

Meeting Report

Summary of the American College for Advancement in Medicine November 2007 Conference on Integrative Medicine: Advancing Science and Clinical Practice

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The autumn 2007 session of the American College for Advancement in Medicine's International Educational Conference on Complementary, Alternative and Integrative Medicine (CAIM) took place between November 14 and November 18 at the Sheraton Wild Horse Pass Resort in Chandler, Arizona, USA. Over 400 physicians gathered at ACAM's (American College for Advancement in Medicine) 'Integrative Medicine: Advancing Science and Clinical Practice' to learn the latest science on a variety of illnesses. From topics in cancer and musculoskeletal disorders, to the science of lipids, these were cutting edge lectures from leading scientists and clinicians around the country.

ACAM is a not-for-profit medical society dedicated to the education of physicians and allied health care professionals. As the leading voice in CAIM for over 30 years, ACAM strives to bring the best of nutritional and environmental research into the arena of clinical practice.

During the meeting, Dr Ken Bock turned over the presidency to Dr Jeanne Drisko, the Riordan Professor of Orthomolecular Medicine and Director of the Program in Integrative Medicine Complementary and Alternative Therapies at the University of Kansas Medical Center. Dr Drisko's academic background and forward thinking leadership will help guide ACAM through the next 2 years. She has continuously demonstrated her commitment to providing advanced education to physicians

through her collaborative efforts within the CAIM community and her research efforts at KUMC.

Her plans include expanding Dr Bock's successful legacy of building bridges by reaching out to the academic CAIM physicians in the Consortium of Academic Health Centers for Integrative Medicine. We look forward to Dr Drisko's visionary efforts on behalf of our organization.

ACAM unveiled its first Integrative Health Guideline on the management of hypercholesterolemia. Graciously sponsored by Employers Resource and authored by Dr Mark Houston and colleagues, this effort promises to be the first in a series that brings fully integrated guidelines to bear on the management of degenerative illnesses.

The pre-conference workshop on Hormone Replacement therapy was co-chaired by our incoming president, Dr Jeanne Drisko and president elect Dr Eleanor Hynote. Presenters included Dr David Rosensweet, Dr Eugene Shippen and Dr Jonathan Wright. Emphasis was placed on individualizing bioidentical hormone replacement therapy. From titration methods of bioidentical hormones to the benefits of iodine in fibrocystic breast disease this workshop was filled with practical information.

ACAM's pre-conference workshop on chelation therapy was co-chaired by Dr James Biddle and Dr Jeffery Morrison. Chelating agents are molecules known for their strong affinity for heavy metals and their ability to remove them from the body. The workshop consisted of lectures describing the general history and biochemical role of chelation therapy, the indications for varied chelating agents, abnormal lab parameters in the setting of heavy metals and the rationale of this therapy in the treatment of chronic degenerative diseases

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potentially induced by heavy metal exposure and excess calcium.

Summary of Presentations

Gina Nick, NMD, PhD

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Inflammation in the brain and depression: advances in the recognition and treatment of sickness syndrome

Dr Nick reviewed the concept of sickness syndrome, a recently coined term she uses to describe chronic elevation of cortisol and the subsequent increase in inflammatory cytokines TNF alpha and IL-6. These inflammatory markers lead to associated depression and poor mental function. She reviewed the importance of detoxication and restoration of adrenal gland and brain function through proper diet, caloric restriction and herbal nutrients. Lastly she emphasized the importance of assessing hormonal balance and the utilization of prayer and meditation in regulating vagal output and production of inflammatory cytokines.

James M. Wright, MD, PhD

Professor—Department of Anesthesiology, Pharmacology and Therapeutics and Department of Medicine at the University of BC, Vancouver, Canada.
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Are lipid lowering guidelines evidence based?

Dr Wright's lecture discussed bias in clinical guidelines identifying those who are likely to benefit from statin therapy and those who are not. He reviewed the fact that all major clinical guidelines ultimately mandate different percentages of patients receive statins and then proceeded to explain the bias inherent in them. He highlighted the fact that serious adverse event data is often missing in primary prevention trials and that this data must be reviewed in order to conclude a true 'net health benefit' in the various populations studied. He concluded that statins do *not* reduce mortality in primary prevention populations (those patients with risk factors, but no proven vascular disease) and their use in this population should be reconsidered. In fact, after a full review of the literature he concluded statins have not been proven to have a net health benefit in most patients taking them today.

Martin L. Pall, PhD

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The NO/NOO— cycle as the cause of previously unexplained illnesses: etiology and effective therapy

Related overlapping illnesses including chronic fatigue syndrome, multiple chemical sensitivity, fibromyalgia and post-traumatic stress disorder appear to be caused by a novel paradigm of human disease known as the NO/NOO— cycle.

The NO/NOO— cycle involves the interaction of Nitric Oxide with superoxide to produce a quite damaging radical: peroxynitrite. Dr Pall reviewed how this model is based on five distinct principles which may in fact help explain the pathogenesis of many inflammatory diseases including: Alzheimer's, Multiple Sclerosis, Autism, Asthma and Parkinson's disease. He suggested that short-term stressors raise nitric oxide levels and initiate this vicious cycle that is self-perpetuating and quite damaging to mitochondria. In order to treat these disorders, one must deal with the major oxidative stressors in this NO/NOO— cycle. He then reviewed promising agents for down regulation of this cycle and the data supporting their rational use. Those with clinical trial data include: ascorbic acid, flavonoids, Acetyl-L-carnitine, mitochondrial regeneration agents, B12, folic acid, NMDA antagonists, Long chain omega 3 fatty acids, Algal supplements, glutathione, magnesium, and hyperbaric oxygen.

Roberts W. Summers, MD, James A. Clifton

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Back to the future: Helminth Ova Therapy in IBD

'The etiology of inflammatory bowel disease represents the interplay between genetic and environmental factors. Helminths have been shown to modulate immune response in animals and protect mice from developing experimentally-induced IBD.' Dr Summers reviewed data showing that in 54 subjects with ulcerative colitis enrolled in a 12-week double-blind placebo controlled clinical trial, 45% of Porcine whipworm ova-treated subjects had a positive response to therapy compared with only 17% in placebo controls. In 29 patients with Crohn's disease, 62% achieved remission after 12 weeks and 76% achieved a clinical response. No significant side effects or complications were identified making this a very promising treatment in a variety of immune-mediated difficult to control diseases.

Bill Cham, PhD

'The Eggplant Cancer Cure: A Treatment for Skin Cancer and New Hope for Other Cancers from Nature's Pharmacy'. E-mail: bill.cham@gmail.com

When does alternative become orthodox? Skin cancer treatment with solasodine rhamnosyl glycosides in its transitional stage, a case study.

Dr Cham's work centers on 'Devil's Apple' derived glycoalkaloids, specifically solasodine rhamnosyl glycoside. He has discovered that many tumors contain receptors for this glycoalkaloid and exhibit a unique binding increasing their susceptibility to its killing effect without harming normal cells. The constant ratio of solasodine glycosides (now known as BEC) available in 'Devil's Apple' have been shown to be non-toxic to normal cells and dramatically reduce the growth of many tumor cells *ex vivo* including ovarian and squamous cell tumors among others. BEC or its main compound solamargine, is reported to show much higher antineoplastic activity and lower toxicities than vinblastin, cisplatin, doxorubicin and camptothecin and should result in a higher therapeutic window when used in the treatment of cancer. He presented data in mice with terminal sarcoma showing that four doses of BEC resulted in >90% survival rates. Other promising tumor responses have been seen with melanoma and merkel cell tumors.

A small phase II clinical trial in humans composed of 40 patients with late stage disease including: glioblastoma multiforme, colon cancer, bladder cancer, liver cancer, metastasized melanoma to the lung and rectal cancer showed improvement in appetite, tumor reduction, improved quality of life and extended life span.

Additionally, the results of Phase 3 clinical trials utilizing BEC topically for skin cancers showed an impressive 100% success rate at 12 weeks of treatment.

Steve Kaufman DC

Author of 75 papers on the topics of nutrition, acupuncture and soft tissue therapies, Dr Kaufman practices in Denver, Colorado, USA.

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Pain neutralization technique: using neurological reflexes to stop musculoskeletal pain instantly, without needles or electronics

Dr Kaufman presented a new method of quickly neutralizing areas of palpatory pain often known as trigger points. With participants on stage he reviewed the nature and definition of trigger points, the three types of pain described as (i) spontaneous pain, (ii) pain on movement and (iii) palpatory pain. He then demonstrated the benefits of his techniques by identifying and manipulating neurological reflexes in a hands on fashion.

Floyd H. 'Ski' Chilton, III PhD

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Women's Center for Botanical Lipids—Wake Forest University Health Sciences.

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The role of natural bioactive for the prevention and treatment of chronic human diseases

Dr Chilton reviewed five key nutritional trends that have taken place in our lifetime and likened them to the perfect storm for poor health. These include: (i) increased calories (ii) reduced fiber (iii) decreased exercise (iv) decreased dietary polyphenols and (v) an increase in dietary omega 6 fatty acids and reduction in dietary omega 3 fatty acids. He noted that most of these trends have been driven by a marked change in our food supply and lays the major illnesses in this country such as asthma, obesity, heart disease, psoriasis and diabetes squarely at their feet.

He reviewed the data on how obesity increases the levels of inflammatory cytokines such as IL1B, TNF-alpha and IL-6. He discussed bioactive compounds in our foods: compounds not necessary for life as are nutrients, but compounds which act as enzyme inhibitors and inducers, inhibitors and inducers of receptor activities and inhibitors of gene expression. Reviewing the concept of nutrigenomics (using or avoiding foods to regulate transcriptional factors and subsequent gene expression) Dr Chilton placed NFkB in the middle of controlling our immune response and noted that incorrect control of this transcription factor is key to the development of disease. He ended the lecture discussing the various bioactives and their ability to ameliorate disease. From polyphenols to Omega 3 fatty acids, the future promise of better health seems clear if we can reconstitute our foods: genetically speaking. Unfortunately, it appears this will come in the form of patented medical foods that extract a considerable financial price. This indeed was my only disappointment with an otherwise excellent lecture.

Lewis Mehl-Madrona, MD, PhD, MPhil

Associate Professor of Family Medicine and Psychiatry—University of Saskatchewan College of Medicine.

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Traditional healing, alternative medicine and diabetes

According to Dr Mehl-Madrona, aboriginal populations have undergone dramatic transformations of culture and lifestyle within the last half-century leading to increases in many diseases, most notably diabetes. In this lecture, Dr Mehl-Madrona reviewed the role of emotional stress and socioeconomic status in the onset of diabetes. He suggests addressing low levels of autonomy and low self-esteem may be two important means of improving management of diabetes as evidenced by a pilot study on the efficacy of lifestyle interventions among the Pima tribe of Arizona.

Richard I. Gracer, MD

Specialist in interventional pain management and regenerative medicine. Author-A New Prescription for Addiction. E-mail: Richard@gracermd.com

A new prescription for addiction

Dr Gracer accurately identified the flaws in the current treatment of addiction and proposed a number of specific solutions to correct these deficits. He noted that nutritional deficiencies were often not addressed and included the assessment of hormonal and neurotransmitter function as an important aspect of his evaluation. Dr Gracer referenced studies, which consistently demonstrate a combination of pharmacotherapy, psychosocial intervention and nutrition education are more successful than current interventions.

Alcohol and cocaine clearly have an impact on cerebral blood flow and neurotransmitter function based on SPECT scanning. Additionally, they impact GABA receptors in an adverse way. Considering that nearly 40% of all brain synapses are GABA this has profound implications for addiction. Dr Gracer reviewed the increased expression of alpha 4 subunits in GABA receptor sites with the excess use of alcohol, cocaine, and methamphetamine citing the alpha 4's tendency to exacerbate cravings and withdrawal symptoms. Normalizing the ratio of GABA alpha 1-alpha 4 receptor subunits is a promising approach to treating anxiety and addictive behavior. He showed the potential benefit of using flumazenil a benzodiazepine antagonist to treat methamphetamine-dependent subjects. Methamphetamine usage was significantly reduced up to 2 months after cessation of medication in one study and 80% of cocaine addicts remained drug free for at least 180 days in another.

Jeffrey Blumberg, PhD, FACN, CNS

Professor-Friedman School of Nutrition and Science and Policy. Director-Antioxidants Research Laboratory Tufts University. E-mail: jeffrey.blumberg@tufts.edu

Evidence-based nutrition and the problem of proof

'The randomized controlled clinical trial is now the 'gold standard' not only for establishing the efficacy and safety of drug therapies but also for recommending changes in diet and the use of dietary supplements' says Dr Blumberg. 'There are however problems with this approach considering the long latency and multifactorial causation of chronic disease and the impossibility of a zero exposure to a nutrient (for a placebo).' Additionally, the multiple thresholds for different actions of a single nutrient in various tissues limit the value and the application of randomized controlled trials to test nutrition hypotheses. Quoting Concato *et al.*, *N Engl J Med* 2000, Dr Blumberg noted, 'the popular belief that

only randomized controlled trials produce trustworthy results and that all observational studies are misleading does a disservice to patient care, clinical investigation, and education of health care professionals' And again, Benson and Hartz, *N Engl J Med* 2000 in their comparison of 136 Observational Studies and RCTs (Randomized Controlled Trials) 'We found little evidence that estimates of treatment effects in observational studies reported after 1984 are either consistently larger than or qualitatively different from those obtained in randomized, controlled trials'. Lastly, Heaney, *Am J Clin Nutr* 2006, 'The randomized controlled trial, which has become the gold standard for establishing the efficacy of pharmacologic agents, is poorly suited to the evaluation of nutritional effects, a fact that I believe many have been reluctant to acknowledge.' He then covered the NIH State-of-the Science Conference on Multivitamin/Mineral Supplements and Chronic Disease Prevention. 'The present evidence is insufficient to recommend either for or against the use of (Multi Vitamins and Minerals) by the American public to prevent chronic disease.' And how did the NIH arrive at this conclusion Dr Blumberg asks? A literature search process identified 11 324 citations from 1996 to February of 2006 that were potentially relevant to the key questions. These citations were found through MEDLINE, EMBASE, Cochrane database, etc. According to AHRQ Publication No. 06-EOI2, May 2006, *the review process for eligibility and study quality assessment excluded consideration of 11,261 reports, so the final report and recommendations were based on only 63 articles.*

Might there be bias in these recommendations? The publication did admit that 'Limiting the focus of our statement to RCTs has some inherent limitation.' Indeed! Dr Blumberg is to be commended for this excellent review of the limitations the randomized controlled trial places on the evaluation of nutrients and their ability to prevent chronic disease.

Frank Antonawich, PhD

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The metabolic role of palladium lipoic acid complex in mitochondrial health and subsequent regulation of cellular death

Dr Antonawich, reviewed the biochemistry of Palladium Lipoic Acid Complex (PdLA). PdLA is a nutritional supplement that is unique to free radical biology since palladium is a transition metal that can catalyze aerobic respiration, thus mimicking the electron transport chain. Research studies with PdLA a novel redox molecule have demonstrated its ability to take advantage of the

metabolic dysfunction of cancer cells by increasing their susceptibility to apoptosis. Additionally, being a redox molecule and a potent free radical scavenger PdLA attenuates reperfusion injury by lessening the impact of free radicals on damaged tissues and implying a role in stroke and other reperfusion induced injuries. In an animal study published in *Free Radical Biology and Medicine*, 2007, Dr Atonawich has shown that after an episode of transient global ischemia, PdLA rescues ~80% of the hippocampal neurons when administered at the time of insult.

The history of cancer bioenergetics including the Warburg effect was reviewed. Dr Atonawich detailed the view of modern molecular biology: cancer is more a disease of genetics, not bioenergetics. Yet, more recent research from the NIH suggests mutations in the p53 gene (commonly linked to cancer) can trigger the Warburg effect leading to abnormal bioenergetics. It is at this crossroad that PdLA may play a role. In cancer, hypoxia triggers a series of physiologic adaptations to this environment via Hypoxia Inducible Factor (HIF). This metabolic dysfunction restricts malignant cells forcing them to rely on anaerobic metabolism (glycolysis) for energy, which is extremely inefficient. By providing an alternative electron source in a hypoxic state such as PdLA, cancer cells cannot survive and die while normal cells are supplemented by it and thrive. PdLA appears to kill cancer cells by facilitating apoptosis.

Allan B. Warshowsky, MD

Board certified OB/GYN. Author- *Healing Fibroids A Doctors Guide To A Natural Cure*.
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Healing fibroids: a doctors guide to a natural cure

Dr Warshowsky attempted to demonstrate how disorders of inflammation, immune response, sugar metabolism, intestinal function and detoxification affect hormone balance and the growth of fibroid tumors. He suggests that proper diet and nutrition, exercise, and stress management can benefit hormone balance and inflammation reducing the need for invasive procedures with uterine fibroids.

Dr Warshowsky reviewed the symptoms of estrogen dominance and how this condition was made worse by impaired detoxification, glucose dysregulation, and intestinal dysbiosis. Reviewing a small study of 37 women in which his methods were applied, he noted a cure of fibroids in three patients and a mean reduction in size of 0.8cm compared with an average increase in size of 1.9cm in controls. He reviewed a number of herbal products felt to be supportive in the quest to prevent or reduce uterine fibroids.

Katherine Falk, MD

Assistant Clinical Professor of Psychiatry Mount Sinai School of Medicine.
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Integrative therapy of depression, anxiety and bipolar disorder.

Dr Falk's lecture centered on facilitation of proper neurotransmitter function in the setting of depression and bipolar disorder. She reviewed neurotransmitter production and the varied nutrients involved as cofactors in their synthesis as well as the impact of Omega 3 fatty acids in depression noting that too much EPA may lead to an agitating influence in bipolar disorder while DHA exerts a more calming effect.

She discussed the neuroprotective role of lithium and its ability to stimulate neuronal growth, even in small dosages. She reviewed the benefit of SAME in methyl donation in over 35 reactions and its necessity in over 100 biochemical reactions. She acknowledged that SAME may induce mania and must be properly monitored. The adverse effects of St. John's Wort were reviewed and the benefit of T3 preparations as a potential neurotransmitter were discussed.

George Gillson, MD, PhD

President and CEO—Rocky Mountain Analytical Lab.
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Transmethylation reactions: critically important, often overlooked

In this lecture, Dr Gillson reviewed the role of common methyl donors including: (i) S-AdenosylMethionine (SAMe), (ii) Trimethylglycine (TMG), (iii) 5-methyltetrahydrofolate(MTHF), (iv) Methylcobalamin(MethylB12) and (v)Methylsulfonylmethane (MSM).

Transmethylation reactions are integral in histamine metabolism, methionine cycling, adrenal function, neurotransmitter balance, myelin stability, estrogen and catecholamine metabolism, cell membrane structure and liver detoxification. Dr Gillson reviewed the importance of SAMe in inactivating histamine thereby successfully neutralizing histamine mediated reactions such as hives and excess acid secretion. He noted the role of elevated homocysteine in many diseases and how it could be reduced using methyl donors. He reviewed liver detoxification and the importance of methylsufonation in clearing PCBs. Other notable roles of methyl donors include protection from CCl₄ exposure, reduction of alcoholic fatty liver (betaine) and prevention of cirrhosis (SAMe). An excellent lecture.

Robert Rountree, MD

Author of five books on Integrative and Nutritional Medicine. Technical editor—Journal of the American Nutraceutical Association. E-mail: roundoc@qwest.net

Enhancing detoxification with glucosinolates from Brassica vegetables.

Broccoli, cabbage, cauliflower, collards, kale and brussel sprouts were just a few of the *Brassica* vegetables that Dr Rountree noted to be helpful in aiding detoxification. Briefly reviewing the consensus of 300 case control studies he summarized their conclusions. *Brassica* vegetables show a protective effect against cancer in the

respiratory tract, the gastrointestinal tract, the genitourinary tract and the reproductive organs. When compared with fruits and vegetables in general, cruciferous vegetables have a better reduction in relative risk for bladder cancer than any other group. He noted the key groups of protective compounds in *Brassica* vegetables are the glucosinolates and their derivatives, isothiocyanates, which are responsible for modulating Phase I and Phase II enzymes. They have been shown to have direct effects on human cancer cells in addition to shifting estrogen metabolism toward healthier 2OH estrogens.

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