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Divider Title: Lindberg

Donald A. Lindberg, M.D.
National Library of Medicine

Testimony of
Donald A.B. Lindberg, M.D.
Director, National Library of Medicine
Before the White House Commission on
Complimentary and Alternative Medicine Policy
May 15, 2001

Thank you for inviting me to participate on this panel that is addressing Approaches to Evaluating Research Literature. The Commission is making an important contribution to advancing research on complementary and alternative medicine (CAM) and to disseminating reliable information on CAM to health care providers and the public. I know that several of my fellow NIH institute directors already have testified before the Commission and I appreciate the opportunity to contribute this discussion. In addition, last March, Sheldon Kotzin, Chief of the National Library of Medicine's (NLM) Bibliographic Services Division testified before your Commission, focusing on access to complimentary and alternative medicine (CAM) resources available through NLM databases. He highlighted our collaborative effort with NIH's National Center for Complementary and Alternative Medicine to create CAM on PubMed. Today I will discuss the coverage of CAM journals in MEDLINE, the process by which items are selected for inclusion in our databases, and the expansion of CAM terms in the thesaurus of medical subject headings (MESH).

The users of MEDLINE are many and varied, including researchers, health care practitioners, educators, administrators, and students in this country and abroad. Now that MEDLINE is easily accessible via the World Wide Web, we also count the general public among our main audiences. Our database, therefore, must reflect this diversity and include journals in many disciplines related to the health sciences broadly. Because

#25

much important research is done in other countries, and published in languages other than English, our scope must be worldwide.

MEDLINE has always contained literature concerning complimentary and alternative medicine. Historically, most of the referenced articles were from non-CAM-related journals. However, in recent years more journals with CAM content have been recommended for inclusion in MEDLINE. The expansion of our coverage of CAM literature relied significantly on advice that we received in 1997 from Dr. Jonas when he was head of the NIH National Center for Alternative and Complimentary Medicine (CAM). The Center compiled a list of 695 journals that published most of the articles in the field. NLM then sent the list to 14 organizations specializing in complementary and alternative medicine for their recommendations. Of the 695, it was found that NLM already held in its collection 79 percent of the titles. Six more titles were added to the Library's collection as a result of that initial review.

We currently index in MEDLINE 75 primarily CAM journals. Appendix A provides a sample list showing the range of CAM journals in MEDLINE. It is important to emphasize that in addition to journals specifically devoted to CAM subjects, articles concerning CAM may be selected from any of the 4,500 journals currently indexed in MEDLINE. Indeed, if one searches CAM on PubMed, you will find more than 230,000 citations.

The Library uses a NIH chartered committee, the Literature Selection Technical Review Committee (LSTRC), to review all new journal titles and recommend those to be indexed. The members of LSTRC, whose appointments are approved by the Director of NIH, come from a broad range of fields in biomedicine, allied health, and life sciences.

They include medical scientists and administrators, health practitioners, and librarians. Although some of the reviewers have knowledge of CAM subject matter, we plan to expand our expertise in this field in the future. The Committee also seeks outside expertise, including from professional societies and through collateral reviews.

LSTRC meets three times each year and considers more than 140 journals at each session, regularly including reviews of CAM journals. Primary and secondary reviewers are assigned to each journal. Based upon the ratings assigned by the Committee to each journal, approximately 25-30% are recommended for inclusion in MEDLINE. Each year, NLM also conducts subject reviews and considers all the journals in a particular subject field. Last year the Committee reviewed pharmacology journals and this year they are considering public health journals.

The final selection is based upon my judgement and that of the reviewers, but NLM has published guidelines that provide a consistent set of critical elements that we use in making these decisions. The scientific merit of a journal's content is the primary consideration in the selection of journals for inclusion in the database. The key factors in determining quality are the journal contents' validity, importance, originality, and contribution to the field. Sometimes journals fill a special niche that is not otherwise well covered in the literature.

Another key factor we consider is the editorial quality of the journal. The process by which the journal selects articles, conducts peer review, ensures objectivity, and adheres to ethical guidelines all contribute to the Committee's rating. Production quality also is important. Reviewers look at the quality of the layout, printing, graphics, and illustration of each journal. Lastly, reviewers consider the value of non-U.S. journals that

report on local or regional health conditions. Fifty-five percent of PubMed's use is from outside the United States and today 59 percent of MEDLINE's journals are published outside the United States. While 85 percent of the journals are in English, foreign material on indigenous health conditions and treatments is vital in today's world where we are all more closely connected and health problems arise on a global scale.

If you look at the content of journals indexed in MEDLINE it generally fits into one of the following categories:

1. Reports of original research
2. Original clinical observations accompanied by analysis and discussion
3. Analysis of philosophical, ethical, or social aspects of the health professions or biomedical sciences
4. Critical reviews
5. Statistical compilations
6. Descriptions of evaluations of methods and procedures
7. Case reports with discussions

I hope that this description provides you with an understanding of how NLM selects items, including those with CAM content, for our databases. I would like to conclude my remarks by highlighting a recent NLM initiative to enhance public access to CAM literature that I believe is of interest to the Commission. NLM has funded 53 projects in 34 states and the District of Columbia to provide training in retrieving online health information for professionals in public libraries and other location institutions. Working through our National Network of Regional Medical Libraries, we have expanded the ability of librarians at local libraries to answer patron questions about

resources for health information and to direct them to useful sites on the Internet, such as CAM on PubMed.

We have received a great deal of positive feedback about the value of this effort for introducing the public to reliable, up-to-date health information. Surveys indicate that while most people search for health information on the Web from the privacy of their own homes, they often find out about these online resources through public libraries and other local institutions. We believe that the kind of programs that NLM sponsors for training local public librarians and for expanding consumer outreach will contribute substantially to making the public aware of helpful information concerning complementary and alternative medicine.

Appendix A

Representative Alternative Medicine Titles in Medline

AAOHN Journal; American Association of Occupational Health Nursing
Acta Pharmaceutica Sinica; Yao Hsueh Hsueh Pao
Acta Pharmacologica Sinica; Chung-Kuo Yao Li Hsueh Pao
Acupuncture and Electro-Therapeutics Research
Acupuncture Research; Chen Tzu Yen Chiu; Zhen Ci Yen Yan Jiu
Advances in Mind Body Medicine
Alternative Medicine Review
Alternative Therapies in Health and Medicine
American Journal of Acupuncture
American Journal of Chinese Medicine; Mei-Chou Chung-Kuo I Hsueh Tsa Chih
American Journal of Clinical Nutrition
American Journal of Health Promotion
American Journal of Preventive Medicine
Annual Review of Nutrition
Applied Psychophysiology and Biofeedback
Arzneimittel-Forschung
British Homoeopathic Journal
British Journal of Clinical Pharmacology
British Journal of Nutrition
China Journal of Chinese Materia Medica
Chinese Journal of Integrated Traditional and Western Medicine
Chinese Journal of Preventive Medicine
Chinese Medical Journal
Chiropractic History
Complementary Therapies in Medicine
Complementary Therapies in Nursing and Midwifery
Culture, Medicine and Psychiatry
Drugs under Experimental and Clinical Research
Environmental Health Perspectives
Forschende Komplementarmedizin
Fortschritte der Medizin
Health Affairs
Holistic Nursing Practice
Hospital Medicine
Human Nutrition. Applied Nutrition
Human Nutrition. Clinical Nutrition
Indian Journal of Experimental Biology
Indian Journal of Medical Research
International Journal for Vitamin and Nutrition Research
International Journal of Psychophysiology
International Journal of Psychosomatics
Journal of Alternative and Complementary Medicine

Alternative Medicine Titles in Medline (Continued)

Journal of Chinese Medicinal Materials
Journal of Ethnopharmacology
Journal of Holistic Nursing
Journal of Manipulative and Physiological Therapeutics
Journal of Natural Products
Journal of Nutrition
Journal of Nutritional Science and Vitaminology
Journal of Psychoactive Drugs
Journal of Spinal Disorders
Journal of Substance Abuse
Journal of the American College of Nutrition
Journal of the American Dietetic Association
Journal of the American Osteopathic Association
Journal of Traditional Chinese Medicine
Medical Anthropology
Medical Hypotheses
Metabolism: Clinical and Experimental
Nutrition and Cancer
Nutrition and Health
Nutrition Reviews
Orvosi Hetilap
Pain
Pharmacology, Biochemistry and Behavior
Phytomedicine
Phytotherapy Research
Planta medica
Proceedings of the Nutrition Society
Progress in Clinical and Biological Research
Social Science and Medicine
Veterinary and Human Toxicology
Women and Health
Women's Health Issues

In addition to these 74 journals, another 600-700 journals included in MEDLINE also publish articles in the field of Complementary and Alternative Medicine. For example, these include such titles as Lancet, British Medical Journal, Canadian Medical Association Journal, the Journal of Biological Chemistry, JAMA, and the American Journal of Physiology.

Donald A.B. Lindberg, M.D.
Director
National Library of Medicine

Donald A.B. Lindberg, M.D., a scientist who has pioneered in applying computer technology to health care beginning in 1960 at the University of Missouri, in 1984 was appointed Director of the National Library of Medicine, the world's largest biomedical library (annual budget $246,351 million; 600 career staff). From 1992-1995 he served in a concurrent position as founding Director of the National Coordination Office for High Performance Computing and Communications (HPCC) in the Office of Science and Technology Policy, Executive Office of the President (annual budget $1.1 billion; 12 federal agencies, including DOD, DOE, NSF, NASA, HHS, VHA, DOC, EPA). In 1996 he was named by the HHS Secretary to be the U.S. Coordinator for the G-7 Global Healthcare Applications Project.

In addition to an eminent career in pathology, Dr. Lindberg has made notable contributions to information and computer activities in medical diagnosis, artificial intelligence, and educational programs. Before his appointment as NLM Director, he was Professor of Information Science and Professor of Pathology at the University of Missouri-Columbia. He has a current academic appointment as Adjunct Professor of Pathology at the University of Maryland School of Medicine.

Dr. Lindberg was elected the first President of the American Medical Informatics Association (AMIA). As the country's senior statesman for medicine and computers, he has been called upon to serve on many boards including the Computer Science and Engineering Board of the National Academy of Sciences, the National Board of Medical Examiners, the Council of the Institute of Medicine of the National Academy of Sciences.

Dr. Lindberg is the author of three books: The Computer and Medical Care; Computers in Life Science Research; and The Growth of Medical Information Systems in the United States, several book chapters, and more than 200 articles and reports. He has served as editor and editorial board member of nine publications including the Journal of the American Medical Association.

Dr. Lindberg graduated **Magna cum Laude** from Amherst College and received his M.D. degree from the College of Physicians and Surgeons, Columbia University. Among the honors he has received are Phi Beta Kappa, Simpson Fellow of Amherst College, Markle Scholar in Academic Medicine, Surgeon General's Medallion, recipient of the First AMA Nathan Davis Award for outstanding Member of the Executive Branch in Career Public Service, the Walter C. Alvarez Memorial Award of the American Medical Writers Association, the Presidential Senior Executive Rank Award, Founding Fellow of the American Institute of Medical and Biological Engineering, the Outstanding Service Medal of the Uniformed Services University of the Health Sciences, *Federal Computer Week's* Federal 100 Award, Computers in Healthcare Pioneer Award, Association of Minority Health Professions Schools Commendation, RCI High Performance Computing Industry Recognition Award, U.S. National Commission on Libraries and Information Science Silver Award, Council of Biology Editors Meritorious Award, Presidential Rank Award of Meritorious Executive in the Senior Executive Service, Medical Library Association President's Award, American College of Medical Informatics Morris F. Collen, M.D. Award of Excellence, Johns Hopkins University School of Medicine Ranice W. Crosby Distinguished Achievement Award, New York Academy of Medicine Information Frontier Award, 2001 Cosmos Club Award, Fellow of the American Association for the Advancement of Science, and honorary doctorates from Amherst College, the State University of New York at Syracuse and the University of Missouri-Columbia.

May 2001

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Kamerow

Divider Title: _____

Douglas B. Kamerow, M.D., M.P.H.

Assistant Surgeon General, USPHS

Dr. Douglas Kamerow, an Assistant Surgeon General in the U.S. Public Health Service Commissioned Corps, is currently Director of the Center for Practice and Technology Assessment (CPTA) of the Agency for Healthcare Research and Quality (AHRQ) in Rockville, Maryland. Since October 1994, Dr. Kamerow has led AHRQ's programs to improve the quality of health care in the U.S. through the development and implementation of evidence-based tools. These tools have included the 19 AHRQ clinical practice guidelines, which were widely disseminated and very influential. CPTA's current programs include 12 Evidence-based Practice Centers, the U.S. Preventive Services Task Force, the National Guideline Clearinghouse, and research on implementation of evidence-based recommendations into health care.

Before joining AHRQ, Dr. Kamerow was for six years Director of the Clinical Preventive Services Staff of the PHS Office of Disease Prevention and Health Promotion (ODPHP). He was managing editor of the first and second editions of the report of the U.S. Preventive Services Task Force, the *Guide to Clinical Preventive Services*. He also conceived and directed the development and implementation of the PHS national clinical preventive services education campaign, "Put Prevention into Practice," including editing the first edition of the *Clinician's Handbook of Preventive Services*, published in 1994.

A family physician with training in epidemiology, Dr. Kamerow graduated with honors from Harvard College and received his medical degree from the University of Rochester and a master's degree in public health from Johns Hopkins University. He is board-certified in family practice and in preventive medicine. During his PHS career, Dr. Kamerow also has served as a general practitioner in the National Health Service Corps and as the Director of the Primary Care Research Program of the National Institute of Mental Health (NIMH).

Dr. Kamerow is also the PHS alternate delegate to the American Medical Association's House of Delegates, working with the Surgeon General to present PHS policies and positions to the AMA. He holds the rank of Clinical Professor in the Department of Family Medicine at Georgetown University, where he teaches medical students and family practice residents.

Dr. Kamerow has edited three books and authored or co-authored more than 40 articles, editorials, book chapters, and monographs on evidence-based medicine, guidelines, preventive services, and mental disorders in primary care. He has received numerous awards for his work at AHRQ, ODPHP, and NIMH, including most recently the DHHS Secretary's Award for Distinguished Service, the AHRQ Administrator's Distinguished Service Award, and the Surgeon General's Exemplary Service Medal.

A native of the District of Columbia, Dr. Kamerow lives in Chevy Chase, Maryland with his wife, Celia Shapiro, and their three children.

12/99

AHRQ, CAM, and EBM

Douglas B. Kamerow, M.D., M.P.H.
Assistant Surgeon General
Agency for Healthcare Research and Quality

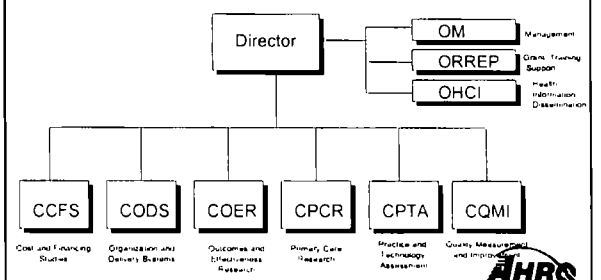
Overview

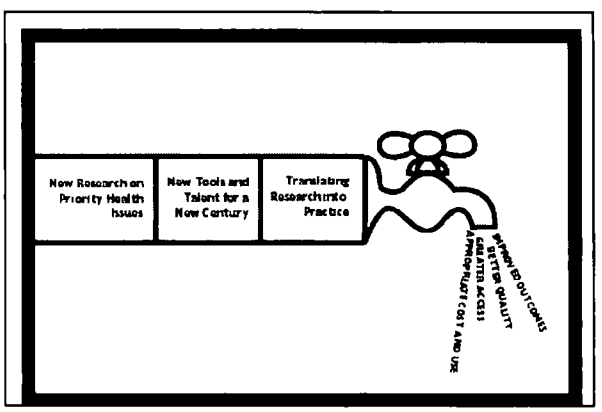
- Agency for Healthcare Research and Quality
- Complementary and Alternative Medicine at AHRQ
- AHRQ's Evidence-based Practice Centers
- EPCs and CAM

AHCPR is Now AHRQ!

- Became official on December 5, 1999 when President signed reauthorization legislation
- Mission: support, conduct, and disseminate research that improves access to care, reduces its cost, and improves the outcomes, quality, and appropriate use of health care services
- Lead Federal agency in improving health care quality through health services research
- FY 2001 budget: $260 million

AHRQ Structure





Overview of AHRQ CAM Activities

- Outcomes and effectiveness research
  - Mainly on back pain, investigating chiropractice and acupuncture
- Surveys
  - Medical Expenditure Panel Survey (MEPS
  - Nationally representative household survey
  - Collecting data on CAM usage by individuals
- Synthesis
  - Evidence-based Practice Centers (EPCs)

Chiropractic

- Chiropractic vs. physical therapy - a randomized trial (included monograph comparing chiropractic and medical school education)
- Low back pain outcomes and efficiency of care (included chiropractic)
- Manual therapy in primary care of acute low back pain
- Chiropractic vs. medical care for low back pain

Acupuncture and Other Alternative Therapies

- Alternative therapies for back pain - a randomized trial (traditional Chinese acupuncture and therapeutic massage)
- Evaluating the efficacy of acupuncture for back pain (pilot study co-funded with NCCAM)
- Acupuncture treatment of depression during pregnancy (pilot study co-funded with NCCAM)

Medical Expenditures Panel Survey (MEPS)

- Annual household survey of 27,000 Americans
- Representative of civilian non-institutionalized population
- Tracks health services and costs
- 1996 data was available in January 2000

MEPS and CAM

- Tracks use of these CAM therapies:
  - Acupuncture
  - Nutritional
  - Massage
  - Herbal
  - Biofeedback
  - Meditation
  - Homeopathy
  - Spiritual
  - Hypnosis
  - Chinese/Indian/ayurvedic

MEPS and CAM

- Counts of use
- Cost of visit
- Allows comparison of use of CAM and conventional therapies

Evidence-based Practice Centers (EPCs)

- Created in 1997
- 12 centers
- Produce evidence reports/technology assessments
- Work with public and private sector partners
- User driven

Evidence-based Practice Centers

- BC/BS
- Duke U.
- ECRI
- Johns Hopkins U.
- McMaster U.
- MetaWorks
- New Eng. Med. Ctr.
- Oregon HSU
- So. Calif. - RAND
- RTI - UNC
- UCSF - Stanford U.
- U. Texas San Antonio

Potential Uses -- To Develop...

- Clinical practice guidelines
- Performance measures
- Quality improvement programs
- Coverage policies

Systematic Reviews

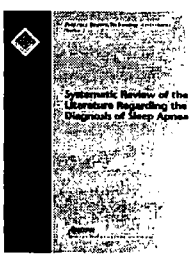
- Concise summaries of the best available evidence addressing sharply defined clinical questions, using explicit and rigorous methods to identify, critically appraise, and synthesize relevant studies (Mulrow C, Cook, D *Systematic Reviews*, ACP, 1998)

Evidence Reports

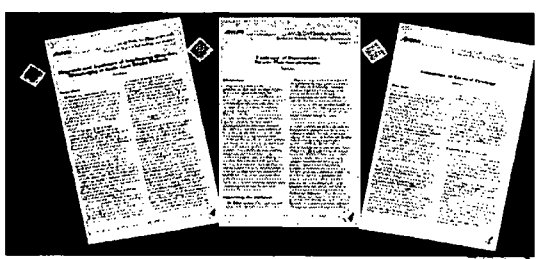
- "Front end" of guidelines, QI programs, coverage decisions
- Focused on a few specific questions
- Systematic and thorough reviews
- Peer reviewed
- Published and widely disseminated

Full Text of EPC Evidence Reports

- Includes all analyses
- Evidence tables and references
- Search strategies
- Available from AHRQ Clearinghouse: 1-800-358-9295



Four-Page Summaries of EPC Evidence Reports



EPCs and CAM

- Sponsored by National Center for Complementary and Alternative Medicine, NIH
  - Routine evidence reports
    - Garlic and heart disease/cancer
    - Milk thistle and liver disease
  - Multi-year task order with RAND
    - Three topics completed, more underway
- Sponsored by the Office of Dietary Supplements
  - Ephedra, others to come

RAND CAM Topics

- Mind-body medicine and gastrointestinal disease
- Ayurvedic medicine and diabetes mellitus
- Methods report on evaluation of non-randomized trials with meta-regression
- More topics in coming year

Uses of AHRQ CAM Evidence Reports

- What works and what has been proven
- What has promise for more research
- Methods and bibliographic research

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Berman

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Brief Biography

BRIAN M. BERMAN, M.D.

University of Maryland School of Medicine
Complementary Medicine Program, Department of Family Medicine
Kernan Hospital Mansion
2200 Kernan Drive, Baltimore, MD 21207-6697
Tel: (410) 448-6871 Fax: (410) 448-6875

Dr. Berman is the founder and director of the Complementary Medicine Program at the University of Maryland School of Medicine and Professor of Family Medicine. Board certified in family medicine and pain management, Dr. Berman has trained extensively in acupuncture and homeopathy and has integrated these therapies into his clinical practice over the past 17 years. He holds a diploma in Traditional Chinese Medicine and, in addition to being a founding member of the American Academy of Medical Acupuncturists, he is a member of the Royal Society of Medicine and the Faculty of Homeopathy in Britain.

Dr. Berman is principal investigator of a National Institutes of Health (NIH) center grant for the study of alternative medicine in the treatment of arthritis and related disorders. He is principal or co-investigator of eight research studies in complementary medicine funded by the NIH, the Department of Defense and private foundations, including a large, multi-site randomized controlled trial of acupuncture in the treatment of osteoarthritis and studies of acupuncture for acute post-operative pain and nausea and vomiting. Interested in investigating the scientific foundation and efficacy of therapies currently outside the mainstream of medicine and evaluating their contribution in the treatment of chronic ailments such as pain, Dr. Berman established the first university-based center in the United States focusing on research, education and clinical care in complementary medicine. He has published widely in the field and was recently awarded the international Seirin award in recognition of his contributions to acupuncture research.

Dr. Berman has served as adviser to the NIH, chairing the first advisory panel to the National Institutes of Health Office of Alternative Medicine (NIH-OAM) and participating as a member of the NIH Alternative Medicine Program Advisory Council for six years. In addition, he chaired the NIH-OAM editorial board for its 350-page report, *Alternative Medicine: Expanding Medical Horizons*. Dr. Berman also serves as Field Coordinator for the Complementary Medicine Field of the international Cochrane Collaboration, an organization dedicated to evaluating all medical practices.

Brian M. Berman M.D.
Professor of Family Medicine
Director, Complementary Medicine Program
University of Maryland School of Medicine

PRESENTATION TO THE WHITE HOUSE COMMISSION ON COMPLEMENTARY AND ALTERNATIVE MEDICINE POLICY
May 15, 2001

Mr. Chairman and members of the Commission, I am extremely honored to be given the opportunity to speak with you today on the evaluation of complementary and alternative medicine (CAM) research literature and the role of the Cochrane Collaboration, as well as research training for CAM practitioners and the integration of CAM research into conventional academic health centers.

I am a board certified family practitioner and pain management specialist with extensive training and clinical experience in a variety of CAM modalities. I am also Director of the University of Maryland Complementary Medicine Program and Principal Investigator of a National Institutes of Health (NIH)-funded Specialized Center of Research in CAM as well as a PI & co-investigator on a number of NIH-funded clinical trials. As such, I am both a clinician and a scientist. As I speak to you today I will mainly be wearing my research hat. One of the main areas of focus of our center at the University of Maryland is the investigation of the safety, efficacy and mechanism of CAM therapies for pain-related problems. We design and conduct original, rigorous research trials, in addition to systematically distilling the best evidence available worldwide and communicating these results to the clinical, scientific and public communities. The first half of my presentation will address the importance of the work in systematically reviewing the CAM scientific literature.

Evaluation of CAM Research Literature and the Role of the Cochrane Collaboration

The Cochrane Collaboration is an international organization founded in 1993 that prepares, maintains and disseminates systematic, up-to-date reviews of health care interventions. It was started in response to the challenge made by Archie Cochrane, an eminent British epidemiologist, that people who want to make informed decisions about healthcare do not have ready access to reliable reviews of the available evidence.

The aims of the Collaboration are to provide information that is:

- Evidence-based
- Easily accessible
- Internationally developed
- Quality controlled
- Clinically useful
- Periodically updated

The Collaboration is being built on nine principles:

- Collaboration
- Building on the enthusiasm of individuals
- Avoiding duplication
- Minimizing bias
- Keeping up to date
- Ensuring relevance
- Ensuring access
- Continually improving the quality of its work
- Continuity

The significance of the work of the Collaboration to medicine has been compared to that of the Human Genome Project. Not only does it provide an invaluable service in overcoming "the great collective ignorance about the effects of health care" (Archie Cochrane), it also provides invaluable information to guide future research efforts.

The Cochrane Library

One of the main outputs of the Collaboration is the Cochrane Library which includes several databases:

- *The Cochrane Database of Systematic Reviews* contains Cochrane systematic reviews.
- *The Cochrane Controlled Trials Register* is a bibliographic database of controlled trials.
- *The Database of Abstracts of Reviews of Effectiveness (DARE)* includes structured abstracts of systematic reviews which have been critically appraised by reviewers.
- *The Cochrane Review Methodology Database* is a bibliography of articles on the science of research synthesis.
- *Reviewers' Handbook* on the science of reviewing research.
- *Glossary* of methodological terms and Cochrane jargon; and contact details for review groups and other groupings in the Collaboration.

At present there are 1081 reviews and 307,872 trials in the Reviews Database and the Registry and 2793 abstracts in DARE, an amazing achievement for an organization that has not yet celebrated its 8th birthday! The Library is available electronically.

The Complementary Medicine Field

In 1996, through the interest of a number of researchers from countries around the globe and the encouragement of Wayne Jonas (Director at the time of the NIH- Office of Alternative Medicine), a Complementary Medicine Field was registered within the Collaboration. The purpose of the Field is to 1) ensure the priorities and perspectives of CAM are reflected in the work of collaborative review groups; 2) compile a database of CAM reviews; 3) compile a registry of trials in CAM for uploading to the central Cochrane Registry, 4) coordinate activities with relevant agencies outside the Collaboration; and 5) comment on systematic reviews relating to CAM. The Field is

coordinated by our Center at the University of Maryland and we now also maintain the CAM Registry. The work of the Field has received support from NCCAM.

The Cochrane CM Field Trials Registry

The CAM Trials Registry has been a significant undertaking since it aims to be inclusive of all randomized controlled trials in CAM, published or unpublished, in any language. Many of the trials and tribulations of finding relevant studies are outlined in an article about the CM Field published in JAMA in 1998. Challenges have included 1) the difficulty of capturing all CAM studies through MEDLINE (and other electronic medical database) searches due to factors such as the limited scope of practices defined by MEDLINE as alternative medicine and the limited number of journals containing CAM literature that have been indexed by MEDLINE, 2) the need to identify and search electronic databases world-wide that may contain CAM literature, and 3) the need to hand-search journals that are published around the world. As part of our effort to increase accessibility of CAM literature, members of the Field have worked with the National Library of Medicine to make recommendations to improve the number of CAM journals indexed by MEDLINE and to make their Medical Subject Headings indexing system more sensitive and precise for searching on CAM. There are now over 5300 randomized controlled trials and controlled clinical trials in the Cochrane CM Trials Registry.

Criteria for Inclusion as CAM

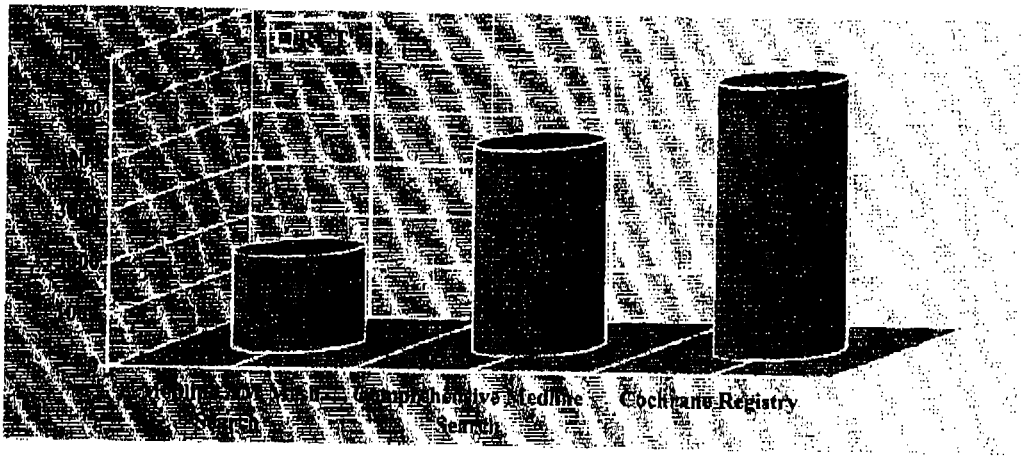
The criteria used in our selection process with regard to CAM topics is based on the definition of CAM developed at the April 1995 NIH, OAM Methodology Conference:

"CAM is a broad domain of healing resources that encompasses all health systems, modalities and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period. CAM includes all such practices and ideas self-defined by their users as preventing or treating illness of promoting health and well-being. Boundaries within CAM and between the CAM domain and that of the dominant system are not always sharp or fixed."

However, since this definition does not necessarily guide decisions about whether an intervention falls under the rubric of CAM, we use the definition as an inclusion criteria and have developed three exclusion criteria. An intervention will be excluded from the Cochrane CAM registry if it meets two of the criteria:

1. Is the intervention, when practiced in this manner, at this dose, with these patients, almost exclusively practiced by those with "conventional medical qualifications"?
2. Is the intervention when practiced in this manner, at this dose, with these patients, a recommended treatment (i.e. a significant number of standard medical or paramedical references refer to use of the therapy as routine)?
3. Does the intervention fail to involve any theoretical divergence with mainstream medicine or science?

In Addendum 1 you will find the CAM search strategy that we have developed for MEDLINE, which also gives an overview of therapies that Cochrane considers to fall under the rubric of CAM. The value of this search strategy is demonstrated in the following graph, comparing the number of trials captured through three different search strategies. The left column reflects a search of MEDLINE using just the "Alternative Medicine" medical subject heading (MeSH) combined with "Randomized Controlled Trial" as a publication type. The middle column is a comprehensive MEDLINE search using the much broader Cochrane defined Complementary Medicine thesaurus and search strategy. The right column reflects a search using the Cochrane Complementary Medicine thesaurus and search strategy on multiple databases as well as conducting hand searches of non indexed journals, conference proceedings and abstracts



Systematic Reviews

Having identified all existing relevant literature, the next step is to conduct systematic reviews which will synthesize the results of these primary investigations. Systematic reviews are concise summaries of the best available evidence that address sharply defined clinical questions. The process of conducting a review is outlined in the following steps:

1. A well-formulated question is asked
2. A comprehensive search is conducted to identify all potentially relevant articles
3. Articles that meet explicit, reproducible criteria are selected
4. The study design and characteristics of each trial are critically appraised – there are 9 checklists and at least 25 different scales for assessing trial quality
5. The data are synthesized
6. The results are interpreted
7. A structured report is written
8. The review is updated periodically as new studies are identified

Looking specifically at steps 3 & 4, a clearly formulated question helps define the criteria that studies must meet to be included in the review. These inclusion criteria can be divided into five categories: 1) type of person (including disease, personal characteristics, population); 2) type of intervention; 3) type of control; 4) type of outcome; 5) type of

study design. In evaluating the quality of the studies Cochrane uses scales, such as the Jadad and Oxman scales, with close attention paid to the recently revised Consort statement published in JAMA, April 18th, 2001. Of particular importance are the randomization process, allocation concealment, and masking (blinding) issues as well as whether there was adequate follow-up and attention to drop-outs. It is well recognized that poorly designed trials can exaggerate treatment outcomes and give misleading information on effectiveness. Likewise, poorly conducted reviews can be misleading, hence the emphasis on a systematic process to minimize error and bias.

There are now 208 systematic reviews in the Cochrane CM Field Reviews Registry. A list is attached (Addendum 2) but reviews range from topics such as acupuncture for low back pain, to echinacea for the prevention and treatment of the common cold.

What Use are Reviews to Us?

The value of a systematic review is that it helps keep us up to date. For consumers, systematic reviews can help cohere conflicting results of research. Policymakers can draw on systematic reviews when developing practice guidelines or conducting risks assessments and economic analyses. Practitioners (already overwhelmed at the number of journals published every year and the daunting task of synthesizing all this information so it is of use to them) can use reviews to answer specific clinical problems. Does this therapy work? Is it safe? Will it be safe and effective for my patient? Researchers can use reviews to define research agendas, summarize the existing data, refine their hypotheses and estimate sample sizes. What reviews cannot do is replace sound clinical reasoning. Knowledge, skills, values and research evidence need to be integrated into each patient clinical encounter. Reviews provide the quality evidence to this mix: evidence that is generated systematically, refined through a comments and criticisms process, and that is kept up to date on a regular basis.

The Value of Reviews – A Brief History in Time

As an example of the impact a systematic review can have there is an interesting short tale about the history of St. John's Wort in the U.S. St. John's Wort was until recently a little known herb in this country. In 1996, however, a founding member of the Cochrane CM Field, Klaus Linde, and some colleagues published a systematic review in the British Medical Journal showing the anti-depressant effects of St. John's Wort. Six months later the television show 20/20 used the review as the basis for a program. By 1997, St. John's Wort had gone from being well below the 20 best selling herbs to being one of the top 10. It reached the radar screen of the NIH and in 1998 they funded a multi-center Phase III clinical trial of St. John's Wort for severe depression. Had Linde never published his review the latter part of this story probably would still not have happened. Most of the literature showing the safety and effectiveness of this herb was published in non-English journals and no-one had ever gathered together this information to critically appraise it and draw out its clinical findings.

The Role of the Consumer in the Cochrane Collaboration

The Collaboration puts a high priority on consumer input throughout all levels of activity, from identifying important questions to commenting on drafts of reviews and helping disseminate results. As a whole, the Collaboration is a highly successful model of international cooperation and, especially in countries such as the United Kingdom, a model of participatory research among consumers, policymakers, investigators and clinicians.

Within the CM Field, our consumer representative, Claire Allen, has been very active in helping reviewers make their reviews more consumer friendly and composing lay summaries. These consumer related changes are timely – since 1999 all Cochrane abstracts of completed reviews appear in MEDLINE. Claire has also been involved with surveying consumers to identify obstacles to becoming involved with Cochrane.

Policy Recommendations Regarding the Evaluation of Research Literature in CAM

The work of the Cochrane CM field and CAM literature evaluation has only just begun. The effort in producing systematic reviews needs to continue and the scope of the work and its impact needs to be broadened. Specifically, I recommend that the infrastructure and collaborative work of the Cochrane CM Field be allocated on-going support allowing for continued maintenance of the registry, and coordination of the Field. With sufficient support the Field can increase its current work and significantly add to its value by:

1. Increasing the availability of reviews and their potential value by:
    a. Making them available in the offices of policymakers, in public libraries and community health centers through on-line subscription to the Cochrane Library.
    b. Developing executive summaries of systematic reviews that clearly and concisely state the results of the reviews.
    c. Developing electronic, jargon-free versions of systematic reviews with hypertext links to allow readers with various backgrounds to access information at different levels of complexity
    d. Expanding the current CM Field web-site (www.compmed.ummc.umaryland.edu) to include access to review summaries and to include consumer-friendly information.
2. Increasing participatory approaches to research in this country to ensure knowledge for action, in contrast to knowledge for understanding.
3. Identifying the public's needs through working with organizations such as the NCCAM Clearinghouse
4. Commissioning topics for reviews so that the questions addressed and the information developed are relevant to users of these treatments
5. Developing methodologies to evaluate non-randomized controlled trials, thus broadening the pool of information that can be drawn from.

With support in the region of $500,000 a year the Field would be able to undertake an ambitious program of generating and disseminating high quality information to the public

The Challenge of Integrating CAM Research into Conventional Academic Institutions and the Training of CAM Practitioners as Research Investigators

The second half of my presentation is focused around issues relative to ensuring that research in CAM meets the highest scientific standards. A great deal of research is needed in this field and to accomplish this task we must tap into the resources of our country's academic institutions, for the infrastructure they provide as well as their intellectual wealth. At the same time, we need to ensure that those involved in CAM research are knowledgeable about the therapies they are investigating and cognizant of their unique paradigms.

Our center at the University of Maryland has been in existence now for 10 years so we are well aware of the challenges of bringing CAM research into an academic medical setting. I would like to emphasize, however, that taking an evidence-based approach to CAM has been the basis of our success in developing positive relationships within the institution. Through research collaborations with colleagues in Departments such as Epidemiology, Medicine and Pediatrics as well as the Schools of Dentistry, Pharmacy and Nursing, we have built a large clinical and pre-clinical trials program. Just as importantly, we have built up trust and respect and nurtured a common curiosity in finding out what works and what doesn't and how this translates to improving the care of our patients.

Lack of knowledge and understanding of CAM among the conventional medical community is perhaps one of the first challenges facing any CAM initiative in a medical school or university. There is still a lot of bias against CAM and unwillingness to look at these therapies. Also, at times, if there is willingness, the interest can be driven more by chasing sources of funding. This latter scenario can lead to the unfortunate event of a highly experienced researcher designing and being funded for a study that is not sensitive to the manner in which a therapy is practiced. In addition, researchers may not have a good understanding of what are the key questions that need to be answered.

Another issue that relates to the above points is the importance of a clinical base in order to build a program of clinical research in CAM. At our own center we have a fully functioning out-patient clinic staffed by practitioners dual-trained in conventional medicine and CAM as well as highly qualified CAM practitioners. We have found the clinic to be vital as a nurturing-ground for research questions that are firmly based in clinical reality. However, establishing a clinic of this sort within an academic medical environment is not always welcomed or readily supported by the institution.

Complementary medicine research has suffered from the lack of CAM practitioners who are knowledgeable about research. The value of an academic-based center is the possibility of developing a team approach to designing and conducting rigorous CAM studies that draws on the expertise of methodologists, clinicians and CAM practitioners.

Nonetheless, the role of these centers should also be to train CAM practitioners to become skilled CAM researchers. These researchers, in turn, will ensure the future leadership of the field.

Even with the best team and with highly skilled CAM investigators, there are many practical issues, common to almost all research, in conducting well-designed studies. First, there is the issue of limited funding resources for the type of large, multi-center trials that are needed. Some of the many challenges then of seeing the research trials through to their conclusion include: availability of adequate space to run the studies; the large amount of paperwork required by Institutional Review Boards and funding bodies; and the difficulty of keeping patients invested in the study especially if they are randomized into an arm of the study that does not include the CAM intervention.

Recommendations

Good science is the key component to evaluating the role CAM can and should play in the health care of Americans. In turn, education and training are key components in creating a community dedicated to rigorous evaluation of CAM. I have a number of recommendations for achieving these aims:

1. Fund a network of centers of excellence at academic institutions dedicated to the investigation of CAM. (Work of this sort has already been started by NCCAM and is creating the infrastructure necessary to support large and far-reaching research programs as well as educate and train a growing pool of investigators dedicated to the CAM field. The scope and number of these centers needs to grow)
2. Encourage collaboration between the CAM community, government, industry, philanthropy, and academic health centers through forged partnerships and joint funding.
3. Fund career development initiatives that would include.
    a. Research fellowships that include didactic teaching and hands-on training with appropriate mentoring aimed at creating skilled CAM clinical researchers.
    b. Master's of science degree in epidemiology with a CAM clinical research track, providing broad, rigorous training in research methods, closely mentored research experience and a specific focus on CAM interventions in a two year curriculum.
    c. Critical appraisals training focused on finding and assessing the scientific literature
    d. A national core curriculum in CAM for conventionally trained practitioners (including medical students, residents, pharmacists, nurses)
    e. CAM "tracks" at medical schools and in residency programs allowing interested individuals to focus on CAM. Ideally, both (d) and (e) would include experiential elements; history, philosophy and clinical uses of therapies; finding and assessing the evidence; self-care; and methodological issues in CAM research.

   f. The creation of a centralized database of curriculum topics and informational material to facilitate integration of CAM into existing courses
4. Encourage the NIH to continue funding and expand evaluation of CAM as well as research training initiatives.
5. Support of technology assessment workshops.

ADDENDUM 1

Cochrane Collaboration
MEDLINE Search Strategy for Complementary and Alternative Medicine

Therapies which are undeniably complementary medicine but which may not be clearly described as such in trial reports

1 ACUPUNCTURE
1.1 Insertion of an acupuncture needle
1.2 Stimulation by any modality of a recognised acupuncture point
1.3 Stimulation by any means other than manual pressure of a trigger point, defined as a locus in a muscle of increased tenderness.
2 HOMOEOPATHY
2.1 Administration of any remedy described as homoeopathic or produced by serial dilution and agitation
3 HERBAL MEDICINE (INCLUDES AROMATHERAPY)
3.1 Administration of any form product derived from plant or fungal material, including essential oils (aromatherapy).
3.2 Any product with fewer than 5 identified chemical constituents derived from plant sources will be excluded.
4. MANIPULATIVE THERAPIES: OSTEOPATHY AND CHIROPRACTIC
4.1 Any intervention brought about by the hands directly on the patient's body where the practitioner is identified as a chiropractor, osteopath or manual therapist
4.2 Manipulation or mobilisation of any bone
4.2.1 Treatments of a break, fracture or dislocation will be excluded
4.2.2 Concomitant use of general or local anaesthetic will be excluded
4.3 Sustained contact between the practitioners hands and the subject's cranium or sacrum.
4.4 Any technique described as cranial therapy / osteopathy, cranio-sacral therapy / osteopathy
5. MASSAGE
5.1 Any form of soft-tissue manipulation in which the intended effects are non-specific, that is, they are intended to bring about general improvements in health
5.2 Use of any of the following techniques: effleurage, gentle stroking, soft-tissue manipulation, myofascial release, sports massage, connective tissue massage, Bidegewebsmassage, caring touch, Hellerwork, Trager, Zero Balancing, Rolfing, Structural integration, Functional integration, Feldenkrais, Bowen therapy, neuromuscular technique, muscle energy techniques, proprioceptive neuromuscular facilitation, contract-relax / hold-relax, post-isometric contraction, strain counterstrain, shiatsu, acupressure, bioenergetics, manual stimulation of trigger points (see above), mechanical massage tools.
5.3 An intervention brought about by the hands directly on the patient's body where the practitioner is identified as a massage or body work therapist or a practitioner of any of the techniques mentioned in 5.2
6. HYPNOSIS
6 1 Induction of any mental state described as hypnotic by non-pharmacological means. The state can be induced by the subject him or herself.

6.2 Use of verbal suggestions by another whilst the subject is in a mental state thought to be receptive to suggestion, for example, in deep relaxation or under anaesthesia.
7. RELAXATION AND MEDITATION TECHNIQUES
7.1 Any method in which the subject undertakes mental exercises in order to reduce mental and / or physical arousal.
7.2 Any method in which the subject changes posture or breathing in order to reduce mental and / or physical arousal
7.3 Use of any of the following techniques: Jacobsen, sequential muscle relaxation, Mitchell method, autogenic training, visualisation, therapeutic imagery, tai chi, chi gong
8. HEALING AND THERAPEUTIC TOUCH
8.1 Attempts to bring about healing by an effort of will
8.2 Manipulation of an unspecified form of energy or aura for healing purposes by placing hands on or near the subject's body.
9. REFLEXOLOGY
9.1 Manual stimulation of points on the foot thought to correspond to the organs and structures of the body
10 IRIDOLOGY
10.1 Diagnosis of disease and dysfunction in organs other than the eye by analysis of characteristic markings of the iris.
11 ALEXANDER TECHNIQUE
11.1 Therapy designed to increase awareness and voluntary inhibition of personal habitual patterns of rigid musculoskeletal constriction
12 KINESIOLOGY
12.1 Diagnosis of non-musculoskeletal disease and dysfunction by looking for patterns of muscle weakness
13 ANIMAL EXTRACTS
13.1 Administration of any form of product derived from animal material
13.2 Any product with fewer than 5 identified chemical constituents derived from animal sources will be excluded
13.3 Any product used to provide specified compounds which are part of a necessary diet will be excluded
14. CANCER OR AIDS TREATMENT
14.1 Interventions offered by any institution self-defined as alternative or unconventional or which treats cancer or AIDS without drugs, surgery or radiotherapy

Therapies which can sometimes be described as complementary medicine

I. NUTRITION
I.I Any form of supplementation with vitamins, minerals or fatty acids to treat or prevent disease apart from:
I.I.I Treatment of deficiency disease (defined as any disease caused by levels of intake of a nutrient which are persistently lower than RDA)
I.I.II prevention of neural tube defects
I.I.III treatment of premature infants
I.I.IV treatment of cancer with b and d vitamin derivatives
I.I.V treatment and prevention of osteoporosis with calcium vitamin D
I.I.VI vitamin e or essential fatty acids to treat dermatological conditions
I.I.VII essential fatty acids to treat or prevent cardiovascular disease
I.I.VIII magnesium supplementation for cardiovascular disease
I.I.IX treatment and prevention of measles using vitamin A
I.I.X prevention of eye disease

I.I.XI prevention of cancer in those not at increased risk
I.I.XII treatment of insulin dependent diabetes mellitus
I.I.XIII treatment of disease in developing countries
I.II Elimination of any food from the diet other than when that food is not thought to cause disease by conventionally understood allergic mechanisms or by raising or reducing levels of an identifiable substance in the body apart from:
I.II.I Treatment or prevention of coeliac disease, ulcer
I.III Adherence to any of following diets: Hay, Dong, macrobiotic, high fibre for weight loss, Cambridge, vegetarian, vegan, "stone age", raw foods, essential fatty acid diet for multiple sclerosis

II PSYCHOLOGICAL INTERVENTIONS
II.I Any form of talking therapy, counselling or social support other than:
II.I.I treatment of any form of mental health problem including problem behaviour (eg. obesity)
II.I.II peer support / self-help groups
II.I.III non-specific social support

III HYDROTHERAPY
III.I Bathing in water in which salts or plant products have been added
III.II Bathing in water chosen because of a high-concentration of salts
III.III Bathing in natural springs and spas
III.IV Bathing in alternatively warm and then cool water or hot air and cool water.
III.V Any of the following: sitz baths, wraps, hydrogalvanic baths, carbon dioxide baths, underwater jet massage, mud packs, hyperthermia.

Complementary Medicine Field Search Strategy

Terms in italics are excluded

001 tai chi.tw.
002 qigong.tw.
003 yoga.tw.
004 yoga/

005 reflexology.tw.

006 therapeutic touch.tw.
007 spiritual healing.tw.
008 faith healing.tw.

"pnf" is short for "proprioceptive neuromuscular facilitation" a technique used by many manual therapists. However, it is also an abbreviation for a variety of phosphorylated compounds and for "primary nonfunction", a problem in transplantation
009 pnf.tw.
010 *phosphorylated.tw.*
011 *primary nonfunction.tw*
012 *exp transplantation/*
013 10 or 11 or 12
014 9 not 13

015 proprioceptive neuromuscular facilitation.tw.

016 effleurage.tw.
017 soft tissue manipulation.tw.
018 myofascial release.tw.
019 aston patterning.tw.
020 connective tissue massage.tw
021 bidegewebsmassage.tw.
022 caring touch.tw.
023 hellerwork.tw.
024 trager.tw.
025 bowen therapy.tw.
026 bowen technique.tw.
027 neuromuscular therapy.tw
028 bowen work.tw.
029 muscle energy technique$.tw
030 neuromuscular facilitation.tw.
031 shiatsu.tw.
032 zero balancing.tw.
033 rolfing.tw.
034 structural integration.tw.
035 functional integration.tw.
036 acupressure.tw.
037 trigger point$.tw.
038 post isometric contract$.tw.
039 contract relax.tw.

040 hold relax.tw.

041 *relaxation/
042 *autogenic training/
043 exp *hypnosis/
suggestion

044 iris diagnosis.tw.
045 iridolog$.tw.

046 shark cartilage.tw.

047 exp *tissue extracts/tu
actihaemyl
cell extracts
liver extracts
pancreatic extracts
pancreatin
placental extracts
thymus extracts

048 *bees/

bee venoms are conventionally used in "immunotherapy".
049 exp *bee venoms/ad,tu
050 *immunotherapy/*
051 *anaphylaxis/*
052 *desensitization, immunologic/*
053 50 or 51 or 52
054 49 not 53

055 *honey/

056 alexander technique.tw.

057 hoxsey.tw.
058 gerson.tw.

059 qi gong.tw.
060 chi kung.tw.
061 chikung.tw.

062 doman delcato.tw.

patterning and conductive education are forms of treatment for brain damaged children
063 patterning.tw.
064 exp *brain damage, chronic/
065 conductive education.tw.
066 (63 or 65) and 64

067 unani.tw.
068 flower remed$.tw.
069 vega test$.tw.

Colonic irrigation is an alternative modality but is used sometimes during surgery or for the treatment of intestinal disease
070 colonic irrigation.tw.
071 *exp surgery, operative/*
072 *exp intestinal diseases/*
073 71 or 72
074 70 not 73

075 *sensory deprivation/
076 restricted environmental stimulation therapy.tw.
077 vitalism/

This bit was a mistake and is corrected nearer the end.
078 *terpenes/ad,tu
079 exp *vitamins/tu,ad
080 exp *retinoids/tu,ad
081 squalene/
082 exp *carotene/
083 exp *antioxidants/
084 or/79-83
085 78 not 84

Some physical therapy procedures are used in complementary medicine

086 exp *physical therapy/
- balneology
  - ammotherapy
- baths
  - baths, finnish
  - mud therapy
- *cryotherapy*
  - *cryosurgery*
- *drainage, postural*
- *electric stimulation therapy*
  - electroacupuncture
  - transcutaneous electric nerve stimulation
- *exercise therapy*
- *motion therapy, continuous passive*
- hydrotherapy
- *hyperthermia, induced*
  - *ammotherapy*
  - *diathermy*
  - *short-wave therapy*
  - *ultrasonic therapy*
- manipulation, orthopedic
- massage
  - acupressure
- *photochemotherapy*
  - *hematoporphyrin photoradiation*
  - *puva therapy*
- photopheresis
- *phototherapy*
  - color therapy
  - heliotherapy
  - ultraviolet therapy
- *rewarming*
- thalassotherapy

These are the ones we are removing

087 *exp *rewarming/*
088 *exp *photochemotherapy/*
089 *exp *postural drainage/*
090 *exp *cryotherapy/*
091 *motion therapy, continuous passive/*
092 *exercise therapy/*
093 *exp phototherapy/*
094 *exp hyperthermia, induced/*
095 **physical therapy/*

Take out orthodpedic manipulation where associated with treatment of fractures or dislocations

096 *manipulation, orthopedic/
097 *exp *fractures/*
098 *exp *dislocations/*
099 97 or 98

Take out water birth

101 *baths/
102 *exp *delivery/*
103 *exp *labor/*
104 102 or 103
105 101 and 104
106 natural childbirth/

107 exp alternative medicine/
alternative medicine
acupuncture
acupuncture anesthesia
acupuncture therapy
acupuncture analgesia
electroacupuncture
meridians
anthroposophy
aromatherapy
"biofeedback (psychology)"
chiropractic
color therapy
diet fads
eclecticism
electric stimulation therapy
electroacupuncture
transcutaneous electric nerve stimulation
homeopathy
"imagery (psychotherapy)"
kinesiology, applied
massage
acupressure
medicine, traditional
medicine, african traditional
medicine, arabic
medicine, unani
medicine, ayurvedic
medicine, herbal
medicine, unani
medicine, oriental traditional
medicine, chinese traditional
shamanism
mental healing
"mind-body relations (metaphysics)"
moxibustion
music therapy
naturopathy
organotherapy
tissue therapy
radiesthesia
reflexotherapy
rejuvenation
relaxation techniques
meditation
therapeutic touch

108 osteopathic medicine/
109 oils, volatile/
110 exp plants, medicinal/
aloe
areca
arnica
artemisia
belladonna
cannabis
capsicum
cinchona
coca
colchicum
digitalis
erythrina
eucalyptus
ferula
garlic
ginseng
legumes
acacia
cassia
glycyrrhiza
mustard
papaver
plantago
podophyllum
rauwolfia
rhamnus
rhubarb
stramonium
valerian
veratrum
viscum
111 exp plant extracts/
cascara
curare
drugs, chinese herbal
guaiac
"ipecac (syrup)"
podophyllin
podophyllotoxin
etoposide
psyllium
senna
tragacanth
turpentine
112 exp plant oils/tu,ad
castor oil
corn oil
cottonseed oil
croton oil
iodized oil
ethiodized oil
linseed oil
safflower oil
sesame oil
soybean oil

Take out studies on chemistry, classification, genetics, ultrastructure or virology of edible plants. Take out studies on plants related to food industry. Take out immunotherapy (which may use plant extracts)

113 *exp *plants, edible/ch,cl,ge,ul,vi*
114 *exp *food services/*
115 **immunotherapy/*
116 or/109-112
117 or/113-115
118 116 not 117

Take out cannabis and areca (betel nut) where this is the disease not the treatment
119 cannabis/
120 areca/
121 *exp *substance use disorders/*

122 (119 or 120) and 121

Take out carotid and ocular massage and treatment of pressure sores
123 **carotid body/*
124 **intraocular pressure/*
125 **glaucoma/*
126 *exp *carotid arteries/*
127 **decubitus ulcer/*
128 *carotid.tw.*
129 *or/123-128*
130 *massage.ti,ab,sh. and 129*

Take out studies which are about bees, rather than their therapeutic use
131 **bees/ah,ch,cl,em,ge,gd,ph,re,ul,vi*

Take out podopyllotoxins and pancreatin which are conventional drugs.
132 *exp podophyllotoxin/*
133 **pancreatin/*

This bit does the physical therapy search
134 *or/87-95,100,105*
135 86 not 134

Take out a variety of other things
136 **dietary fiber/*
137 *electric stimulation therapy/*
138 *immunotherapy.tw.*
139 *exp iodized oil/*
These bits connect up the various bits of the search. 140 is what we do want, 141 what we don't.

140 or/1-8,14-48,54-62,66-69,74-77,85,106-108,118,135 83
141 or/122,130-133,136-139

Terpenes are substances derived from plants. Some, like certain vitamins, squalene, retinoids etc. are conventional drugs.
142 exp *terpenes/ad,tu
- cannabinoids
  - cannabidiol
  - cannabinol
  - tetrahydrocannabinol
- *carotenoids*
  - *bacterorhodopsin*
  - *carotene*
  - *beta carotene*
- canthaxanthin
- xanthophyll
- diterpenes
  - aphidicolin
  - dolichol
    - dolichol phosphates
  - forskolin
  - phorbols
    - phorbol esters
  - phytanic acid
  - phytol
- *retinoids*
  - *acitretin*
  - *etretinate*
  - *fenretinide*
  - *isotretinoin*
  - *retinaldehyde*
  - *tretinoin*
  - *vitamin a*
- eugenol
- gefarnate
- menthol
- norbornanes
  - bornanes
  - camphor
  - mecamylamine
  - toxaphene
- polyisoprenyl phosphates
  - dolichol phosphates
- polyisoprenyl phosphate sugars
- polyisoprenyl phosphate monosaccharides
  - dolichol monophosphate mannose
- polyisoprenyl phosphate oligosaccharides
- pyrethrins
  - allethrin
- sesquiterpenes
  - farnesol
  - santonin
- trichothecenes
- t- toxin
- trichodermin
- thapsigargin
- thymol
  - bromthymol blue
- triterpenes
  - glycyrrhetinic acid
  - carbenoxolone
  - gossypol
  - sapogenins
  - oleanolic acid
  - *squalene*

143 *exp *vitamins/ad,tu*
144 *exp *retinoids/ad,tu*
145 *squalene/*
146 *exp *carotene/*
147 *exp *antioxidants/*
148 or/143-147
149 142 not 148

150 exp *herbs/
151 140 or 149 or 150
152 151 not 141

152 is the total search for complementary medicine

All the folowing is the cochrane search for clinical trials

153 randomized controlled trial.pt
154 controlled clinical trial.pt.
155 randomized controlled trials.sh.
156 random allocation.sh.
157 double blind method.sh.

158 single blind method.sh.
159 or/153-158
160 (animal not human).sh
161 159 not 160
162 clinical trial.pt.
163 exp clinical trials/
164 (clin$ adj25 trial$).ti,ab.
165 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mas
166 placebos.sh.
167 placebo$.ti,ab.
168 random$.ti,ab.
169 research design.sh.
170 or/162-169
171 170 not 160
172 171 not 161
173 comparative study.sh.
174 exp evaluation studies/
175 follow up studies.sh.
176 prospective studies.sh.
177 (control$ or prospectiv$ or volunteer$).ti,ab.
178 or/173-177
179 178 not 160
180 178 not (161 or 172)
181 161 or 172 or 180

Combine complementary medicine and cochrane search
182 152 and 181

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Complementary Medicine and the Cochrane Collaboration

EVERY YEAR, millions of US consumers spend billions of dollars on alternative and complementary medical treatments.[1] A similar trend exists in the United Kingdom and Australia.[2-4] As people increasingly use these treatments, questions arise from consumers, clinicians, payers, and policymakers as to the effectiveness of these interventions.

The Cochrane Complementary Medicine Field

To meet the increasing demand for evidence-based complementary medicine (CM), a CM Field, funded by the National Institutes of Health Office of Alternative Medicine, was established within the Cochrane Collaboration[5] in 1996. The goal of the Cochrane Collaboration is to produce, maintain, and disseminate systematic reviews on all topics in health care. The CM Field focuses on CM topics. Two major products of the Cochrane Collaboration are a database of systematic reviews and the Cochrane Controlled Trials Registry, the largest registry of its kind.[6] Both databases are updated quarterly with information added regularly by the CM Field.

The systematic review is a method par excellence for synthesizing evidence on a given topic, and policy agencies are increasing use of it to summarize evidence.[7] Cochrane reviews are more transparent than other reviews,[8] so that conclusions are replicable and methods are explicit. Systematic reviews are valuable even when the results are inconclusive because reviews point out where knowledge gaps exist.

Search Strategies to Retrieve Randomized Trials of CM

Since the CM Field has been functioning, a great deal of effort has focused on laying the groundwork for reviews by con-

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structing a database of randomized controlled trials (RCTs) on CM topics. Capturing all relevant trials in MEDLINE has yielded surprising challenges. The scope of practices defined as complementary within the CM Field is broader than those captured in a MEDLINE search of the term *alternative medicine*. For example, Chinese movement therapies such as Qigong and Tai Chi are considered complementary therapies by the Field's standards, but are not accessed by a hierarchical MEDLINE search of the term *alternative medicine*. Similarly, herbal remedies may be described by MEDLINE as plant extracts rather than by any alternative medicine term. To aid MEDLINE searching, a 250-line MEDLINE search strategy has been written and is available for public use.[9]

Assessments of MEDLINE sensitivity (the proportion of RCTs identified by a MEDLINE search relative to a "gold standard" of the known number of RCTs) have demonstrated that on average, MEDLINE searches yield only half of all known trials on a given topic, with CM topics usually scoring below average (eg, 17% for homeopathy, 31% for *Ginkgo biloba*, and 58% for acupuncture).[10] The first reason for low MEDLINE sensitivity may be that articles are appearing in journals not indexed by MEDLINE. This is true for acupuncture[11] and vitamin C for the common cold.[12] Of approximately 16 000 serial medical journals worldwide, MEDLINE references about 3700 (28%).[10] Of the 695 CM journals worldwide identified by the Office of Alternative Medicine and the National Library of Medicine, MEDLINE indexes 69 (10%). Collaborations between the National Library of Medicine, the CM Field, and the Office of Alternative Medicine should soon result in increasing the number of indexed CM journals and expanding the MEDLINE thesaurus to include more CM search terms.

To retrieve studies indexed in other databases, the CM Field is searching both standard medical databases and specialized CM databases. By mid-1998, the Cochrane CM Trials Registry contained more than 3500 RCTs, with only 33% identified by a MEDLINE search for RCTs in alternative medicine and 20% not found in MEDLINE. Periodically, the CM registry uploads its trials to the Cochrane Controlled Trials Registry, making these trials available to individuals with access to the Cochrane library. The CM Field maintains the CM registry, adds new trials, assists reviewers doing CM reviews, and proactively provides references to all 40 Cochrane Collaboration reviews and protocols that have a CM component. A second reason for low MEDLINE sensitivity is that articles exist in journals that are not indexed by any electronic database. Volunteers within the CM Field are now searching by hand approximately 40 indexed and nonindexed journals in English, German, Italian, Japanese, and Spanish and are reading every article published in these journals back to their first issues to locate every RCT.

Publication Bias

A third reason for low MEDLINE sensitivity is that studies exist that have never been fully published in any journal ("gray literature").[10] Estimates from conventional medicine show that only about 50% of the RCTs that appear as conference proceedings ever materialize into published journal articles.[10] Some observations[13] estimate CM gray literature to be at least as plentiful. Complementary medicine gray literature includes expected sources, such as conference proceedings and dissertations, and unexpected sources such as US patents records.[14]

Beyond the hard-to-find trials in the gray literature lie the even harder to find studies that do not appear in print anywhere and exist only in homeopathic company data files or researchers' file drawers.[13] Gray literature plus unpublished data are collectively termed unpublished studies.[15] Publication bias is "the tendency of investigators, reviewers, and editors to differentially submit or accept manuscripts for publication based on the direction or strength of the findings."[15] To the extent that publication bias exists, systematic reviews that omit unpublished studies risk overestimating treatment effects. Bias has been demonstrated both in what investigators submit to journals[16] and what conference abstracts editors accept.[17] However, whether to include unpublished studies in reviews is still a source of debate.[15] The influence of unpublished studies in CM systematic reviews is being analyzed by the CM Field as part of a review of 154 CM systematic reviews.[9] Until the value of including CM unpublished studies can be answered more conclusively, the CM Field will continue to search for unpublished studies to help answer a frequently asked question: How much evidence exists in CM?

Examining how publication bias skews the CM evidence is important for the CM Field because some forms of publication bias may be unique to CM. One question is whether both positive and negative publication biases exist in CM. Asked another way, do CM journals tend to publish results favoring CM treatments and conventional medical journals publish results not favoring CM treatments?

Examining publication bias is not always straightforward. A study by the CM Field found that studies published in Russia and China had a disproportionately high number of statistically significant results (97% and 99%, respectively) when compared with England (75%).[18] It is not yet evident whether these high proportions are due to extreme forms of publication bias or low study quality, which overestimated treatment effects.[19,20] The CM Field is obtaining translations of these studies to examine study quality. The qualitative results will determine whether it is practical to devote efforts to the tedious task of identifying unpublished studies.

Language Bias

Moher and colleagues[21] demonstrated that the quality of studies published in French, German, Spanish, and Italian is comparable with those published in English. The present research of the CM Field will extend methodological quality knowledge into studies from Russia and China. Egger and colleagues[22] demonstrated that a language-related publication bias exists in which authors who publish in both German and English tend to report nonsignificant findings in German and significant findings in English. Preliminary observations suggest that an additional language bias may exist for CM. Regardless of whether results are significant, some CM topics are almost exclusively published initially in languages other than English. A systematic review on St John's wort for depression[23] noted that none of the trials had been originally published in English, although some were subsequently published in English. A similar experience has been reported for *Gingko biloba* for cerebral insufficiency,[24] which suggests that for certain topics in CM, there may be a language-related publication lag time—a trend not reported for conventional medicine. Trends such as this underscore the importance of the CM Field's effort to retrieve trials in languages other than English and to identify biases that may be unique to CM.

Quality Assessment of RCTs

Assessing study quality also may improve the validity of systematic reviews. The finding that low-quality studies have re-

Titles of Cochrane Systematic Reviews Pertaining to Complementary Medicine

- Reviews completed
  - Acupuncture for asthma
  - Acupuncture for nicotine addiction
  - Balneotherapy (spa therapy) for arthritis
  - Cabbage leaves to reduce breast engorgement in nursing mothers
  - Garlic for lower-limb atherosclerosis
  - Homeopathy for asthma
  - Hypnosis for smoking cessation
  - Massage for low-birth-weight infants
  - St John's wort for depression
  - Vitamin E for intermittent claudication
  - Vitamin C for the common cold
- Reviews in progress
  - Acupuncture for lower back pain
  - Acupuncture for headache
  - Acupuncture for osteoarthritis
  - Alexander technique for asthma
  - *Echinacea* for the common cold
  - Evening Primrose Oil for premenstrual syndrome
  - *Gingko biloba* for dementia
  - *Gingko biloba* for intermittent claudication
  - Manual therapy for neck pain
  - Manual therapy for asthma
  - Marine oil supplementation for type 2 diabetes mellitus
  - Music therapy for dementia
  - Padma 28 for intermittent claudication
  - *Pygeum africanum* for benign prostatic hyperplasia
  - *Secale cereale* for benign prostatic hyperplasia
  - *Serenoa repens* for benign prostatic hyperplasia
  - Spinal manipulation for low back pain
  - Therapeutic Touch for wound healing
  - Yoga for epilepsy

peatedly yielded exaggerated treatment effects has been documented for conventional medicine[19,20] and acupuncture.[25] Yet, methodological assessments are sometimes absent from non–Cochrane Collaboration CM systematic reviews. A summary of 29 meta-analyses of mind-body techniques, for example, demonstrated that only about half assessed study quality.[26] Although assessing study quality cannot compensate for fraudulent or inaccurate reporting, it can provide additional validity-related information to guide reviewers' conclusions. For CM, quality assessments will provide needed answers to another commonly asked question: How good is the quality of CM trials?

This quality question is usually raised as an implication that CM trials reflect lower methodological quality than conventional medicine trials. To examine this notion, Cochrane Collaboration methodologists are collaborating with members of the CM Field to compare the methodological quality of CM trials with conventional medicine trials on the same diseases. Low-quality meta-analyses for analgesic interventions have been found to be associated with more positive results than high-quality meta-analyses.[27] The analysis of CM reviews is to examine whether this can be replicated in low-quality vs high-quality CM reviews, and how conclusions of low-quality vs high-quality CM reviews on the same topic differ.

Reviews Completed by the CM Field

The CM Field has completed systematic reviews on acupuncture, massage, homeopathy, and herbal medicine. Nineteen reviews are in process (Table),[28] and the CM Field has commented on protocols of 12 planned and completed reviews.[29]

Conclusions

Although there is no guarantee that systematic reviews will result in changing policy and practice, there is increasing evidence that policy organizations rely on systematic reviews more than they have in the past[7] and that practitioners rely on reviews as a primary information source.[30] It has also been suggested that consumers can use reviews to guide decision making.[30] Traditional literature reviews, however, have lacked explicit methods and have been susceptible to biases that generally tend to overestimate treatment effects.[7] Therefore, at a time when the public is using CM treatments in record numbers and an explicit peer-reviewed and regularly updated systematic review method exists, it is imperative to apply this method to CM. The Cochrane Collaboration provides a forum of interdisciplinary cooperation in which to produce these reviews that we hope will result in improved patient care.

Jeanette Ezzo, PhD
Brian M. Berman, MD
Andrew J. Vickers, MA
Klaus Linde, MD

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Cochrane Collaboration Complementary Medicine Field Newsletter

Message From The Field Coordinator

The Complementary Medicine (CM) Field continues to grow in supporting the Cochrane Collaboration and in producing systematic reviews. As you will note, seven new reviews are complete and ten new reviews are in progress. These reviews are now available through our website.

The increased access to Cochrane reviews related to CM is thanks to the hard work of our Registry Coordinator Mac Beckner and web developer Ralph Reckly. That access as well as the indexing of Cochrane reviews on MEDLINE will go far to increase the awareness of the Cochrane Collaboration and to increase research related to CM. We still have a way to go, however. According to the World Health Organization, 70% of the world uses complementary and alternative therapies. In keeping with that, we continue to look for ways to increase international participation in the CM Field and to enhance the diversity of those involved. Language difficulties and cultural norms that can present challenges in conducting systematic reviews (see article on page 2) challenge us, in turn, to improve any language and cultural imbalances that exist in the Field. One suggestion offered to the Steering Group at its meeting in March 2000 was to add promoting inclusiveness to the list of Cochrane Collaboration principles.

I look forward to the continued growth of the CM Field and certainly welcome your suggestions on how we might improve and expand the Field.

Brian Berman, Field Coordinator

Conducting a Cochrane Review

Who can do a Cochrane systematic review? In general, there are no exclusion criteria for who can undertake a review. There are some definite requirements, though: access to a computer, time, enthusiasm, and a sense of adventure! All Cochrane reviewers are volunteers and while we do not commission reviews on particular topics, we do recognize that volunteers are more likely to be able to review a question that they themselves want answered.

You'll find that Cochrane has resources available to help in the review process. RevMan is the Cochrane Collaboration's software for preparing and maintaining reviews in the appropriate format. Using RevMan, the reviewer can create protocols and reviews with text, study characteristics, comparisons, and study data and then perform a meta-analysis, if appropriate. There are also training and support resources available, both self-paced exercises and more formal workshops. For details, visit www.cochrane.org/cochrane/.

Inside

Information for the editor or the newsletter is welcome at jlewis @compmed.ummc.umaryland.edu
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Design:
Amy Hardcastle

The Complementary Medicine Field Registry of Randomized Controlled Trials now contains approximately 5300 RCT's and CCT's, and another 5400 possible RCT's with nearly 1900 hard copy reports in the article archive. In June the updated registry was sent to the New England Cochrane Center (NECC) and it will be available on Issue 4 of the Cochrane Library by searching the keyword "compmed". Additionally, there are now 49 CM systematic reviews including 7 new reviews (see page 7) and 53 CM protocols registered on the Cochrane Library, with the total number of identified reviews in CM now over 200 (Linde).

We are continuing to execute database specific search strategies on all major bibliographic databases including the Cochrane library, as well as continuing to conduct hand searches of high priority CM journals. Additionally, in an effort to make the CM field registry more accessible to consumers, researchers and healthcare providers, we have mounted the registry so that it can be searched on the University of Maryland Complementary Medicine Program (CMP) website [http://www.compmed.ummc.umaryland.edu]. Additional CM field information on the CMP website includes the CM field progress report and CM field advisory board members along with hyperlinks to Cochrane resources. In planning for the future, we are now evaluating Meerkat software as a means for managing the CM registry.

Individuals wishing to obtain a copy of the registry should contact the Registry Coordinator.

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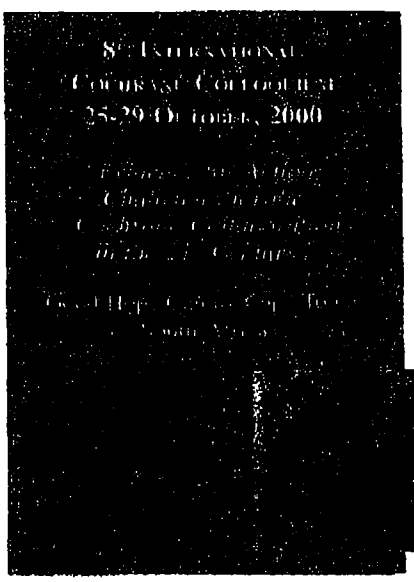
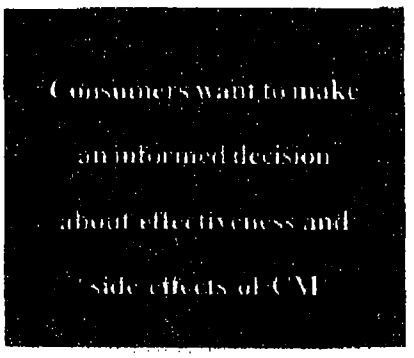
The Colloquium theme will highlight key methodological, logistical, and social challenges that need to be addressed by the Collaboration in order to further its goals. The Colloquium includes plenary sessions, workshops, poster presentations and social events, providing Collaboration members with an opportunity to discuss their work and to look at the achievements of the Collaboration. This is the first Colloquium to be held in a developing country and it is hoped this will focus attention on recruiting participants from the developing world and making the work of the Collaboration more universally accessible.



Consumer Update

Can Complementary Medicine be Intergrated into the National Health Service in the United Kingdom?

In June I attended the above Drug and Therapeutics Bulletin seminar. It was an interesting afternoon with presentations on different aspects of complementary medicine. A number of different complementary medicine practitioners attended, the majority from the UK, and the afternoon generated a great deal of discussion.



The afternoon started with David Peter giving the Cochrane Collaboration's definition of complementary medicine: 'Complementary and alternative medicine (CAM) is a broad domain of healing resources that encompass all health systems, modalities and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period. CAM also includes all such practices and ideas self-defined by their users as preventing or treating illness or promoting health and well-being. Boundaries within CAM and the CAM domain and that of the dominant system are not always sharp or fixed.' This definition became a theme throughout the afternoon. However it became apparent that complementary medicine (CM) has different meanings for different people.

It became clear that doctors' attitudes are changing, from CM being at the fringe of modern medicine to it becoming increasingly available on the NHS. It was reported also that adverse effects are rare, but that more primary research should be and is being carried out (there are 49 systematic reviews of CM in Issue 3, 2000 of *The Cochrane Library*[1]). Most of the main complementary therapies are now covered by university degree courses apart from 'touch' based therapies. However, there seemed to be a general lack of confidence among general practitioners to learn complementary therapies and everyone agreed that better education and communication needs to take place between general and complementary practitioners.

The second presentation by George Lewith, Senior Research Fellow, Centre for the Study of Complementary Therapies, University of Southampton, confirmed the view that consumers want to make an informed decision about effectiveness and side effects of CM (or, in fact, conventional medicine). There was general consensus that CM is under-funded and under-resourced in the UK and that, if used more commonly, it could provide cost savings to the NHS. Again, it was emphasized that more research is needed before CM becomes part of the NHS provision.

Sarah Cant, Senior Lecturer from the University of Surrey, spoke at length about why consumers find CM attractive. She suggested that consumers believe CM is more natural than conventional medicine and they have fewer concerns about side effects. Usually they have experienced failure from conventional practitioners and longer consultations with complementary providers give them a feeling of empowerment in their health care decisions. Because complementary practitioners treat consumers on an individual as well as holistic basis, consumers begin to have a greater understanding of their body and its reaction to the medical condition.

Tina Raphael, a Lecturer in health care law and ethics, outlined the legal obligations of practitioners noting that although some CM practitioners are regulated, there is voluntary self-regulation for others. She also questioned how, in the absence of evidence, a complementary practitioner can inform the consumer of all the possible risks and benefits. She discussed obstacles to integrating CM into the NHS, the need to establish efficacy and safety, adequate training of practitioners, and the need for negotiation. It seems that CM will only be integrated if it is shown to be cost effective, if practitioners want it and if more research is undertaken.

Last, Michael Fox, Chief Executive of the Foundation for Integrated Medicine, reviewed the current position of the NHS in terms of complementary medicine. He reported that £0.80 in every £100 was spent on research in CM and this needs to be increased. He stated that the current position on regulation is unsatisfactory; there are over 150 different regulatory bodies for CM practitioners. One in five consumers is using CM in the UK with the most popular therapies being Herbal medicine (34%), Aromatherapy (21%), Acupuncture (20%), Homeopathy (17%), Massage (6%), Reflexology (6%), and Osteopathy (4%). Approximately 49,000 CM practitioners provide a huge variety of therapies at a cost of £1.6 billion, most of which is spent outside the NHS.

Claire Allen
Consumer Representaive

[1] *Information on obtaining the Cochrane Library is found on page 5.*

Find synopses of Cochrane reviews written for consumers at the Consumer Network web site: http://hiru.mcmaster.ca/cochrane/cochrane/consumer.htm

Include Dissertations in Systematic Reviews or Not?

One of the principles for systematic review is that all unpublished data should be included, if appropriate, but there is little information about doing so. Locating such data takes considerable time, effort, and expense, particularly if the author has not published the study and is no longer at the host institution. To what extent does the inclusion of dissertation research alter the findings or conclusions of a review?

In reviewing massage therapy for infants, we identified 17 dissertations. Almost all (13 studies) were excluded from the review, 11 because of no or improper randomization. Another three studies were subsequently published as a journal paper. That left one original dissertation that was included in our review although that one study made no difference to our review.

We also checked the Cochrane library and we found that 24 of the 878 reviews claimed to search for dissertations. However, only five reviews appeared to have identified at least one dissertation: three as an included study and two as an excluded study. In only one review did incorporating dissertation data affect the conclusion.

So what do we recommend? Allocate time and resources to the identification, retrieval and analysis of dissertations but be prepared that dissertations may not change the findings or conclusions of the review.

Andrew J. Vickers and Claire Smith

Lessons Learned while Doing a Systematic Review

Although I fully support Cochrane guidelines for conducting systematic reviews, there are a number of challenges that may be encountered due to the different scientific cultures and reporting conventions encountered in some countries. As an example, after I presented preliminary data on low energy laser irradiation (LELI) interventions in Russia at the Rome Colloquium in 1999, I was invited by the Infectious Diseases group to review LELI as adjuvant treatment for tuberculosis. While searching for publications, obtaining copies, writing letters to authors, and analysing the contents, I learned some lessons although some questions remain unanswered.

Of the 18 publications of controlled studies — all in Russian — only one stated that there was randomization. Not one author offered explanations in reply to my detailed letters, although one did send a letter of refusal. Analysis of the published texts revealed that only three publications could be considered for my review. Others were duplicates or suspected to be duplicates. For example, in a second publication from the same group of researchers using similar research methods, the number of patients was almost duplicated and some outcomes were the same. Without explanations from the authors about the design, the only option available to me was to analyse the phrases used to describe the origin of the control group. All studies showed a significant positive effect of LELI, almost duplicating the outcomes (pulmonary cavities closed, perifocal infiltration reduced, no bacterial discharge).

All these authors believe that they not only conduct research, but that they save lives with LELI while evaluating it. However, in one study two physicians described the experimental application of LELI through rigid bronchoscope to children 1 to 4 years of age, under narcosis, using up to 12 procedures during one hospitalization.

Given that the quality of reporting for many of the studies was low, researchers did not use randomization, and authors did not reply to requests for further explanations, I am left to wonder: Can I believe that the one study where randomisation was mentioned really used this procedure? And, if not, how much reliance can we place upon systematic reviews based upon studies such as these?

Vasiliy Vlassov

At the 8th International Cochrane Colloquium meeting in Cape Town, South Africa, October 25-29, 2000, Dr. Vlassov will present a paper entitled "Low energy lasers for treatment of tuberculosis."

MEDLINE Listing

Cochrane Reviews are now listed in MEDLINE. The source is listed as the Cochrane Database of Systematic Reviews with the citation "(Cochrane Review)" appended to the title. This makes it difficult to identify cochrane reviews by searching for titles, but discussion is underway with the National Library of Medicine to amend the entries. If you have questions or comments about the MEDLINE indexing, contact Mark Starr, e-mail: mstarr@update.co.uk.

Introduction for Chinese Editors

The First National Exploratory Meeting on "Introduction to the Cochrane Collaboration and Evidence-Based Medicine" for the chief editors of leading Chinese medical journals was held in Chengdu in April 2000.
Cochrane News, Issue 18, June 2000.

Alternative Medicine Foundation, Inc.

The HerbMed® project continues to grow and gain recognition. HerbMed® is a non-affiliated evidence-based herbal database, providing independent scientific information on the use of herbs for health. Researchers find it a useful first point for tracking down RCTs for systematic reviews.

HerbMed® was chosen as Hot Pick in Science Magazine in June 2000 and Hot Site in USA Today in July 2000. The Western Journal of Medicine has featured the database and the foundation continues to receive testimonials and a record number of visitors.

We take suggestions. If you need scientific information on a herb or herbal mixture that you would like us to research, contact the HerbMed® project director:

Jackie Wootton, M.Ed.
Tel: 301-581-0116; Fax: 301-581-0119
E-mail: jcw@amfoundation.org

Symposium on Systematic Reviews

For information about the 4th Symposium on Systematic Reviews: Beyond the Basics, contact Rochelle Seifas, Centre for Statistics in Medicine, Institute of Health Sciences, Old Road, Oxford, OX3 7LF, UK (e-mail: r.seifas@icrf.icnet.uk).

White House Commission Appointment

Dr. Wayne Jonas, CM Field Board Member, has been appointed to serve as a member of the White House Commission on Complementary and Alternative Medicine Policy.

How to Obtain the Cochrane Library

The Cochrane Library is published and distributed by Update Software. It is updated quarterly and is available in CD-ROM for Windows or 3-1/2 inch disk for Windows. Subscriptions are for one year and include current issue plus four quarterly updates. The Library contains the following information:

- The Cochrane Database of Systematic Reviews (CDSR)
- The York Database of Abstracts of Reviews of Effectiveness (DARE)
- The Cochrane Controlled Trials Register (CCTR)
- The Cochrane Review Methodology Database (CRMD)

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News From The CM Field Board

Publications

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Presentations

Berman B.

"The University of Maryland Complementary and Alternative Medicine Program." Harvard State of the Science Symposium. Boston, MA (March 2000).

"Overview of Complementary Medicine." Supportive Care in Cancer. Washington DC (March 2000).

"Integration of Conventional and Complementary Medicine: The University of Maryland Experience." Association of American Medical Colleges Council of Deans. Puerto Rico (April 2000).

Jonas WB.

"Balancing Belief and Evidence in Alternative Medicine Decisions" (Workshop) 31st Annual Meeting of the Association of Applied Psychophysiology and Biofeedback. Denver, CO (April 2000).

"Applying Evidence-based Medicine Principles to Complementary Medicine." 48th Annual Clinical Meeting of the American College of Obstetrics and Gynecology. San Francisco, CA (May 2000).

"Complementary and Alternative Medicine: Actions and Interactions." 48th Annual Clinical Meeting of the American College of Obstetrics and Gynecology. San Francisco, CA (May 2000).

Jonas WB, Linde K.

"Homeopathy: State of the Science". International Conference Evidence-based Complementary Medicine, University of Munich, Munich, Germany (April 2000).

Romoli M.

"Changes and Limits in Evidence Based Research in Acupuncture." Conference sponsored by the Italian and Chinese Ministry of Health, Rome, Italy (September 2000).

Other

Dr. Mary Ann Richardson, M.P.H., Dr.P.H., CM Field Board Member, has been appointed program officer for extramural research at the National Center for Complementary and Alternative Medicine (NCCAM), National Institutes of Health. Dr. Richardson will direct NCCAM's oncology initiatives and manage the growing portfolio of oncology projects. She was previously Director of the University of Texas Center for Alternative Medicine Research in Cancer.

Dr. Kiichiro Tustani is handsearching two more acupuncture journals in Japanese for the Cochrane Registry: Nihon Shinkyu Chiryo Gakkai Shi (The Journal of the Japan Acupuncture and Moxibustion Society) 1951-1980 and Ido no Nippon (The Journal of Japanese Acupuncture and Moxibustion) 1948-2000.

- Dietary marine fatty acids (fish oil) for asthma
- Feverfew for preventing migraine
- Low level laser therapy for OA
- Low level laser therapy for RA
- Manual therapy for asthma
- Nutritional supplementation in stable chronic obstructive pulmonary disease
- Psychological therapies for sickle cell disease and pain

Low Level Laser Therapy (LLLT) in the Treatment of RA
(Brosseau L, Welch V et al., 2000)

Objective: To assess the effectiveness of LLLT in the treatment of RA.
Selection criteria: Randomized controlled trials of LLLT for the treatment of patients with a clinical diagnosis of RA.
Main Results: Five placebo-controlled trials with a total of 204 patients. LLLT reduced pain by 70%, reduced morning stiffness duration by 27.5 minutes, and increased tip to palm flexibility by 1.3 cm reltive to placebo. Functional assessment, range of motion and local swelling did not differ between groups.

Feverfew for preventing migraine
(Pittler MH, Vogler BK, Ernst E, 2000)

Objective: To systematically review evidence for or against the efficacy of feverfew versus placebo for the prevention of migraine.
Selection Criteria: Randomized, placebo-controlled, double-blind trials assessing the efficacy of feverfew for preventing migraine.
Main results: Four trials met inclusion criteria and majority suggested beneficial effects of feverfew compared with placebo. Highest quality trial, however, found no significant difference.
Conclusions: The efficacy of feverfew for the prevention of migraine has not been established.

LLT (continued)

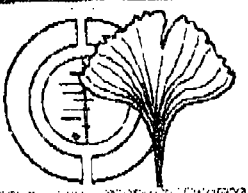
Conclusions: LLLT could be considered for short-term relief of pain and morning stiffness for RA patients. There is a need for RCTs that investigate the effects of wavelength, treatment duration of LLLT, dosage and site of application over nerves instead of joints on LLLT effectiveness.

Reviews in Progress

- Acupuncture for chemotherapy-induced nausea or vomiting among cancer patients *
- Acupuncture for lateral elbow pain in adults
- Acupuncture for osteoarthritis *
- Aerobic exercise interventions for people with HIV/AIDS
- Alexander Technique for chronic asthma
- Anti-oxidant foods or supplements for preventing cardiovascular disease in patients with and without ischemic heart disease
- Asthmatic exacerbations and magnesium sulphate
- Behavioral treatment of chronic low back pain
- Behavioural and cognitive interventions for faecal incontinence in children *
- Behavioural interventions for primary and secondary dysmenorrhoea *
- Breathing exercises in asthma
- Calcium and phosphate supplementation of human milk for promoting growth in preterm infants
- Cernilton for Benign Prostatic Hyperplasia
- Chinese herbal medicine for atopic eczema *
- Chinese medicinal herbs for chronic hepatitis B *
- Cognitive behaviour therapy for depressed carers of people with Alzheimer's disease and related disorders
- Complementary therapies for acne
- Cow's milk and childhood asthma
- Dietary marine fatty acids in asthma control
- Electrical stimulation for pressure sores
- Evening primrose oil or other essential fatty acids for premenstrual syndrome
- Food or supplements rich in omega-3 fatty acids for prevention of cardiovascular disease in patients with ischaemic heart disease
- Galantamine for Alzheimer's disease
- Gingko biloba in dementia and cognitive impairment
- Gingko biloba in intermittent claudication
- Manual therapy for mechanical neck disorders
- Marine oil supplementation in NIDDM
- Massage and aromatherapy for symptom relief in patients with cancer *
- Massage for low back pain *
- Mind/Body Therapy for Fibromyalgia
- Noninvasive physical treatments for chronic headache
- Omega-3 fatty acids supplementation for rheumatoid arthritis
- Omega-3 fatty acids for cystic fibrosis
- PFMT and/or biofeedback for faecal incontinence
- Phytoestrogens for menopausal symptoms
- PMS: Evening primrose oil
- Psychological interventions for non-ulcer dyspepsia *
- Pygeum africanum for Benign Prostatic Hyperplasia
- S-adenosyl-L-methionine for alcoholic liver diseases *
- Spinal manipulation for low back pain
- Tartrazine exclusion and asthma
- Therapeutic touch in wound healing
- Vitamin A for measles in children
- Vitamin B6 and placebo in premenstrual syndrome

* New for this issue

Would You Like To Participate In The Cochrane Collaboration Complementary Medicine Field?



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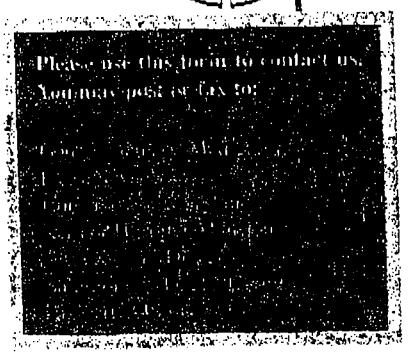

Support Work of Collaborative Review Groups (CRGs)

___ Prepare and maintain Cochrane Complementary Medicine reviews
List topics of interest below
___ Liaison between CM Field and a CRG
___ Identify and prioritize needed Cochrane Reviews
___ Train and/or recruit reviewers
___ Other

How I Will Contribute to the Field

Identify Trials

___Hand search journals *Language (s)*
___Translate articles *Language(s)*
___Other

Dissemination

___Promote The Cochrane Library
___Act as contact person from non-Cochrane Organization for CM Field
___Other

Tell us about your interests. _____

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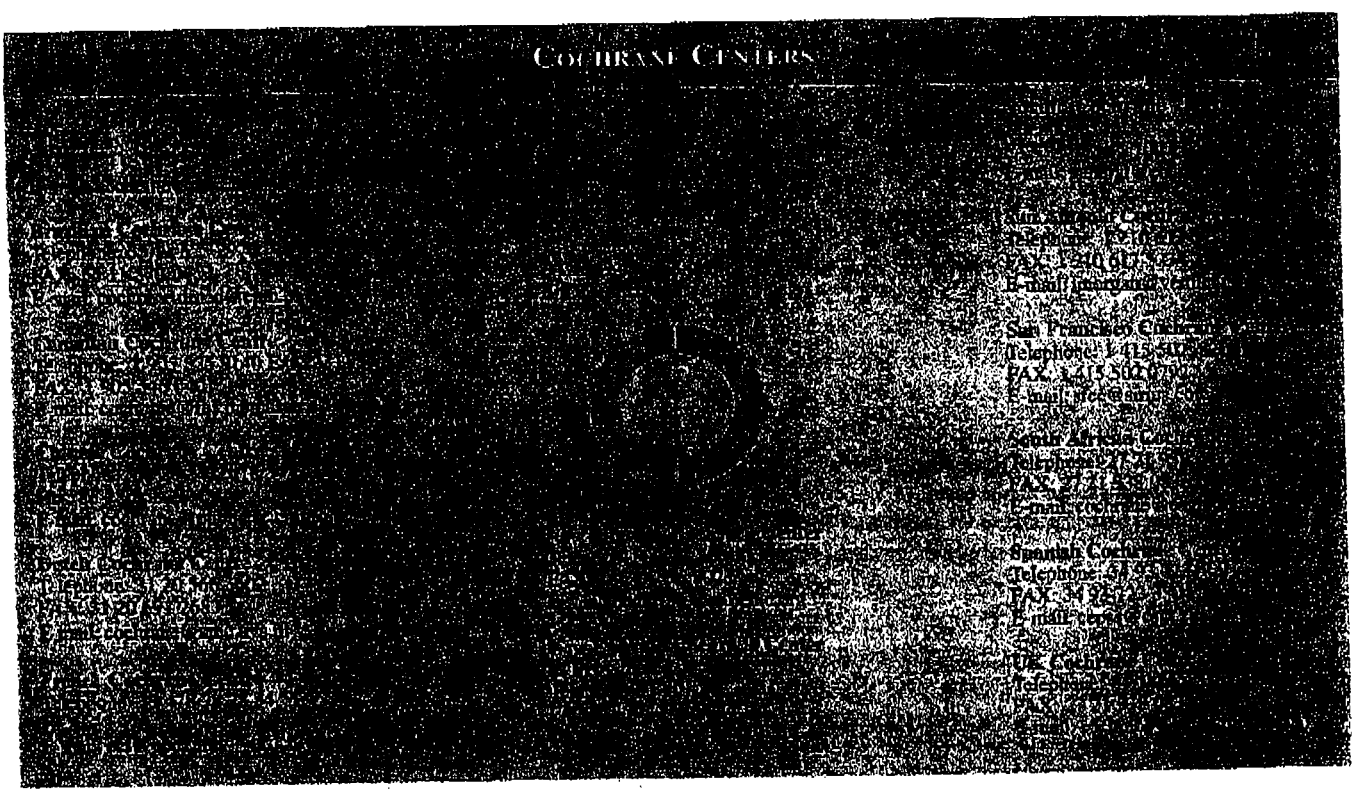

ADDENDUM 2

Cochrane Collaboration
Complementary Medicine Field Systematic Reviews and Protocols

I.CM Field Completed Reviews

	1) Linde, K. Jobst, K. Panton, J.	Acupuncture for chronic asthma	1996, *Issue* 3
New	2) Melchart, D. Linde, K. Fischer, P. Berman, B. White, A. Vickers, A. Allais, G.	Acupuncture for Idiopathic headache	2001, *Issue* 1
New	3) Smith, CA. Crowther, CA	Acupuncture for induction of labour	2001, *Issue* 1
	4) Tulder MW, van. Cherkin, DC. Berman, B. Lao, L. Koes, BW	Acupuncture for low back pain	1999, *Issue* 1
	5) White, AR. Rampes, H. Ernst, E.	Acupuncture for smoking cessation	1997 *Issue* 1
	6) Dennis, J.	Alexander Technique for chronic asthma	2000, *Issue* 2
	7) Evans, JR. Henshaw, K.	Antioxidant vitamin and mineral supplements for preventing age-related macular degeneration.	1999, *Issue* 4
	8) Evans, JR.	Antioxidant vitamin and mineral supplements for age related macular degeneration.	1998, *Issue* 1
	9) Nixon, S. O'Brien, K. Glazier, RH. Wilkins, AL.	Aerobic exercise interventions for people with HIV/AIDS	2001, *Issue* 1
	10) McIntosh, HM. Olliaro, P.	Artemisinin derivative for treating uncomplicated malaria	1998, *Issue* 2
	11) McIntosh, HM. Olliaro, P	Artemisinin derivatives for treating severe malaria	1998, *Issue* 3
	12) Verhagen, AP. De Vet, HCW. de Bie, RA. Kessels, AGH. Boers, M. Knipschild, PG.	Balneotherapy for rheumatoid arthritis and osteoarthritis	1999, *Issue* 3
	13) Norton, C. Hosker, G. Brazzelli, M.	Biofeedback and/or sphincter exercises for the treatment of faecal incontinence in adults.	2000, *Issue* 2
	14) Wilt, T. Ishani, A. Mac Donald, R. Stark, G. Mulrow, C. Lau, J.	Beta-sitosterols for benign prostatic hyperplasia	2000, *Issue* 2

	15) Karjalainen, K. Malmivaara, A. van Tulder, M. Roine, R. Jauhiainen, M. Hurri, H. Koes, B	Biopsychosocial rehabilitation for upper limb repetitive strain injuries	2000, *Issue* 3
	16) Holloway, E. Ram, FSF	Breathing exercises for asthma	1998, *Issue* 4
New	17) Kelly, AJ Kavanagh, J Thomas, J	Castor oil,bath and/or enema for cervical priming and induction of labor	2001, *Issue* 2
	18) Wilt, T. Mac Donald, R. Ishani, A. Rutks, I. Stark, G.	Cernilton for benign prostatic hyperplasia	1998, *Issue* 2
New	19) Liu, JP McIntosh, H. Lin, H	Chinese medicinal herbs for asymptomatic carriers of hepatitis B.	2001, *Issue* 2
New	20) Liu, JP. McIntosh, H. Lin, H.	Chinese medicinal herbs for chronic hepatitis B	2001, *Issue* 1
	21) Renfrew, MJ. Lang, S. Martin, L. Woolridge, MW	Treatments to relieve breast engorgement (Previous review title: Cabbage leaves for breast engorgement this review has been withdrawn see protocol 14)	1999, *Issue* 4
	22) Price, JR. Couper, J.	Cognitive behavior therapy for chronic fatigue syndrome in adults	1998, *Issue* 3
	23) Jones, C. Cormac, I. Mota, J. Campbell, C	Cognitive behavior therapy for schizophrenia	1999, *Issue* 1
	24) Jepson, RG. Mihaljevic, L. Craig, J.	Cranberries for the prevention of urinary tract infections	1998, *Issue* 4
	25) Jepson, RG. Mihaljevic, L. Craig, J.	Cranberries for the treatment of urinary tract infections	1998, *Issue* 4
	26) Woods, RK. Thien, FCK. Abramson, MJ.	Dietary marine fatty acids (fish oil) for asthma.	2000, *Issue* 3
	27) Van den Ende, CHM. Vliet Vlieland, TPM. Munneke, M. Hazes, JMW.	Dynamic exercise therapy for rheumatoid arthritis	2000, *Issue* 3
	28) Melchart, D. Linde, K. Fischer, P. Kaesmayr, J.	Echinacea for the prevention and treatment of the common cold	1999, *Issue* 1
	29) Ram, FSF. Robinson, SM Black, PN.	Physical training for asthma.	1999, *Issue* 1
New	30) Flemming, K, Cullum, N	Electromagnetic therapy for the treatment of pressure sores	2001, *Issue* 1
New	31) Flemming, K. Cullum, N.	Electromagnetic therapy for the treatment of venous leg ulcers	2001, *Issue* 1
	32) Pittler, MH.	Feverfew for preventing migraine	2000, *Issue* 3

	Vogler, BK. Ernst, E.		
New	33) Olin, J. Schneider, L.	Galantamine for Alzheimer's disease	2001, *Issue* 1
	34) Jepson, RG. Kleijnen, J. Leng, GC.	Garlic for peripheral arterial occlusive disease	1997, *Issue* 3
New	35) Towheed, TE. Anastassiades, TP. Shea, B. Houpt, J. Welch, V. Hochberg, MC.	Glucosamine therapy for osteoarthritis	2001, *Issue* 1
	36) Evans, JR.	Ginkgo biloba extract for age related macular degeneration	1999, *Issue* 3
New	37) Little, CV. Parsons, T	Herbal therapy for treating osteoarhritis	2001, *Issue* 1
New	38) Little, C. Parsons, T.	Herbal therapy for treating rheumatoid arthritis	2001, *Issue* 1
	39) Linde, K. Jobst K, A	Homeopathy for chronic asthma	1998, *Issue* 3
	40) . Vickers, AJ. Smith, C.	Homoeopathic Oscillococcinum for preventing and treating influenza and influenza like syndromes.	1999, *Issue* 4
	41) Abbot, NC. Stead, LF. White, AR. Barnes, J. Ernst, E.	Hypnotherapy for smoking cessation	1998, *Issue* 2
	42) Roberts, L. Ahmed, I. Hall, S.	Intercessory prayer for the alleviation of ill health	1999, *Issue* 1
	43) Jewell, D. Young, G.	Interventions for nausea and vomiting in early pregnancy	1996, *Issue* 4
New	44) Campbell, K. Waters, E. O'Meara, S. Summerbell, C	Interventions for treating obesity in children	2001, *Issue* 1
	45) Flemming, K. Cullum, N.	Laser therapy for venous leg ulcers	1998, *Issue* 4
New	46) Higgins, JPT. Flicker, L.	Lecithin for dementia and cognitive impairment.	2000, *Issue* 2
	47) Brosseau, L. Welch, V. Wells, G. deBie, R. Gam, A. Harman, K. Morin, M. Shea, B.Tugwell, P.	Low level laser therapy for OA	2000, *Issue* 4
	48) Brosseau, L. Welch, V. Wells, G. deBie, R. Gam, A. Harman, K. Morin, M. Shea, B.Tugwell, P.	Low level laser therapy fio RA	2000, *Issue* 4
	49) Hondras, MA. Linde, K. Jones, AP	Manual therapy for asthma.	2000, *Issue* 3

	50) Furlan, AD. Brosseau, L. Welch, V. Wong, J.	Massage for low back pain	2000, *Issue* 4
	51) Vickers, A. Ohlsson, A. Lacy, JB. Horsley, A	Massage to promote development in preterm and/or low birth weight infants	1998, *Issue* 3
New	52) Herxheimer, A. Petrie, KJ.	Melatonin for preventing and treating jet lag	2001, *Issue* 1
New	53) Koger, SM. Brotons, M	Music therapy in dementia	2001, *Issue* 1
	54) Ferreira, IM. Brooks, D. Lacasse, Y. Goldstein, RS	Nutritional supplementation in stable chronic obstructive pulmonary disease	2000, *Issue* 2
	55) Wilkinson, EAJ. Hawke, CI.	Oral zinc for arterial and venous leg ulcers	1998, *Issue* 3
	56) Joy, CB. Mumby-Croft, R. Joy, LA.	Polyunsaturated fatty acid supplementation (fish or evening primrose oil) for schizophrenia	2000, *Issue* 1
	57) Anie, KA; Green, J	Psychological therapies for sickle cell disease and pain	2000, *Issue* 3
	58) Wilt, T. Ishani, A. Stark, G. Mac Donald, R. Mulrow, C. Lau, J.	Serenoa repens (saw palmetto) for benign prostatic hyperplasia	1998, *Issue* 4
New	59) Suresh, GK; Davis, JM; Soll, RF	*Superoxide dismutase for preventing chronic lung disease in mechanically ventilated preterm infants*	2001, *Issue* 1
	60) Beamon, S. Falkenbach, A. Fainburg, G. Linde, K.	Speleotherapy for the treatment of asthma	2000, *Issue* 1
	61) Linde, K. Mulrow, CD	St. John's Wort for depression	1998, *Issue* 2
	62) Douglas, RM. Chalker, EB. Treacy, B	Vitamin C for preventing and treating the common cold	1998, *Issue* 1
	63) Kleijnen, J. Mackerras, D	Vitamin E for intermittent claudication	1996 *Issue* 2
	64) Soares, KVS. McGrath, JJ	Vitamin E for neuroleptic induced tardive dyskinesia	2000, *Issue* 3
	65) Tabet, N. Birks, J. Grimley Evans, J. Orrel, M.Spector, A	Vitamin E in Alzheimer's disease	2000, *Issue* 4
	66) Ramaratnam, S. Sridharan, K	Yoga in the treatment of epilepsy	1999, *Issue* 3
	67) Marshall, I	Zinc in the treatment of the common cold	1999, *Issue* 2
	68) Mahomed, K	Zinc supplementation in pregnancy	1997, *Issue* 3

II. CM Field Protocols

New	1) He, L. Zhou, D. Wu, B. Li, N.	Acupuncture for bell's palsy	2001, *Issue* 1
	2) Richardson, MA. Allen, C. Ezzo, J. Lao, L. Ramirez, G. Ramirez, T. Zhang, G	Acupuncture for chemotherapy-induced nausea or vomiting among cancer patients	2000, *Issue* 1
	3) Green, S. Buchbinder, R. Hall, S. Barnsley, L. Forbes, A. Smidt, N. Assendelft, W.	Acupuncture for lateral elbow pain in adults	1999, *Issue* 1
	4) Ezzo, J. Hadhazy, V. Berman, B. Birch, S. Kaplan, G. Hochberg, M.	Acupuncture for osteoarthritis	1998, *Issue* 3
	5) Correia, M. Veloso, M. Correia, C	Antioxidants for acute stroke	1998, *Issue* 3
	6) Correia, M. Silva, C. Veloso, M.	Antioxidants for secondary prevention after stroke or transient ischaemic attack	1999, *Issue* 3
New	7) Orrell, RW. Lane, RJM. Ross, M.	Antioxidant treatment for amyotrophic lateral sclerosis / motor neuron disease	2001, *Issue* 1
	8) Hooper, L. Capps, N. Clements, G. Davey Smith, G. Ebrahim, S. Higgins, J. Ness, A. Riemersma, RA. Summerbell, CD.	Anti-oxidant foods or supplements for preventing cardiovascular disease	1999, *Issue* 2
	9) Brazzelli, M. Griffiths, P.	Behavioural and cognitive interventions for faecal incontinence in children	2000, *Issue* 2
	10) Wilson, ML. Murphy, PA. Pattison, HM. Farquhar, CM.	Behavioural interventions for primary and secondary dysmenorrhoea	2000, *Issue* 3
	11) Snowden, HM. Renfrew, MJ. Woolridge, MW	Treatments to relieve breast engorgement during lactation	2000, *Issue* 2
	12) Hoare, C. Leonard, T. Williams, HC.	Chinese herbal medicine for atopic eczema	2000, *Issue* 2
	13) Charlesworth, G. Riordan, J. Shepstone, L.	Cognitive behavior therapy for depressed carers of people with Alzheimer's disease and related disorders	1999, *Issue* 4
	14) Coates, P. Eady A, E. Cove J, H.	Complementary therapies for acne	1999, *Issue* 2
	15) Caraballoso, M. Bonfill, X. Serra, C	Drugs for preventing lung cancer	2000, *Issue* 1
	16) Flemming, K.	Electrotherapy for chronic wounds	2000, *Issue* 3

	Cullum, N.		
	17) Flemming, K. Cullum, N	Electrotherapy for pressure sores	2000, *Issue* 3
	18) Flemming, K. Cullum, N	Electrotherapy for diabetic ulcers	2000, *Issue* 3
	19) Ruether, A; Bueschel, G; Leipner, J; Linde, K; Rostock, M; Horneber, M	Enzyme therapy in oncology	2000, *Issue* 4
	20) Strid, J. Jepson, R. Moore, V. Kleijnen, J. Iasco, SM	Evening primrose oil or other essential fatty acids for premenstrual syndrome	1998, *Issue* 2
	21) Kleijnen, J.	Ginkgo biloba for intermittent claudication	1996, *Issue* 2
New	22) Birks J, Grimley Evans J, Dongen M	Ginkgo biloba for dementia and impairment	2001 *Issue* 2
	23) Novak, F. Avenell, A. Heyland, DK. Croal, BL. Drover, JW. Jain, M. Noble, D. Su, X.	Glutamine supplementation for critically ill adults	2000, *Issue* 3
	24) Wilson, ML. Murphy, PA. Farquhar, CM	Herbal and dietary therapies for primary and secondary dysmenorrhoea	1999, *Issue* 2
New	25) Bennett M, Heard R	Hyperbaric oxygen therapy for multiple sclerosis	2001, *Issue* 2
	26) Beamon, S. Falkenbach, A. Jobst, K.	Hydrotherapy for asthma	1999, *Issue* 4
	27) Blackhall K, Appleton S	Ionisers for chronic asthma	2000 *Issue* 3
	28) Bent, S. Tsourinas, C. Romoli, M. Linde, K.	Kava for Anxiety Disorder	1999, *Issue* 3
	29) Beamon, S. Falkenbach, A. Jobst, K.	Hydrotherapy for asthma	1999, *Issue* 4
	30) Shaw, K. Turner, J. Spinks, A. Del Mar, C	Management of Depression with Tryptophan and 5-Hydroxytryptophan	1999, *Issue* 3
	31) Gross, AR. Hondras, MA. Aker, PD. Peloso, P. Goldsmith, CH.	Manual therapy for mechanical neck disorders	1997, *Issue* 3

	32) Lockhart-Wood, K. Gambles, M. Wilkinson, S	Massage and aromatherapy for symptom relief in patients with cancer	2000, *Issue* 3
New	33) Urrutia, G Bonfill, X Del, 34) Pozo, P Fernandez A	Neuroreflexology for low back pain	2001 *Issue* 2
	35) Hadhazy, V. Ezzo, JM. Berman. BM. Creamer, P. Bausell, B	Mind/Body Therapy for Fibromyalgia	2000,*Issue* 3
	36) Greener, J. Enderby, P. Whurr, R.	Pharmacological treatment for aphasia following stroke	1998, *Issue* 2
	37) Bronfort, G. Nilsson, N. Assendelft, WJJ. Bouter, LM. Goldsmith, C. Evans, R. Haas, M.	Noninvasive physical treatments for chronic headache.	1999, *Issue* 3
	38) Salinas, A. Berchuk, M. Welch, V. Fortin, P. Shea, B.	Omega 3 fatty acids supplementation for rheumatoid arthritis.	1997, *Issue* 3
	39) Farmer, A. Dineen, S	Omega 3 fatty acids on glycaemic control of plasma lipids in type II diabetes mellitus	1997, *Issue* 3
	40) Juni, P. Fux, C. Hertog, MGL. Egger, M. Ernst, E	Padma 28 (a Tibetan herbal preparation) for intermittent claudication.	1997, *Issue* 4
	41) Beckles Willson, N. Elliott, TM. Everard, ML	Omega-3 fatty acids for cystic fibrosis	2000, *Issue* 3
	42) Lethaby, AE Kronenberg, F. Roberts, H. Eden, J.	Phytoestrogens for menopausal symptoms	1998, *Issue* 4
	43) Soo, S. Moayyedi, P. Deeks, J. Delaney, B. Forman, D.	Psychotherapy for non-ulcer dyspepsia	1999, *Issue* 3
	44) Wilt, T. Ishani, A. Mac Donald, R. Rutks, I. Stark, G	Pygeum africanum for Benign Prostatic Hyperplasia	2000, *Issue* 2
New	45) Gambles, MA. Lockhart-Wood, K. Wilkinson, SM	Reflexology for symptom relief in patients with cancer	2001, *Issue* 1
	46) Rambaldi, A. Ghud, C.	S-adenosyl-L-methionine for alcoholic liver diseases	1999, *Issue*3

	47) Wilson, ML. Murphy, PA. Johnson, TC. Farquhar, CM	Spinal manipulation for primary and secondary dysmenorrhoea	1999, *Issue* 3
	48) Assendelft, WJJ. Shekelle, PG.	Spinal manipulation for low back pain	1996, *Issue* 1
New	49) Rees, K. Bennett, P. Vedhara, K. West, R. Davey Smith, G. Ebrahim, S	Stress management for coronary heart disease	2001, *Issue* 1
New	50) Szatmari, Sz Whitehouse, PJ	Vinpocetine for cognitive impairment and dementia	2001 *Issue* 2
	51) O'Mathuna, D.	Therapeutic touch in wound healing	1998, *Issue* 3
	52) Iasco, SM. Castro, AA. Atallah, AN	Vitamin B6 and placebo in premenstrual syndrome	1998, *Issue* 4
	53) Kaur, B.	Vitamin C supplementation for asthma	1997, *Issue* 3

III. CM Field Newly Registered Titles

2001	Li, Zi	Chinese herbal medicine for chronic renal failure	March, 2001
2001	Xiong, Dylan	Compound red sage root (radix salviae miltiorrhiaze) versus nitrate for angina	March, 2001
2001	Zeng, Xianrong	Gingko biloba extract for acute ischaemic stroke	March, 2001

Compiled by:
University of Maryland
Complementary Medicine Program
Cochrane Collaboration
Complementary Medicine Field

CAM evaluation comes into the mainstream: NIH Specialized Centers of research and the University of Maryland Center for Alternative Medicine Research in arthritis

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SUMMARY. In September of 1999 the National Institutes of Health (NIH) announced the funding of five Specialized Centers of Research in complementary and alternative medicine (CAM), bringing the total number of centers being supported to nine. The NIH center grant model provides a tremendous boost to the scientific investigation of CAM, nurturing an emerging field through the support of a step-wise research program of clinical and pre-clinical trials and developmental and feasibility studies; the building of infrastructure; and the training of a new cadre of scientific investigators in the field. This article explains the overall objectives of the NIH Specialized Centers program and focuses on one of the oldest CAM research centers in the USA, exploring some of the challenges faced in conducting CAM research while developing a center, and some of the goals and activities of the center. © 2000 Harcourt Publishers Ltd

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In September 1999 the National Institutes of Health (NIH) announced the funding of five Specialized Centers of Research in complementary and alternative medicine (CAM), bringing the total number of centers being supported to nine. These grants are an encouraging jump-start into the new millennium and a fittingly symbolic ending to the last decade of the old millennium–a decade in which CAM research in the USA has experienced a changing of the tides and a slow, but steady, rise in its acceptability as a target for federal support. Each of the centers will be receiving approximately $7.5 million in funding over the next 5 years and is expected to conduct clinical and pre-clinical research; encourage developmental and feasibility studies; and educate and train a new cadre of scientific investigators in the field. The nine centers are located around the country and each will have a disease or therapy area of focus (Table 1). Two of the centers funded last year (Columbia University and University of Maryland) were previously funded by the NIH and will be building on the initiatives started over the past 4 years.

The NIH center grant model draws from the experience of more mature disciplines and is designed to nurture an emerging field through a carefully staged research process. This process

Area of Focus	Institution	Principal Investigator
Addiction	Minneapolis Medical Research Foundation	Thomas Kiresuk, PhD
Arthritis and Related Disorders	University of Maryland	Brian Berman, MD
Cardiovascular Diseases	University of Michigan	Steven Bolling MD
Cardiovascular Diseases and Aging in African-Americans	Maharishi University	Robert Schneider, MD
Chiropractic	Palmer Center for Chiropractic Research	William Meeker, DC, MPH
Craniofacial Disorders	Kaiser Foundation Hospital, Oregon	Alexander White, DDS
Neurological Disorders	Oregon Health Sciences University	Barry Oken, MD
Pediatrics	University of Arizona	Fayez Ghishan, MD
Women's Health & Aging	Columbia University	Fredi Kronenberg, PhD

includes generating information on the effectiveness of a therapy through a range of methodological designs, the phasing of studies leading up to large randomized, controlled trials, and the building of infrastructure through support of core resources (such as data management, statistical analysis, and administration) and the training of new investigators. Hence, a minimum of three studies are supported under each center grant and are expected to lead on to large, randomized, controlled clinical trials. At the same time, innovative preliminary projects will be funded (subject to rigorous peer review) by the centers' development and feasibility programs. Junior faculty and post-doctoral fellows will be provided education and training in CAM and research, thus growing a new generation of investigators who are sensitive to the issues and challenges particular to CAM.

The University of Maryland Center

The Center for Alternative Medicine Evaluation and Research in Arthritis is housed within the University of Maryland's Complementary Medicine Program. This center grant is a competitive renewal of one of the initial 10 center grants awarded by the NIH in 1995 and builds upon a research program that is focused around pain related conditions. While each of the CAM centers undoubtedly has its own valuable stories to share, the University of Maryland program, as one of the oldest centers in this country, will be the focus of this article. We will explore some of the challenges we have faced in conducting CAM research while developing a center, and outline the goals for our center.

Edging into the academic arena

Everyone involved in the scientific investigation of CAM as well as its clinical practice is aware of the many obstacles that have confronted this field in its struggle for legitimacy in the medical and research arenas. At the time that the University of Maryland CAM program was established in 1991, one of the most often voiced criticisms of CAM was the lack of scientific data on its effectiveness and safety. However, at the same time, the CAM field lacked the infrastructure and research capacity with which to support and foster the sorely needed studies and trials. Most CAM practitioners themselves had little training in research, nor were there sources for the funding of research. Our program was fortunate to receive core funding from a private foundation and to find an academic institution open to embracing CAM evaluation at a time when the prevalent attitude to CAM in academic medical circles was characterized by hostility or distrust. With these resources at our disposal we were able to begin pilot studies which could generate crucial preliminary data allowing us to be competitive in applications to funding institutions such as the NIH.

Embarking on a research program

Before starting any studies and in order to assure ultimate usage of our limited means as well as identify the most needy and/or promising areas of investigation, we drew up a strategic plan for the center and set a research agenda. Our research agenda was based on surveys of CAM therapy usage rates, conditions identified as major public health problems, and review of the existing CAM literature.[1] As a result of this process we chose to focus on pain-related conditions and to initially examine therapies where there was the greatest body of evidence suggesting their usefulness, as well as evidence of their use by consumers.

Multiple preliminary studies based upon strong theory and the empirical work of previous investigators is always necessary before a definitive study is mounted. In our experience, following a step-wise progression of studies (somewhat mirroring the Federal Drug Administration guidelines for phasing of studies) has allowed for consideration of methodological issues, such as appropriate control groups, and other therapy-specific issues, such as appropriate dosage and safety, before embarking on full-blown, Phase 3, randomized controlled trials (RCT).

As an example of our approach, our group used the Phase I pilot studies to test suitable outcomes measurements and determine standardized acupuncture treatment protocols in studies of acupuncture for postoperative dental pain and for osteoarthritis. On the basis of this work we were able to successfully compete for some of the initial developmental grants funded by the newly-created NIH Office of Alternative Medicine. We then followed this work with two Phase 2 studies: one small trial (n = 39) comparing acupuncture to a mock acupuncture control (which involved no needle insertion) for acute pain; one larger study (n = 73) comparing acupuncture plus standard care to standard care alone with osteoarthritis patients.[2,3] These studies allowed us to: 1) test our hypothesis on a small, cost-effective scale; 2) conduct a power calculation for a larger trial; 3) assess the feasibility of the research setting; and 4) resolve unforeseen problems and thus design a solid study protocol for the RCT. Both studies are now funded by the NIH at the Phase 3 stage and, with large sample sizes and multi-site location, will be more definitive efficacy studies. The osteoarthritis study is a three arm parallel design (n = 570) comparing real versus sham acupuncture versus an education control group; while the dental trial is a two experiment, two site study that combines elements of both Phase 2 and 3 trials.

Finding and evaluating the existing evidence

One stumbling block we encountered early in our investigation of CAM was establishing what is known already. Without a thorough knowledge of the literature it is impossible to set a research agenda, know the pertinent questions to be asked, the study designs that are needed, or the methodological issues to be confronted. Much of the literature on CAM had not been published in mainstream medical journals, was published in languages other than English, and was not available through traditional medical literature databases and libraries. In our search for the literature on pain we confronted this problem and were able, as part of our first NIH center grant funding, to compile a database of the literature in CAM and pain (CAMPAIN). We drew from electronic sources worldwide as well as carrying out extensive hand-searching of journals and conference proceedings. A review we conducted of acupuncture treatment for chronic pain problems serves as an example of the hurdle of finding the literature in CAM.[4] In this study, a search of our CAMPAIN database yielded 58% more citations than a similar search of the National Library of Medicine's (NLM) Medline database. The CAMPAIN database (available on our website: www.compmed.ummc.umaryland.edu) currently contains 12 000 citations, testimony to the fact that there is existing evidence on CAM, although it has just been more difficult to access than other medical literature. Our reviews to-date, however, suggest that the quality of the science is generally poor and there are many gaps in our knowledge.[5,6]

At the international level, efforts to collect and evaluate the CAM literature have been substantially improved through the establishment in 1996 of a complementary medicine (CM) field within the Cochrane Collaboration.[7] The field is coordinated through our center and we maintain a comprehensive registry of RCTs in CAM which is uploaded to the central Cochrane library (which contains all known RCTs for all of medicine). The registry lays the groundwork for collaborators worldwide to conduct systematic reviews which will summarize existing evidence while minimizing bias. Furthermore, the CM field has also been working with the NLM to identify journals and to refine their thesaurus of CAM subject headings for Medline.

Evaluating CAM in a clinical setting

Some of the greatest challenges our center has faced has been in our clinical program. At the program's out-patient clinic, based at one of the University of Maryland hospitals, we have been assessing the value of integrating CAM therapies with conventional medicine in the treatment of patients with pain related conditions. However, generating truly useful data from outcomes research is extremely difficult due to the hectic, uncontrolled nature of clinical practice. On the whole, any data generated is generally less controlled than even our crudest pilot studies. For example, it is difficult to employ prospective exclusion/inclusion criteria for clinical patients and to administer outcomes measures specific to a particular diagnosis in a clinical setting. Although the clinic continues to be popular among patients and our data shows high satisfaction levels, developing meaningful outcomes data will continue to be a challenge for our center and the CAM community in general.

On a more practical level, obstacles we have faced in our clinical program have included distrust and unfamiliarity with CAM amongst many of the University's faculty and clinicians who have been opposed to CAM therapies being offered under the University's umbrella. However, we have sought to build confidence among our colleagues by offering only those CAM therapies for which there is some body of evidence to support their clinical usefulness and safety. Over time, the clinic has offered an excellent opportunity to build bridges through shared patient care, and has generated ideas for collaborative research endeavors. We have also had some interesting instances where some of our most skeptical research collaborators have resorted to acupuncture for relief of their own pain conditions. Personal experience of relief has often done more to change attitudes than objective research data!

Other hurdles we have faced have included staffing and reimbursement. The CAM therapists involved with our clinic have had extensive training in their respective fields and have been credentialed, however, with little standardized credentialing in most CAM professions to-date, finding suitable practitioners has not always been straightforward. Furthermore, lack of experience with or training in CAM has meant that there have been few physicians who can work at the clinic and coordinate integrated programs of care. Insurance coverage of CAM has only recently begun to improve and, while this obviously creates problems in making the clinic financially viable, it has also created problems in tracking long-term costs of CAM care.

Looking to the future

It will be exciting to observe how each Specialized Center confronts the issues and challenges of CAM evaluation. The NIH center grant mechanism, with its emphasis on rigorous scientific process, a structured progression of research, innovation, as well as training, provides the structure for CAM investigation to make huge advances in the new millennium. Our center will continue with efficacy trials (e.g. one study funded by our center grant will evaluate mind/body therapies for fibromyalgia), as well as studies of basic mechanism involved in CAM therapies (e.g. another program of research involves identifying the antagonist receptor system as well as the descending modulating pain pathway in the brain stem involved in electro-acupuncture using an animal model that we have pioneered in our basic science laboratory). We will also explore the long-term outcomes; patterns of health services utilization and costs of patients who are treated by acupuncture in the osteoarthritis RCT that is currently underway; as well as begin the investigation of the use of various herbs in the treatment of inflammation and immune mediated arthritis. In addition to our own primary research, we will continue to synthesize the results of CAM trials in order to make summary judgments regarding effectiveness. Equally exciting, the Specialized Center mechanism has provided a budget of approximately three quarters of a million dollars to fund projects involving promising investigators outside our program to continue the process that we have been involved with for the past decade. In this manner we hope to add to the scientific body of information on CAM and broaden the spectrum of evidence based treatments for chronic pain problems.

ACKNOWLEDGEMENTS

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Complementary medicine and medical education

Teaching complementary medicine offers a way of making teaching more holistic

Education and debate p 154

Complementary and alternative medicine is no longer an obscure issue in medicine. Our patients are using alternative therapies in addition to conventional care[1–3] and sometimes do not share this information with us. But even if they did would we know how best to advise them about safety issues or about the effectiveness of a particular therapy for their problem? Surveys indicate that doctors and medical students are increasingly interested in complementary and alternative therapy,[4–5] yet lack of knowledge is one of the greatest barriers to its appropriate use. Although many medical schools and training programmes now include teaching on complementary and alternative therapies, the approaches are variable and often superficial.

In this issue Owen et al ask provocative questions about our attitudes and behaviour towards complementary and alternative therapy (p 154),[6] and point out that few of us encountered such therapy as medical students or during later training. Nevertheless, there are signs of change, and Owen et al describe initiatives to include complementary and alternative therapy in medical education in the United Kingdom. Similar changes are occurring in the United States. In 1995 a national conference on complementary and alternative therapy education involving the National Institutes of Health recommended that complementary and alternative therapy should be included in nursing and medical education. Two years later a survey of all 125 US medical schools found that 75 of them offered some form of education on complementary and alternative therapy.[7]

Teaching includes elective modules, core curriculum lectures, and inclusion in problem based learning at undergraduate and residency level. Institutions such as Harvard and Stanford offer continuing postgraduate education courses, and the universities of Maryland and Arizona offer research and clinical fellowships. In addition, special interest groups in complementary and alternative therapy have been formed in professional organisations such as the Association of American Medical Colleges, and the Society for Teachers of Family Medicine has issued guidelines on including complementary and alternative therapy in the curriculum for residents.[8] The NIH-National Center for Complementary and Alternative Medicine recently issued funding initiatives to support the development of teaching on complementary and alternative therapy in medical, dental, and nursing education. The centre also supports career development and training programmes at several of its research centres around the country

BMJ 2001;322:121–2

When in 1992 we developed a complementary and alternative therapy curriculum at the University of Maryland we thought it was important to present the therapies in the context of their own philosophies and models of health and illness. Students and residents have the opportunity to experience the clinical practice of these therapies both in the community and in our own integrated medical clinic. We also teach students how to find and evaluate the evidence for the safety and efficacy of complementary and alternative therapies. Our goal is to encourage the additional skills of openness, sensitivity to cultural influences and beliefs, communication, and critical appraisal of the literature of complementary and alternative therapy treatments.

Nevertheless, great heterogeneity exists in the content, format, and requirements of complementary and alternative therapy courses for medical students and physicians in training. Typically, courses give an overview of the main complementary and alternative therapies and their uses and possible effects, but they do not teach skills to a clinical level of competence. Decisions about which complementary and alternative therapies to include in teaching will necessarily be dictated by usage patterns and resources in one's locality. However, guidance about the main complementary and alternative therapy categories can be obtained from sources such as the National Center for Complementary and Alternative Medicine (http://nccam.nih.gov). In addition, however, some general consensus needs to be reached on the essentials of a core curriculum. This should aim to improve doctors' knowledge of complementary and alternative therapy practices and their place in patient care; their ability to advise and guide patients about these therapies; their ability to refer patients to practitioners of complementary and alternative therapy; and their knowledge of the practicalities, such as credentials and legal and reimbursement issues.

Most medical schools have a packed curriculum, so complementary and alternative therapy options tend to be electives with only a smattering of core curriculum lectures. Given the shift towards problem based and case based learning, it is a realistic goal to have complementary and alternative therapy treatment options integrated into existing teaching at all levels. This highlights the need for faculty development. Academics who are not experts in complementary and alternative therapy but accept its legitimacy at some level must gain knowledge of the subject in order for students to receive this exposure. Complementary and alternative therapy educators will need clearly to define their objectives and goals and be rigorous in evaluating whether their aims are being met. Nevertheless, until qualification requirements include components on complementary and alternative therapy it may seem an indulgence to curriculum committees and students to dedicate time to complementary and alternative therapy.

We know from research that people are drawn to complementary and alternative therapy mostly out of a desire for a more humanistic, "holistic" approach.[9 10] Medical education should re-examine the emphasis it places on the importance of the integration of mind, body, and spirit and acknowledge the role of social, cultural, and environmental influences and the power of self care and healing. Healthcare professionals, patients, and our healthcare system can only benefit if medical education bridges the gap with complementary and alternative therapy.

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Divider Title: Concerns About CAM

IV

Questions for the Panel on Concerns about CAM and CAM Research Panel:

What are your major concerns about CAM practices and products and about CAM research?

When addressing the need to find research methods and approaches to establish the safety and effectiveness of CAM practices and products, in addition to data collection and clinical trial methodology, consider how we can study the complex questions inherent in CAM such as multiple interventions; complex systems and complex compounds; mind-body interactions; individualization; the placebo effect; qualitative research; energy medicine; provider/patient interaction; multiple populations including culture/race, gender, age; and so forth?

What policy recommendations can you offer regarding research on CAM practices and procedures for the Commission's consideration as it develops its report to the President and Congress?

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Divider Title: London

William M. London

William M. London, EdD, MPH is the president of The National Council Against Health Fraud, Inc. He is an associate professor of health care management and the director of the Graduate Program in Health Care Management, College of St. Elizabeth in Morristown, New Jersey. He also has an appointment as a specialized faculty mentor in the Master of Science in Public Health program of Walden University. Dr. London is a contributing editor to *The Scientific Review of Alternative Medicine and Aberrant Medical Practices*. He is a co-author of sixth edition of the college textbook *Consumer Health: A Guide to Intelligent Decisions* and a co-author of the seventh edition of the textbook, which is scheduled for publication in July 2001.

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2. WHCCAM should promote opportunities for research to increase knowledge about quackery/health fraud as a public-health problem associated with the "complementary" and "alternative" medicine marketplace.[8]
3. WHCCAM should declare that it is misleading to use the terms "complementary" and "alternative" to refer to questionable, unproven, and disproved methods. Reliable and useful information must be grounded in principles of consumer protection and science.
4. WHCCAM should recommend that appropriate access and delivery of healthcare be based on principles of consumer protection and science.

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Quackery: "Promoting health products, services, or practices of questionable safety, effectiveness, or validity for an intended purpose." [NCAHF, 1986]

Health fraud/quacks: "Health fraud is the promotion, for financial gain, of fraudulent or unproven devices, treatments, services, plans or products (including, but not limited to, diets and nutritional supplements) that alter or claim to alter the human condition. Those who promote such medical remedies that do not work or have not been proven to work are called 'quacks.'" [The Assembly Republican Task Force on Health Fraud and the Elderly, New York State Assembly, June 1986]

Health fraud: "The deceptive promotion, advertisement, distribution or sale of articles, intended for human or animal use, that are represented as being effective to diagnose, prevent, cure, treat, or mitigate disease (or other conditions), or provide a beneficial effect on health, but which have not been scientifically proven safe and effective for such purposes. Such practices may be deliberate, or done without adequate knowledge or understanding of the article." [Compliance Policy Council of the U.S. Food and Drug Administration. Announced in a letter from M. L. Frazier, Director, State Information Branch, June 18, 1993.]

Recommendations

1. The education and training of health care practitioners must address principles of consumer protection and science. Health care practitioners must learn to recognize quackery/health fraud associated with "complementary" and "alternative" medicine.

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- Providing a center for communication between individuals and organizations concerned about health misinformation, fraud, and quackery.
- Supporting sound consumer health laws.
- Opposing legislation that undermines consumer rights.
- Encouraging and aiding legal actions against those who violate consumer protection laws.
- Sponsoring a free, weekly e-mail newsletter.

NCAHF's publications rely on the following definitions:

Fraud: "An intentional perversion of truth for the purpose of inducing another in reliance upon it to part with some valuable thing. . . . a false representation of a matter of fact, whether by words or by conduct, by false or misleading allegations, or by concealment of that which should have been disclosed, which deceives or is intended to deceive another so that he shall act upon it."[Black's Legal Dictionary, 4th Edition, 1968]

Misinformation: "Untrue or misleading information." [Webster's Seventh New Collegiate Dictionary, 1972]

Promote: "To contribute to the growth or prosperity of; to present for public acceptance through advertising and publicity." [Webster's New Collegiate Dictionary, 1975]

Quack: "Anyone who promotes medical schemes or remedies known to be false, or which are unproven, for a profit." [United States House of Representatives, Select Committee on Aging, Subcommittee on Health and Long-term Care. Quackery: A $10 Billion Scandal. Washington, DC, 1984, US Government Printing Office.]

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- Professionals in the health sciences, academia, law and business as well as government agencies share a responsibility to help consumers protect themselves from deception and exploitation in health-related matters.
- The scientific process is essential for discovering truths and validating health claims and information.
- Health products and services should be:
    - proved safe and effective before marketing with proponents bearing the burden of such proof.
    - accurately labeled or fully described.
    - truthfully advertised.
- As noted in the Consumer Bill of Rights, consumers have:
    - The right to free and informed choice.
    - The right to accurate information.
    - The right to safety.
    - The right to be heard.
    - The right to consumer education.

Activities and Purposes

NCAHF's activities and purposes include:

- Investigating and evaluating claims made for health products and services.
- Educating consumers, professionals, business people, legislators, law enforcement personnel, organizations and agencies about health fraud, misinformation, and quackery.

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motto of The National Council against Health Fraud is: "Enhancing freedom of choice through reliable information."

About The National Council Against Health Fraud, Inc.

The National Council Against Health Fraud is a nonprofit, tax-exempt voluntary health agency that focuses its attention upon health fraud, misinformation, and quackery as public health problems. It is private, nonpartisan, and nonsectarian. Its members are health professionals, educators, researchers, attorneys, and other concerned citizens. Its officers and board members serve without compensation.

Background History

The Council originated in 1977 as the Southern California Council Against Health Fraud, Inc. and became the California Council Against Health Fraud in 1978. The Council became national in 1984. It is now incorporated in California and has members in all 50 states, the District of Columbia, and several foreign countries. Nearly all of our funding comes from membership dues and individual contributions.

Basic Principles

NCAHF bases its claim to be a consumer organization on its founding principles derived from consumer protection law and the scientific process. Included are the beliefs that:

- "Consumer" is not a special class but a role played by all; everyone in a free enterprise society has a stake in maintaining high standards for health products and services.

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According to a usage dictionary, "First, *alternative* may suggest adequacy for some purpose...; and second, it may suggest compulsion to choose.[7] Questionable and dubious methods are not adequate for their intended purposes. And consumers should not feel compelled to choose them.

It is unavoidable for legitimate practitioners to use unproven methods. Medicine will never have all the answers. Clinical judgment and innovation will always be important to the art of delivering healthcare. However, responsible healthcare professionals do not promote unproven methods. The promotion of unproven methods through such methods as advertising and publicity is objectionable because it is deceptive. It violates the ethical principles of veracity and non-maleficence.

Everyone wants alternatives, but they want genuine alternatives. Many promoters of "alternative" medicine exploit this by calling for "freedom of choice" for consumers. What these promoters really want is freedom from accountability to consumers. They support the concept of caveat emptor, "let the buyer beware," but they have a problem with the concept of caveat vendor, "let the seller beware." Caveat vendor provides a rationale for consumer protection laws to compensate for the disadvantageous bargaining position consumers have in the health marketplace. It is difficult to evaluate claims for health products and services. We are vulnerable to mistaken perception and deception especially when we feel threats to our well-being and when we are desperate for answers. It is important to protect consumers from both intentional and unintentional deception. And it is also important to preserve true freedom of choice. Thus, the

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Genuine alternatives or genuinely complementary methods tend not to require the justification of labels like "alternative" or "complementary" in marketing.

Experimental methods are unproven, but are studied responsibly with extra care given to seeking informed consent from study participants and protecting them from exploitation. It is reasonable for taxpayers to expect that their financial support will be used to study promising rather than implausible methods. But many taxpayers don't realize that alternativists do not espouse such values. Alternativists have no problem with taxpayers supporting the study of implausible methods.

Remarkably, NCCAM is currently funding a study of an "alternative" protocol involving enzyme supplements and coffee enemas. The protocol is implausible.[5] had been used on a Hodgkin's lymphoma patient who died. Last year a jury found that the patient was 51% responsible for her harm. The jury said that the patient was "negligent" in letting the physician treat her and for foregoing the standard care her original doctors had recommended.[6]

Questionable methods are those for which scientific evidence is insufficient to support the claims made by proponents. The most implausible questionable methods are legitimately described as dubious. (Perhaps I should add a fourth category of plausible alternatives with clear benefits and clear risks when used for an intended purpose, but for which it is unclear whether proven benefits outweigh the risks. Estrogen replacement therapy for postmenopausal women might belong in this fourth category.)

hunches, clinical impressions, subjectivity, anecdotes, reports of best cases, legends, and so-called "other ways of knowing," as sufficient "proof" to justify their promotional efforts. They tend not to value efforts to identify sources of clinical illusions and to reduce the problems of systematic and nonsystematic errors leading to faulty conclusions.

Alternativists also value different credentials and standards of practice than most consumers expect. "Alternative" credentials and standards of practice tend to be different in that they don't espouse the need for professional accountability. I believe the WHCCAM should note that this poses a problem for consumers.

"Alternative" medicine methods generally do not allow or necessitate a choice between two or more things, as suggested by dictionary definition number 1 above for "alternative." Drs. Marcia Angell and Jerome P. Kassirer, former editors of *The New England Journal of Medicine* have pointed out: "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."[3]

I have proposed that alternatives be classified into three categories: genuine, experimental, and questionable.[4]

Genuine alternatives are backed by sufficient scientific evidence showing that the potential for benefit exceeds the potential for harm to specific populations for specific intended purposes.

methods. Traditionalists and true-believers cling to unsafe and ineffective methods as a matter of faith.

I am unaware of any efforts by OAM and later by NCCAM to identify methods promoted as "complementary" or "alternative" that should be discarded. In order to provide reliable and useful information about complementary and alternative medicine, it is necessary to identify methods that should be discarded. I ask that the WHCCAM to make recommendations to accomplish this based on principles of consumer protection and science discussed later in this paper.

Much has been written about the established institutions and systems of delivering medical care. I think it is fair to note the existence of the "alternative" medical establishment which is composed of prominent promoters, practitioners, organizations, foundations, retail businesses, wholesale businesses, politicians, the NCCAM, the WHCCAM, and other institutions. The "alternative" medical establishment has even extended its reach into medical schools, other professional schools, colleges and universities, hospitals, and insurance plans. In so doing, alternativists have increased their power and, in effect, invalidated the NCCAM definition of complementary and alternative medicine.

"Alternative" medicine *is* alternative in the sense of espousing or reflecting values that are different from those of the establishment (definition 2a above), if by establishment we mean people who insist that health products and services be proved safe and effective—with proponents bearing the burden of such proof—before promoting them. Alternativists often value

complements anything else in providing benefit to health. The claim that a particular method is complementary to anything else is misleading unless the claim can be supported by evidence. If a method doesn't add to the outcome then it isn't complementary; it just adds to the cost. Few, if any, methods, marketed as "complementary" medicine have been shown to complement anything else.

What Would Make "Alternative" Medicine Alternative?

The *American Heritage Dictionary of the English Language, Third Edition* defines alternative, when used as an adjective, as: "**1.** Allowing or necessitating a choice between two or more things. **2.a** Existing outside traditional or established institutions or systems : *an alternative lifestyle*. **b.** Espousing or reflecting values that are different from those of the establishment...." (p. 55.)

The NCCAM definition suggests that "alternative" medicine is "alternative" in the sense of dictionary definition 2a. To some extent this is a fair characterization. However, "alternative" medicine is largely "traditional" itself and it has become its own "establishment." Promoters of "alternative" medicine often promote traditional systems for alleged healing. Strong reliance on tradition is one of "alternative" medicine's biggest problems. Tradition-bound systems resist change. Their proponents selectively seek affirming evidence while rejecting disconfirming evidence and criticism. Proponents adhere to orthodoxy.

On the other hand, science/evidence-based medicine is iconoclastic. Medical practice changes over time because scientifically-based practitioners learn to discard unsafe and ineffective

"unconventional.") The study reported on a national telephone survey of the use by adults of methods such as relaxation techniques, massage, exercise, prayer, self-help groups such as Alcoholics Anonymous, imagery, biofeedback, and hypnosis. Many of the methods discussed in the survey are either methods of self-care or, in contradiction to the definition used for "unconventional medicine" in the study, are methods with established medical uses.[2] The study showed that few survey respondents used commercially promoted methods such as acupuncture, homeopathy, energy healing, megavitamin therapy, and herbal medicine. Strangely, 30% of respondents who reported use of chiropractic didn't actually see a provider of chiropractic services.

The NCCAM definition has little to do with what the words "complementary" and "alternative" actually mean. To refer to "complementary" and "alternative" methods is to imply that such methods actually complement other methods or serve as alternatives to other methods. The "complementary" and "alternative" medicine marketplace is dominated by products, services, and regimens that have not been shown to complement or serve as a genuine alternative to any other method for significant intended purposes.

What Would Make "Complementary" Medicine Complementary?

The *American Heritage Dictionary of the English Language, Third Edition* defines complementary as: "**1.** Forming or serving as a complement; completing. **2.** Supplying mutual needs or offsetting mutual lacks." (p. 386). Thus, to refer to something as "complementary medicine" implies that it completes what some other medicine does not do on its own. However, just because someone refers to a method as complementary does not mean it actually

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Problems with Terminology

According to Executive Order 13147, the White House Commission on Complementary and Alternative and Medicine shall provide a report on recommendations addressing: "(a) the education and training of health care practitioners in complementary and alternative medicine; (b) coordinated research to increase knowledge about complementary and alternative medicine practices and products; (c) the provision to health care professionals of reliable and useful information about complementary and alternative medicine that can be made readily accessible and understandable to the general public; and (d) guidance for appropriate access to and delivery of complementary and alternative medicine."

In order to make these recommendations, I recommend that the Committee acknowledge that the term "complementary and alternative medicine" implies much more than what is in the definition of complementary and alternative medicine used by the National Center for Complementary and Alternative Medicine (NCCAM). According NCCAM: "Complementary and alternative medicine (CAM) covers a broad range of healing philosophies, approaches, and therapies. Generally , it is defined as those treatments and healthcare practices not taught widely in medical schools, not generally used in hospitals, and not usually reimbursed by medical insurance companies."

The NCCAM definition is similar to the definition used for "unconventional medicine" in a paper by Eisenberg et al,[1] which is often misrepresented as providing evidence that Americans are so interested in "complementary and alternative medicine" that NIH funding of CAM research is needed. ("Complementary" and "alternative" have far more promotional value than

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A Call to Oppose Health Fraud and Quackery Promoted as "Complementary" and "Alternative" Medicine

Statement to the White House Commission on Complementary and Alternative Medicine
May 15, 2001

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Margolis

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Simeon Margolis, M.D., Ph.D.

Dr. Margolis received his M.D. and Ph.D. degrees at the Johns Hopkins University School of Medicine. He was appointed to the Hopkins faculty upon completion of his residency on the medical service at Johns Hopkins Hospital in 1965. He is presently a Professor of Medicine and Biological Chemistry. He was the Director of the Division of Endocrinology and Metabolism in the Department of Medicine from 1968 to 1981 and from 1985 to 1990. He served as the Associate Dean for Academic Affairs from 1984 to 1990 and subsequently was Associate Dean for Faculty Affairs for 18 months. He has been a consultant to the Food and Drug Administration and to the National Institutes of Health as a member of the Metabolism Study Section, the General Clinical Research Centers Committee, and the Committee on Specialized Centers for Atherosclerosis Research. Dr. Margolis' laboratory research had focused on the factors that regulate the synthesis and breakdown of cholesterol in isolated liver cells. His clinical research has involved studies on the effects of diet and drugs on the levels of serum lipids and lipoproteins. He was an active participant in the Lipid Research Clinics Coronary Primary Prevention Trial which showed that lowering cholesterol levels led to a significant reduction in the complications of coronary heart disease.

Dr. Margolis' practice has been directed to the prevention of premature coronary heart disease, mainly by proper management of abnormalities of serum lipids and lipoproteins. He has been very active in teaching the principles of diagnosis and treatment of these disorders to both medical students and practicing physicians and has written many articles and book chapters on this subject. Over the last decade he has written and edited a number of books and other publications directed at the lay public, including the monthly Johns Hopkins newsletter Health After 50.

Dr. Simeon Margolis: Summary of Remarks

Let me preface my remarks by stating that I would enthusiastically welcome any alternative and complementary product or practice that is proven to be effective.

As you have heard or will hear from other members of the panel, the major problems with CAM are well recognized:

Most CAM products and practices are either untested or based on unreliable research.

Nonetheless, they are aggressively promoted, usually with guarantees of success. Yet any experienced physician knows that no treatment or procedure is always effective.

These promotions and promises mean that patients may waste money on unproven measures, and at the same time fail to seek medical attention and obtain medications or procedures with proven effectiveness for illnesses that may have serious consequences.

People are urged to use CAM products because they are "natural", apparently forgetting that poison ivy, floods, hurricanes and tornadoes prove that natural isn't necessarily good.

And finally, because CAM products are unregulated, patients can be subjected to serious risks.

I will take one example - chelation therapy - and have included an article I have written on the subject as a reference.

Chelation involves a course of 2 to 3 weekly, 2-hour long intravenous infusions of EDTA for a total of 30 treatments. Based on a number of uncontrolled studies, chelation therapy is reputed to improve the activity-related pain of coronary artery disease and peripheral vascular disease by binding calcium and heavy metals that may cause damage by enhancing the oxidation of tissues and blood proteins. With the exception of one small, short study, all of the CAM-based studies of chelation had no control group. Two earlier randomized, blinded studies, done in Scandinavia and New Zealand on patients with claudication, injected either EDTA or saline alone in a control group. After treatment, there were no differences between the EDTA group and the control group in how long they could walk on a treadmill before developing leg pain. A recent study from Canada of 80 angina patients, reported this March at a meeting of the American College of Cardiology, found no differences between the EDTA and control groups in how long they could walk on a treadmill before developing ischemic changes on an ECG. BUT in all three studies patients in both the EDTA and control groups had modest improvements in how long they could walk before developing leg pain or angina. These findings emphasize the importance of a control group in studies of chelation, or any other CAM product or procedure.

In the Canadian study, patients in both groups reported on questionnaires that they had less angina and better quality of life after the treatments. Chelation patients often feel they were improved by the treatment; but I suspect that anyone in this audience would tell their doctors they were better, and indeed believe they were improved, after they underwent 30 intravenous infusions and spent about $5000 out-of-pocket.

Most distressing to me is the statement made in response to the Canadian study by Dr. Michael Janson, past president of the American College for Advancement in Medicine, who is quoted as saying

"I've been doing it for 18 years and have seen some dramatic differences. I've been really impressed with it". He also said that 75% of his patients respond and are able to walk farther and have less chest pain. His reaction raises the concern that CAM practitioners will not accept the negative results of scientifically valid studies and alter their practices accordingly.. If that is true, properly conducted research by either CAM investigators or NIH-supported investigators at academic institutions will be nothing more than a waste of time and money.

A second question we were asked to address is how valid research can study the complex issues inherent in CAM research.

I submit that the problems associated with CAM research are inherently no different than those faced in other areas of clinical research. What is needed is some ingenuity, the design of carefully controlled studies, and the willingness of investigators to roll up their sleeves and do the work.

My recommendations to the Commission are:

1. CAM research requires large well-controlled studies which provides scientific evidence that either supports or rejects the value of all CAM products, such as herbs and vitamins, as well as procedures, like chelation and therapeutic touch. Such studies on safety and efficacy must be done before marketing and promotion of products because it would exorbitantly expensive for government agencies to fund such studies on every herbal product, for example, reputed to be beneficial. The failure to carry out such studies means that the public will lose out on two scores:

First, the public will continue to waste money using ineffective and possibly risky CAM products.

Secondly, they will not have widespread access to CAM products and practices that really are effective.

2. The Commission should urge Congress to revise the "dietary supplement " act of 1994 so that the FDA has some control over CAM products and procedures.

3. Finally, the Commission and CAM practitioners must accept and act appropriately if the results of sound studies prove that a CAM product or practice is ineffective or dangerous.

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POINT

EDTA CHELATION THERAPY SHOULD BE MORE COMMONLY USED IN THE TREATMENT OF VASCULAR DISEASE

L Terry Chappell, MD

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EDTA chelation therapy is safe, effective, and more economical than commonly used surgical treatments for vascular disease. This article includes evidence of effectiveness, mechanisms of action of EDTA, a discussion of studies that have been done regarding the therapy, and some brief case reports. The conclusion is that EDTA chelation therapy should be a therapeutic option for vascular disease, either by itself or in conjunction with standard protocols. (Alternative Therapies in Health and Medicine. 1995;1(2):53-57)

Standard treatments of coronary, cerebral, and peripheral vascular disease are expensive and have high complication rates and significant mortality. The integration of ethylenediaminetetraacetic acid (EDTA) chelation therapy with these treatments would make them safer and more cost-effective and would often result in better clinical outcomes.

The following facts are supported by the literature:

- The mortality rate of coronary bypass is 4% to 10%,[1] and is even higher in elderly patients.[2] Common complications are restenosis within 7 years[3] and significant cerebral dysfunction after the procedure.[4]
- Only a limited number of vessels can be treated by angioplasty, and restenosis rates are as high as 40% within 6 months.[5]
- A cardiac bypass procedure costs about $50,000[6]; EDTA

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CHELATION THERAPY IS INEFFECTIVE FOR THE TREATMENT OF PERIPHERAL VASCULAR DISEASE

Simeon Margolis, MD, PhD

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The case against chelation therapy for cardiovascular disease (CVD) can be summarized in one sentence: Although advocates of chelation therapy have reported favorable results based on uncontrolled, usually retrospective "studies," two double-blind, randomized, placebo-controlled, prospective trials have shown that infusions of ethylenediaminetetraacetic acid (EDTA) are no more effective in improving the manifestations of peripheral vascular disease (PVD) than are infusions of a placebo.

Proponents have claimed that chelation therapy improves liver function, memory, and vision; lowers cholesterol; relieves symptoms of arthritis, Parkinson's disease, and multiple sclerosis; and reduces the incidence of cancer. The major use of chelation therapy, however, has been to treat CVD. In at least 50 published papers, chelation therapists have reported remarkable improvements in symptoms and objective findings following a course of chelation treatment. Unfortunately, these reports provide no acceptable scientific evidence for the benefits of chelation therapy because none of them included a control group.

In a meta-analysis Chappell and Stahl[1] selected 19 of 40 articles describing the effects of chelation treatment on CVD. They concluded that 87% of the patients included in their analysis "demonstrated clinical improvement by objective testing." A letter by Jonas[2] points out that this meta-analysis is fatally flawed despite a reasonable statistical approach. The absence of a control group in all but one of the studies is sufficient to reject the validity of the analysis. As shown in controlled studies described below, chelation therapy does provide some objective, short-term improvement in patients with PVD, but similar improvement occurred in the control patients. In addition to the other weaknesses cited by Jonas, 94% of the subjects included in the meta-analysis (21,629 of 22,765 subjects) were from two

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chelation therapy costs about one tenth that amount.

In the last 20 years, mortality due to cardiovascular disease has declined somewhat.[7] This improvement is probably due more to lifestyle changes than to new therapeutic interventions.[8]

Good, clean, precise, double-blind controlled trials on cardiovascular therapies are desirable, but because of the number of variables, such studies are very difficult to conduct with high accuracy, and they often conflict. None have been performed for bypass, angioplasty, or EDTA chelation.

A preponderance of evidence shows that EDTA and other chelating agents are effective in treating vascular disease and are dramatically effective in certain patients. When given according to the published protocol, EDTA is safe, with a mortality rate that approaches zero and very low morbidity.[9]

EVIDENCE OF EDTA EFFECTIVENESS

Chappell and Stahl[10] did a meta-analysis to determine whether correlation between treatment with EDTA and improvement in vascular disease was significant. Meta-analysis is a technique that is particularly well-suited for determining the net effect of multiple studies with somewhat different designs, and for evaluating controversial therapies.[11,12] Of the 41 studies we found in a literature search, 19 that were published or submitted for publication met our criteria that objective data be listed on individual patients with vascular disease. A total of 22,765 patients had been enrolled in these studies; 87% of them had measurable improvement with treatment, and the correlation coefficient was highly positive at .88. To ensure that there was no type I publication bias by excluding unpublished data, a follow-up study[13] on 1241 patients from 32 investigators was done. That meta-analysis also showed a correlation coefficient of .88, and 88% of the patients improved. Our conclusion was that EDTA was indeed effective in treating vascular disease. Using the square of the correlation coefficient as an estimate of the variability, it was estimated that 77% of the variability in improvement was due to EDTA and the rest to unknown factors. The improvement rate of 87% is comparable to that in the primary trials of pentoxifylline[14] for the treatment of peripheral vascular disease (84%).

Several clinical studies merit special mention. Olszewer and Carter[15] published a study of 2870 patients with various chronic degenerative diseases, primarily vascular. Almost 90% of them showed good to excellent outcomes. They also completed a small double-blind, crossover, controlled study[16] on cardiovascular patients that was strongly positive. Van der Schaar[17] demonstrated that by using the double and triple product on treadmill testing, almost all patients improved with EDTA treatment. Rudolph et al[18] documented consistent improvement on Doppler ultrasound readings for patients with carotid artery obstruction and recently published a case study[19] with retinal photographs showing improvement in macular degeneration. Brittenham and associates[20] used the iron chelator deferoxamine to prevent vascular

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studies.[3,4] The size of these two studies so dominates the outcome of the meta-analysis that the other 17 studies don't affect the results.

Are these two large studies examples of careful clinical investigation? Judge for yourself. In the larger study, with 19,147 subjects, which was unpublished at the time of the meta-analysis, investigators apparently used only thermography to measure improvement. Although a survey[6] showed that the majority of authors and half the responding editors felt that it was acceptable to include unpublished data in a meta-analysis, the scientific rigor and validity of this large study, which accounts for the vast bulk of the patients included in this meta-analysis, are impossible to evaluate. Both of these studies were retrospective, included no controls, and involved a mixture of patients with PVD, coronary artery disease (CAD), and cerebrovascular disease. The lack of validity in lumping these three aspects of CVD together in a meta-analysis is evident from another publication by the authors of the smaller of these two studies,[6] in which marked improvement in 91% of patients with PVD, 77% with CAD, and only 24% with "cerebral diseases" was reported. No improvement was seen in the 88 patients who had suffered a stroke at least 6 months before the initiation of treatment.

A placebo-controlled study of chelation therapy was started in 10 patients with PVD by Olszewer and coworkers,[7] but after 10 infusions they noted that "some patients were improving substantially but others were not." When the code was broken, these investigators found that the five subjects who had not improved were receiving the placebo infusions. Accordingly, all subjects were then treated with 10 infusions of EDTA, and those initially in the control group improved nearly as much as those receiving the full 20 infusions. Incidentally, this raises the question of whether 30, 20, 10, or even fewer treatments with EDTA are needed to achieve the improvements claimed for chelation therapy. This issue has never been carefully evaluated.

To date, three reports have described the results of two randomized, double-blind, placebo-controlled studies of EDTA chelation for treatment of PVD. The first[8] reported results from a subset (30 patients) of 153 Danish patients with claudication treated with 20 infusions of either sodium EDTA or saline. They found no differences between the 15 treated with EDTA and the 15 control patients in angiograms, ankle-brachial indices, transcutaneous oxygen tension, walking distance, or subjective improvement measured before, during, and after the infusions. This paper was soundly criticized in an unsigned editorial[9] as a "harsh critique" revealing "political bias" rather than welcoming it as the first careful, controlled study of the issue. The editorial suggested that the 30 patients selected for inclusion in the study might not be representative of the whole group of 153 subjects and that "the authors may conveniently forget to publish the entire data." The absence of a bibliography was deemed "unusual."

The results from all 153 subjects *were* published,[10] along

complications in patients with iron overload. Casdorph[21,22] used technetium-99 isotope techniques that demonstrated improvement in coronary and carotid disease.

Researchers in two studies (published in three journals[23-25]) have claimed the studies to be randomized, well-controlled, double-blind clinical trials; they supposedly did not confirm the effectiveness of EDTA chelation treatment. Subjects in both groups were primarily smokers who had severe disease and were given minimal treatment (20 sessions, instead of the 30 or 40 suggested for such patients by physicians experienced with chelation). The fact that so many were smokers greatly limits the usefulness of the studies. But despite the limitations, 50% to 60% of the treated patients improved in both studies. Sloth-Nielson and colleagues did not follow the protocol for EDTA use established by the American College for Advancement in Medicine, although they claimed to have done so. The study was criticized in at least four journals[26-28] and also by the Danish Council on Scientific Dishonesty.[30] The trial by Van Rij and colleagues[25] actually compared two chelating solutions, one with EDTA and the other without. Intermittent claudication patients treated with both solutions showed significant improvement, the former (60%) slightly more than the latter (59%). Since this improvement is much higher than expected in similar patients treated with placebo,[14] the study actually confirms the therapeutic effect of chelating solutions.

Of 65 patients who were on a waiting list for cardiac bypass surgery, 58 were able to cancel their surgery after chelation therapy by Hancke and Flytlie.[31] Similarly, 24 of 27 patients awaiting amputation were able to cancel their surgery after EDTA chelation treatment. Chappell[32] applied these figures to such cases in the United States and speculated that if chelation therapy had been used as a primary treatment in 1992, 363,000 of 407,000 bypasses might have been avoided and 102,000 limbs might have been saved. The estimated direct cost savings in that year alone would have been close to $8 billion.

MECHANISMS OF ACTION

Multiple mechanisms of action have been documented for EDTA therapy: it decreases plaque formation and has a positive influence on cell membrane function. Kaman and associates[33] demonstrated the removal of metastatic calcium from rabbit aortas. Kindness and Frackelton[34] showed a dramatic inhibition of platelet aggregation and prolongation of partial thromboplastin time. Gutteridge[35] identified increased effectiveness of hydroxyl-radical scavengers in the presence of EDTA. Rudolph et al[36] showed a reduction of iron with chelation treatment. Further effects include improved lipid levels[37] and the restoration of electromagnetic potential across cell membranes.[38] Several detailed reviews of these mechanisms have been published.[39-42]

Free radicals have been shown to cause ischemic cardioplegia after bypass.[43] Grech and associates[44] recently demonstrated a marked increase in free-radical activity after primary coronary

with 21 references. When examined 3 and 6 months after the two courses of treatment, identical numbers of subjects in both groups reported that their symptoms were unchanged or improved; and there were no differences between the two groups in objective measurement of distance the subjects could walk before developing leg pains. The above-mentioned editorial made the following criticisms of this study: the use of sodium EDTA instead of magnesium EDTA would cause local pain and unblind the study; mineral and vitamin supplementation was not provided; the load of 8.4 g of sodium with the EDTA was detrimental; and two thirds of the patients continued to smoke.

The authors of the Danish paper mentioned in their Discussion section that the incidence of local pain and phlebitis was the same in those treated either with EDTA or saline alone. Others have reported the same beneficial effects from sodium and magnesium EDTA. A daily oral supplement of vitamins and minerals was given throughout the study. The amount of sodium added with the EDTA is trivial compared with the amount of sodium in the saline used for both sets of infusions, and it is not clear why chelation would be ineffective in smokers. The major benefits of chelation are now attributed to their antioxidant effect; and a recent epidemiological study[11] showed that intake of the antioxidant β-carotene reduced CAD in current and former male smokers, but not in men who had never smoked.

The latest double-blind, randomized, placebo-controlled trial of chelation therapy for PVD was carried out in New Zealand.[12] The 32 subjects received 20 saline infusions each, oral and intravenous vitamins, and sodium EDTA plus magnesium in the treatment group of 15 patients. Subjects were not permitted to smoke. No clinically significant differences were detected between the two groups up to 3 months after treatment in subjective and measured walking distance, ankle/brachial pulse indices, mood state, activities of daily living, or quality of life factors. It is particularly instructive to note that an improvement in walking distance was reported in 60% of the chelation group and 59% of the control group. Similar results were obtained in the Danish study; 50% of the placebo patients and 48% of those treated with EDTA reported mild to great improvement in their symptoms. These findings once more demonstrate the strong placebo effect of many treatments and the questionable validity of claims for benefits from any therapeutic approach unless a comparison is made with some type of placebo treatment.

One wonders what kind of criticism of this study will emerge from the advocates of chelation treatment. Perhaps the answer is best predicted by quoting the last paragraph from the editorial supporting chelation therapy.[3] "Our obligation as physicians and scientists is to prove by well-planned studies that this technique which we use constantly in our practices is beneficial to the long-suffering chronically sick people who are our patients. Thus, and only by such measures, do we remove the ugly bias which stalks the subject of EDTA chelation. This is, indeed, why ACAM [American College of Advancement in

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angioplasty in acute myocardial infarction. Since chelating agents can often control free-radical activity, they appear to be ideal agents for improving outcomes in patients with coronary artery disease.[45-47]

Certainly, well-designed, randomized studies on the use of EDTA for vascular disease should be completed. But the above evidence is sufficient at this time for the off-label use of chelating agents with informed consent.

DRAMATIC CASES

Physicians who offer chelation therapy often have successfully treated patients who had had multiple surgical procedures and been told that nothing remained to be done except to go home and die. I have had two patients who were previously on the heart transplant waiting list. After EDTA treatment, both were removed from the list by their cardiologists and both lead active lives. Another patient, a 59-year-old man, had spent 120 days per year in the hospital for 3 years. He had a history of five myocardial infarctions, seven angioplasty procedures, and one bypass. He required a meperidine injection to walk a block without chest pain. In the 2 years since EDTA treatment was begun, he has been in the hospital for only 2 days (for noncardiac pain). He takes no oral medication whatsoever and he bowls and plays golf for the first time in years. His insurance company paid approximately $600,000 for functionally ineffective hospital care (although it may have kept him alive) and reimbursed none of the $5000 he spent on the highly successful EDTA treatment.

INTEGRATION OF EDTA CHELATION THERAPY INTO CURRENT PROTOCOLS

EDTA treatment is not a "magic bullet." Physicians who use it must be well-trained.[9] The American Board of Chelation Therapy has a rigorous certification process to identify specialists in the field. The therapy is only part of a comprehensive program that includes lifestyle changes and a continuation of medications that appear beneficial. Overall, 87% of patients who use the treatment demonstrate improvement with objective testing. Many are able to reduce medications and significantly improve function. The therapy is perhaps most important for those who are able to avoid the risks of surgery and for those who have responded poorly to standard protocols and improve dramatically with EDTA. Many of the latter patients would be disabled or perhaps dead without the benefits of EDTA treatment. A few patients require bypass surgery, angioplasty, or other interventions despite receiving chelation therapy.

Modern protocols should include EDTA therapy as an option for all types and degrees of vascular disease. This therapy should be encouraged before bypass or amputation (unless a life-threatening situation exists) in an attempt to avoid surgery and improve outcome. Chelation therapy should be used in nonsurgical candidates who are doing poorly. Some will show dramatic improvement. Furthermore, EDTA should be studied as a postbypass

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Medicine] founded its Journal, to be used as a proper instrument for reporting appropriate clinical and scientific studies which *support what we are doing*" (my emphasis). This last sentence does not seem to reflect a desire to learn the truth about chelation therapy, and now well planned studies, not an ugly bias, have shown that chelation therapy has no place in the treatment of PVD.

The bias frequently referred to by the advocates of chelation therapy suggests that their "opponents" fear the potential financial loss associated with the cure of CVD by chelation therapy. My guess is that others, like myself, have no fear that conventional treatments will be replaced by chelation therapy. Rather, we are concerned that a multitude of sufferers will continue to spend about $5000 each out of pocket (since insurers do not cover the costs of chelation) for a treatment proven to be ineffective. Never mentioned is the potential bias of the chelation practitioners, who face significant financial loss if patients are finally convinced that chelation treatment is a waste of money.

The ball is now in the court of the proponents of chelation therapy. This treatment does appear to provide short-term improvement, although it is probably a placebo effect. The real question, however, is whether chelation treatments give long-term benefits for patients with PVD or other CVD. None of the studies has yet addressed this issue. If those carrying out chelation therapy wish to justify the practice, their obligation is to prove by well-planned studies that this technique provides long-term benefits to the sick people who are their patients.

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and/or angioplasty treatment to prevent restenosis and also as a prevention technique for type I cardiac patients, especially those with high risk factors for cardiovascular disease and stroke.

EDTA treatment is not a substitute for the judicious use of surgery or the appropriate use of pharmaceuticals, nor does its use preclude the appropriate use of either when indicated. When conscientiously applied by a trained physician in a comprehensive program that includes lifestyle modification and rational pharmacotherapy, EDTA chelation is scientifically sound, clinically effective, exceptionally safe, and comparatively inexpensive. And it is compatible with other treatment modalities. What more can be asked from a medical therapy?

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