

Scientific scrutiny of "alternative" therapies by CRAIG LAMBERT

N THE 1950s the American Cancer Society had a Committee on Quackery. Later that turned into a committee on "unproven methods of cancer management," superseded by one on "questionable methods." The names indicate a gradual acceptance of the unconventional; today the cancer society has a Committee on Complementary and Alterna-

tive Medicine (CAM). The evolving vocabulary also reflects a sea change underway throughout medicine. In the last few years, the term "alternative,"

suggesting something done *instead of* conventional medicine, has been giving way to "complementary," a therapy done *along with* mainstream treatment. Both words may ultimately be replaced by "integrative medicine"—the use of techniques like acupuncture, massage, herbal treatments, and meditation in regular medical practice.

Such therapies, which mainstream doctors once considered useless, puzzling, or even dangerous, are now welcomed into the labs, classrooms, and clinics of academic medical centers, including those of Harvard Medical School (HMS). "Medical care is both a science and a connection between patient and healer," HMS

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dean Joseph B. Martin has declared. "As in the past, some treatments that are now 'alternative' will become standard treatments."

Martin made that remark at an October reception celebrating a \$10-million grant from the Bernard Osher Foundation for the medical school's new Division for Research and Education in Complementary and Integrative Medical Therapies, launched in the spring of 2000. (Philanthropist Osher, a Maine resident who relocated to San Francisco, cofounded Golden West Financial. He also owned the Butterfield & Butterfield auction house, which he sold to eBay in 1999.) Augmented by \$2 million from HMS, the foundation's gift to Harvard endows several positions and programs, including an Osher professorship in complementary and integrative medical therapies.

That chair's first occupant, David M. Eisenberg '76, M.D. '80, is an impeccably credentialed academic doctor who directs the division and has emerged as a leading figure in this new field poised at the confluence of several healing traditions. "Any new therapy is temporarily an 'alternative' therapy," he says. "In the past, the environment didn't allow for the application of skeptical science to these unconventional treatments. But that environment now exists."

It exists because of a grassroots, bottom-up revolution in the nation's patterns of healthcare. "Integrative medicine's time has come," declared Bernard Osher at the reception. "It is here because of patient demand, and it has come about only because of patient demand." In a landmark 1993 New England Journal of Medicine article, Eisenberg and several colleagues documented the vast extent of that demand, describing what is virtually a parallel industry to standard medicine. The article reported a 1990 national survey ("a way to biopsy what is happening in the marketplace," Eisenberg says) showing that 34 percent of American adults had used at least one unconventional therapy in the previous year, and estimated that Americans made 425 million visits to providers of such therapies-exceeding the number to primary care physicians (388 million). This, despite the fact that 75 percent of CAM therapy expenditures were paid out of pocket-for a total annual out-of-pocket expense approximating the comparable figure for all hospitalizations in the United States.

The report, which described a phenomenon underway for at least half a century, made a splash. ("That article is cited everywhere," Martin says.) And the trend has only strengthened since 1990; by 1997, visits to CAM providers had increased 47 percent, to 625 million. Today, half of all adults use CAM treatments, creating a \$30-billion growth industry. Health insurers, HMOs, and Fortune 500 companies are

now endorsing some alternative treatments as part of health benefits. In 1992, the National Institutes of Health (NIH) created an Office of Alternative Medicine with a \$2-million budget; in 1998 the office became the National Center for Complementary and Alternative Medicine, and today its research budget has increased fifty-fold, to \$100 million. Furthermore, with 70 percent of their generation routinely using CAM therapies, today's medical students increasingly demand education in this area.

The 1990 survey also identified a factor of special import for practicing physicians. Of patients who used unconventional therapies for serious medical conditions, 83 percent also sought treatment from a medical doctor—but 72 percent of that group did not inform their doctors about their CAM treatments. "It's not that they think their doctor will disapprove or discourage these therapies," Eisenberg says. "The perception is that the physician won't know enough about these treatments to incorporate them into the patient's care." However, CAM treatments can interact with conventional therapies, perhaps in unexpected ways, so overall patient care may suffer when physicians are unaware of the full range of treatments in play.

Hence the need to bring CAM into the mainstream of medical education and research—a task that amounts to a fair summary of Eisenberg's life mission. "David is a pioneer," says Jon Kabat-Zinn, professor of medicine emeritus at the University of Massachusetts Medical School and author of Full Catastrophe Living, a best-selling book on stress management. "There are a dozen prestigious medical centers in the United States moving in this direction, but when Harvard invests in something, other institutions look up and take notice." Perhaps partly due to Harvard's influential status, the NIH recently awarded the new HMS division a \$2-million grant to build the first clinical model of integrative care within an academic teaching hospital—a model that could eventually be replicated throughout the United States. The first clinical trial in the proposed integrative-care center will involve lower back pain, the leading complaint for which people seek CAM treatment. The volunteer subjects will be nurses from Harvard teaching hospitals who have thrown out their lower backs while lifting patients and have been out of work four weeks; they will be invited to be randomly assigned to conventional or integrative treatment to compare the modalities.

A survey of the 5,000-member Medical School faculty drew 436 responses expressing a variety of interests in CAM research and education—"an extremely high return for a mailing to faculty," says Walter Distinguished Professor of medicine and medical education Daniel D. Federman '49, M.D. '53, formerly dean for medical educa-

Western and Chinese remedies, including honeysuckle tea, tiger balm, tangerine peel, and dried litchi fruit. The Chinese character opposite is *qi* ("chee"), which means, roughly, "life energy."

tion. Yet Federman adds, "Among people whose lives are based on rigorous scientific evidence, there is plenty of suspicion of such treatments. I have friends who think it's all nonsense, all placebo effects; I could name 10 doctors who are household names who would tell you that this is not the way to go—an inappropriate area for a medical school's involvement." Federman uses a literary metaphor to indicate the scorn that parts of the medical establishment have for such treatments: "Coleridge said that poetry deserves the willing suspension of disbelief. So does complementary medicine. But we can't even get *unwilling* suspension of disbelief!"

A COMBINATION OF PERSONAL LOSSES and world events propelled Eisenberg along his unique career path, which was in place by the time he was 25. The grandson of Jewish immigrants who escaped persecution in Poland and Russia, Eisenberg grew up on Long Island. His father, a baker, and mother, a lawyer, had four children. When Eisenberg was 10, both his grandmothers died of illnesses within a week of each other; then, only six weeks later, his father died of a heart attack at age 39. Within two years he lost his remaining grandfather. The deaths of his father and three grandparents within two years "molded my personality and subsequent choice of profession," he says. One grandmother, he later learned, had perished from a misdiagnosed bacterial infection. The other one died of multiple medical problems, and his father's death had been sudden and early. The mystery of human health and disease took on a compelling interest for the teenager.

Eisenberg matriculated at Harvard in the fall of 1972, barely six months after President Richard Nixon made his groundbreaking visit to the People's Republic of China. Then-New York Times columnist James Reston had accompanied the Nixon delegation to China, only to undergo emergency surgery for acute appendicitis in Beijing. Reston wrote a front-page story in the Times—"an obituary to his appendix," as Eisenberg recalls it—that described how his intense postoperative pain was relieved by acupuncture, an ancient technique of Chinese medicine then unknown in the West. "This was an intellectual shot heard round the world," Eisenberg says. "It resulted in NIH sending teams of scientists and clinicians to China to see if acupuncture anesthesia had any validity."

The 17-year-old Har-

vard freshman was fascinated. "It was something out of Star Trek—the idea that acupuncture needles could change pain sensations in a human being was like magic," Eisenberg recalls. He won approval for an independent study on acupuncture anesthesia, supervised by the late Nobel Prize-winning biologist George Wald and his wife, Ruth Hubbard '45, Ph.D. '50, now professor of biology emerita. But Eisenberg could not find a single word in English on the subject in all the Harvard libraries. He did discover one gem: The Yellow Emperor's Classic of Internal Medicine, a book written circa 400 B.C. that remains a primary reference for traditional medicine throughout the Pacific rim. The text included two quotations (see pages 49 and 100)—one on prevention, the other on mind-body interactions-whose profundity impressed Eisenberg. He was already pre-med, so he thought, "I'll just study Chinese medicine, too. The next logical step was to study Chinese language, philosophy, and history, with great teachers like John King Fairbank. I fell in love with Chinese culture and civilization."

During the summer before his second year at Harvard Medical

School, Eisenberg went to Taipei on a Paul Dudley White Traveling Fellowship. He studied both the Chinese language and traditional Chinese healers—herbalists, acupuncturists, faith healers. He also had a lifechanging experience. "In China and all East Asian countries, there's a long history of training children who are blind to go into the profession of massage," he explains. "Massage therapists are highly valued and can make a good living. Blind massage therapists can use their heightened tactile abilities. I was fascinated by this, and invited the local blind massage therapist to

work on me. He spoke Taiwanese and I spoke Mandarin-we didn't have one word in common. Yet, after only 90 seconds of scanning my body with his hands, he understood a lot about me. And within five minutes he had put me into a state I have never experienced before or since. It was complete relaxation—every part of my body felt like Jell-O; yet at the same time, I was acutely aware of the environment with all my senses, almost hypervigilant. This is what meditation does, fusing relaxation with hyperacuity; he did it with a few well-placed fingertips. In that moment I knew he had something to teach me with his hands that I was probably not going to be exposed to on my rounds at Harvard Medical School. That was enough to convince me I needed to go back to Asia.

"If and when we build an integrative medicine clinic at a Harvard teaching hospital," Eisenberg continues, "one idea I carry with me is to work with local schools for the blind and local massage therapy institutes to develop a special curriculum for people who are visually impaired."

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David M. Eisenberg in his office

"To administer medicine to diseases which have already developed and thereby suppress bodily chaos which has already occurred is comparable to the behavior of those who would begin to dig a well after they had grown thirsty, or those who would begin to cast weapons after they have engaged in battle. Would these actions not be too late?" The Yellow Emperor's Classic of Internal Medicine, circa 400 B.C.

In 1978, Eisenberg returned to China as the only medical student—and only Chinese speaker—among 15 members of the first HMS delegation to that country. He needed permission to miss several weeks of classes, but then-admissions dean Gerald S. Foster, M.D. '51, now associate clinical professor of medicine, immediately saw the trip's value and passed on a bit of received wisdom: "Don't ever let your schooling get in the way of your education." President Jimmy Carter normalized diplomatic relations with Beijing that year, and in 1979, Eisenberg returned to China as the first American

Healing implements (left) east and west: a reflex hammer, a Japanese massage roller, a tuning fork, and a hemostat. At right, a plastic model marked with points for acupuncture.

medical-exchange student to visit since 1949. (In 1993, when television host Bill Moyers and Eisenberg traveled to China to film the first episode of the public TV series *Healing and the Mind*, they interviewed some of Eisenberg's Chinese teachers for the show.) In 1985, Eisenberg published his book *Encounters with* Q*i*, describing his experiences with traditional Chinese healing treatments. (Q*i*, pronounced *chee*, is a Chinese word meaning "life energy.")

In China, "Whenever I saw beneficial effects of unfamiliar treatments, I intuitively asked, 'Is it the *therapy*, or *belief* in the *(please turn to page 99)*

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THE NEW ANCIENT TREND IN MEDICINE *(continued from page 49)*

therapy? The needle or belief in the needle?" Eisenberg recalls. "A central research question is: to what degree can belief or cultural conditioning increase or decrease the effect of any therapy—including radiation or chemotherapy? Can the patient's belief—or the clinician's belief, or both affect the result? This is testable."

IN FACT, EISENBERG ASSERTS, the vast majority of CAM treatments are testable. His mantra is "open-minded skepticism," the intellectual attitude that he considers to be Harvard's strength. "In the clinical world," he says, "the language is shifting from 'Does it work?"—a black-and-white question—to 'What is sufficiently proven by science to recommend its use?' The field is entering the mainstream logic of clinical medicine." The new HMS division applies this open-yet-skeptical approach to its research and education activities (it does not yet offer clinical treatments), continuing and extending work that Eisenberg has pursued since 1994, when he founded the Center for Alternative Medicine Research and

Glass cupping jars, tools of traditional Chinese medicine, are used on the skin as an adjunct to acupressure therapy. Education at Beth Israel Hospital (now Beth Israel Deaconess Med-

The Center for Wellness and Health Communication

"YOU CAN BE PHYSICALLY FIT without being well," says Keli M. Ballinger, suggesting the holistic approach of the University Health Services' (UHS) "wellness center," where she is program manager. Ballinger is also clinic/administrative director and clinical provider for the UHS Mind/Body Medical Institute (MBMI), an outpost of the eponymous program that Mind/Body Medical Institute associate professor of medicine Herbert Benson, M.D. '61, founded at New England Deaconess Hospital in Boston in 1988.

The wellness center offers a variety of resources—including yoga classes, nutritional consultation, and mind-body tech-

niques for reducing stress to Harvard faculty, students, and staff. "The techniques we provide have hundreds of studies supporting them," Ballinger says. "I practice these things myself!"

For the past three years, five times a year, MBMI has offered a 10-week Medical Symptom Reduction Program for groups of 12 to 15 people who may have only one thing in common: they are suffering from a symptom exacerbated by stress. This can mean insomnia, asthma, hypertension, gastrointestinal disorders, or migraines, as well as serious conditions like breast cancer. cardiovascular illness. and AIDS. For some condi-



tions, "The diagnosis itself is a stressful event," Ballinger says. A fundamental component of the program is the "relaxation response," a meditative mind-body technique that Benson popularized in his 1975 book of that name. The aim is to help people reexamine thought patterns that sometimes distort or "catastrophize" their condition. This isn't simply "putting pink paint over a black spot and saying, 'It's all pretty now,'" cautions Ballinger. "It doesn't mean that the condition is going to change. But you may be able to think more rationally about the situation you are in."

Using similar techniques, MBMI also offers a six-week Maximize Your Potential program for students who may not be struggling with any medical condition, but often put unneces-

sary stress on themselves. (Ballinger and her colleagues eventually hope to monitor levels of the stress-related hormone cortisol while following a cohort of freshmen through their four years of college.) "A student who gets a B on an exam may think, 'I will be a failure for the rest of my life, and I will always be second-rate. If I don't succeed in this way, my parents won't love me,'" says Ballinger. Preliminary research indicates that the program significantly reduced perceived levels of stress, as well as emotional symptoms such as anxiety and depression.

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"I have heard that in early times the people lived to be over 100 years old. But these days people only reach half that age and must curtail their activities. Does the world change from generation to generation or does man become negligent of the laws of nature?...Today people do not know how to find contentment within. They are not skilled in the control of their spirits. For these reasons they reach only half of their 100 years and then they degenerate."

The Yellow Emperor's Classic of Internal Medicine, circa 400 B.C.

ical Center), a Harvard teaching hospital.

"I am passionate in my view that the tools we have are adequate to investigate the overwhelming majority of alternative and complementary therapies," Eisenberg says. "And we have new tools that didn't exist 10 years ago." There are now all sorts of scanning technologies to look at brain states, reports Jon Kabat-Zinn. "Neuro-imaging tools can help explore the connection between subjective intrapsychic states and more objective measures of cognitive functioning, and so expand our knowledge of the mind-body interface." A recent Science article on Parkinson's disease, for example, reported how positron-emission tomography (PET scans) detected the release of the neurotransmitter dopamine in the brain in response to placebos. In another area, Eisenberg mentions "robotic tools for drug discovery that in one day can screen thousands of herbal extracts and other biological substances for their effects on biological targets."

There is also a whole new horizon of basic science unfolding that explores the mechanisms by which CAM treatments work. "There's no doubt that you can do certain types of surgery under acupuncture anesthesia," says Federman. "But no one knows why. There's work needed on the brain, on pain pathways in the brain, and how acupuncture affects perceptions of pain. And there are herbal remedies crying out for study. The use of many of these herbs goes back thousands of years, and it seems hard to imagine that everybody has been duped all this time, or that the placebo mechanism is the only factor. There are active ingredients in some herbal medicines, but how do they have their effect? Cell-biology researchers study herbals in the lab, rather than in the patient. Drug companies are now trying to detect their clinically effective components."

Eisenberg is interested in "unbundling"

the placebo phenomenon, the well-established observation that belief in a treatment enhances its effectiveness. "In every randomized study there are a handful of subjects who have an extraordinary response to the placebo. What are the characteristics of those extraordinary responders? What about their brains, bodies, or mental sets distinguishes them from others? Are they high responders across all treatments or only a particular one?"

Admittedly, there are a few therapies that do not neatly lend themselves to scientific testing. "Teaching someone to think in a particular way is difficult to control," Eisenberg says. "It's also hard to

> create a sham control for acupuncture or massage." But innovations are underway. German researchers, for example, have developed springloaded acupuncture devices that position the needle inside a guiding tube, and prick the skin without penetrating

it — giving control subjects the sensation of acupuncture without the actual treatment.

"Today, the basic science community is fascinated by the mechanisms involved in these treatments—how do they alter physiology?" says Eisenberg. "This field used to have a very high 'anti-tenure titer.' Someone eager to investigate these phenomena

Medicinal needles: both syringes and acupuncture needles come in various sizes. was seen as their advocate—but advocacy is unscientific. Since NIH began funding the area and has seen its value and potential, young scientists are no longer shying away. It's now a politically correct field for a neuroscientist, or any biomedical investigator. And that is new—the shift has occurred in the last two or three years. One of the most pleasurable aspects is that the skeptics are now interested, if not in the actual research question, then in how to answer the question. When the challenge of creating a methodology becomes intellectually stimulating and fun, that's when a field has staying power."

INDEED complementary therapies are here to stay, and appear to be on their way to increasing use in Western medicine. In some ways they hold out great promise. The Moyers television program showed a Chinese doctor performing brain surgery on a conscious patient primarily anesthetized with acupuncture, using

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less than half the chemical anesthesia typical in the West. Clinical trials funded by NIH—some now in Phase III—suggest that ginkgo extract may be effective for Alzheimer's disease, that chondroitin sulfate may affect osteoarthritis, and that saw-palmetto extract might ameliorate benign prostatic hypertrophy. An NIH consensus conference agreed that meditapopular demand for CAM treatments practiced with the oversight and support of traditional academic medicine. If this happens, medical institutions that dismiss or ignore patients' desire for CAM will risk being left behind.

Eisenberg foresees medical schools "teaching everybody a modest amount about these treatments. Then, in every

The Zakim Center for Integrated Therapies

THE LEONARD P. ZAKIM BUNKER HILL BRIDGE, the new span connecting Boston and Charlestown, honors the memory of a Boston citizen with a gift for building bridges between communities. Zakim died in December 1999 of multiple myeloma, a form of cancer affecting bone marrow. While being treated by oncologists at the Dana-Farber Cancer Institute, Zakim also made use of acupuncture, massage, meditation, exercise, nutrition, and support groups to ameliorate his symptoms. The regimen of complementary therapies, he said in a videotaped interview, "put me in the best physical shape I've been in since the days I played high-school football."

In November 2000, Dana-Farber opened the Zakim Center for Integrated Therapies, offering cancer patients a range of options that includes acupuncture, mindbody techniques, exercise programs (like yoga), therapeutic touch (including Japanese reiki), nutritional consultation, music therapy, and massage therapy. Most health insurers do not yet cover any of these resources. But if research demonstrates that such interventions reduce the need for pain medication (and hence drug costs), the insurance benefits could change, says Oliver professor of hygiene and University Health Services director David S. Rosenthal '59, medical director of the Zakim Center and former president of the American Cancer Society. Rosenthal notes that clinical evidence indicates that acupuncture is effective for pain, and can also decrease some side effects of chemotherapy, like nausea—as well as improve emotional states such as anxiety, stress, and depression.

tion and other mind-body techniques can help treat pain and insomnia. At Massachusetts General Hospital, associate professor of psychiatry Andrew Nierenberg is running a clinical trial exploring the value of St. John's wort for mild to moderate depression.

Such innovative treatments will probably enter conventional practice in varied ways. Best-selling author Andrew Weil '64, M.D. '68, has launched a two-year fellowship program in integrative medicine at the University of Arizona that offers doctors a broad training in the field. Yet integrative medicine may never become a board-certified specialty; instead, it may gradually infuse the whole of medical practice. It might become another standard tool of the medical arts, and like any medical innovation, some of its practices could eventually supplant conventional therapies. Integrative clinics tied to teaching hospitals may some day become a truly "disruptive technology" by meeting a vast domain, there would be somebody more expert than his or her peers. In every oncology group, each dermatology group, and so on, there would be someone who had studied herbs, massage, or meditation, who could inform colleagues on a given case."

Federman sees complementary therapies as something that will be "integrated into patient care by the people who have the patients—rather than referring them to the Qi specialist down the street." He cites a bit of medical history: "The proposition that obstetricians were carrying puerperal infections from one patient to another was extremely unpopular until it was seen that the evidence was overwhelming. If something works, it should be incorporated into medical care. In the long run, there is no such thing as alternative medicine."

Craig A. Lambert '69, Ph.D.'78, is deputy editor of this magazine.



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