Preface to Position Statements

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As with any medical specialty, controversy abounds in the area of Medical Toxicology. In order to summarize the pertinent literature in a concise form, the ACMT has developed various position statements. The *Journal of Medical Toxicology* will periodically publish official ACMT position statements (in the original form) that can also be viewed at **www.acmt.net**.

Position Statement Development Process

All position statements are edited by the ACMT practice committee and then referred to the ACMT Board of Directors for review. The authors and the committee assess all comments. After endorsement by the board, position statements are posted on the ACMT web page for a two week period for review and comment by all members. All position statements are introduced by a disclaimer indicating that **while individual practitioners may differ, this is the position of the college at the time written, after a review of the issue and pertinent literature.** All statements are reviewed on a periodic basis and as needed when new data or questions arise. The original author(s) must address any questions, indicating the date of any revisions on the statement. Each author must sign a disclosure form discussing any potential sources of bias and conflict of interest.

ACMT Position Statement: Dietary Supplements

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DISCLAIMER

While individual practitioners may differ, this is the position of the College at the time written, after a review of the issue and pertinent literature.

INTRODUCTION

1n 1938 with the passage of the FD & C Act, pre-existing plant-based drugs, such as atropine, codeine, and morphine, were "grandfathered" into approved use in the United States along with everything listed in the United States Pharmacopoeia-National Formulary. Herbals were exempted from registration as drugs following a review commissioned by the FDA (authorized by the Kefauver-Harris amendments in 1962) from the National Academy of Sciences.

Herbals are now considered dietary supplements. They are being widely utilized; however, treating physicians may not be aware that patients are taking them. The Eisenberg report in JAMA (1998) stated that 42% of those surveyed used some alternative forms of medical therapy (increased from 34% in a 1991 survey). While the percentage that used herbals was relatively low at 12%, this was dramatically increased from 2.5% in the 1991 survey. Other published estimates of herbal medication use have ranged as high as 30% in certain ethnic or patient populations. In 1994, the United States Dietary Supplement Health Education Act (USDSHEA) was passed, designating the FDA Center for Food Safety and Applied Nutrition (CFSAN) with responsibility for developing regulations for dietary supplements, which include amino acids, biological extracts, herbals, minerals, and vitamins. In 1995, a National Center for Complementary and Alternative Medicine (NCCAM) was established at NIH with a growing budget for sponsored research. In May 1998, the dietary supplement branch of CFSAN published a container labeling requirement, and a 10-year plan was issued in January 2000 for the total regulation of dietary supplements.

DATA

How orthodox medicine relates to these alternative forms is important, given the extent of their use by patients. A valid concern is that patients may self-administer an inefficacious or poorly efficacious alternative medication when an efficacious pharmaceutical product is available. On the other hand, there is an accumulating body of case-control studies of certain single agents, such as ginger, St. John's wort, saw palmetto, and an NIH study of ginko biloba, in which effectiveness has been shown. There are also three trade organizations, including the American Herbal Products Association, which self-regulate members and have codes of ethics that should impose regulations on harmful products, such as ephedra (Ma huang). This particular agent has been associated with many serious cardiovascular reactions and death; its sale and labeling have been regulated by several states, although regulation efforts by the FDA have been unsuccessful. It appears that most manufacturers have limited the amount available in a single dose and instituted the use of some warning labels.

Medical toxicology is primarily focused on problems with poisoning or overdose, rather than therapeutic options. As such, potential toxicity and herb-drug interactions of these preparations are our major concern. In addition, there are preparations in which multiple ingredients are included, making this a confusing issue.

Toxicity

Concerning toxicity, one needs to consider the origin of the substance. Is the product produced and labeled in the United States or Europe? Is it an Asian, ayuvedic, or mixture of other origin that could be combined with other herbals, sometimes containing misidentified plant material, or even heavy metals such as lead, arsenic, antimony, or mercury? Could the preparation have a non-labeled inclusion of a pharmaceutical product, such as butazolidine in antiarthritics or a benzodiazepine in calmatives?

There are certain naturally-occurring substances which have been withdrawn from internal use due to hepatoxicity, including comfrey tea, chapparal, and pennyroyal oil. Central nervous system toxicants include henbane, jimson weed, and mandrake, all more likely to be encountered in substances harvested by amateurs rather than in products sold by the herbal medication industry. This also applies to the cardiovascular toxicants monkshood, ch'an su, foxglove, oleander, and squill. Gastrointestinal toxicants, such as aloe, buckthorn, cascara, pokeweed, and senna, have often been used for dyspepsia or constipation and can be abused with resultant electrolyte loss. This could result in cardiac arrhythmias or perturb the therapeutic effects of various cardiac medications.

Interactions

Herb-drug interactions of most concern involve ephedra and St. John's wort. Ephedra, which contains 6 isomers including ephedrine, is a sympathomimetic amine which interacts with other amines as well as with digoxin and other cardiac drugs, resulting in cardiac arrhythmias or hypertension. St. John's wort, the most commonly used antidepressant in Germany, can result in mild serotonin syndrome in combination with sertraline, trazodone, and nefazodone; lethargy and incoherence in combination with paroxetine; and can decrease digoxin, cyclosporine, and theophylline levels when co-administered. These are thoroughly reviewed in the provided references. Ongoing reports through the FDA's MedWatch system (*www.fda.gov/medwatch*) and the American Association of Poison Control Centers Toxic Exposure Surveillance System help update this information.

Conclusions

Herbal medication use as a dietary supplement is common. Many Americans use these products, federal legislation has implemented the USDSHEA, and there is now a National Center for Complementary and Alternative Medicine at NIH. Ethical herbal medication use of those single substances shown to be effective is growing. When patients are taking dietary supplements or herbal medications, the ingredients, origin, and potential toxicity or herb-drug interactions need to be determined. Education concerning these products and their potential toxicity, adverse effects, and interactions should become an essential component of medical toxicology. Clinicians caring for patients who may self-administer these products should attempt to obtain this history and familiarize themselves with the potential problems. The American College of Medical Toxicology strongly recommends consultation with or care by a medical toxicologist in cases of suspected or confirmed toxicity, adverse effects, or interactions from dietary supplements. We further encourage patients to report their use of these supplements to their physicians. FDA supervised labeling now requires a "Supplement Facts" label on each dietary supplement bottle marketed in the U.S. that describes and quantitates ingredients; supplements that do not have such a label should be used cautiously, if at all. The ACMT strongly supports the FDA's plan to further review and regulate dietary supplements where clinical experience or scientific information suggests the possibility of harm.

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WEBLINKS

MEDLINEplus "*Herbal Medicine*" website is a list of links, including to the NCCAM (National Center for Complementary and Alternative Medicine) at NIH, a Pandora's box of information in itself.

ACMT Position Statement: Institutions Housing Venomous Animals

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BACKGROUND

There are no published standards regarding the responsibilities of institutions housing venomous animals. Manifestations and management of the envenomations of non-native venomous animals are unfamiliar to most potential local treating physicians. Proper planning for such envenomations includes proper storage, transport and use of non-licensed antivenoms, Emergency Medical System coordination, receiving medical facility coordination, regional poison center involvement and the involvement of an appropriately trained or experienced clinician. Therefore: When an institution houses, displays or otherwise has possession of venomous animals, it is incumbent upon that institution to assure that the likelihood of human envenomation is minimized and that there is a written plan to respond to any envenomation that may occur.

1. **Acquisition and Housing:** Venomous animals with significant envenomation risks should only be acquired and maintained by institutions that have the resources and capabilities to properly care for them and where the regional resources and capabilities exist to manage envenomations. Venomous animals should be housed and displayed in properly designed enclosures.
2. **Antivenom Acquisition:** When antivenom is available, it should be obtained prior to the institution's acquisition of the venomous animal. When an FDA approved species-specific antivenom is available, the institution should procure an amount adequate to treat a moderately to severely envenomated victim. When FDA approved antivenom is not available, an antivenom that is approved for use in another country is preferred over antivenom with no governmental regulatory approval. Decisions regarding which antivenom to obtain and in what amounts should be made by the physician or clinical toxicologist identified below. When only non-FDA approved species-specific antivenom(s) are available, it is the responsibility of the institution to obtain an importation permit and FDA investigational new drug (IND) application for appropriate antivenom. Replacement antivenom should be obtained prior to expiration of old stock.