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Alternative Medicine -- The Risks of Untested and Unregulated Remedies

What is there about alternative medicine that sets it apart from ordinary medicine? The term refers to a remarkably heterogeneous group of theories and practices -- as disparate as homeopathy, therapeutic touch, imagery, and herbal medicine. What unites them? Eisenberg et al. defined alternative medicine (now often called complementary medicine) as "medical interventions not taught widely at U.S. medical schools or generally available at U.S. hospitals." (1) That is not a very satisfactory definition, especially since many alternative remedies have recently found their way into the medical mainstream. Medical schools teach alternative medicine, hospitals and health maintenance organizations offer it, (2) and laws in some states require health plans to cover it. (3) It also constitutes a huge and rapidly growing industry, in which major pharmaceutical companies are now participating. (4)

What most sets alternative medicine apart, in our view, is that it has not been scientifically tested and its advocates largely deny the need for such testing. By testing, we mean the marshaling of rigorous evidence of safety and efficacy, as required by the Food and Drug Administration (FDA) for the approval of drugs and by the best peer-reviewed medical journals for the publication of research reports. Of course, many treatments used in conventional medicine have not been rigorously tested, either, but the scientific community generally acknowledges that this is a failing that needs to be remedied. Many advocates of alternative medicine, in contrast, believe the scientific method is simply not applicable to their remedies. They rely instead on anecdotes and theories.

In 1992, Congress established within the National Institutes of Health an Office of Alternative Medicine to evaluate alternative remedies. So far, the results have been disappointing. For example, of the 30 research grants the office awarded in 1993, 28 have resulted in "final reports" (abstracts) that are listed in the office's public on-line data base. (5) But a Medline search almost six years after the grants were awarded revealed that only 9 of the 28 resulted in published papers. Five were in 2 journals not included among the 3500 journal titles in the Countway Library of Medicine's collection. (6,7,8,9,10) Of the other four studies, none was a controlled clinical trial that would allow any conclusions to be drawn about the efficacy of an alternative treatment. (11,12,13,14)

It might be argued that conventional medicine relies on anecdotes, too, some of which are published as case reports in peer-reviewed journals. But these case reports differ from the anecdotes of alternative medicine. They describe a well-documented new finding in a defined setting. If, for example, the Journal were to receive a paper describing a patient's recovery from cancer of the pancreas after he had ingested a rhubarb diet, we would require documentation of the disease and its extent, we would ask about other, similar patients who did not recover after eating rhubarb, and we might suggest trying the diet on other patients. If the answers to these and other questions were satisfactory, we might publish a case report -- not to announce a remedy, but only to suggest a

hypothesis that should be tested in a proper clinical trial. In contrast, anecdotes about alternative remedies (usually published in books and magazines for the public) have no such documentation and are considered sufficient in themselves as support for therapeutic claims.

Alternative medicine also distinguishes itself by an ideology that largely ignores biologic mechanisms, often disparages modern science, and relies on what are purported to be ancient practices and natural remedies (which are seen as somehow being simultaneously more potent and less toxic than conventional medicine). Accordingly, herbs or mixtures of herbs are considered superior to the active compounds isolated in the laboratory. And healing methods such as homeopathy and therapeutic touch are fervently promoted despite not only the lack of good clinical evidence of effectiveness, but the presence of a rationale that violates fundamental scientific laws -- surely a circumstance that requires more, rather than less, evidence.

Of all forms of alternative treatment, the most common is herbal medicine. (15) Until the 20th century, most remedies were botanicals, a few of which were found through trial and error to be helpful. For example, purple foxglove was found to be helpful for dropsy, the opium poppy for pain, cough, and diarrhea, and cinchona bark for fever. But therapeutic successes with botanicals came at great human cost. The indications for using a given botanical were ill defined, dosage was arbitrary because the concentrations of the active ingredient were unknown, and all manner of contaminants were often present. More important, many of the remedies simply did not work, and some were harmful or even deadly. The only way to separate the beneficial from the useless or hazardous was through anecdotes relayed mainly by word of mouth.

All that began to change in the 20th century as a result of rapid advances in medical science. The emergence of sophisticated chemical and pharmacologic methods meant that we could identify and purify the active ingredients in botanicals and study them. Digitalis was extracted from the purple foxglove, morphine from the opium poppy, and quinine from cinchona bark. Furthermore, once the chemistry was understood, it was possible to synthesize related molecules with more desirable properties. For example, penicillin was fortuitously discovered when penicillium mold contaminated some bacterial cultures. Isolating and characterizing it permitted the synthesis of a wide variety of related antibiotics with different spectrums of activity.

In addition, powerful epidemiologic tools were developed for testing potential remedies. In particular, the evolution of the randomized, controlled clinical trial enabled researchers to study with precision the safety, efficacy, and dose effects of proposed treatments and the indications for them. No longer do we have to rely on trial and error and anecdotes. We have learned to ask for and expect statistically reliable evidence before accepting conclusions about remedies. Without such evidence, the FDA will not permit a drug to be marketed.

The results of these advances have been spectacular. As examples, we now know that treatment with aspirin, heparin, thrombolytic agents, and beta-adrenergic blockers greatly reduces mortality from myocardial infarction; a combination of nucleoside analogues and a protease inhibitor can stave off the onset of AIDS in people with human immunodefiency virus infection; antibiotics heal peptic ulcers; and a cocktail of cytotoxic drugs can cure most cases of childhood leukemia. Also in this century, we have developed and tested vaccines against a great many infectious scourges, including measles, poliomyelitis, pertussis, diphtheria, hepatitis B, some forms of meningitis, and pneumococcal pneumonia, and we have a vast arsenal of effective antibiotics for many others. In less than a century, life expectancy in the United States has increased by three decades, in part because of better sanitation and living standards, but in large part because of advances in medicine realized through rigorous testing. Other countries lagged behind, but as scientific medicine became universal, all countries affluent enough to afford it saw the same benefits.

Now, with the increased interest in alternative medicine, we see a reversion to irrational approaches to medical practice, even while scientific medicine is making some of its most dramatic advances. Exploring the reasons for this paradox is outside the scope of this editorial, but it is probably in part a matter of disillusionment with the often hurried and impersonal care delivered by conventional physicians, as well as the harsh treatments that may be necessary for life-threatening diseases.

Fortunately, most untested herbal remedies are probably harmless. In addition, they seem to be used primarily by people who are healthy and believe the remedies will help them stay that way, or by people who have common, relatively minor problems, such as backache or fatigue. (1) Most such people would probably seek out conventional doctors if they had indications of serious disease, such as crushing chest pain, a mass in the breast, or blood in the urine. Still, uncertainty about whether symptoms are serious could result in a harmful delay in getting treatment that has been proved effective. And some people may embrace alternative medicine exclusively, putting themselves in great danger. In this issue of the Journal, Coppes et al. describe two such instances. (16)

Also in this issue, we see that there are risks of alternative medicine in addition to that of failing to receive effective treatment. Slifman and her colleagues report a case of digitalis toxicity in a young woman who had ingested a contaminated herbal concoction. (17) Ko reports finding widespread inconsistencies and adulterations in his analysis of Asian patent medicines. (18) LoVecchio et al. report on a patient who suffered central nervous system depression after ingesting a substance sold in health-food stores as a growth hormone stimulator, (19) and Beigel and colleagues describe the puzzling clinical course of a patient in whom lead poisoning developed after he took an Indian herbal remedy for his diabetes. (20) These are without doubt simply examples of what will be a rapidly growing problem.

What about the FDA? Shouldn't it be monitoring the safety and efficacy of these remedies? Not any longer, according to the U.S. Congress. In response to the lobbying efforts of the multibillion-dollar "dietary supplement" industry, Congress in 1994 exempted their products from FDA regulation. (21,22) (Homeopathic remedies have been exempted since 1938. (23)) Since then, these products have flooded the market, subject only to the scruples of their manufacturers. They may contain the substances listed on the label in the amounts claimed, but they need not, and there is no one to prevent their sale if they don't. In analyses of ginseng products, for example, the amount of the active ingredient in each pill varied by as much as a factor of 10 among brands that were labeled as containing the same amount. (24) Some brands contained none at all. (25)

Herbal remedies may also be sold without any knowledge of their mechanism of action. In this issue of the Journal, DiPaola and his colleagues report that the herbal mixture called PC-SPES (PC for prostate cancer, and spes the Latin for "hope") has substantial estrogenic activity. (26) Yet this substance is promoted as bolstering the immune system in patients with prostate cancer that is refractory to treatment with estrogen. (27) Many men taking PC-SPES have thus received varying amounts of hormonal treatment without knowing it, some in addition to the estrogen treatments given to them by their conventional physicians.

The only legal requirement in the sale of such products is that they not be promoted as preventing or treating disease. (28) To comply with that stipulation, their labeling has risen to an art form of doublespeak (witness the name PC-SPES). Not only are they sold under the euphemistic rubric "dietary supplements," but also the medical uses for which they are sold are merely insinuated. Nevertheless, it is clear what is meant. Shark cartilage (priced in a local drugstore at more than $3 for a day's dose) is promoted on its label "to maintain proper bone and joint function," saw palmetto to "promote prostate health," and horse-chestnut seed extract to "promote... leg vein health." Anyone can walk into a health-food store and unwittingly buy PC-SPES with unknown amounts of

estrogenic activity, plantain laced with digitalis, or Indian herbs contaminated with heavy metals. Caveat emptor. The FDA can intervene only after the fact, when it is shown that a product is harmful. (28)

It is time for the scientific community to stop giving alternative medicine a free ride. There cannot be two kinds of medicine -- conventional and alternative. There is only medicine that has been adequately tested and medicine that has not, medicine that works and medicine that may or may not work. Once a treatment has been tested rigorously, it no longer matters whether it was considered alternative at the outset. If it is found to be reasonably safe and effective, it will be accepted. But assertions, speculation, and testimonials do not substitute for evidence. Alternative treatments should be subjected to scientific testing no less rigorous than that required for conventional treatments.

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