a heterogeneous group of techniques, and theoretical approaches, which can be divided into several groups: (1) manual therapy, (2) body movement or body re-education techniques, and (3) energy work. Theories vary with the specific approach used. Generally, bodywork techniques are used as an adjunct therapy for reduction of stress, and “holding patterns” in the body, improvement of local circulation, and well-being. (1) Manual therapy implies physical contact from the therapist. This category would include Swedish massage, Rolfing, and Myofascial Release releasing tension and muscular and fascial holding patterns as well as increasing circulation. (2) Body movement/education techniques such as Feldenkrais and Alexander technique re-educate the body giving improved balance, better alignment and a sense of well-being.

(3) Energetic bodywork such as Reiki, Therapeutic Touch, and Polarity Therapy are considered healing practices influencing the body on an energetic level. The Chinese arts of Tai Chi Chuan and Qi Gong would fall into this last category.

Massage is a very common technique that most people associate with relaxation and feeling of well-being. However, certain massage techniques are used adjunctively for a variety of medical conditions and is increasingly being employed in hospital settings for patients. Common to all techniques is relaxation of the soft tissues, increased circulation to the massaged area resulting in decreased pain. There are other physiological and psychological effects that can be therapeutic as well. For example, massage is thought to activate the relaxation response and decrease respiratory rate, loosen tight respiratory muscles, and fascia which can help loosen and discharge phlegm. All forms of massage can be adapted for children. There are a few techniques that are specifically used in children: infant massage, Ayurvedic (Indian), and Tui Na (Chinese) massage for children. Some of these are also regarded as energy work as well.

Efficacy

Few well-designed studies exist for manual bodywork. Most benefits such as the sense of well-being are subjective. However, massage therapy in premature infants has been shown to promote a more stable response to stresses, increased weight gain and earlier discharge from the hospital.¹³⁵ Massage has been shown to benefit many different medical conditions such as insomnia, colic, as well as chronic pulmonary disorders such as asthma and cystic fibrosis. In two clinical studies on asthma and CF, parents were taught to do massage to their child while control group used relaxation technique only. Positive response to massage therapy included reduction in anxiety, improvement in mood, and increase in peak flows.^{136,137}

ENERGY WORK

The use of energy healing therapies has tripled between 1990 and 1997.¹³⁸ Two types of energy fields are bioelectromagnetic based therapies: (1) use of magnetic fields (generally used for pain syndromes) (2) biofield therapies that are intended to affect the energy fields that surround and penetrate the human body and are not directly measurable; examples include therapeutic touch, Reiki, The goal of the latter is balancing the energy field in the body either through laying hands on or with nontouch interventions. These have in common the idea of facilitating the body's own natural healing ability. Spiritual healing or prayer is amongst the oldest and most widespread interventions used, but the most recent Cochrane database reveals no evidence yet in support of prayer as an intervention.¹³⁹ Therapeutic touch is a well known noninvasive

biofield therapy and is most frequently used in pediatrics for anxiety, subjective dyspnea related to asthma, pain, insomnia, and isolation. Many patients seek therapeutic touch practitioners because they find they derive comfort and benefit from them. Currently, there is no consensus regarding the scientific mechanism of action involved. There are numerous peer-reviewed articles indicating patient perceived benefit as well as two meta-analysis of therapeutic touch that concluded a positive effect on physiological and psychologic variables.¹⁴⁰ However, one study in 1998 concluded that all therapeutic touch claims were groundless.¹⁴¹ Subsequently, there have been at least four published papers critical of the procedures involved in that study; that it violated the essential practice requirement of therapeutic touch and claim that this resulted in inappropriate conclusions.^{142–145} A study on Reiki showed significant reduction in anxiety, blood pressure, and increase in salivary IgA levels indicating stress reduction response.¹⁴⁶ But convincing research data on many of these therapeutic effects of these therapies are lacking at this time.

Qigong, literally meaning energy work, has many different forms. Often with little body movement, the purpose is to move the “Qi” and enhance health. Medical Qigong, is a branch of CM and Qigong exercises are prescribed for specific medical problems. One meta-analysis review of past Qigong Random-controlled trials (26 trials) reports effects on a number of physiological parameters including increased number of white cells, FVC, and FEV1.¹⁴⁷ *Tai Chi Chuan* is also an energy (Qi) enhancement exercise contained within a martial art. There are two conflicting reviews of the effect of Tai chi exercises in adults: One meta-analysis with an inclusion of seven trials concludes an increase in aerobic capacity.¹⁴⁸ The second review (five trials) found no convincing evidence of an effect of Tai Chi on aerobic capacity.¹⁴⁹

Safety and Practical Issues

The more gentle techniques of body movement or re-education and energetic forms of bodywork are considered very safe. Manual massage is safe in almost all situations with the exception of acute febrile illness, local infection, certain skin disorders, phlebitis, thrombosis, and bleeding disorders. While massage can be provided at home by parents, a licensed massage therapist would be able to provide medical massage that is targeted towards a particular therapeutic effect.

CONCLUSION

General concerns that arise when evaluating any potential new therapeutic approach are: safety, effectiveness, and practical issues such as ease of administration and cost. CAM modalities such as homeopathy, mind-body

medicine, bodyworks, and acupuncture are generally regarded as safe. Others, like herbs and supplements, may require more careful selection and monitoring due to pharmacologic activity, product variability, and lack of regulation. This is especially true for children as there is often less information and data in this age group.

While there is a lack of clinical studies in CAM for many individual pulmonary diseases in children, the general safety and efficacy data that do exist can help guide us in its potential use or further investigation. It is recognized that research in CAM faces unique obstacles.^{150,151} For example, there is difficulty finding true sham acupuncture; blinding in mind–body studies; standardizing herbal and supplement products tested. With some therapies it is difficult to achieve the optimal effect when that modality is isolated from its accompanying synergistic therapies. Some question whether clinical studies in CAM should even be done using the standard methods that are used in conventional medicine. This is evident in view of the fact that many CAM therapies have to be tailored to the individual with the underlying premise that each individual has a different constitution and a unique reaction—“one medicine does not fit all.” This is somewhat parallel to pharmacogenetics and the recognition of the variances in individual response to drugs.

It should be noted that publication biases can affect our attitudes towards CAM therapies: negative studies in CAM are more likely to be published in mainstream western journals, and positive studies more likely to be published in foreign-language journals.¹⁵² Regardless, there remains a great need for CAM therapies to undergo rigorous clinical trials and investigations to elucidate the mechanisms involved. It is understandable that this is needed in order for the practitioner to have a comfort level when discussing CAM therapies with their patients who may be seeking these treatment modalities. Open dialogue with experienced CAM practitioners is essential for improved understanding and optimizing research.

While many of us sit on the sidelines waiting for more solid evidence-based data on CAM, patients have been turning to many of these CAM therapies with or without their physicians’ participation. We need to develop a knowledgeable understanding of these approaches and use the best available evidence along with safety and experiential profiles to assist in guiding our patients.

ACKNOWLEDGMENTS

We gratefully acknowledge Susanna McColley, MD for her ideas and advice regarding this review.

REFERENCES

- Eisenberg DM, Kessler RC, Foster C, Norlock FE, Calkins DR, Delbanco TL. Unconventional medicine in the United States: prevalence, costs, and patterns of use. *N Engl J Med* 1993; 328:246–252.
- Kemper JK, Vohra S, Walls R. The task force on complementary medicine and alternative medicine and the provisional section on complementary, holistic and alternative medicine. The use of Complementary and Alternative Medicine in Pediatrics. *Pediatrics* 2008;122:1374–1386.
- Mark JD. Integrative medicine and asthma. *Pediatr Clin N Am* 2007;54:1007–1023.
- Ernst E. Use of complementary therapies in childhood asthma. *Pediatr Asthma Allergy Immunol* 1998;12:29–32.
- Stern RC, Canda ER, Doershuk C. Use of nonmedical treatment by cystic fibrosis patients. *J Adolescent Health* 1992;13:612–615.
- Ramsay D, Bowman M, Greenman P, Jiang S, Kushi L, Leeman S, Lin K, Moerman D, Schnoll S, Walker M, et al. National Institute of Health Consensus Development Conference Statement. *Acupuncture* 1997;15:1–34.
- World Health Organization. Traditional Chinese Medicine and Acupuncture Health Information Organization: acupuncture research: review and analysis of reports on controlled clinical trials. World Health Organization. 2003. www.tcm.health-info.org/WHO-treatment-list.htm.
- Jobst KA. Acupuncture in asthma and pulmonary disease: an analysis of efficacy and safety. *J Altern Complement Med* 1996;2:179–206.
- McCarney RW, Brinkhaus B, Lasserson TJ, Linde K. Acupuncture for chronic asthma. *Cochrane Database Syst Rev* 2004;1: CD000008.
- Fleischman GF. Possibilities for the treatment of cystic fibrosis with acupuncture and Chinese herbs: theory and case study. *Am J Acupunct* 1996;24:135–142.
- Maa S, Tsou T, Wang K, Wang C, Lin H, Huang Y. Self administered acupressure reduces the symptoms that limit daily activity in bronchiectasis patients. *J Clin Nurs* 2007;16:794–804.
- Maa S, Sun M, Hsu K, Hung T, Chen H, Yu C, Wang C, Lin H. Effect of acupuncture or acupressure on quality of life of patients with chronic obstructive asthma: a pilot study. *J Altern Complement Med* 2003;9:659–670.
- Manheimer E, Cheng K, Linde K, Lao L, Yoo J, Wieland S, van der Windt DA, Berman BM, Bouter LM. Acupuncture for peripheral joint osteoarthritis. *Cochrane Database Syst Rev* 2010;1:CD001977.
- Lewis K, Abdi S. Acupuncture for lower back pain: a review. *Clin J Pain* 2010;26:60–69.
- Lin JG, Chen WL. Review: acupuncture analgesia in clinical trials. *Am J Chin Med* 2009;37:1–18.
- Selfe TK, Taylor AG. Acupuncture and osteoarthritis of the knee: a review of randomized, controlled trials. *Fam Community Health* 2008;31:247–254.
- Madsen MV, Gøtzsche PC, Hróbjartsson A. Acupuncture treatment for pain: systematic review of randomised clinical trials with acupuncture, placebo acupuncture, and no acupuncture groups. *Br Med J* 2009;338:a3115.
- Sun Y, Gan TJ. Acupuncture for the management of chronic headache: a systematic review. *Anesth Analg* 2008;107:2038–2047.
- Sun Y, Gan TJ, Dubose JW, Habib AS. Acupuncture and related techniques for postoperative pain: a systematic review of randomized controlled trials. *Br J Anaesth* 2008;101:151–160.
- Lin YC, Ly H, Golianu B. Acupuncture pain management for patients with cystic fibrosis: a pilot study. *Am J Chin Med* 2005;33:151–156.
- Loo M. Acupuncture. In: Loo M, editor. *Integrative medicine for children*. Saunders: Elsevier; 2009. p 81.
- White A. A cumulative review of the range and incidence of significant adverse events associated with acupuncture. *Acupunct Med* 2004;22:122–133.

23. Carson C, Riley T. Toxicity of the essential oil of *Melaleuca alternifolia* or tea tree oil. *J Toxicol Clin Toxicol* 1995;33:193–194.
24. Ernst H. Herbal medicines for asthma: a systematic review. *Thorax* 2000;55:925–929.
25. Clark CE, Arnold E, Lasserson TJ, Wu T. Herbal interventions for chronic asthma in adults and children: a systematic review and meta-analysis. *Prim Care Respir J* 2010;19:307–314. pii: pcrj-2010-04-0047. DOI: 10.4104/pcrj.2010.00041 [Epub ahead of print]. Available on www.thepcrj.org.
26. Ammon HP. Boswellic acids in chronic inflammatory diseases. *Planta Med* 2006;72:1100–1116.
27. Ernst E. Frankincense: systematic review. *Br Med J* 2008; 337:1439–1441.
28. Moussaieff A, Mechoulam R. Boswellia resin from religious ceremonies to medical uses: a review of in-vitro, in-vivo and clinical trials. *J Pharm Pharmacol* 2009;61:1281–1293.
29. Gupta I, Gupta V, Parihar A, Gupta S, Ludtke R, Safayhi H, Ammon HP. Effects of *Boswellia serrata* gum resin in patients with bronchial asthma: results of a double-blind, placebo-controlled, 6 week clinical study. *Eur J Med Res* 1998;3:511–514.
30. Gopalakrishnan C, Shankaranarayanan D, Kameswaran L, Natarajan S. Pharmacological investigations of tylophorine, the major alkaloid of *Tylophora indica*. *Indian J Med Res* 1979;69:513–520.
31. Gopalakrishnan C, Shankaranarayanan D, Nazimudeen SK, Kameswaran L. Effect of tylophorine, a major alkaloid of *Tylophora indica*, on immunopathological and inflammatory reactions. *Indian J Med Res* 1980;71:940–948.
32. Ganguly T, Sainis KB. Inhibition of cellular immune responses by *Tylophora indica* in experimental models. *Phytomedicine* 2001;8:348–355.
33. Udupa AL, Udupa SL, Guruswamy MN. The possible site of anti-asthmatic action of *Tylophora asthmatica* on pituitary-adrenal axis in albino rats. *Planta Med* 1991;57:409–413.
34. Shivpuri DN, Menon MP, Prakash D. A crossover double-blind study on *Tylophora indica* in the treatment of asthma and allergic rhinitis. *J Allergy* 1969;43:145–150.
35. Shivpuri DN, Singhal SC, Parkash D. Treatment of asthma with an alcoholic extract of *Tylophora indica*: a crossover, double-blind study. *Ann Allergy* 1972;30:407–412.
36. Mathew KK, Shivpuri DN. Treatment of asthma with alkaloids of *Tylophora indica*: a double-blind study. *Aspects Allergy Appl Immunol* 1974;7:166–179.
37. Thiruvengadam KV, Haranath K, Sudarsan S, Sekar TS, Rajagopal KR, Zacharian MG, Devarajan TV. *Tylophora indica* in bronchial asthma. *J Indian Med Assoc* 1978;71:172–177.
38. Gupta S, George P, Gupta V, Tandon VR, Sundaram KR. *Tylophora indica* in bronchial asthma—a double-blind study. *Indian J Med Res* 1979;69:981–989.
39. Wang W, Bernard K, Li G, Kirk KL. Curcumin opens cystic fibrosis transmembrane conductance regulator channels by a novel mechanism that requires neither ATP binding nor dimerization of the nucleotide-binding domains. *J Biol Chem* 2007; 16:4533–4544.
40. Menon VP, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. *Adv Exp Med Biol* 2007;595:105–125.
41. Sharma RA, Steward WP, Gescher AJ. Pharmacokinetics and pharmacodynamics of curcumin. *Adv Exp Med Biol* 2007;595: 453–470.
42. Cartiera MS, Ferreira EC, Caputo C, Egan ME, Caplan MJ, Saltzman WM. Partial correction of cystic fibrosis defects with PLGA nanoparticles encapsulating curcumin. *Mol Pharm* 2010;7:86–93.
43. Thomet OA, Schapowal A, Heinisch IV, Wiesmann UN, Simon HU. Anti-inflammatory activity of an extract of Petasites hybridus in allergic rhinitis. *Int Immunopharmacol* 2002; 2:997–1006.
44. Danesch UC. Petasites hybridus (Butterbur root) extract in the treatment of asthma—an open trial. *Alter Med Rev* 2004;9: 54–62.
45. Lee DK, Haggart K, Robb FM, Lipworth BJ. Butterbur, a herbal remedy, confers complementary anti-inflammatory activity in asthmatic patients receiving inhaled corticosteroids. *Clin Exp Allergy* 2004;34:110–114.
46. Persson T, Hansen TH, Rasmussen TB, Skindersø ME, Givskov M, Nielsen J. Rational design and synthesis of new quorum-sensing inhibitors derived from acylated homoserine lactones and natural products from garlic. *Org Biomol Chem* 2005; 3:253–262.
47. Bjarnsholt T, Jensen PÄ, Rasmussen TB, Christophersen L, Calum H, Hentzer M, Hougen HP, Rygaard J, Moser C, Eberl L, Høiby N, Givskov M. Garlic blocks quorum sensing and promotes rapid clearing of pulmonary *Pseudomonas aeruginosa* infections. *Microbiology* 2005;151:3873–3880.
48. Smyth AR, Cifelli PM, Ortori CA, Righetti K, Lewis S, Erskine P, Holland ED, Givskov M, Williams P, Câmara M, Barrett DA, Knox A. Garlic as an inhibitor of *Pseudomonas aeruginosa* quorum sensing in cystic fibrosis—a pilot randomized controlled trial. *Pediatr Pulmonol* 2010;45:356–362.
49. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trial* 1996;17:1–12.
50. Jane Brody: vitamins and supplements. *New York Times* 1997. October 26.
51. Portal BC, Richard MJ, Faure HS, Hadjian AJ, Favier AE. Altered antioxidant status and increased lipid peroxidation in children with cystic fibrosis. *Am J Clin Nutr* 1995;61:843–847.
52. Wood LG, Fitzgerald DA, Gibson PG, Cooper DM, Collins CE, Garg ML. Oxidative stress in cystic fibrosis: dietary and metabolic factors. *J Am Coll Nutr* 2001;20:157–165.
53. Back EI, Frindt C, Nohr D, Frank J, Ziebach R, Stern M, Ranke M, Biesalski HK. Antioxidant deficiency in cystic fibrosis: when is the right time to take action? *Am J Clin Nutr* 2004;80:374–384.
54. Grey V, Mohammed SR, Smountas AA, Bahlool R, Lands LC. Improved glutathione status in young adult patients with cystic fibrosis supplemented with whey protein. *J Cyst Fibros* 2003; 2:195–198.
55. Lands LC, Iskandar M, Beaudoin N, Meehan B, Dauleibaev N, Berthiuame Y. Dietary supplementation with pressurized whey in patients with cystic fibrosis. *J Med Food* 2010;13:77–82.
56. Zavorsky GS, Kubow S, Grey V, Riverin V, Lands LC. An open-label dose-response study of lymphocyte glutathione levels in healthy men and women receiving pressurized whey protein isolate supplements. *Int J Food Sci Nutr* 2007;58:429–436.
57. Kongerud J, Crissman K, Hatch G, Alexis N. Ascorbic acid is decreased in induced sputum of mild asthmatics. *J Inhal Toxicol* 2003;15:101–109.
58. Allen S, Britton JR, Leonardi-Bee JA. Association between anti-oxidant vitamins and asthma outcome measures: systematic review and meta-analysis. *Thorax* 2009;64:610–619.
59. Gao J, Gao X, Li W, Zhu Y, Thompson PJ. Observational studies on the effect of dietary antioxidants on asthma: a meta-analysis. *Respirology* 2008;13:528–536.
60. Kaur B, Rowe BH, Arnold E. Vitamin C supplementation for asthma. *Cochrane Database Syst Rev* 2009;21:CD000993.
61. Wood LG, Fitzgerald DA, Lee AK, Garg ML. Improved antioxidant and fatty acid status of patients with cystic fibrosis after antioxidant supplementation is linked to improved lung function. *Am J Clin Nutr* 2003;77:150–159.

62. Shaheen SO, Newson RB, Rayman MP, Wong AP, Tumilty MK, Phillips JM, Potts JF, Kelly FJ, White PT, Burney PG. Randomised double blind, placebo-controlled trial of selenium supplementation in adult asthma. *Thorax* 2007;62:483–490.
63. Hasselmark L, Malmgren R, Zetterstrom O, Unge G. Selenium supplementation in intrinsic asthma. *Allergy* 1998;48:30–36.
64. Allam MF, Lucance RA. Selenium supplementation for asthma. *Cochrane Database Syst Rev* 2004;2:CD003538.
65. Duntas LH. Selenium F inflammation: underlying anti-inflammatory mechanisms. *Horm Metab Res* 2009;41:443–447.
66. Lau BH, Riesen SK, Truong KP, Lau EW, Rohdewald P, Barreta RA. Pycnogenol as an adjunct in the management of childhood asthma. *J Asthma* 2004;41:825–832.
67. Hosseini S, Pishnamazi S, Sadrzadeh SM, Farid F, Farid R, Watson RR. Pycnogenol® in the management of asthma. *J Med Food* 2001;4:201–209.
68. Simopoulos AP. Essential fatty acids in health and chronic disease. *Am J Clin Nutr* 1999;70:560S–569S.
69. Wall R, Ross RP, Fitzgerald GF, Stanton C. Fatty acids from fish: the anti-inflammatory potential of long-chain omega-3 fatty acids. *Nutr Rev* 2010;68:280–289.
70. McKarney C, Everard M, N'Diaye T. Omega-3 fatty acids (from fish oils) for cystic fibrosis. *Cochrane Database Syst Rev* 2007;17:CD002201.
71. Reisman J, Schachter HM, Dales RE, Tran K, Kourad K, Barnes D, Sampson M, Morrison A, Gaboury I, Blackman J. Treating asthma with omega-3 fatty acids: where is the evidence? A systematic review. *BMC Complement Altern Med* 2006;19:6–26.
72. Woods RK, Thien FC, Abramson MJ. Dietary marine fatty acids (fish oil) for asthma in adults and children. *Cochrane Database Syst Rev* 2002;3:CD001283.
73. Olveira G, Olveira C, Acosta E, Espíldora F, Garrido-Sánchez L, García-Escobar E, Rojo-Martínez G, Gonzalo M, Soriguer F. Fatty acid supplements improve respiratory, inflammatory and nutritional parameters in adults with cystic fibrosis. *Arch Bronconeumol* 2010;46:70–77.
74. Britton J, Pavord I, Richards K, Wisniewski A, Knox A, Lewis S, Tattersfield A, Weiss S. Dietary magnesium, lung function, wheezing and airway hyperreactivity in a random population sample. *Lancet* 1994;344:357–362.
75. Rowe BH, Camargo CA, Jr. The role of magnesium sulfate in the acute and chronic management of asthma. *Curr Opin Pulm Med* 2008;14:70–76.
76. Gontijo-Amaral C, Ribeiro MA, Gontijo LS, Condino-Neto A, Ribeiro JD. Oral magnesium supplementation in asthmatic children: a double-blind randomized placebo-controlled trial. *Eur J Clin Nutr* 2007;61:54–60.
77. Bruzzese E, Raia V, Gaudiello G, Polito G, Buccigrossi V, Formicola V, Guarino A. Intestinal inflammation is a frequent feature of cystic fibrosis and is reduced by probiotic administration. *Aliment Pharmacol Ther* 2004;20:813–819.
78. Infante Pina D, Redecillas Ferreiro S, Torrent Vernetta A, Segarra Cantón O, Maldonado Smith M, Gartner Tizziano L, Hidalgo Albert E. Improvement of intestinal function in cystic fibrosis patients using probiotics. *An Pediatr (Barc)* 2008;69:501–505.
79. Bruzzese E, Raia V, Spagnuolo MI, Volpicelli M, De Marco G, Maiuri L, Guarino A. Effect of lactobacillus GG supplementation on pulmonary exacerbations in patients with cystic fibrosis: a pilot study. *Clin Nutr* 2007;26:322–328.
80. Weiss B, Bujanover Y, Yahav Y, Vilozni D, Fireman E, Efrati O. Probiotic supplementation affects pulmonary exacerbations in patients with cystic fibrosis: a pilot study. *Pediatr Pulmonol* 2010;45:536–540.
81. Honeycutt TC, El Khashab M, Wardrop RM III, McNeal-Trice K, Honeycutt AL, Christy CG, Mistry K, Harris BD, Meliones JN, Kocis KC. Probiotic administration and the incidence of nosocomial infection in pediatric intensive care: a randomized placebo-controlled trial. *Pediatr Crit Care Med* 2007;8:452–458.
82. Whelan K, Myers CE. Safety of probiotics in patients receiving nutritional support: a systematic review of case reports, randomized controlled trials, and nonrandomized trials. *Am J Clin Nutr* 2010;91:687–703.
83. Liou MT. Safety of probiotics: translocation and infection. *Nutr Rev* 2008;66:192–202.
84. Snydman DR. The safety of probiotics. *Clin Infect Dis* 2008;1: S104–S111.
85. Rey L. Thermoluminescence of ultra-high dilutions of lithium chloride and sodium chloride. *Physica A* 2003;323:67–74.
86. Elia V, Niccoli M. New physico-chemical properties of extremely diluted aqueous solutions. *J Therm Anal Calorimetry* 2004;75: 815–836.
87. Roy R, Tiller WA, Bell IR, Hoover MR. The structure of liquid water: novel insights from materials research; potential relevance to homeopathy. *Mater Res Innov* 2005;94:577–608.
88. Rao ML, Roy R, Bell IR, Hoover R. The defining role of structure (including epitaxy) in the plausibility of homeopathy. *Homeopathy* 2007;96:175–182.
89. Belon P, Cumps J, Ennis M, Mannaioni PF, Sainte-Laudy J, Roberfroid M, et al. Histamine dilutions modulate basophil activity. *Inflamm Res* 2004;53:181–188.
90. Witt CM, Bluth M, Albrecht H, et al. The in vitro evidence for an effect of high homeopathic potencies—a systematic review of the literature. *Complement Ther Med* 2007;15:128–138.
91. Frenkel M, Mishra BM, Sen S, Yang P, Pawlus A, Vence L, Leblanc A, Cohen L, Banerji P, Banerji P. Cytotoxic effects of ultra-diluted remedies on breast cancer cells. *Int J Oncol* 2010;36:395–403.
92. Linde K, Clausius N, Ramirez G, Melchart D, Eitel F, Hedges LV, Jonas WB. Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. *Lancet* 1997;20:834–843.
93. Kleijnen J, Knipschild P, ter Riet G. Clinical trials of homeopathy. *Br Med J* 1991;302:316–323.
94. Cucherat M, Haugh MC, Gooch M, Boissel JP. Evidence of clinical efficacy of homeopathy. A meta-analysis of clinical trials. HMRAG. Homeopathic Medicines Research Advisory Group. *Eur J Clin Pharmacol* 2000;56:27–33.
95. Shang A, Huwiler-Müntener K, Nartey L, Jüni P, Dörig S, Sterne JA, Pewsner D, Egger M. Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. *Lancet* 2005;2:726–732.
96. Rutten AL, Stolper CF. The 2005 meta-analysis of homeopathy: the importance of post-publication data. *Homeopathy* 2008;97: 169–177.
97. Reilly D, Taylor MA, McSharry C, Aitchison TC. Is homeopathy a placebo response? Controlled trial of homeopathic potency, with pollen in hayfever as model. *The Lancet* 1986;344:881–886.
98. Reilly D, Taylor MA, Beattie NG, Campbell JH, McSharry C, Aitchison TC, Carter R, Stevenson RD. Is evidence for homeopathy reproducible? *The Lancet* 1994;344:1601–1606.
99. Vickers AJ, Smith C. Homeopathic Oscilloccoccinum for preventing and treating influenza and influenza-like syndromes. *Cochrane Database Syst Rev* 2000;3:CD001957.
100. Barnes J, Resch KL, Ernst E. Homeopathy for postoperative ileus? A meta-analysis. *J Clin Gastroenterol* 1997;25:628–633.
101. Jacobs J, Jimenez LM, Gloyd SS, Gale JL, Crothers D. Treatment of acute childhood diarrhea with homeopathic medicine: a randomized clinical trial in Nicaragua. *Pediatrics* 1994;93: 719–725.

102. Jacobs J, Jonas WB, Jimenez-Perez M, Crothers D. Homeopathy for childhood diarrhea: combined results and meta-analysis from three randomized controlled trials. *Pediatr Infect Dis* 2003;22:229–234.
103. Linde K, Jobst KA. Homeopathy for chronic asthma. *Cochrane Database Syst Rev* 2000;1:CD000353.
104. Frass M, Dielacher C, Linkesch M, et al. Influence of potassium dichromate on tracheal secretions in critically ill patients. *Chest* 2005;127:936–941.
105. Dantas F, Rampes H. Do homeopathic medicines provoke adverse effects? A systematic review. *Br Homeopath J* 2000;89:235–238.
106. Haczku A, Panettieri RA, Jr. Social stress and asthma: the role of corticosteroid insensitivity. *J Allergy Clin Immunol* 2010;125:550–558.
107. Chen E, Miller GE. Stress and inflammation in exacerbations of asthma. *Brain Behav Immun* 2007;21:993–999.
108. Chen E, Hanson M, Paterson L, et al. Socioeconomic status and inflammatory processes in childhood asthma: the role of psychological stress. *J Allergy Clin Immunol* 2006;117:1014–1020.
109. Cohen DP. A pediatric perspective on mind-body medicine. In: Culbert TP, Olness K, editors. *Integrative Pediatrics*. New York: Oxford University Press; 2010. pp. 267–301.
110. NIH Technol Assess Statement. Integration of behavioral and relaxation approaches into the treatment of chronic pain and insomnia. NIH Technol Assess Statement. 1995; October 16–18: 1–34.
111. Anbar R, Hummell K. Teamwork approach to clinical hypnosis at a pediatric pulmonary center. *Am J Clin Hypn* 2005;48:45–49.
112. Anbar RD. Self-hypnosis for management of chronic dyspnea in pediatric patients. *Pediatrics* 2001;107:E21.
113. Belsky J, Khanna P. The effects of self-hypnosis for children with cystic fibrosis: a pilot study. *Am J Clin Hypn* 1994;36:282–292.
114. Anbar RD. Self-hypnosis for patients with cystic fibrosis. *Pediatr Pulmonol* 2000;30:461–465.
115. Brown D. Evidence-based hypnotherapy for asthma: a critical review. *Int J Clin Exp Hypn* 2007;55:220–249.
116. Lahmann C, Nickel M, Schuster T, Sauer N, Ronel J, Noll-Hussong M, Tritt K, Nowak D, Rohricht F, Loew T. Functional relaxation and guided imagery as complementary therapy in asthma: a randomized controlled clinical trial. *Psychother Psychosom* 2009;78:233–239.
117. Delk KK, Gevirtz R, Hicks DA, Carden F, Rucker R. The effects of biofeedback assisted breathing retraining on lung functions in patients with cystic fibrosis. *Chest* 1994;105:23–28.
118. Grasso M, Button BM, Allison DJ, Sawyer SM. Benefits of music therapy as an adjunct to chest physiotherapy in infants and toddlers with cystic fibrosis. *Pediatr Pulmonol* 2000;29:371–381.
119. Holloway E, Ram F. Breathing exercises for asthma. *Cochrane Database Syst Rev* 2004;1:CD001277.
120. Pomidori L, Campigotto F, Amatya TM, Bernardi L, Cogo A. Efficacy and tolerability of yoga breathing in patients with chronic obstructive pulmonary disease: a pilot study. *J Cardiopulm Rehabil Prev* 2009;29:133–137.
121. Vempati R, Bijlani RL, Deepak KK. The efficacy of a comprehensive lifestyle modification programme based on yoga in the management of bronchial asthma: a randomized controlled trial. *BMC Pulm Med* 2009;30:37.
122. Sodhi C, Singh S, Dandona PK. A study of the effect of yoga training on pulmonary functions in patients with bronchial asthma. *Indian J Physiol Pharmacol* 2009;53:169–174.
123. Donesky-Cuenco D, Nguyen HQ, Paul S, Carrieri-Kohlman V. Yoga therapy decreases dyspnea-related distress and improves functional performance in people with chronic obstructive pulmonary disease: a pilot study. *J Altern Complement Med* 2009;15:225–234.
124. Galantino ML, Galbavy R, Quinn L. Therapeutic effects of yoga for children: a systematic review of the literature. *Pediatr Phys Ther* 2008;20:66–80.
125. Sabina AB, Williams AL, Wall HK, Bansal S, Chupp G, Katz DL. Yoga intervention for adults with mild-to-moderate asthma: a pilot study. *Ann Allergy Asthma Immunol* 2005;94:543–548.
126. Cooper S, Osborne J, Newton S, Harrison V, Thompson Coon J, Lewis S, Tattersfield A. Effect of two breathing exercises (Buteyko and pranayama) in asthma: a randomised controlled trial. *Thorax* 2003;58:674–679.
127. Haldeman S. Principles and practice of chiropractic. New York: McGraw-Hill Professional; 2004. p. 755.
128. Bonfort G, Evans R, Kubic P, Filkin P. Chronic pediatric asthma and chiropractic spinal manipulation: a prospective clinical series and randomized clinical pilot study. *J Manipulative Physiol Ther* 2001;24:369–377.
129. Kaminskyj A, Frazier M, Johnstone K, Gleberzon J. Chiropractic care for patients with asthma: a systematic review of the literature. *J Can Chiropr Assoc* 2010;54:24–32.
130. Stern RC, Canda ER, Doershuk CF. Use of nonmedical treatment by cystic fibrosis patients. *J Adolesc Health* 1992;13:612–615.
131. Thiel HW, Bolton JE, Docherty S, Portlock JC. Safety of chiropractic manipulation of the cervical spine: a prospective national survey. *Spine* 2007;32:2375–2378.
132. Gouveia LO, Castanho P, Ferreira JJ. Safety of chiropractic interventions: a systematic review. *Spine* 2009;15:E405–E413.
133. Vohra S, Johnston BC, Cramer K, Humphreys K. Adverse events associated with pediatric spinal manipulation: a systematic review. *Pediatrics* 2007;119:275–283.
134. Paccou J, Zeboulon N, Combescure C, Gossec L, Cortet B. The prevalence of osteoporosis, osteopenia, and fractures among adults with cystic fibrosis: a systematic literature review with meta-analysis. *Calcif Tissue Int* 2010;86:1–7.
135. Field T, Hernandez-Reif M, Diego M, Figueiredo B, Schanberg S, Kuhn C. Prenatal cortisol, prematurity and low birthweight. *Infant Behav Dev* 2006;29:268–275.
136. Hernandez-Reif M, Field T, Krasnegor J, Martinez E, Schwartzman M, Mavanda K. Children with cystic fibrosis benefit from massage therapy. *J Pediatr Psychol* 1999;24:175–181.
137. Field T, Henteleff T, Hernandez-Reif M, et al. Children with asthma have improved pulmonary function after massage therapy. *J Pediatr* 1998;132:854–858.
138. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, Kessler RC. Trends in alternative medicine use in the United States 1990–1997: results of a follow-up national survey. *JAMA* 1998;280:1569–1575.
139. Roberts L, Ahmed I, Hall S, Davison A. Intercessory prayer for the alleviation of ill health. *Cochrane Database Syst Rev* 2009;2:CD000368.
140. Ott MJ, Bossi I, Colbath J. A pediatric perspective on energy therapies. In: Culbert TP, Olness K, editors. *Integrative pediatrics*. New York: Oxford University Press; 2010. pp. 180–203.
141. Rosa L, Rosa E, Sarner L, Barrett S. A close look at therapeutic touch. *JAMA* 1998;279:1005–1010.
142. Cox T. A nurse-statistician reanalyzes data from the Rosa therapeutic touch study. *Altern Ther Health Med* 2003;9:58–64.
143. Dossey L. Therapeutic touch at the crossroads: observations on the Rosa study. *Altern Ther Health Med* 2003;9:38–39.
144. Achterberg J. Clearing the air in the therapeutic touch controversy. *Altern Ther* 1998;4:100–101.
145. Leskowitz E. Un-debunking therapeutic touch. *Altern Ther* 1998;4:101–102.

146. Wardell D, Engebretson J. Biological correlates of Reiki Touch (sm) healing. *J Adv Nurs* 2001;33:439–445.
147. Ng BH, Tsang HW. Psychophysiological outcomes of health qigong for chronic conditions: a systematic review. *Psychophysiology* 2009;46:257–269.
148. Taylor-Piliae RE. The effectiveness of Tai Chi exercise in improving aerobic capacity: an updated meta-analysis. *Med Sport Sci* 2008;52:40–53.
149. Lee MS, Lee EN, Ernst E. Is Tai Chi beneficial for improving aerobic capacity? A systematic review. *Br J Sports Med* 2009;43: 569–573.
150. Shekelle PG, Morton SC, Suttorp MJ, Buscemi N, Friesen C. Challenges in systematic reviews of complementary and alternative medicine topics. *Ann Intern Med* 2005;142:1042–1047.
151. Mason S, Tovey P, Long AF. Evaluating complementary medicine: methodological challenges of randomised controlled trials. *Br Med J* 2002;325:832–834.
152. Pham B, Klassen TP, Lawson ML, Moher D. Language of publication restrictions in systematic reviews gave different results depending on whether the intervention was conventional or complementary. *J Clin Epidemiol* 2005;58:769–776.