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Current perspectives

Complementary and alternative medicine for the allergist-immunologist: Where do I start?

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Complementary and alternative medicine (CAM) therapies present a growing information management challenge for physicians because nearly 40% of their patients may be using and another 50% may be considering use of CAM as part of their healthcare regimen. The National Health Statistics Reports for 2007 described the most commonly used nonvitamin, nonmineral therapy as natural products (eg, herbals at 17.7%). More than 5% of children under the age of 18 years used CAM for allergic conditions including asthma. The amount and quality of information available and concerns about liability risk represent a challenge for most physicians. This review focuses on considerations for approaching a CAM-related consultation, incorporating legal and logistic factors affecting how such an encounter should be approached. A 10-step process is presented that addresses different components of CAM consultations and what should be documented. Access to timely, high-quality information regarding product specific efficacy and safety data, as found in the Natural Medicines Comprehensive Database, is needed to support CAM consultation efficiently. Understanding of serious adverse events associated with CAM is limited; an international need exists for improved safety surveillance and information sharing. Allergy-immunology, as a specialty with expertise in adverse drug reaction evaluation and management, has a unique opportunity to support enhanced CAM-related adverse events evaluations, reporting, and research. (J Allergy Clin Immunol 2009;123:309-16.)

Key words: *Complementary and alternative medicine, integrative medicine, herbals, herbs, adverse reactions, risk communication, quality of care*

Abbreviations used
CAM: Complementary and alternative medicine
FDA: Food and Drug Administration
NCCAM: National Center for Complementary and Alternative Medicine
NIH: National Institutes of Health

COMPLEMENTARY AND ALTERNATIVE MEDICINE CHALLENGES FOR CLINICIANS

Health care workers trained in allopathic medicine frequently encounter patients who expect patient-centric holistic care with a potential to discuss complementary and alternative medicine (CAM) therapies. This discussion is not a topic that is included in any current medical competency training, and most health care workers have limited knowledge on the subject. Unfortunately, if there is a perceived reluctance or derogatory attitude from the provider, the patient may use CAM therapies without informing the health care team, potentially affecting the benefit and risk of traditional medicines. Ironically, as traditional/conventional medical practices are squeezed by reduced fees and insurance-related barriers to care delivery, the world of CAM therapists and therapies is enjoying an expanding market in which patients are willing to pay out of pocket.[1] In 2007, almost 4 of 10 adults had used CAM therapy in the past 12 months, with the most commonly used therapies (nonvitamin, nonmineral) including natural products (17.7%) and deep breathing exercises (12.7%).[2] Although mainstream physicians have confidence in the safety and efficacy of evidence-based medical practices, and managed care organizations cite such evidence in developing treatment pathways, patients seeking CAM treatment are often distrustful of these practices. The Institute of Medicine report on medical errors[3] shows that the safety of traditional medical practices can be questioned. Furthermore, a recent literature review of published managed care strategies designed to reduce cost and improve the quality of medication demonstrated an adverse outcome: patients with chronic illness had reduced access to essential medicines due to shift in the cost burden from the managed care organization to the patient.[4]

Taken together, these factors may contribute to an atmosphere in which patients may not fully discuss all therapeutic approaches taken with their allopathic healthcare providers. The unintended dilemma for the physician is a limited amount of time, energy, and resources to focus on conventional medicine and a distrust of CAM therapies in the face of limited knowledge and predominantly negative increased risk perceptions for unfamiliar CAM treatments. The unintended dilemma for the patient, who has rapid

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access to a bewildering array of unfiltered information via the Internet as well as vast promises of success through CAM (or natural) therapies, is a perception that traditional medicine is intimidating and unresponsive to holistic concerns, whereas CAM therapies and therapists are more approachable and/or trustworthy.

Given the time and cost constraints found in mainstream medicine, incorporating within the traditional medical encounter the 6 interactive components of the patient-centered clinical method (exploring both disease and the patients' illness experience, understanding the whole person, finding common ground, enhancing the patient-doctor relationship, being realistic, and incorporating prevention and health promotion) is frequently difficult.[5] Ultimately, patients and their caregivers/guardians are seeking to optimize their quality of life and well being as an outcome with a desire to exhaust all treatment options that might improve disease management. The search for "remembered wellness" (p 194) or what many perceive as the placebo effect is frequently the focus of a patient-centric encounter.[6] The measurable clinical and quality of life benefits from the placebo effect may represent at least a part of this "remembered wellness" outcome.

Allergy-immunology specialists are faced with the challenge of how to respond practically to the evolving information presented by the expanding world of CAM. The spectrum of positions on CAM within conventional medical practices ranges from "don't ask, don't tell" to establishing a partnership with the patient who may be seeking or is already using CAM therapies. A small percentage of practitioners are incorporating both conventional and nontraditional medical therapies, reflecting a movement toward integrative medicine. Many physicians and health care workers in general are interested in learning more about CAM but are overwhelmed by the amount of information and afraid of entering into any discussions with their patients because of a possible liability risk and/or time requirement. This review focuses on practical considerations for approaching a CAM-related consultation and incorporates updates on legal and logistic factors that affect how such an encounter could be managed and documented.

RESPONSE TO PATIENTS SEEKING INFORMATION ABOUT CAM THERAPIES

In 1997, Eisenberg[7] published his landmark article titled "Advising patients who seek alternative medical therapies." The passionate responses in subsequent comment letters illustrate the trepidation generated by Eisenberg's step-by-step proposed strategy whereby "conventionally trained medical providers and their patients can proactively discuss the use or avoidance" (p 61) of CAM therapies. Concerns about time and expertise required, resource diversion from proven therapies, and physicians' ethical right to not participate in unproven therapies were just some of the issues. Strategies for shared decision-making that focused on doing no harm and documenting legally defensible behavior on the part of the physician were detailed and reinforced in subsequent articles, including an Institute of Medicine report titled "Complementary and Alternative Medicine in the United States."[8-11] It is noteworthy that the Institute of Medicine report was strongly contested by some,[12] but for many clinicians seeking more information and a more intellectually open approach to the study of unconventional therapies (if indicated by positive outcomes), the report represented a needed catalyst for examining CAM therapies for useful and valuable therapeutic options.[13]

In the past 10 years, the presence of CAM therapies in different patient populations has increasingly affected a broad range of medical specialties. The 2002 National Health Information Survey, which was limited in the scope of CAM content, showed that 36% of adults used CAM (62% if prayer was included), with follow-up surveys demonstrating continued increases, particularly in the use of herbals.[1-2] At the same time, health care provider knowledge of CAM or awareness of CAM use by their patients remains deficient, and an evolving need for a CAM-focused education curriculum in medical schools and residencies is presented in the literature.[14-19] The fact that 50% of Americans would consider trying CAM therapy in addition to conventional therapies is a staggering statistic that makes the need for developing tools and resources to support clinicians in meeting this challenge ever more urgent. Avoidance and denial are no longer sustainable options for conventional practitioners.[1]

PROPOSED 10-STEP APPROACH TO PATIENT-PHYSICIAN PARTNERSHIPS IN EXPLORING THERAPEUTIC ALTERNATIVES

Although Eisenberg's work[7-9] has laid significant ground work for discussing CAM treatments with patients, controversy continues surrounding the evolving fiscal, ethical, and legal questions that may accompany such discussion. It has been argued that use of CAM treatments is analogous to the situation encountered when US Food and Drug Administration (FDA)–approved drugs are used for off-label indications. However, even when used for off-label indications, FDA-approved therapies have undergone quality control scrutiny and include a safety profile as required by the FDA licensure requirements. In the CAM arena, products such as herbal supplements may not have been manufactured with stringent quality controls, so content, amount, or contaminants present may be confounding variables that affect the outcome of a therapeutic trial.

There is a need for standardizing clinical guidelines to address complex medical management, particularly when the level of evidence for a wide range of therapeutic options is variable and multidisciplinary competencies are involved. Yet when patients ask that CAM approaches be included in medical management, there are limited efficacy and safety data available to providers, and most CAM interventions have not been reviewed by broad-based national expert panels, like the National Heart, Lung, and Blood Institute panel, which has developed the National Asthma Education and Prevention Program asthma care guidelines. The National Center for Complementary and Alternative Medicine (NCCAM) at the National Institute of Health (NIH) has supported the development of expanded educational resources and funded research to address the questions related to the efficacy and safety of specific CAM therapies that are necessary for informed clinical choices.[20]

Building on Eisenberg's[6] approach, this article's Table E1 in the Online Repository at www.jacionline.org presents a 10-step summary of the critical elements to be considered in developing a patient-provider partnership that includes CAM therapeutic options.[7,8] The key elements of physician-patient interactions that involve CAM questions and/or therapeutic impact include the following: (1) exploring factors driving interest in CAM; (2) documenting clinical reasons for seeking CAM options; (3) assessing current disease/health status and therapies to date; (4) documenting patient's preferences and reasons; (5) assessing and documenting adequacy of medical evaluation; (6) defining a plan for follow-up visits; (7) providing good risk communications

with option for additional consultative visits; (8) acknowledging evolving expectations and goals; (9) educating about new safety and/or efficacy issues related to CAM choices during each visit; and (10) addressing need for further consultations and how these consultations can be optimized (see Table E2 in this article's Online Repository at www.jacionline.org). Nonetheless, significant issues and controversies confront licensed conventional health care providers when considering inclusion (or exclusion) of elements of CAM therapy in medical decision-making. Physicians cannot be forced to adapt any practice with which they do not feel comfortable or they believe is harmful, futile, or too much of an unknown. Providing consultation on CAM therapies may be complex and time-consuming with an initial steep learning curve for both patient and physician. The growing questions about reimbursement for such services cannot be ignored or minimized and require clarification because physicians are stressed by the business of medicine.

TOOLS AND RESOURCES TO SUPPORT GATHERING UP-TO-DATE INFORMATION ON THE EFFICACY, SAFETY, AND DISEASE EXACERBATION RISKS OF A CAM THERAPY

Gathering reliable, unbiased, and comprehensive data about CAM therapies can be a challenge. In the early 1990s, when patient use of CAM therapies began to accelerate across North America, many clinicians sought data on these therapies to counsel patients better, but there simply was not an easy way to find information. In many cases, reliable information did not exist. It is noteworthy that the first *Physicians' Desk Reference* on herbal supplements did not appear until 1998.[21] Today, the landscape has changed, thanks to expanded research in the area of CAM and improved availability of new resources with rapid cycle information updating.

One trustworthy source of information on a wide variety of CAM treatments and interventions is the NCCAM of the NIH. The NCCAM began as the Office for Alternative Medicine with a Congressional funding allocation in 1991. Since that time, support for objective research of CAM interventions has grown, and in 1998, NCCAM was authorized in its current form by Congress. NCCAM oversees a robust research portfolio designed to identify promising CAM approaches and show safety and efficacy. In addition, the NCCAM maintains a large database on CAM treatments, and this is easily available to providers and patients through the NCCAM website (http://nccam.nih.gov/).

The Natural Medicines Comprehensive Database is another trustworthy resource for data on CAM treatments that was developed by the publishers of *Prescriber's Letter* and *Pharmacist's Letter* in the mid-1990s.[22] This database provides evidence-based information (using standardized approach to evidence quality/ranking[23]) on CAM that includes practical evidence-based reviews on nearly 1100 natural ingredients (representing many thousands of different generic names, depending on the culture in which it is used) as well as supplements and more than 30,000 commercially available brand name products. It cites more than 16,000 references and includes reviews of more than 2000 new scientific articles for potential inclusion every year. This database includes evidence-based information on traditional Chinese medicine, Kampo medicine, Ayurvedic medicine, and several alternative treatment modalities such as acupuncture, reflexology, and many others. The database also provides an evidence-based rating on commercially available CAM products based entirely on the evidence for safety and effectiveness for product ingredients plus evidence for product quality using data from international regulatory bodies.

Research for the Natural Medicines Comprehensive Database is critically assessed on the basis of key factors such as randomization, allocation concealment, adequate blind, and other factors using the principles from the Cochrane Collaboration[24] and is regularly maintained and updated. Research results are selected that have the potential to provide relevant information related to safety, effectiveness, and clinical use, mechanism of action or pharmacology, interactions with drugs, laboratory test interference, or other practice information that is relevant to health professionals. After the initial search and review of the literature, new research findings are identified through systematic searching of literature for updated data on specific CAM approaches. Examples of information regarding CAM approaches for allergic diseases, interactions of CAM treatments with FDA-approved drugs, and CAM treatments that exacerbate allergic disease are shown in Tables I to III. A more complete description of this database can be found at http://www.naturaldatabase.com.

EMPOWERING THE PATIENT TO PARTNER IN THE SEARCH FOR RELIABLE INFORMATION, ENABLING THE CLINICIAN TO PRACTICE GOOD MEDICINE SAFELY: LEGAL IMPLICATIONS AND ETHICS

There is concern about the potential legal liability of physicians and other licensed providers when they choose to provide consultation about or direct care with CAM treatments (either individually or through an integrative medicine clinic environment) or refer their patients to nonphysician CAM providers. Much of this discussion ignores the increasing focus on patient-directed care and choice empowerment, positioning the provider as a consultant, not as the person in charge. The ethical conundrum comes when perceived legal liability drives a physician to refuse care, only further enhancing the well documented and higher risk behavior of don't ask, don't tell. What are the potential liability risks when the physician does not want to abandon the patient but wants to minimize risk for the practice? Liability is the legal responsibility for one's acts or omissions, and there are 2 primary areas of liability concern for physicians who choose to incorporate CAM into their practices or refer patients to CAM providers.

The first is in the realm of health care licensure, which determines who can be licensed. The extent of the scope of practice varies among the jurisdictions and is a matter of state law. Generally, the scope of practice for physicians in the United States is unlimited, meaning that they can generally use all methods that their profession accepts as safe and effective to treat a given disease.[25] Because the practice of medicine is licensed and regulated at the state level, individual physicians are accountable to their respective state medical boards for the quality of care they deliver. If physicians choose to incorporate nontraditional methods in their practices and provide patients with CAM therapies that are unsafe and ineffective, they may face allegations of unprofessional conduct or may be disciplined by their respective state medical boards should these physicians depart from the standard of care (may be defined as any departure from acceptable and prevailing medical practice) in that particular jurisdiction.[26,27] CAM, under some definitions, is considered a departure from conventional norms of practice.[28] Unlike the standard of care applied by courts in medical malpractice cases, medical board disciplinary cases do

TABLE I. Selected natural medicines used for atopic conditions

Natural medicine	Use/indication	Effectiveness rating	Practice pearl
Bifidobacteria	Eczema	Possibly Effective	Some evidence in infants only.
Bitter orange	Asthma/allergic rhinitis	Insufficient Evidence to Rate	Bitter orange contains a stimulant similar to ephedra; linked to several reports of severe adverse events including myocardial infarction.
Butterbur	Allergic rhinitis	Possibly Effective	Some evidence that a specific butterbur extract is comparable to Zyrtec (cetirizine; McNeil-PPC, Raritan, NJ) and Allegra (fexofenadine; Sanofi-Aventis, Bridgewater, NJ); a specific extract (Ze 339) standardized to 8 mg total petasine has been used.
Choline	Asthma	Possibly Effective	
Fish oil	Asthma	Possibly Effective	Benefits seen in children but not adults.
Honey	Allergic rhinitis	Insufficient Evidence to Rate; preliminary evidence suggests that honey does not improve symptoms	
Lactobacillus	Eczema/atopic disease	Possibly Effective	Specific product used in clinical trials – *Lactobacillus* GG (Culturelle, Amerifit Brands, Cromwoll, Conn)
Magnesium	Asthma	Possibly Effective	Intravenous magnesium beneficial for acute attacks; by mouth magnesium supplements do not improve chronic asthma.
Phleum pratense	Allergic rhinitis	Possibly Effective	A specific standardized product (Grazax, ALK-Abelló, Denmark) has been used.
Pycnogenol	Asthma	Possibly Effective	Benefits seen in children.
Quercetin	Asthma/allergic rhinitis	Insufficient Evidence to Rate	Thought to work similarly to cromolyn; however, no clinical data to support use.
Serrapeptase	Bronchitis, sinusitis	Insufficient Evidence to Rate; preliminary evidence suggests some benefit	
Sinupret (Bionorica, San Clemente, Calif)	Sinusitis	Possibly Effective	This is a brand name product containing 5 herbal ingredients.
Stinging nettle	Allergic rhinitis	Insufficient Evidence to Rate; preliminary evidence suggests some benefit.	If used, stinging nettle should be started at the first sign of symptoms.
Tinospora cordifolia	Allergic rhinitis	Possibly Effective	A specific extract (Tinofend, Verdure Sciences, Noblesville, Ind) has been used.
Vitamin C/citrus fruits	Asthma	Insufficient Evidence to Rate; preliminary evidence that eating vitamin C–rich fruits 1-2 times/wk improves lung function; some conflicting data; preliminary evidence that vitamin C supplements might decrease exercise-induced asthma	Grapefruit, kiwi fruit, orange, and other fruits.
Whey protein	Atopic disease	Possibly Effective	Some evidence in infants only.

From Jellin J, Gregory P, editors. Natural medicines comprehensive database. Stockton (CA): Therapeutic Research Faculty; 2008. Available at: http://www.naturaldatabase.com.[22] Accessed January 1, 2009. Not a complete list. For additional data, go to http://www.naturaldatabase.com.

not have to establish that the medical care under review caused any injury to the patient.[26] Therefore, physicians can be subject to license revocation even if there is no injury to the patient. Even though disciplinary action for failure to meet the standard of care is possible, most charges against physicians who practice CAM tend to be related to "failure to perform adequate patient evaluations, testing, monitoring, and record-keeping," and generally such failures are actions under the physician's control[26] (p 71).

To avoid charges of unprofessional conduct from their state medical licensing boards, physicians must continue to monitor patients conventionally and perform adequate evaluations, order necessary tests, and document encounters carefully in the medical record. Physicians are advised to follow the Federation of State Medical Boards "guidelines for the use of complementary and alternative therapies in medical practice."[27,29]

A second area of potential liability concern is the potential risk of allegations of medical malpractice if the CAM treatment provided to a patient falls below the standard of care and injures the patient.[27,30] Medical malpractice is governed by the law of torts. A tort is any wrongful act that one person commits against another, and a negligent tort is defined as a failure to exercise reasonable care under the circumstances.[31] Medical malpractice based in negligence provides that liability likely exists when a given therapy falls below the standard of care and subsequently injures the patient.[30]

Ultimately the standard of care will be determined by expert witness testimony in a court of law and is the same for all physicians regardless of whether they use conventional or CAM therapy.[26,28,30] The standard of care is determined by whether a particular treatment deviated from accepted medical practice in

TABLE II. Potential interactions between selected natural medicines used for atopic conditions and conventional medicines

Natural medicine	Interactions	Mechanism	Interaction rating
Bitter orange	QT-interval–prolonging drugs Stimulant drugs	Bitter orange contains a stimulant called synephrine. Combining bitter orange with drugs that prolong QT-interval might increase the risk of arrhythmia; combining with other stimulants can result in additive stimulant activity.	Moderate; be cautious with this combination.
Fish oil	Antiplatelet/anticoagulant drugs Orlistat (Xenical, Roche, Nutley, NJ; Alli, GlaxoSmithKline, London, United Kingdom)	High-dose fish oils (>3 g/day) can modestly inhibit platelet aggregation and might increase the risk of bleeding; however, there are conflicting data. Orlistat might decrease the absorption of fish oils when they are taken together.	Moderate; be cautious with this combination.
Grape extract	Cytochrome P450 1A2 substrations (eg, Plavix, Bristol-Myers Squibb, New York, NY; Valium, Roche; Zyprexa, Eli Lilly and Co, Indianapolis, Ind; warfarin, many others)	Grape juice induces cytochrome P450 1A2 drug metabolism and might decrease levels of substrates of this enzyme; although grape juice might interact with these medications, it is not known whether grape extract has the same effect.	Moderate; be cautious with this combination.
Stinging nettle	Diabetes drugs Hypertension drugs Warfarin (Coumadin)	Stinging nettle might lower blood glucose levels and could have additive effects when combined with diabetes drugs. Stinging nettle might lower blood pressure and could have additive effects when combined with blood pressure drugs. Stinging nettle contains vitamin K and therefore might decrease the anticoagulant effects of warfarin.	Moderate; be cautious with this combination.

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the community.[26] Because efficacy and safety data about CAM therapies are often limited, the standard of care for CAM is not as well defined as for conventional medicine.[30] Courts may, therefore, view a nonstandard CAM therapy as equivalent to substandard therapy or care.[28] To avoid allegations of medical malpractice, physicians who wish to incorporate CAM therapies into their practice must be familiar with the efficacy and safety data relevant to the CAM therapy and must assure that it has been addressed with the patient and a benefit-risk assessment for the recommended use well documented.[33]

Information about the safety and efficacy of a specific CAM therapy can be classified into 4 categories of relative potential liability risks:[30]

1. Evidence supports both safety and efficacy of the CAM therapy
2. Evidence supports safety of the CAM therapy, but evidence regarding efficacy of the CAM therapy is inconclusive
3. Evidence supports efficacy of the CAM therapy, but evidence regarding safety of the CAM therapy is inconclusive
4. Evidence indicates either serious risk or inefficacy of the CAM therapy

If a CAM treatment falls into category 1, liability risk is minimized and probably comparable to the use of any other conventional therapy. If a treatment falls within category 4, liability risk is high, and defense of use would be difficult when responding to a negligence allegation. However, most CAM therapies fall into categories 2 and 3, with the issue of safety more important than efficacy.[27] Evidence regarding any specific CAM therapy safety and efficacy may change with evolving research, so it is important to recognize that the risk category of a CAM therapy may change over time.

To minimize the potential for medical malpractice liability, physicians who choose to use CAM therapies should consider incorporating the following strategies within the treatment regimen:[26,27,30]

1. Determine and document the clinical risk level by reviewing existing medical literature to assess the evidence for safety and efficacy of a given CAM therapy
2. Provide adequate informed consent by engaging in a clear discussion of the risks and benefits of using the CAM therapy and document informed consent process
3. Continue to monitor the patient during conventional and CAM therapies
4. If a CAM therapist is involved, advise the patient to seek objective information about the provider and report adverse events

There is potential medical malpractice liability when a conventional provider refers their patient to a nonphysician CAM provider and/or functions in a team approach with implied supervisory responsibility or integrated medical practice. Generally, courts have been reluctant to impose liability for a referral to another provider, but there exist notable exceptions.[32] Vicarious

TABLE III. Selected natural medicines that can cause or exacerbate atopic conditions

Natural medicine	Comment
Anise	Inhaled anise can cause rhinoconjunctivitis and asthma in some patients.
Butterbur	Some patients can experience pruritus, itchy eyes, and asthma after oral ingestion of butterbur.
Camphor	Some patients can experience contact eczema after topical application.
Chlorella	Some patients can experience allergic reactions including asthma and anaphylaxis.
Chondroitin	One case report linking chondroitin plus glucosamine to exacerbation of asthma.
Chymotrypsin	Rare anaphylactic reactions have occurred including dyspnea, urticaria, edema, and others.
Cranberry	Cranberry contains a significant amount of salicylic acid; theoretically, large amounts of cranberry could trigger a reaction in patients with asthma.
Echinacea	Allergic reactions to *Echinacea* are more likely in patients with atopy.
Garlic	Allergic reactions associated with garlic include rhinitis, conjunctivitis, urticaria, anaphylaxis, and angioedema.
German chamomile	Topical application can cause allergic dermatitis and eczema in some patients.
Glucosamine	One case report linking glucosamine plus chondroitin to exacerbation of asthma.
Gotu kola	Some patients can experience eczema when gotu kola is applied topically.
Green tea	Some patients can experience allergic reactions including cough, dyspnea, and asthma.
Milk thistle	Some patients can experience allergic reactions including pruritus, urticaria, eczema, and anaphylaxis.
Pomegranate	Topical application can cause contact hypersensitivity in some patients resulting in urticaria, angioedema, rhinorrhea, itchy eyes, and dyspnea.
Propolis	Propolis allergens can worsen asthma symptoms.
Royal jelly	Royal jelly causes a high rate of allergic reactions in patients with asthma or atopy. Royal jelly can also worsen symptoms of dermatitis.
Saffron	Rhinoconjunctivitis and asthma has occurred in patients taking saffron.
Schisandra	Some patients have experienced allergic skin rashes and urticaria.
Senna	Some patients taking senna can experience asthma and allergy symptoms.
Sweet cherry	Sweet cherry can cause allergic reactions in sensitive patients such as mucosal irritation, urticaria, angioedema, dyspnea, cough, and gastrointestinal symptoms.
Tea tree oil	Topical application can cause contact eczema in some patients.
Willow bark	Willow bark contains a significant amount of salicylic acid; theoretically, willow bark could trigger a reaction in patients with asthma.

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liability risk may exist if 1 or more of the following conditions are met:

1. The referral can be considered negligent because of delay of diagnosis or accepted treatment[32]
2. The CAM provider is known to be incompetent and/or the therapy is ineffective[26]
3. The physician has exercised supervisory responsibility or was involved in jointly treating the patient with a provider known to be incompetent or who has been officially disciplined for unsafe practices[26,27,30,32]

Malpractice cases relating to CAM are less frequent than for conventional medical therapy.[26,32] Should an allegation of medical malpractice be asserted, physicians have 2 major arguments to raise in their defense. The first defense is the 2 schools of thought or respectable minority defense, and takes the position that physicians may choose between alternative approaches to diagnosis and treatment, "so long as a respectable minority in the medical community accepts the alternative approach"[28] (p 192). The definition of *respectable minority* varies among courts and jurisdictions.[26,28] Competent legal advice should be sought within the physician's state of practice for clarification. The second defense is the assumption of risk argument. This defense asserts that the patient assumes the risk of a particular treatment and has chosen to relieve the physician of any associated liability.[28] Although this argument does not completely eliminate liability for the physician, it can help to decrease malpractice exposure. The assumption of risk defense varies widely by jurisdiction, with some allowing it as a complete defense and others severely limiting it.[27,28] The unanswered ethical question is, by what right can a provider deny care to patients who execute their right to choose CAM therapy or therapists despite negative recommendations? In some cases, competent legal advice should be sought within the physician's state of practice for clarification, and a medical ethics consultation may be also be considered.

To address concerns related to CAM practices, many state legislatures have enacted medical freedom acts to assuage concerns of physicians who choose to practice CAM. However, such acts vary by state and are a patchwork quilt that does not adequately change the underlying, parochial nature of medical practice in the United States. Lasting reform that will serve the interests of all stakeholders is required. These reforms must emerge from within the context of the new, integrative health care environment in which physicians and CAM providers are free to practice from within their respective philosophical systems. By fostering interaction, cross-disciplinary research, and collaborative care, redefined standards of care will emerge that are scientifically based and interdisciplinary in nature. The outgrowth of such a paradigm shift will change the legal environment from one of fear to freedom.

In most discussions about the liability risk of CAM therapies and therapists, there is a remarkable void regarding the fact that everything advertised on the Internet, on television, in magazines and newspapers, and in the corner grocery store recommends consulting with your physician. If the physician or provider is committed to the patient and respects the concepts behind patient-centered care, how can we continue to

recommend caution and avoidance, ignoring the need to engage on CAM therapy questions coming from patients and their caregivers?[33] Perhaps it is time and reasonable to embrace the following concept:[34]

> Although all discussions need not end in agreement, they are still opportunities for shared decision making and relationship-centered care. Ultimately, we should not be concerned with practicing what is perceived to be traditional versus alternative and complementary medicine or biomedicine versus naturalistic medicine but only what is truly good medicine.[34]

As in all areas of medicine, competency training is critical to support high-quality practices. The need for a CAM-relevant curriculum has become a topic in the literature, with a 2007 publication describing a needs assessment survey in relation to family practice residents.[35] The majority of respondents rarely ask patients about CAM use, with 92% rating their awareness of CAM resources as poor or fair in all categories.

IS IT TIME TO CONSIDER EVIDENCE-BASED SAFE AND EFFECTIVE HERBAL THERAPIES?

The expanding effort to define how and when to incorporate CAM into patient care has been heavily criticized with a focus on the existence and funding of the NCCAM at the NIH.[36,37] Claims that nothing has come from this NIH effort are difficult to understand in the face of the growing challenges to physicians and health care workers with the reality of patient use (whether the medical establishment approves or not) that will not be contained by simply ignoring the need. Valuable advances and resources have been generated from the efforts of the past 10 years. From traditional Chinese medicine herbal combinations that may finally provide us a treatment for refractory peanut allergy and asthma[38] to the common cold,[39] the healing arts are on an exciting threshold of advances that many hope will improve the quality of the care delivered and help to improve care greatly for those patients who are currently therapeutic orphans.

Remedies for the common cold represent a $17 billion dollar industry, with Americans spending $2.9 billion annually on over-the-counter cold preparations and an estimated $1.1 billion in unnecessary antibiotics.[40] The common cold represents the third most common diagnosis in physicians' offices according to the 2005 National Ambulatory Medicine Care Survey.[41] There is no well established therapy that has been defined to reduce morbidity and duration of these viral infections significantly, and approximately 200 million days of work are lost annually.[42] The herbal remedy known as *Pelargonium sidoides*, also known as the South African geranium, available through herbal vendors for years in health food stores and over the Internet, is associated with a growing body of evidence supporting its efficacy for the treatment of the common cold and bronchitis.[43,44] It has a biologically plausible mechanism through induction of the IFN system and upregulation of cytokines important in protecting host cells from viral infection. The *Journal of Family Practice* in its popular Priority Updates from the Research Literature section recommends offering patients "*Pelargonium sidoides* (30 drops 3 times a day) to reduce the severity and duration of common cold symptoms and to get patients back to work sooner." The article even provides a brand name considered reliable in content, Umcka Coldcare, Nature's Way, Springville, Utah. Although more research is certainly needed to clarify the role of this supplement as a potential antibiotic-sparing drug, there is also a need to define and document the range of side effects and even more serious rare adverse reactions that may become more evident as use increases. As the product is being licensed in more countries besides Germany with potentially many millions of users in Europe and through over-the-counter use in the United States, the article by De Boer et al[45] in *Drug Safety* identifies potential safety concerns based on 34 adverse reaction reports including 12 cases of severe, potentially life-threatening anaphylaxis. Although proof of causality is not established for each of these cases, the report describes a signal that merits further study and validation as a potentially increased risk within an expanded population. It is interesting to speculate what role the increasing use of herbal supplements might have in the increasing incidence of anaphylaxis.[46-49]

CONCLUSION

Complementary and alternative medicine therapy is a growing part of medical interventions available to and used by the public. It is unlikely that this reality will change in the future. There is a need to incorporate substantive but balanced education about these therapies into continuing education programs as well as initial medical training in medical schools and residency programs. Allergy-immunology as a specialty with expertise in adverse drug reaction diagnosis and management has a unique opportunity to expand its scope of practice and relevance by supporting enhanced CAM-related clinical adverse events evaluations, reporting, and research.

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TABLE E1. Ten-step approach to physician-patient partnerships in exploring therapeutic alternatives

Step no.	Elements of physician-patient interaction	Actions and/or special consideration
1	Explore factors driving interest in CAM therapy/therapist Document instigating factors: current use, intent for future use, considering future use and seeking information, desire to access alternative provider Reasons: desire for greater efficacy, safety, and/or acceptability	Options to engage or not Support request but indicate limitations of that support, payment issues, time limits Refer to another provider for in-depth consultation (may be difficult to find)*
2	Document clinical reasons for seeking CAM options Exhausted conventional medicine with unsatisfactory outcomes Disease with bad prognosis or disability impact Fear of conventional therapies	Physician-patient perceptions shared Clinical status, options, and understanding Need for enhanced care/diagnostics Need for other therapeutic options
3	Assess current disease/health status and therapies to date Symptom diary, validated quality of life survey tools Objective measure of disease (blood pressure, peak flow meter) Duration of treatment trial	Educates patient about issues Disease evaluation, treatment options/risks Acceptance or refusal of partnership (may refer elsewhere, if possible)
4	Document patient's preferences and reasons Reason for CAM therapy choice (if defined by patient) Attitude toward CAM and conventional medicine Level of trust in exploring all therapeutic options	Caveats that influence patient's comfort with discussion/disclosure Neutrality of questions asked Atmosphere: caring/supportive
5	Assess adequacy of medical evaluation (document) Need for additional testing and/or consultation Explain all options to optimize diagnosis/treatment Quality-of-life impact of medical concerns	Provider options or recommendations Discuss overall risks and benefits of using treatments for which data are limited Opportunity for questions, dialogue
6	Define plan for follow-up visits† Agreement between provider and patient regarding therapeutic partnership: yes or no (with referral rather than refusal of care) Consider providing a fact sheet that includes reliable information and/or other resources about CAM therapy‡ Provider may opt out of further involvement if available "evidence indicates serious risk or inefficacy" Risk: patient will agree but potentially use anyway	May require out-of-pocket costs for patient Time for visit may not be covered by existing health insurance plan Future visits required with nonreimbursed payment rates (per-hour rate) Patient choice may result in provider suggesting move to a new provider Challenge: avoiding patient abandonment
7	Provide good risk communication, additional visit options Define, respectfully and clearly, what physician can do about request Determine whether insurance will cover the therapy or time for consultation on CAM therapy Define provider's perception of liability risk concerns	Perspectives: communication optimized if Honest and caring about patient issues Explains limitations: time (separate visits), cost-time for information, risks for provider Provides alternatives for how to proceed
8	Acknowledge evolving expectations (each visit) Shared goals for disease and/or symptom control Detail shared responsibility to gather more information Establish provider's ability to support request or validate the safety and efficacy of the CAM therapy of interest Clarify the roles of therapy team involved in care management	Consider Level of patient's suffering and/or fear Psychological factors: eg, depression Patient need for validation, trust Disclaimers that need to be documented Ethical considerations in care plan
9	Educate about new safety and/or efficacy issues Monitor patient and literature concerning specific CAM therapy trial Define guidelines for stopping trial, ethical concerns about supporting continuation of treatment: consider ethics committee consultation for complex benefit-risk analyses if controversial Document patient preferences and understanding of issues	Safety and efficacy: levels of evidence Communicate balanced clinical considerations: nothing is risk-free; there are defined/undefined risks Explain levels of evidence definitions: benefit-risk ratio vs alternatives?

(*Continued*)

TABLE E1. (*Continued*)

Step no.	Elements of physician-patient interaction	Actions and/or special consideration
10	Further consultations: critical elements to consider	Additional information and consideration
	Discuss factors in choosing a CAM-qualified provider	Resources available to assess providers*‡
	Address questions of suitability, licensure, competencies*‡	State certification requirements for CAM therapists (eg, acupuncture), other resources
	Document how provider or practice was identified by patient	
	Educate patient about questions for CAM therapy consultation§	Checklist for patient use during CAM visit§
	Support of patient seeking input for an informed choice	Action items to recommend to patient before starting unconventional treatment
	Empower patient to critically assess treatment trial	
	Referring provider responsibilities	Education to empower patient choice‖
	Document permission to release medical information	Establish ground rules for appointments: level of continued physician engagement
	Provide disclaimer regarding conflict of interest	
	Focus on patient choice tempered by benefit-risk considerations and the concept of "do no harm"	MedWatch for reporting adverse events to drugs/devices, use for CAM reports (http://www.fda.gov/medwatch/)
	Report adverse events, unethical and/or untested practices	

Adapted and updated from Eisenberg DM. Advising patients who seek alternative medical therapies. Ann Intern Med 1997;127:61-9. Comment in: Ann Intern Med 1998;128:328; author reply 329-30. Ann Intern Med 1998;128:328; author reply 329-30. Ann Intern Med 1998;128:329; author reply 329-30. Ann Intern Med 1998;128:329; author reply 329-30.

*Referral to another provider: What are considerations of such a referral?

Questions to consider: Is this a compassionate trial based on balanced review of all therapies available? Can a patient request for a compassionate trial (even in the absence of efficacy evidence) be supported by physician/provider?

Support access of patient to information regarding validity, suitability and/or licensure of alternative providers: published literature, clinical trial in progress, state licensure process available for practitioner type of interest, unbiased sources of information such as NIH/NCCAM (http://nccam.nih.gov/), consumer reports, and so forth.

Educate about conflict of interest considerations: internet search for user experiences, lawsuits, reports of unethical practices with caution about biased testimonials and limitations of single user experiences, conflicts of interest.

Traditional Medicine Provider: Federation of State Medical Boards, PO Box 619850, Dallas, TX 619850; phone 817-868-4000; fax: 817-868-4099; http://www.FSMB.org.

State certification requirements available for CAM therapists of interest (eg, acupuncture: http://www.acupuncture.com/statelaws/statelaw.htm).

†Physician/provider education focus

Establish ground rules for appointments: eg, how many pages of information can the patient bring in for review?

Empower patient to seek more information regarding safety and efficacy of therapies.

Define limits of provider responsibility in the therapeutic trial with therapies outside of conventional practice: ie, buyer beware.

MedWatch for reporting adverse events to drugs/devices, use for CAM reports? http://www.fda.gov/medwatch/.

‡Strategies to identify reliable, impartial information and data relevant to safety/efficacy of therapy or providers

Natural Medicines Comprehensive Database consumer information sheets on individual herbs or supplements.

Information resources that represent unconflicted independent reviewers (eg, *Consumer Reports*, Cochrane Database Reports).

Guidelines for use of CAM in medical practice at http://www.fsmb.org/pdf/2002_grpol_Complementary_Alternative_Therapies.pdf. Accessed December 1, 2008.

§Questions patients should ask their CAM therapy practitioners

Is the provider's belief in the effectiveness of the therapy (for example, acupuncture) based on clinical experience with similar patients? How many patients have received the treatment, and what was their outcome (the good and bad)?

What will the therapy consist of? What is the recommended frequency and duration of therapy? What are the known side effects and serious adverse events?

What is the cost of evaluation and therapy trials? Is third-party reimbursement available?

What criteria will be used and when to assess therapy benefit or failure? How many patients have received treatment and how many got better, worse, or had no change? Beware of 100% or 0% because these statistics are never true and raise suspicion.

Are there written instructions about the treatments and how success or failure will be defined by the CAM therapist?

Is the provider willing to communicate diagnostic findings, therapeutic plans, and follow-up with the patient's primary care provider and/or specialist? Are there any limitations to this communication? Who actually administers the therapy?

‖Action items to recommend to patient before starting unconventional treatments

Talk to other patients who have been treated and search the Internet for experiences related to this provider by other patients.

Ask for written instructions about the treatments and how success or failure will be defined by CAM therapist.

Search for specifics about side effects using such resources as the Natural Medicines Comprehensive Database and the published medical literature via PubMed.

TABLE E2. Criteria for Natural Medicines Comprehensive Database evidence-based safety ratings and effectiveness ratings

Evidence-based criteria for safety ratings
Likely Safe: Product has a very high level of reliable clinical evidence showing its safe use when used appropriately. Products rated likely safe are generally considered appropriate to recommend. To achieve this safety rating, a product is supported by all of the following:
Safety data are available from multiple (2+) randomized clinical trials or meta-analysis or large-scale postmarketing surveillance including several hundred patients (level of evidence = A), or the product has undergone a safety review consistent with or equivalent to passing a review by the FDA, Health Canada, or a similarly rigorous approval process.
Studies have a low risk of bias and a high level of validity by meeting stringent assessment criteria (quality rating = A).
Studies adequately measure and report safety and adverse outcomes data and consistently show no significant serious adverse effects without valid evidence to the contrary.
Possibly Safe: Product has some clinical evidence showing its safe use when used appropriately; however, the evidence is limited by quantity, quality, or contradictory findings. Products rated possibly safe appear to be safe, but do not have enough high-quality evidence to recommend for most people. To achieve this safety rating, a product is supported by all of the following:
Safety data are available from 1e or more randomized clinical trials, meta-analysis (level of evidence = A or B), case series, 2 or more population based or epidemiologic studies (level of evidence = B), or limited postmarketing surveillance data.
Studies have a low to moderate risk of bias and moderate to high level of validity by meeting or partially meeting assessment criteria (quality rating A or B). Studies adequately measure and report safety and adverse outcomes data and show no significant serious adverse effects without substantial evidence to the contrary. Some contrary evidence may exist; however, valid evidence supporting safety outweighs contrary evidence.
Possibly Unsafe: Product has some clinical evidence showing safety concerns or significant adverse outcomes; however, the evidence is limited by quantity, quality, or contradictory findings. People should be advised not to take products with a possibly unsafe rating. To achieve this safety rating, a product is supported by all of the following:
Safety data are available from 1 or more randomized clinical trials, meta-analysis (level of evidence = A or B), 2 or more population-based or epidemiologic studies (level of evidence = B), or limited postmarketing surveillance data. Or multiple, reliable case reports show a potential causal relationship between a product and serious adverse outcome.
Studies have a low to moderate risk of bias and moderate to high level of validity by meeting or partially meeting assessment criteria (quality rating A or B).
Studies adequately measure and report safety and adverse outcomes data and show significant serious adverse effects without substantial evidence to the contrary. Some contrary evidence may exist; however, valid evidence supporting potential safety concerns outweighs contrary evidence.
Likely Unsafe: Product has a very high level of reliable clinical evidence showing safety concerns or significant adverse outcomes. People should be discouraged from taking products with a likely unsafe rating. To achieve this safety rating, a product is supported by all of the following:
Safety data are available from multiple (2+) randomized clinical trials, meta-analysis, or large-scale postmarketing surveillance including several hundred patients to several thousand patients (level of evidence = A).
Studies have a low risk of bias and high level of validity by meeting stringent assessment criteria (quality rating = A).
Studies adequately measure and report safety and adverse outcomes data and consistently show significant serious adverse effects without valid evidence to the contrary.
Unsafe: This product has a very high level of reliable clinical evidence showing safety concerns or significant adverse outcomes. People should be discouraged from taking products with an unsafe rating. To achieve this safety rating, a product is supported by all of the following:
Safety data are available from multiple (2+) randomized clinical trials, meta-analysis, or large-scale postmarketing surveillance including several hundred to several thousand patients (level of evidence = A).
Studies have a low risk of bias and high level of validity by meeting stringent assessment criteria (quality rating = A).
Studies adequately measure and report safety and adverse outcomes data and consistently show significant serious adverse effects without valid evidence to the contrary.
Evidence-based criteria for efficacy ratings
Effective: This product has a very high level of reliable clinical evidence supporting its use for a specific indication. Products rated effective are generally considered appropriate to recommend. To achieve this effectiveness rating, a product is supported by all of the following:
Evidence consistent with or equivalent to passing a review by the FDA, Health Canada, or similarly rigorous approval process.
Evidence from multiple (2+) randomized clinical trials or meta-analysis including several hundred to several thousand patients (level of evidence = A).
Studies have a low risk of bias and high level of validity by meeting stringent assessment criteria (quality rating = A).
Evidence consistently shows positive outcomes for a given indication without valid evidence to the contrary.
Likely Effective: This product has a very high level of reliable clinical evidence supporting its use for a specific indication. Products rated likely effective are generally considered appropriate to recommend. To achieve this effectiveness rating, a product is supported by all of the following:
Evidence from multiple (2+) randomized clinical trials or meta-analysis including several hundred patients (level of evidence = A).
Studies have a low risk of bias and high level of validity by meeting stringent assessment criteria (quality rating = A).
Evidence consistently shows positive outcomes for a given indication without significant valid evidence to the contrary.
Possibly Effective: This product has some clinical evidence supporting its use for a specific indication; however, the evidence is limited by quantity, quality, or contradictory findings. Products rated possibly effective might be beneficial, but do not have enough high-quality evidence to recommend for most people. To achieve this effectiveness rating, a product is supported by all of the following:
One or more randomized clinical trials or meta-analysis (level of evidence = A or B) or 2 or more population based or epidemiologic studies (level of evidence = B).
Studies have a low to moderate risk of bias and moderate to high level of validity by meeting or partially meeting assessment criteria (quality rating A or B).
Evidence shows positive outcomes for a given indication without substantial valid evidence to the contrary. Some contrary evidence may exist; however, valid positive evidence outweighs contrary evidence.

(*Continued*)

TABLE E2. (*continued*)

Evidence-based criteria for efficacy ratings
Possibly Ineffective: This product has some clinical evidence showing ineffectiveness for a specific indication; however, the evidence is limited by quantity, quality, or contradictory findings. People should be advised not to take products with a possibly ineffective rating. To achieve this effectiveness rating, a product is supported by all of the following:
One or more randomized clinical trials or meta-analysis (level of evidence = A or B) or 2 or more population-based or epidemiologic studies (level of evidence = B).
Studies have a low to moderate risk of bias and moderate to high level of validity by meeting or partially meeting assessment criteria (quality rating A or B).
Evidence shows negative outcomes for a given indication without substantial valid evidence to the contrary. Some contrary evidence may exist; however, valid positive evidence outweighs contrary evidence.
Likely ineffective: This product has a very high level of reliable clinical evidence showing ineffectiveness for its use for a specific indication. People should be discouraged from taking products with a likely ineffective rating. To achieve this effectiveness rating, a product is supported by all of the following:
Evidence from multiple (2+) randomized clinical trials or meta-analysis including several hundred patients (level of evidence = A).
Studies have a low risk of bias and high level of validity by meeting stringent assessment criteria (quality rating = A).
Evidence consistently shows negative outcomes for a given indication without significant valid evidence to the contrary.
Ineffective: This product has a very high level of reliable clinical evidence showing ineffectiveness for its use for a specific indication. People should be discouraged from taking products with an ineffective rating. To achieve this effectiveness rating, a product is supported by all of the following:
Evidence from multiple (2+) randomized clinical trials or meta-analysis including several hundred to several thousand patients (level of evidence = A).
Studies have a low risk of bias and high level of validity by meeting stringent assessment criteria (quality rating = A).
Evidence consistently shows negative outcomes for a given indication without valid evidence to the contrary.