

Alternative medicine for allergy and asthma

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Orthodox medical approaches to asthma and allergic respiratory diseases are provided in guidelines developed by professional societies and national or state organizations that represent organized medicine. Alternative therapies may include such orthodox medical therapies as obsolescent formerly used agents, unusual but accepted agents, and agents that are in favor for orthodox therapy in other countries. However, the current growth of complementary and alternative medicine is based on the use of nonorthodox remedies that are becoming increasingly popular with patients and that should be familiar to physicians. Asthma and allergies are frequently treated with such remedies by patients, either as part of self-therapy or on the advice of a complementary and alternative medicine practitioner. The most popular alternative medical treatments are herbs (Western and Asiatic), acupuncture, various types of body manipulation, psychologic therapies, homeopathy, and unusual allergy therapies. There is little evidence in favor of most of these unorthodox treatments, although they are very often reported on favorably by patients. The published evidence that might support some alternative medical practices is reviewed so as to help physicians select alternatives that could appropriately be integrated into orthodox practice. (*J Allergy Clin Immunol* 2000;106:603-14.)

Key words: Asthma, alternative medicine, herbal therapy, homeopathic remedies, acupuncture, marijuana, psychologic therapies

Complementary and alternative medicine (CAM) has become an increasingly appealing component of standard medical care, with physicians accepting the need to integrate CAM with orthodox allopathic practices.^{1,2} Asthma is one of a number of common disorders for which there is a varied literature in support of CAM therapies.³⁻⁵ However, the extreme variety of approaches that can be successfully used indicates that the majority of unusual therapies must work on the overall mind-body relationship that is a factor in the control of asthma.⁶ Many of these unorthodox therapies are fraudulent or are ridicu-

Abbreviations used

CAM: Complementary and alternative medicine
MDI: Metered-dose inhaler
sGaw: Specific airway conductance
TCM: Traditional Chinese medicine
THC: Tetrahydrocannabinol

lous placebos,⁷ whereas others are adjuvants that may work through important and acceptable mechanisms, such as by alleviating anxiety. Similar remarks may apply to nonorthodox diagnostic and therapeutic modalities used in the treatment of allegedly allergic disorders. Nevertheless, in spite of these reservations, there is a surprising amount of clinical and laboratory information that has been published in support of some of the alternative remedies for asthma and hayfever.^{5,8} In this review particular emphasis will be given to the more scientific literature on herbs, homeopathy, unusual drugs (including marijuana), and acupuncture.

HISTORICAL HIGHLIGHTS

Some of the historical theories, techniques, and treatments that have been used in the management of breathing disorders and chest diseases have persisted over thousands of years.⁹ The favored drugs for asthma that were used in the second half of the twentieth century had their origins in folk remedies discovered by our ancestors. Thus ephedrine was developed from *ma huang*, a favorite Chinese herbal remedy in use for thousands of years. Ancient asthmatic subjects may have breathed in the smoke of heated henbane leaves, which released anticholinergic drugs, as did the stramonium cigarettes that were introduced into Europe from India in the nineteenth century.⁹⁻¹¹ Asia also provided the herbal origin of theophylline, which is found in tea leaves. Interestingly, the related herbal product caffeine and its congeners in coffee offered a favorite asthma remedy during the same century. Cromolyn was a derivative of the chromones found in *Ammi visnaga*, the source of the ancient Middle Eastern bronchodilator khella. Even steroids have a historical precedent, such as the use of placenta or pubescent boys' urine in treating asthma, whereas in the first half of the nineteenth century, ground adrenal glands were used. Some of these ancient sources of therapy are still made available today.

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TABLE I. Representative Chinese remedies for asthma

Herbs	Bupleurum, cordyceps, ephedra (Ma huang), ginkgo, licorice, magnolia, pinellia, platycodon, polygonum, scute
Minerals	Gypsum, mercury salts
Animals	Worms, lizard tail, crocodile bile
Mixtures	Ge Jie Anti-asthma Pill, Crocodile Bile Pill, Minor Blue Dragon
Kanpo*	Saibuko-to, shoseiryu-to, moku-boi-to, sho-saiko-to, bakumondo-to

The majority of Chinese drugs are not of proven value; ephedra and cordyceps appear to be the most effective of these agents.

*These are Japanese combination products, which may have antileukotriene activities.

Herbal products and associated chemicals and animal parts in great profusion have been used as folk remedies to treat cough, chest pain, wheeze, expectoration, rhinorrhea, dyspnea, and associated problems, such as fever, malaise, and debility.¹² These historical therapies can be classified as follows.

1. **Inhalants.** Inhaled remedies have varied from sacred incenses to cigarettes and from pungent chemicals to natural climates, such as sea air. Some, such as those derived from solanaceous plants containing anticholinergic drugs, would have eventually been recognized to act as bronchodilators, whereas others would have been used just to cause an irritant expectorant effect.
2. **Magical potions.** Witch doctors, shamans, priests, and protophysicians relied on various forms of magical healing that could be delivered through the medium of inspired concoctions of medicaments. These varied from the toxic, such as herbal emetics, to the disgusting, such as foul-tasting mixtures. Each might have been thought to work by driving out evil spirits, and in fact, they could help by inducing expectoration. Other magical remedies varied from the symbolic fox lungs or flowers that look like lungs to impressive expensive products from distant sources, such as imported guaiac wood from America, which led to the development of guaiafenesin. It is of interest that magical asthma remedies are still in use today, such as swallowing new-born live mice, eating fried bat, or consuming gecko tails or earthworms.¹³
3. **Pharmacologic drugs.** Most of the drugs in persistent use during the last century were derived from natural products, particularly herbs and chemicals, such as salts. Careful observation by astute healers or physicians established the objective value of many of these, such as ma huang for asthma, cough, and rhinosinusitis.

Other historical approaches of relevance include the elimination of dusts and animal products (eg, feathers), climate changes, regulation of daily activities and sleep, and other adjustments that are classified as holistic. Maimonides, in the twelfth century, gained fame for recommending such life-regulation approaches for asthma, and his concept of using spicy chicken soup persists to this day.¹⁴

HERBAL THERAPIES

Traditional Chinese medicine (TCM) is the most interesting systematized alternative medical system available in the West, and it is largely based on the use of hundreds of unfamiliar herbs, many of which have been used for hundreds of years (Table I).¹⁵ The typical TCM herbal prescription may contain 10 to 16 herbs, and ma huang (ephedra) is usually the only one with proven pharmacologic benefit. However, *Ginkgo biloba* has been used as an asthma remedy, although its clinical value appears to be negligible. Nevertheless, ginkgo extracts have been shown to have platelet-activating factor-antagonist effects, as do a number of other traditional respiratory herbs, such as coltsfoot, which is used as an antitussive.¹⁶ Some TCM herbs, such as various *Datura* plants, have anticholinergic effects. Some (eg, *Cordyceps sinensis*, licorice, skullcap, and *Perilla frutescens*) have been shown to have anti-inflammatory properties, and others may have nonspecific mucokinetic actions. Many of the numerous herbs used by Chinese practitioners for asthma and allergy have been carefully reviewed in a comprehensive analysis by Bielory and Lupoli,¹⁷ but their clinical value remains uncertain. However, individual preparations and combinations are readily obtained, and adventuresome patients may be using them. Popular proprietary products include Ge Jie (Fig 1) and Crocodile Bile Pill (Fig 2); these and others, such as Minor Blue Dragon Mixture, are based on ma huang and also contain such herbs as goldenthread, peony, orange peel, cinnamon, ginger, licorice, pinellia, and schizandra, along with such signature constituents as gecko tails and cinnabar (mercuric sulfide). Other combination products include Kan-Lin and Wen Yang, which also contain herbs such as aconite, rehmannia, yam, epimedium, psoralae, dodder, astragalus, poria, angelica, bupleurum, atracylodes, codonopsis, ginger, date, and scute. Similar herbal formulas are available for allergic rhinitis; examples include Turtle Shell, Cistanche combination, and Jade Screen powder.¹⁵ Unfortunately, exotic drug preparations are likely to be unreliable in the amount of active drug content, and they may be contaminated with active drugs, such as corticosteroids, or with hazardous agents, such as lead.

Kanpo is the Japanese traditional medical system that is related to TCM. A number of well-known herbal combinations are widely used by Japanese practitioners for asthma and hayfever.¹⁸ Representative ones, such as saibuko-to and sho-saiko-to, contain such constituents as ephedra, licorice, asarum, schisandra, peony, poria, scute, Chinese date, bupleurum, perilla, pinellia, ginseng, ginger, and magnolia. Syo-seiryu-to has been shown to be effective in nasal allergy. Studies suggest that some of these Kanpo combinations have useful properties, including the ability to suppress lipoxygenase and cyclooxygenase activity, and they may affect corticosteroid metabolism.¹⁹ However, it should also be recognized that these agents can be toxic, and thus sho-saiko-to use could be a cause of acute pneumonitis.²⁰

In Indonesia a similar herbal system is used, but the Jamu pharmacopeia has not been adequately evaluated.



FIG 1. Ge Jie Anti-asthma Pill contains apricot kernels, cinnabar, coptidis, ephedra, gecko lizard tail, licorice, ophiopogon, and scutellaria.



FIG 2. Crocodile Bile Pill for Asthma contains adenophora, asparagus, aster, calcium sulfate, crocodile bile, ephedra, gypsum, lily, ophiopogon, orange peel, peony, perilla, peudanum, platycodon, scutellaria, and tricosanthese.

Other systems of drug therapy exist in many Southeast Asian countries, but no additional remedies of value seem to have emerged from this vast repertoire of historical phytomedical experience.

Indian systems of traditional medicine are well systematized but are largely unrecognized in the West. Ayurveda is gaining greater visibility; related systems, such as Unani-Tibb, Siddha, Tibetan and the Indosynic system of Pakistan, are likely to remain obscure.^{21,22} Some Ayurvedic drugs of interest for consideration in asthma include *Datura* plants (the historical source of atropine); *Tylophora asthmatica*, which is used for asthma; and the malabar nut, from which the European mucokinetic agent bromhexine was derived. *Coleus forskohlii* is a plant from which an interesting β -sympathomimetic drug has been obtained; forskolin (colforsin) enters cells and directly stimulates the production of cyclic 3,5-adenosine monophosphate, but its clinical value in asthma has not been adequately established.²³ Other agents used for asthma and coughs include spices, frankincense, jaggery, Indian gooseberry, costus, and myrobalm. Studies on frankincense, which contains

boswellic acid, have demonstrated that it can inhibit 5-lipoxygenase.²⁴

European herbs are relatively disappointing, and no major drugs for asthma or allergies have been derived from them. Most of the respiratory herbs indigenous to Europe are nonspecific mucokinetics; in this respect mustard and horseradish are possibly the most effective.²⁵ Of course, European studies helped establish the value of imported foreign herbal remedies, including atropinic cigarettes (Fig 3) and theophylline. A curious absence has been that of significant herbal antihistaminic or anti-inflammatory drugs other than cromolyn. A German herbal product for sinusitis and bronchitis (that is now available in the US) contains elderberry, gentian, primrose, sorrel, and vervain, and careful laboratory and clinical studies show that this combination may be effective, having antiviral, anti-inflammatory, and mucokinetic effects.²⁶ Other German remedies for colds and coughs include linden, ivy, soapbark, chamomile, birch, willow, peppermint, rose hips, mallow, pine, myrtol, thyme, and meadowsweet; these are often used in teas, but their value is uncertain.²⁷



FIG 3. Lancelot Cigarettes for Asthma contained stramonium. Similar cigarettes were marketed that contained belladonna. Added to these were other plant materials, such as tobacco, marijuana, coltsfoot, mullein, hyssop, and cubeb. Some contained potassium nitrate, arsenic, or other chemicals.

American herbal remedies of the past came mainly from Central and South America; ipecacuanha, pepper, and guaiac are the best known. However, most South American phytomedicines in use today for respiratory disease are of dubious benefit (eg, lettuce, oregano, okra, and copaiba).²⁸ Traditional North American herbal drugs, such as lobelia, yerba santa, senega, and creosote, are largely obsolescent, whereas emerging respiratory drugs, such as echinacea, goldenseal, and sundew, are not indicated for asthma or hayfever. However, meta-analyses suggest that echinacea can help prevent and alleviate common colds. It is of interest that some promoters of echinacea claim that its immunostimulating effect should be a contraindication to its use in asthma.

Universally popular respiratory remedies include eucalyptus, menthol, anise, fennel, tolu balsam, and camphor; some of these are incorporated in products such as Vicks VapoRub and Tiger Balm.²⁴ These aromatic agents, when inhaled as vapors, can soothe the inflamed nasal mucosa and seem to benefit the tracheobronchial tree. Other soothing remedies of the throat include menthol, marshmallow, Iceland moss, mullein, plantain, and

slippery elm. It would be expected that honey, candies, or other nonspecific throat drops may be just as effective as the mucilaginous contents of these phytomedicines.

In contrast to herbs, it is possible that some foods (onion, garlic, pungent spices, antioxidants, omega-3 fatty acids, and essential oils from citrus fruits) and vitamins are of physiologic value in helping improve natural body defenses.²⁹⁻³¹ There is some evidence, which is not uniform, that the addition of such food derivatives to the diet of patients with chronic airway hyperreactivity may be beneficial. Similarly, epidemiologic studies suggest that increasing magnesium intake and decreasing salt and sugar consumption can help stabilize brittle asthma.³² In contrast, food allergy is only an occasional cause of asthma.³³

It can be concluded that herbal remedies offer a melange of nonspecific mucokinetics and placebos, with occasional bronchodilator and anti-inflammatory remedies being discernible. However, the best of these ancient remedies, ma huang, is grossly inferior to orthodox drugs, in terms of both prime effects and side effects. Thus herbs offer an alternative for only milder forms of asthma or hayfever. Representative herbs are listed in Table II.

HOMEOPATHIC REMEDIES

The enthusiasm of many patients and some physicians for homeopathic treatment in asthma illustrates that completely opposite approaches may be equally effective. Thus Chinese herbal medicines may contain 10 or more components, which are boiled in water and used as a soup. In contrast, classical homeopathy uses single herbs diluted to the point that the final prescribed solution may be totally free of any physical remnants of the original drug. In each of these situations, there is an assumption that some essential quality of the administered cure serves to enhance the body's ability to heal itself.

Traditional homeopathy uses unusual drugs, such as bryony, sabadilla, spikenard, and burnt sponge, for asthma and hayfever.^{34,35} However, some formerly popular allopathic drugs are also used, including stramonium, lobelia, onion, honey, nettle, and ipecacuanha. A more recent form of homeopathy, termed isopathy, uses dilutions of allergens or drugs that provoke bronchospasm. This variation of homeopathic therapy has been the source of most of the clinical trials in asthma and hayfever.³⁴ Finally, homeopathic treatment can be self-selected, with patients using over-the-counter remedies, such as the popular isopathic preparation Oscilloccinum for colds; this product is a diluted autolysate of the heart and liver of a duck. Because classical homeopathy uses very dilute solutions of drugs that cause the same symptoms that are to be treated, it is not surprising that onion is a treatment for rhinitis. Theoretically, a very dilute solution of a β -blocker could be used to treat asthma.

When a patient seeks traditional homeopathy, he or she will be carefully evaluated by the therapist with respect to symptoms and aspects of daily living; the patient's personality type is also given consideration.³⁶ The most suit-

TABLE II. Representative Western herbs for asthma

Possible expectorant effect*	Possible immune effect*	Possible bronchodilator effect
Angelica	Echinacea	Belladonna
Balsams	Licorice	Coffee
Coltsfoot	Wheatgrass	Henbane
Creosote		Stramonium
Garlic		Tea
Ginger		Vitamins (eg, A, C, and E)
Goldenseal		
Guaiacol		
Horehound		
Horseradish		
Marshmallow		
Mullein		
Mustard		
Peppers (eg, capsicums and cubeb)		
Sarsaparilla		
Snakeroot		
Skunk cabbage		
Squill		
Storax		
Sundew		
Terpene		
Thyme		

*None of these agents is of proven value for asthma or allergic respiratory diseases.

able homeopathic preparation is then selected from a special therapeutic guidebook or repertory. Thus the personal attention given to the patient may be a potent factor leading to a therapeutic response. This explanation does not apply to the use of off-the-shelf remedies, yet several studies of such products have shown a benefit over placebo therapy in the treatment of asthma and allergic rhinitis. Moreover, a famous study showed that sensitized basophils could be degranulated by a solution of anti-IgE antibodies diluted to 10^{-120} ; such a solution contains not even one molecule of anti-IgE, although it may "retain the memory" of the antibody.³⁷

Reilly et al³⁸ have studied homeopathic treatments in hayfever and in asthma. One hundred and fifty-eight patients with seasonal rhinitis were given either a homeopathic remedy or a placebo twice a day for 2 weeks and followed up 2 weeks later.³⁸ Fifty-six patients receiving the remedy were suitable for evaluation, as were 52 receiving placebo. The responses were judged by using a visual analogue scale, and this showed a significantly greater response to the homeopathic therapy; a corresponding reduction in the need for antihistamines was also seen in these patients. The homeopathic preparation of mixed grass pollens was diluted to 1 in 10^{-6} , and thus none of the active material existed in the remedy. A similar study was carried out on asthma patients.³⁹ Thirteen such patients received the allergen remedy diluted to 1 in 10^{60} , and 15 received placebo. The actively treated group showed significant improvement on the visual analogue scale, as well as in forced vital capacity and FEV₁. Although the results may not be totally convincing, they

are certainly worthy of some respect in that they suggest that homeopathy is more than simply placebo therapy.⁴⁰ The existence of favorable results for asthma and hayfever in double-blind, placebo-controlled studies of homeopathic remedies baffles and disturbs orthodox physicians, but if one wishes to reject those peer-reviewed publications that show favorable outcomes for homeopathy, one should be equally skeptical of favorable findings in double-blind, placebo-controlled studies on orthodox drugs.⁴¹

The problem with homeopathic medications is that their beneficial effects in asthma and allergy may depend on nonmaterial mechanisms that require an expanded dimension in thinking about the therapeutic actions of medications. Thus it is worth reflecting on the early concepts of Hahnemann, who formulated the practice of homeopathy. He believed that treating an inner disease would initially drive it outwards, giving the example that when asthma improves, eczema may appear. Furthermore, homeopathic theories provide a link between the therapeutic achievements of psychoanalysis on the one hand and trace minerals and hyposensitization therapy on the other. It is not surprising that attempts are made to explain homeopathy's therapeutic successes with exotic theories on the basis of electromagnetism, nuclear magnetic resonance, energy fields, and quantum physics. Of course, one could use similar rationales to explain the actions of pure placebos.^{39,42,43} Because placebos can exert significant therapeutic effects, there is still a need to explore all possible mechanisms by which any therapy may bring about an inexplicable benefit.

It must be concluded that homeopathy today is a very variable alternative practice, with patients using self-therapy at one extreme or relying on knowledgeable, dedicated, careful homeopathic practitioners at the other extreme. Because patients may be equally satisfied by either approach, it is probable that most improvements are explicable by the placebo effect. However, the intellectual challenge remains because for many years evidence has been published that would suggest a true benefit may be attributed to homeopathy.⁴⁴ One major criticism of quality homeopathic studies that show favorable results is that the techniques that are used differ from those used in everyday practices, and thus any findings of benefit from such studies cannot be used as an endorsement for current clinical practices in homeopathy and isopathy.

OSTEOPATHY AND CHIROPRACTIC

In the nineteenth century, osteopathy and chiropractic were born in the United States, and they are currently accepted as effective health disciplines. These manipulative arts can be compared with TCM. Classical practitioners profess that by resolving the imbalance of energy flow in the body (as is supposed to occur particularly with acupuncture), the body's ability to heal itself is enhanced. Osteopaths often practice orthodox medicine and may incorporate manipulative therapy as adjuncts to routine drug prescriptions. In contrast, chiropractors do not prescribe drugs and may incorporate herbs, vitamins, and other therapies along with manipulation.

The various techniques of osteopathy—such as infraspinatus muscle injection with local anesthetic, a steroid, or both, or thoracic pumping and lymphatic massage, along with spinal and joint adjustments—may make patients feel better, but they have not been proved to be of significant specific benefit for asthma or respiratory allergies. Recently, a study on chiropractic manipulation in children with asthma suggested that genuine techniques were no more effective than sham techniques. Both appeared to have an equal and measurable outcome, suggesting a placebo and Hawthorne effect attributable to the added attention that the patient receives during the course of the study.⁴⁵

Numerous other body manipulation techniques are advocated by CAM practitioners for a large variety of disorders, including asthma.^{1,6} Some of the better known ones include reflexology, shiatsu, Reiki, various types of bodywork exercises and massage, breathing exercises, yoga exercises, qi gong exercises, spa therapy, and health club activities. All may improve the general perception of health, and although there is no evidence of specific benefit, such treatments may be valuable adjuncts to orthodox medical treatment and can be used as part of integrative and holistic management. The patient who makes a dedicated commitment to these therapeutic practices invests considerable faith in the techniques, and this element will assure a placebo response of significant degree. However, there is some evidence in support of

treating asthma with yoga breathing exercises and postures,^{33,46,47} while Chinese qi gong practices⁴⁸ can be of benefit. Panic control and relief of anxiety are probably of importance, and cognitive behavioral therapy can be of benefit in such situations.⁴⁹

PSYCHOLOGIC THERAPIES

Religious experiences have a long history of value in the treatment of disease. Prayer, miraculous curing, faith healing, therapeutic touch, cult behavior, and shamanism can still benefit those who are believers, although extreme approaches verge into exploitative or fraudulent manipulation of a patient's gullibility. Mesmerism, hypnotism, biofeedback, and related practices can help improve autonomic imbalance in diseases such as asthma.^{33,50} Transcendental meditation can reduce the wasted energy of breathing and can decrease oxygen consumption. Thus training patients to relax; to breathe; to sing, chant, or listen to music; to exercise more economically; and to cough more effectively may result in measurable improvements. Positive imagery, in which a patient conjures up imaginary scenes or feelings of improved body function, also leads to measurable benefit. Similarly, verbalizing or even writing about stress factors can result in benefits in asthma.⁵¹ Rehabilitation programs for patients with severe airway disease emphasize comparable techniques and can also be of benefit by introducing socialization, motivation, compliance, anxiety control, and relaxation practices (perhaps with the help of music)⁵² into the patient's daily life. Optimization of diet and weight, daily exercise, and removal of bad habits (including smoking) may also be achieved with such programs. However, some patients require more radical experiences, such as a visit to a shrine or a guru, or they need to make a pilgrimage or make a major commitment to a religious group. Such experiences may be expected to increase patients' tolerance to disease and to help them control unfavorable psychologic reactions that might contribute to the escalation of the symptomatic reactions that result from exposure to stress. However, some fashionable techniques, such as therapeutic touch, may not prove their value when subjected to scientific study.⁵³ Many of the popular alternative therapies are listed in Table III.

ACUPUNCTURE IN ASTHMA

At present, acupuncture is one of the most popular alternative therapies for asthma in the United States, and with the help of competent practitioners, it is readily available in major population centers. Acupuncture involves the insertion of thin needles into the skin at specified locations to regulate the flow of energy (Chi) that is believed to control psychophysical function.⁵⁴ Once Chi is accessed at points on the meridians along which energy flows, it can be regulated by gently manipulating the needle at different frequencies or by other means, such as electrical stimulation or burning the herb *Artemisia vulgaris* on the end of the needle (moxibus-

TABLE III. Major CAM choices

Herbal	Western: herbs, phytochemicals, botanical; Chinese: CTM, Kanpo, Jamu; Indian: Ayurveda, Unani, Siddha
Dietary	Elimination: additives, processed foods, salt, allergens (eg, spices, milk, nuts, eggs), toxins, yeast products; addition: magnesium, selenium, omega-3 fatty acids, antioxidants (eg, vitamins), coffee, teas, pungent spices
Homeopathy	Classical, modified, isopathy, pseudohomeopathy
Osteopathy	Manipulation, lymphatic massage, exercise
Chiropractic	Correction of subluxations, massage, postural adjustments, vitamins, diet
Exercise	Breathing technique, yoga, Chinese (eg, qi gong, tai chi)
Environment	Climate, spas, air purifiers, aromatherapy
Massage	Numerous types (eg, shiatsu, reflexology)
Immune	Unusual vaccines or desensitization techniques, embryonic cell derivatives, thymus stimulation
Surgical	Vagal, chest wall, lung and esophageal procedures; thymectomy, splenectomy, adenoidectomy
Naturopathy	Fruit and vegetable diets, elimination diets, hydrotherapy, enemas, wheatgrass juice
Acupuncture	Classical, electroacupuncture, acupressure, moxibustion
Unusual drugs	Magnesium preparations, heparin, local anesthetics, and a host of others

TABLE IV. Results and quality of published placebo-controlled trials of acupuncture in asthma

Author	No. of subjects	Random allocation	Type of asthma	Outcome	Quality score (0-100)*
Double-blind trials					
Tashkin, 1977 ⁵⁵	12	Yes (crossover)	Acute (methacholine challenge)	β -Agonist > RA > SA > saline > no treatment (positive)	67
Dias, 1982 ⁵⁶	20	Yes	Chronic	SA > RA (negative)	61
Christensen, 1984 ⁵⁷	17	Yes	Chronic	Electro RA > SA (positive)	51
Tashkin, 1985 ⁵⁸	25	Yes (crossover)	Chronic	RA = SA (negative)	72
Mitchell, 1989 ⁵⁹	31	?	Chronic	RA = SA (negative)	Not scored
Tandom, 1989 ⁶⁰	16	Yes	Acute (histamine challenge)	RA = SA (negative)	55
Single-blind trials					
Yu, 1976 ⁶¹	20	No	Chronic	β -Agonist > RA > SA (positive)	43
Berger, 1977 ⁶²	12	No	Acute	RA > SA (positive)	26
Virsik, 1980 ⁶³	20	No	Acute	RA > SA (positive)	31
Takishima, 1982 ⁶⁴	10	No	Acute	RA > SA (positive)	31
Chow, 1983 ⁶⁵	16	Yes	Acute (exercise challenge)	RA = SA (negative)	31
Luu, 1985 ⁶⁶	16	Yes	Chronic	RA > SA (positive)	36
Fung, 1986 ⁶⁷	19	Yes	Acute (exercise challenge)	β -Agonist > RA > SA > no treatment (positive)	67

*Quality of methodology scored by Kleijnen et al.⁶⁸

RA, Real acupuncture; SA, sham acupuncture.

tion). Acupuncture has the appeal offered by a nearly risk-free, relatively low-cost, nonpharmacologic form of treatment.

Although acupuncture has been used in China for thousands of years for the treatment of asthma, only a limited body of studies of the efficacy of acupuncture in asthma have been carried out, mainly within the last 25 years, that use accepted Western scientific methods for clinical research. In the case of acupuncture, it is not possible or practical to blind the acupuncturist, but the evaluators (nonacupuncturist clinician-investigator and technical assessors) can and should be masked to the treatment condition (real vs sham acupuncture). Sham acupuncture is usually accomplished by injecting acupuncture needles at false points (ie, locations not designated as true acupuncture points on the meridians in any of the classical TCM texts). These sham points are generally selected 2 to 3 cm from the true point or in adjacent dermatomes.⁵⁴

Many reports of the efficacy of acupuncture in asthma published in the Chinese and Russian literature are based on uncontrolled observations and will not be further commented on here. Only 13 controlled clinical trials of real versus sham acupuncture in asthma have been published, of which 6 were double-blind,⁵⁵⁻⁶⁰ and 7 were single-blind.⁶¹⁻⁶⁷ Most of these have been reviewed by Kleijnen et al.⁶⁸ Two of the authors of the latter article independently scored each of these studies for the scientific quality of their methodology. The maximum possible score was 100, and interrater agreement was good. Features of these 13 studies are summarized in Table IV.

Unfortunately, most of the published clinical trials have methodologic shortcomings, including lack of double-blinding, random allocation to treatment, or both; small numbers of patients; and inadequate description of statistical analysis. Of the 6 double-blind studies, 4 were negative, whereas 6 of the 7 single-blind studies were positive. All but one of the negative studies that were scored for

methodologic quality had scores of greater than 50, whereas all but one of the positive studies had quality scores of less than 50. Therefore on the basis of the published literature, claims of the efficacy of acupuncture have not yet been convincingly supported by adequately designed clinical trials. Also, in all 3 studies that included a β -agonist as a positive comparator, the β -agonist was unequivocally superior to real acupuncture.

Jobst⁵⁴ has catalogued the side effects of acupuncture used in the treatment of asthma on the basis of reports from 16 published studies involving a total of 320 cases. Side effects were reported in only 23 (7%) of the 320 cases, and these have generally been mild (eg, vasovagal reactions, earache, and gastrointestinal symptoms), indicating that acupuncture therapy for asthma is generally safe. On the other hand, 5 cases of pneumothorax and one case of cardiac tamponade have been reported. In addition, one case of hepatitis B caused by needle contamination has been documented. It is therefore essential that acupuncture be performed only by well-trained practitioners and that only sterilized needles be used. Acupuncture is best reserved as an optional form of therapy that complements, rather than replaces, conventional therapeutic modalities of proven effectiveness.

ALLERGY THERAPIES

Although it is reasonable to insist that patients avoid obvious exacerbating factors in asthma and allergic disorders, alternative practitioners take elimination techniques to excess. Some of the diagnostic methods that are used, such as evaluating the cytotoxic response to allergies, are frankly fraudulent.^{7,8} Others seem to incorporate folie à deux, where the patient and practitioners believe in extraordinary phenomena. Thus, in applied kinesiology, practitioners claim the ability to detect an allergic response when a patient holds the offending food in one hand and demonstrates a consequent weakness in the other hand.⁶⁹

Very few patients have hidden allergies, and elaborate efforts to restrict diets and detect any adverse response to incremental reintroduction of foods may cause more harm than benefit. The adding of enzymes and special food products to improve digestion and reduce allergic manifestations is based solely on anecdotal reports. Some practitioners try to desensitize patients by administering injections of the patient's own urine or blood. Other extraordinary approaches include eye movement desensitization, reprocessing, and related psychologically directed techniques.⁵⁶ These treatments are accompanied by pseudoscientific explanations to justify their use. However, occasionally an extraordinary technique may be of benefit, such as drinking wheatgrass to progressively diminish allergy to wheat pollens or administering a rapid course of immunotherapy or giving intravenous IgG.⁷⁰ Currently, it is in vogue to blame *Candida albicans* as a cause of allergies and illness, such as hyperactivity, and to eliminate *Candida albicans* from the diet, or to treat with antifungal agents. These practices are

claimed to benefit some patients, although rigorous proof is lacking. It is probable that more consideration should be given in treating patients with severe allergies to the role of possible sensitizers, such as spices, fruits, food preservatives, and coloring agents.⁷¹ The appropriate balance between good, thorough, practical care and the temptation to use alternative or even magical techniques may be tilted in favor of the latter when treating a highly susceptible and demanding patient who favors exotic therapies.

UNUSUAL DRUGS

Throughout history, numerous drugs and chemicals have been used in the treatment of asthma.^{9,12,25} Ephedrine and pseudoephedrine in ma huang have each been used as pure drugs to treat asthma, but they are of limited value, and their effect diminishes because tachyphylaxis develops. Many other sympathomimetics are no longer mainstream or have entirely failed to enter the American market. The value of these was limited for various reasons, including, in some cases, their toxicity. These include methoxyphenamine and protoktyol, which were used in the United States and broxaterol, carbutoleol, clenbuterol, etafedrine, fenoterol, hexoprenaline, quinterenol, rimiterol, ritodrine, soterenol, trimetoquenol, and others that were used abroad. Phosphodiesterase inhibitors that are not in use at this time include bamiphylline, dyphylline, proxiphylline, enprophylline, etophylline, and quazodine. Anticholinergic drugs that have been used in asthma include atropine, hyoscine (scopolamine), hyoscyamine, and glycopyrrolate; in addition, asthma cigarettes containing stramonium (Fig 3), and similar sources of atropinic drugs were formerly in favor. Before the modern drug era of the second half of the twentieth century, asthma remedies included lobelia, potassium nitrate, amyl nitrate, pituitary extracts, khellin (from which cromolyn was derived), and a host of largely useless drugs, such as pyridine and turpentine derivatives. Asthma cigarettes often contained stramonium mixed with tobacco, mullein, coltsfoot, hyssop, horehound, black tea leaves, marijuana, arsenic, and so on in imaginative combinations.

More recently, methotrexate gained favor for steroid-dependent asthma, as had triacetyloleandomycin previously. Neither agent nor other immunosuppressive drugs, such as cyclophosphamide or cyclosporin, are in favor today.³³ Magnesium sulfate given intravenously may be of value in the management of a severe asthma attack, and giving the drug by aerosol or incorporating it in the diet may help stabilize brittle asthma. However, the true value of magnesium given as an aerosol preparation or in the diet has not been established, and therefore it is an alternative.²⁹

Local anesthetics, such as lidocaine or mexiletine, have been given by inhalation, with apparent benefit in asthma. Heparin, which may have anti-inflammatory properties, has also been reported to be of value when given topically into the lungs. Furosemide has for some

years been reported on favorably as an aerosol agent for asthma, but its clinical value and its mode of action are undetermined.

It is probable that at one time or another, almost every class of drug has been described as being of benefit in asthma, although the supporters of agents such as aspirin, phenytoin, hydroxyzine, calcium channel blockers, progesterone, and so on have failed to substantiate their claims. Similarly, many drugs over the years that appeared to be promising never got far beyond animal studies before falling into oblivion. However, some of these unusual drugs may still be used as alternative therapies in some countries. Antihistamines, including ketotifen, as a group have been disappointing in the treatment of asthma, despite their value in treating extrapulmonary allergies.

MARIJUANA

Preparations from the hemp plant, *Cannabis sativa*, which contains the psychoactive principle Δ^9 -tetrahydrocannabinol (Δ^9 -THC), produce a pleasant intoxicating effect. By the middle of the nineteenth century, marijuana was prescribed as a bronchodilator. Its medicinal value declined by the early twentieth century with the introduction of synthetic drugs.⁷² During the last two decades, potentially beneficial effects of smoked marijuana and oral and inhaled synthetic Δ^9 -THC in asthma have been investigated in human volunteers.

Two independent groups of investigators demonstrated a short-term bronchodilator response in healthy male volunteers to inhalation of the smoke of marijuana in concentrations of 1.0% to 2.6% Δ^9 -THC^{73,74} that was not seen after inhalation of placebo. The bronchodilator response to smoked marijuana was of greater magnitude than that observed after administration of a nebulized β -agonist. A dose-dependent bronchodilator response was also noted in healthy subjects to oral administration of 10 to 20 mg of synthetic Δ^9 -THC.⁷⁴ Subsequently, 2% smoked marijuana was observed to produce a similar magnitude of bronchodilation in 10 stable asthmatic subjects to that observed in normal subjects (approximately 50% peak improvement in specific airway conductance [sGaw]), with a duration of action of 2 hours.⁷⁵ However, the peak magnitude of bronchodilation produced by 15 mg of oral THC was slightly less in asthmatic than normal subjects (20% vs 30% increase in sGaw, respectively).^{74,75} Moreover, the magnitude of bronchodilation achieved with the oral formulation was modest (mean peak increase in sGaw of only ~20%-30%) compared with an approximately 50% mean peak increase noted with smoked marijuana, although the duration of bronchodilation was slightly longer after 15 mg of oral THC (2-4 hours) than that of 2% smoked marijuana (2 hours).^{74,75} In comparison with placebo, smoked marijuana (500 mg of 2% Δ^9 -THC) also caused prompt correction of the bronchospasm and associated hyperinflation provoked by methacholine and, on a separate occasion, by exercise in 8 subjects with clinically stable asthma and a history of exercise-induced asthma.⁷⁶

Δ^9 -THC-induced airway smooth muscle relaxation has not been found to be due to an adrenergic-mediated or muscarinic-antagonist effect⁷⁷ or to direct effects in isolated human bronchiolar smooth muscle.⁷⁸ Smoking marijuana is the simplest and most reliable method of administration,⁷⁹ but habitual inhalation of the toxic smoke components⁸⁰ has been shown to cause extensive airway injury and depressant effects on alveolar macrophage function in cannabis smokers.^{81,82} The oral route is not suitable because it is associated with variable and, at best, only modest bronchodilation, and unwanted psychotropic and cardiovascular effects. Therefore the possibility has been explored that inhalation of pure Δ^9 -THC as an aerosol might have therapeutic advantages.⁸³ A metered-dose inhaler (MDI) was specially formulated with Δ^9 -THC dissolved in 95% ethanol and chlorofluorocarbon as the propellant, generating 1 mg of Δ^9 -THC per actuation. Five to 20 actuations from this MDI produced bronchodilation in 11 healthy subjects of a magnitude less than that produced by smoked marijuana; moreover, cough and chest discomfort were noted in a few healthy subjects. In 2 of 5 stable asthmatic subjects, 5 to 10 mg of aerosolized Δ^9 -THC caused moderate-to-severe bronchoconstriction, along with cough and chest discomfort. The latter findings were presumably caused by a local irritant effect of THC on the airways, leading to reflex bronchospasm, which could have been related to the dose of Δ^9 -THC administered (equivalent to the amount of Δ^9 -THC in a 500-mg cigarette of 2% marijuana), the aerosol particle size, or both.⁸³

In contrast, Williams et al⁸⁴ noted significant bronchodilation without any occurrences of bronchospasm in 10 stable asthmatic subjects after administering a much smaller dose of THC aerosol from an MDI (50 μ g per actuation). No associated side effects were noted on mood, behavior, or the cardiovascular system. The onset of bronchodilation was delayed compared with that of albuterol (100 μ g), but the bronchodilator effect was comparable at 1 hour. In a subsequent study the same group demonstrated a dose-response effect of 50 to 200 μ g of THC in 5 asthmatic subjects, with achievement of a plateau of bronchodilation at 100 μ g.⁸⁵ No further investigations of the potentially therapeutic benefits of aerosolized THC in asthma have been published to date.

The possibility that some cannabinoids other than Δ^9 -THC might also exhibit bronchodilator effects has been investigated. Evaluation of Δ^8 -THC and cannabidiol failed to demonstrate any bronchodilation, except for a modest effect of Δ^8 -THC in a 75-mg dose that also produced unwanted side effects.⁸⁶ Similarly, no significant bronchodilation was observed with nabilone (2 mg), a synthetic 9-keto cannabinoid that is chemically related to THC.⁸⁷

The biologic effects of Δ^9 -THC are known to be mediated by two specific G protein-coupled receptors that are expressed on cells in the central nervous system (CB1 receptors) and on cells outside the central nervous system, including immune cells (CB2 receptors).⁸⁸ Mammalian tissue produces two families of endogenous cannabinoid ligands (anandamide and 2-arachidonyl

glycerol) that bind to these receptors, yielding biologic effects similar to those of plant-derived THC. Recent unpublished observations have disclosed CB1 receptors on postganglionic parasympathetic nerve endings in bronchial tissue (D. Piomelli, personal communication, 1999) that have been linked in other tissues (eg, guinea pig ileum) to inhibition of release of acetylcholine. These observations suggest that THC (and related CB1 agonists) may exert a local bronchodilator effect in the airway through stimulation of CB1 receptors on efferent vagal nerve endings, leading to a parasympatholytic effect. It is hoped that novel ligands of high affinity and selectivity for the cannabinoid receptors may ultimately prove to be useful antiasthma medications. Until such time, however, administration of THC in the smoked form should be discouraged because of the well-documented pulmonary toxicity of smoked marijuana, including its potential to cause head and neck and other respiratory cancers.^{89,90}

SURGICAL AND PHYSICAL PROCEDURES

Although surgeons can contribute to the management of asthma with sinus surgery and correction of swallowing or reflux disorders, many more surgical procedures have failed to remain in orthodox practice. Thus bilateral carotid body resection, an operation that could reduce the sensation of dyspnea, has fallen into disrepute because it often resulted in hypoventilation and hypoxemia. Vagal denervation procedures and operations to correct chest wall function or to reinforce collapsing airways have largely been relegated to history. A curious variant, organ vagotonia, which depended on readjusting vagal tone with pharmacologic and physical therapies, was popular in Japan but is no longer being recommended. Bronchoscopic lavage is rarely used; breathing exercises with postural drainage to help eliminate secretions are accepted alternatives, although their value has not been clearly established.

CONCLUSIONS

Numerous alternative therapies that have been used in asthma and allergies are being recommended by those who focus on the inherent disadvantages of current orthodox therapies. Furthermore, new variants, including herbs and nonscientific but impressive-sounding techniques, are being introduced through public media. Many patients are confused about the array of choices and the current options in alternative therapies that they can readily obtain without the advice of a physician. This new paradigm in therapy cannot be ignored, and the alternatives should always be discussed with patients. However, the availability of so many options that appear to work through the mechanism of the placebo response imposes on the medical profession the need to understand and incorporate placebo therapy in a scientific manner. The acceptance of the value of the therapeutic placebo also necessitates that physicians critically evaluate some of

their own accepted therapies, including second- and third-line prescription drugs and the use of diagnostic and therapeutic modalities, such as desensitization therapy. The final outcome for physicians and patients is the incorporation of a tailor-made regimen that matches the physiologic and psychologic needs of individual patients. The medical profession must serve as a resource of information and skills that can be incorporated in an integrative manner with the specific complementary regimen that resonates with the cultural and individualistic needs of each patient. Thus physicians should question each patient carefully about any alternative therapies that he or she may use, and an effort should be made to provide thoughtful advice about the potential value or possible harm of incorporating such modalities into an integrated therapeutic program on the basis of the orthodox management of asthma or allergies.

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