Life Raft Group

July 14, 2018

Integrative, Functional Medicine

Jorge Bordenave MD

What is Integrative Medicine?

- Practice of medicine where patient and practitioner are partners in the healing process.
- All factors that influence health, wellness, and disease are considered, including the mind, body, and spirit.
- Use of conventional and complementary methods to facilitate the body's innate healing response.
- Use of natural and less invasive interventions whenever possible.
- Science based medicine.

National Institutes of Health (NIH);

National Center for Complementary and Alternative Medicine

Integrative Medicine as: “Combination of mainstream medical therapies & Complimentary Alternative Medical (CAM) therapies for which there is some high-quality scientific evidence of safety and effectiveness."

- Alternative Medicine: treatment used in place of standard medical care, ex: treating heart disease with chelation therapy (removing excess metals from the blood) instead of a standard of care approach.*** (NIH)

Alternative Medicine is NOT the same as Integrative, Complementary Medicine

National Institutes of Health (NIH)

~~National Center for Complementary and Alternative Medicine~~

National Center for Complementary and Integrative Health

(2014)

- Integrative Medicine: INTEGRATES Western medicine (U.S./N.A) with proven (whole-istic) therapies from medical systems from across the world…

- Ayurvedic Medicine (>3000yrs)
- Chinese Medicine (2500yrs)
- Chiropractic
- Naturopathic

Ayurveda

- Yoga
- Meditation
- Plant based oils and spices
- Aromatherapy
- Herbs and minerals
- Massage therapy
- Nutrition
- Breathing yoga (pranayama)

Traditional Chinese

- Acupuncture
- Cupping
- Tai-Chi
- Chi-Gong
- Balance and stress control
- Yin and Yang
- Energy medicine: Reiki
- Nutrition
- Guided therapy

Functional Medicine

- Functional Medicine: individualized, patient-centered, science-based approach, empowers patients & practitioners to work together to address the underlying causes of disease and promote optimal wellness.
- It requires a detailed understanding of each patient's genetic, biochemical, and lifestyle factors to direct personalized treatment plans that leads to improved patient outcomes.
- It addresses root cause, rather than symptoms.

THE INSTITUTE FOR FUNCTIONAL MEDICINE®

FUNCTIONAL MEDICINE MATRIX

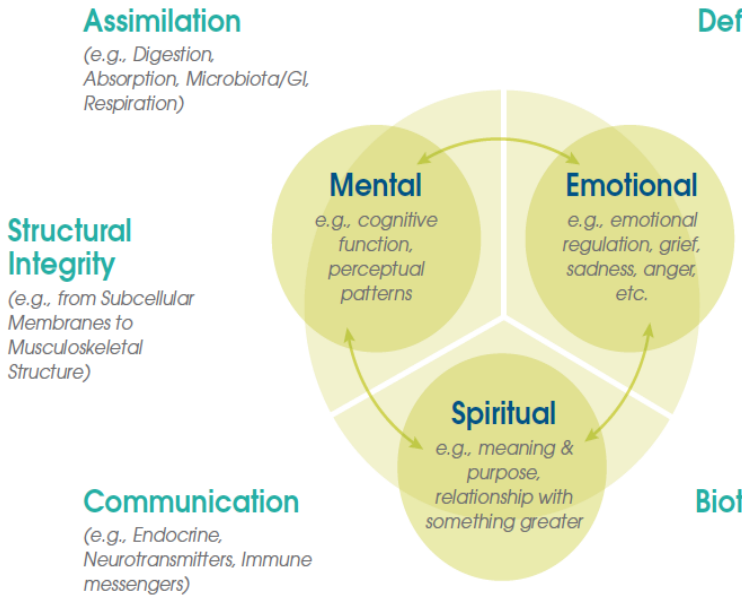
Retelling the Patient's Story

Antecedents
(Predisposing Factors—Genetic/Environmental)

Triggering Events
(Activators)

Mediators/Perpetuators
(Contributors)

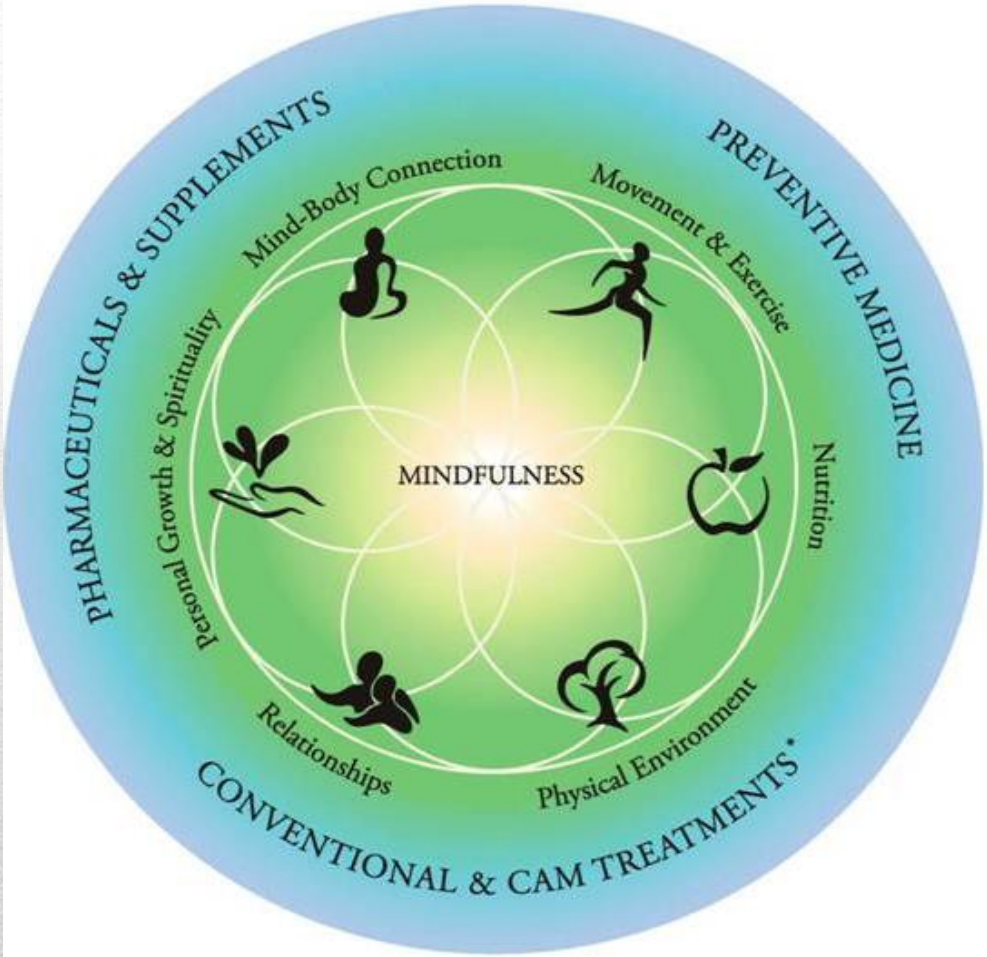
Physiology and Function: Organizing the Patient's Clinical Imbalances



Modifiable Personal Lifestyle Factors

Sleep & Relaxation	Exercise & Movement	Nutrition	Stress	Relationships

Wheel of Health



Mindfulness Self Care Professional Care

*CAM Treatments - Complementary & Alternative Medicine Treatments

- Integrative, Functional Medicine is WHOLE-istic Medicine

Start of U.S. Integrative/Complementary medical care?

- 1890's. Michigan brothers advocated Nutrition and lifestyle as a foundation of health.
- Developed flaked grain cereal (1897). Advocated "alternative" tx:

  diets low in fat & animal protein, advocated consumption of yogurt, nuts, whole grains, fermented & fiber-rich foods.

  Emphasized the importance of fresh air, exercise and hygiene

  including yogurt enemas as treatment.
- Ran sanitariums (health spas).
- Proponent of whole foods and vegetarianism.

John Harvey Kellogg MD

- Current “Modern Medicine”

- Early 20th century. Flexner Report-more science.
- Refinement of the microscope, microbes, bacteria.
- WWII: PNC, discovery of subatomic particles, atoms.
- Technologies able to discover smaller “parts” of the whole.

- Rene Decarte's philosophy of reductionism … the belief that complex phenomena can be understood by reducing them, fragmenting them to their smaller constituent parts.

- Reductionism is pervasive in medical sciences today. It is the way medicine is taught in U.S. medical schools and affects the way we diagnose, and treat diseases.

- Reductionism lead to specialization in medicine.

- From general practioners treating the individual for life, to limiting treatment a body part or system…

Cardiology, Neurology, Gastroenterology, Infectious Disease, Psychiatry, Endocrinology, Dermatology, Rheumatology, Oncology, Hematology…

- U.S. healthcare is fractionated.
- We are a country of specialists, each focused on a specialized, specific area of the body.
- We have become disease centered. We treat ailments instead of the patient.
- We love our technology and our medications.
- We practice a one-size-fits-all, Guideline based, checklist approach medical care.
- Its not healthcare, its disease management.

What do we have to show for this? 2018 …

U.S. maternal mortality continuously increases while decreasing in every industrialized countries around the world. (National Acad of Science 2018)

U.S. is 11 of 11 among industrialized nations in healthcare outcomes, while remaining the most expensive.

U.S. is 34th in the world according to W.H.O. in quality and cost, 2 places ahead of communist Cuba.

- In 2016, healthcare spending was $3.3 trillion, or $10,348 per capita, which is 17.9% of the U.S. economy (CMS).
- Double of that of the other western countries.

- Integrative / Functional Medicine IS
  21st century medicine.

Treats the entire person; body, mind, spirit.

Individualizes, personalizes care.

Identifies cause using genomics, disease modulation-epigenetics.

Lifestyle change: stress control, community, sleep, exercise/movement and NUTRITION, as the foundation of maintaining and achieving wellness.

- **Let food be thy medicine and medicine be thy food.”**

hippocrates

460-370BC

Integrative/Functional Medicine in GIST.

- Work as part of the team with your primary care physicians, oncologist, hematologist, gastroenterologist and other caregivers.

- Post surgical symptoms
- Symptoms related to chemotherapy/radiation
- Emotional issues related to cancer

- Imatinib Gleevec

- Systemic side effects: vomiting, diarreah, myalgias, headaches, fluid retention, bruising, GI bleeds, loss of appetite, bone marrow suppression, liver issues, LV dysfunction (HF) <5%.
- Metabolism: Liver-P450 (CYP3A4, CYP2D6).

  St. Johns wart decreases Gleevec activity, activity.

  Grapefruit increases Gleevec activity as well as blood levels of warfarin, metoprolol, simvastatin + …).

Stress, Emotional Support

- Mindfulness
- Meditation
- Journaling
- Relationships, friends
- Community; The Life Raft Group (support)
- Gratitude

Movement

- Walking, biking, rowing, swimming
- Tai-chi
- Low impact exercise and increase as tolerated
- Yoga

Sleep

- Aromatherapy
- Visualization
- Sleep apnea
- Cortisol levels
- Thyroid function

GI Tract / Digestion / Nutrition

Post surgical changes. Mainly GI.

Absorption issues: supplements, vitamins.

Organic, whole foods.

Lots of vegetables, greens, multi-colored foods.

Mediterranean type diets.

Smaller portioned, more frequent.

Microbiome changes:

Probiotics: lactobacilli, bifidus, sachromyces. Prebiotics.

- Emerging roles of the microbiome in cancer
  Scott J. Bultman
- *Carcinogenesis*, Volume 35, Issue 2, 1 February 2014, Pages 249–255.

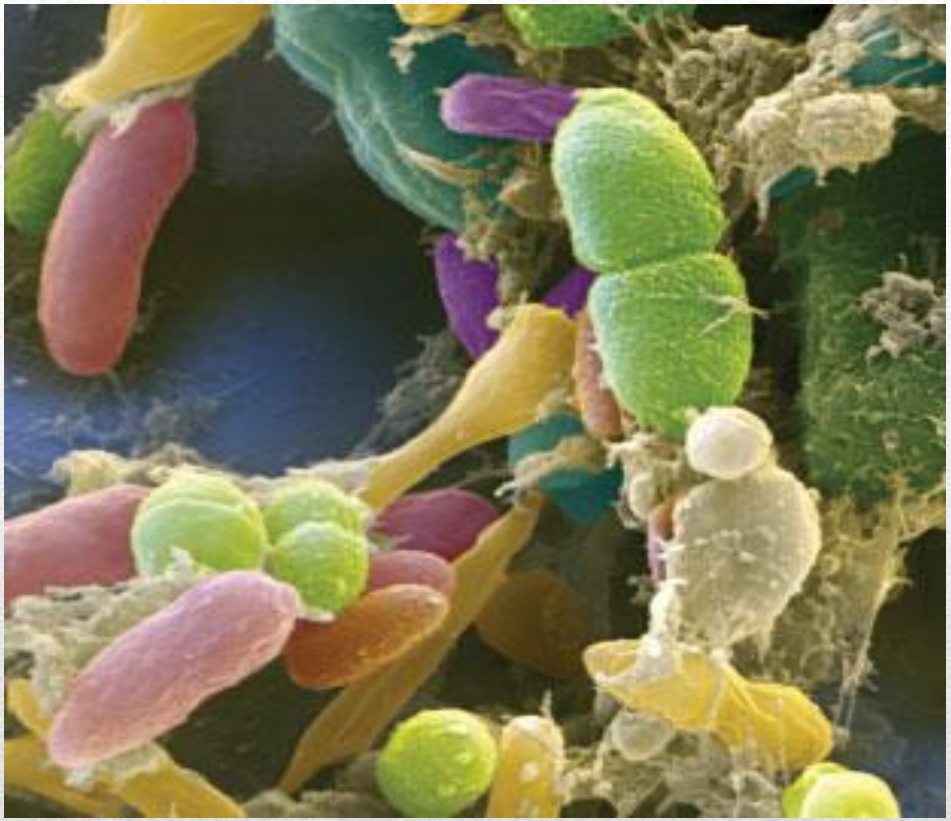
- Gene–environment interactions underlie cancer susceptibility and progression. We still have limited knowledge of which environmental factors are important and how they function during tumorigenesis. However, our microbiota are environmental factors that we are exposed to continuously, and human microbiome studies have revealed significant differences in the relative abundance of certain microbes in cancer cases compared with controls.

The microbiome and cancer

Robert Schwabe & C. Jobin

Natl. Rev Cancer. 2013 Nov: 13 (11): 800-812

Microbiome and host form a complex ‘super-organism’ in which symbiotic relationships confer benefits to the host in many key aspects of life. Defects in the regulatory circuits that control bacterial sensing and homeostasis, or alterations of the microbiome, through environmental changes (infection, diet or lifestyle), may disturb this symbiotic relationship and promote disease. Increasing evidence indicates a key role for the bacterial microbiota in carcinogenesis.

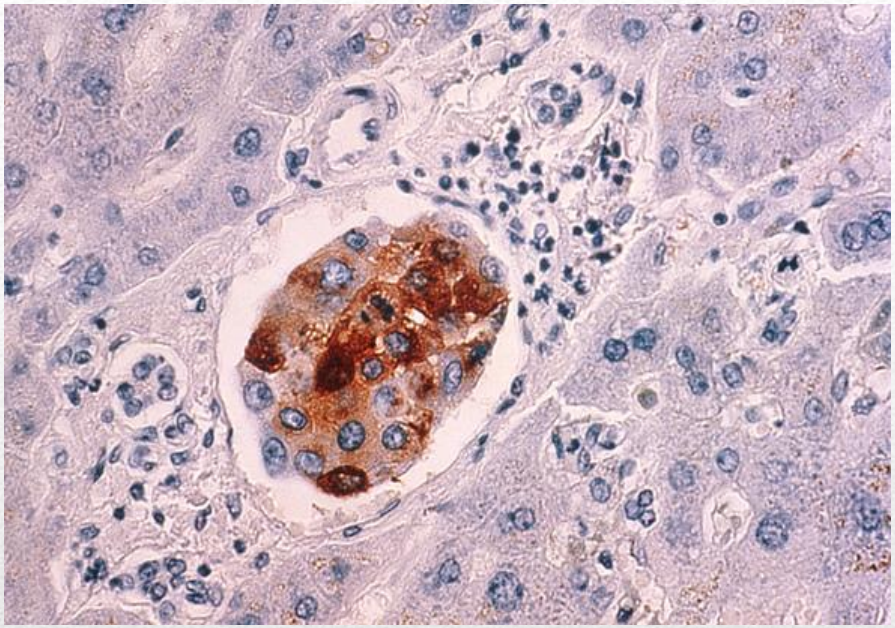


MICROBIAL STOWAWAYS: Bacteria of the human gut microbiome are intimately involved in cancer development and progression, thanks to their interactions with the immune system.
Microbes, such as *Helicobacter pylori*, increase the risk of cancer in their immediate vicinity, while others, such as some *Bacteroides* species, help protect against tumors by boosting T-cell infiltration.

The Scientist April 2016 Issue

Microbes Meet Cancer

Understanding cancer's relationship with the human microbiome could transform immune-modulating therapies.



Gut microbes affect antitumor activity in liver

- A connection between bacteria in the gut and antitumor immune responses in the liver enhances our understanding of liver cancer and suggests new approaches to treat it.

- From the NIH:
- Mediterranean diet may slow Alzheimers disease
- Ebstein Barr virus and auto-immune disease
- Daily stresses may impact long term health
- Sleep deprivation increases Alzheimers protein

VIEWPOINT

The Microbiome and Risk for Atherosclerosis

Anthony L. Komaroff, MD
Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

"Hot" new areas of biomedicine sometimes generate cool skepticism. Little more than a decade ago, investigators proposed that the gut microbiome might be contributing to obesity. Since then, the microbiome has been linked to numerous major diseases, including atherosclerosis, although some have been skeptical about this association.

How could the gut microbiome influence the course of any disease? The central argument is simple and compelling. Humans actually have 2 genomes: human genes and the collective genes (the "microbiome") of the trillions of microbes (the "microbiota") that coexist with each human.

The advent of rapid nucleic acid sequencing has revealed an astonishing fact: the microbiome contains more than 100 times as many genes as there are human genes. More remarkably, these microbial genes generate proteins, including hormones, neurotransmitters, and molecules of inflammation, that can enter the circulation and affect human physiology. Thus, the microbiome is not only a second genome: it is also like an additional endocrine organ.

Considerable evidence indicates that the human gut microbiome may affect the development and progression of atherosclerosis, both by influencing risk factors for atherosclerosis and by direct effects on the initiation and progression of atherosclerotic plaques.

The Microbiome and Risk Factors for Atherosclerosis

As summarized previously, the microbiome may influence the development of both obesity and type 2 diabetes,[1] both of which are atherogenic.

Obesity

It is not the calories that people ingest that affect weight: it is the calories people digest (absorb from the gut). By increasing or decreasing the amounts of digestible sources of energy, particularly monosaccharides and short-chain fatty acids, gut bacteria affect the number of calories that humans absorb.

Consider a study of human twin pairs (mostly monozygotic), one of whom was obese. Lean mice were fed feces from the human twins. Feces from the fat twins caused lean mice to become fat, and feces from the lean twins allowed mice to remain lean. When the fat and lean mice were housed together, and ate each other's feces, the obese mice became lean and their gut flora came to resemble the flora of the lean mice (and the lean human twins).

Type 2 Diabetes

Besides the diabetogenic influence of obesity, the gut microbiome also influences an individual's risk for type 2 diabetes in other ways. For example, a microbiome that produces relatively more acetate and less butyrate increases insulin resistance, and also increases the gut's production of ghrelin (an appetite-stimulating hormone).

The gut microbiome also can promote inflammation. This, in turn, makes the gut epithelial barrier more permeable ("leaky gut") to bacterial products such as endotoxins and allows the escape of bacteria from the gut lumen into the circulation. The resulting systemic activation of the innate immune system increases insulin resistance.

One experimental study suggests that these effects on short-chain fatty acids and inflammation, demonstrated largely in rodents, also may apply to humans. Gut flora were eliminated in treatment-naive individuals with metabolic syndrome. Then, at random, the study participants received small intestinal infusions of either their own feces or feces from lean male donors. The donations from lean male donors increased the insulin sensitivity of the recipients, along with levels of butyrate-producing microbiota.

Lipid Metabolism

Cholesterol is the precursor to bile acid synthesis in the liver. The microbiome can decrease the rate of bile acid synthesis, thereby increasing levels of circulating low-density lipoprotein cholesterol.[2]

Blood Pressure

Several studies have linked gut microbiota to hypertension in rodents through effects on the angiotensin II system, and by affecting the production of short-chain fatty acids.[3] Recently, investigators reported that the microbiome may mediate the effect of a high-salt diet on hypertension. They found that particular members of the *Lactobacillus* species protected against the development of hypertension in rodents and humans, and that a high-salt diet reduced the number of these protective gut bacteria.[4]

The Microbiome and Atherosclerotic Plaques

Inflammation

Activation of the innate immune response—both within and around the atherosclerotic plaque (such as epicardial adipose tissue) and systemically—appears to enhance plaque progression and plaque rupture. When the gut microbiome triggers low-grade inflammation in the gut, allowing entry of bacteria and bacterial products into the circulation, it results in chronic systemic inflammation. In addition, some studies have found the DNA of gut bacteria within plaques, which could trigger inflammation in the plaque.

Endothelial Function

Oral and gut microbiota can affect nitric oxide signaling, and the production of hydrogen sulfide gas. Both nitric oxide and hydrogen sulfide affect vascular smooth muscle relaxation, which is of particular importance during an acute coronary syndrome.

Corresponding Author: Anthony L. Komaroff, MD, Brigham and Women's Hospital, 1620 Tremont St, Boston, MA 02120 (komaroff@hms.harvard.edu).

Alternative Medicine: treatment used in place of standard medical care, ex: *treating heart disease with chelation therapy* (removing excess metals from the blood) instead of a standard of care approach.*** (NIH definition)

ORIGINAL CONTRIBUTION

Effect of Disodium EDTA Chelation Regimen on Cardiovascular Events in Patients With Previous Myocardial Infarction

The TACT Randomized Trial

Gervasio A. Lamas, MD
Christine Goertz, DC, PhD
Robin Boineau, MD, MA
Daniel B. Mark, MD, MPH
Theodore Rozema, MD
Richard L. Nahin, PhD, MPH
Lauren Lindblad, MS
Eldrin F. Lewis, MD, MPH
Jeanne Drisko, MD
Kerry L. Lee, PhD
for the TACT Investigators

Importance Chelation therapy with disodium EDTA has been used for more than 50 years to treat atherosclerosis without proof of efficacy.

Objective To determine if an EDTA-based chelation regimen reduces cardiovascular events.

Design, Setting, and Participants Double-blind, placebo-controlled, 2×2 factorial randomized trial enrolling 1708 patients aged 50 years or older who had experienced a myocardial infarction (MI) at least 6 weeks prior and had serum creatinine levels of 2.0 mg/dL or less. Participants were recruited at 134 US and Canadian sites. Enrollment began in September 2003 and follow-up took place until October 2011 (median, 55 months). Two hundred eighty-nine patients (17% of total; n=115 in the EDTA group and n=174 in the placebo group) withdrew consent during the trial.

Interventions Patients were randomized to receive 40 infusions of a 500-mL chelation solution (3 g of disodium EDTA, 7 g of ascorbate, B vitamins, electrolytes, procaine, and heparin) (n=839) vs placebo (n=869) and an oral vitamin-mineral regimen vs an oral placebo. Infusions were administered weekly for 30 weeks, followed by 10 infusions 2 to 8 weeks apart. Fifteen percent discontinued infusions (n=38 [16%] in the chelation group and n=41 [15%] in the placebo group) because of adverse events.

Main Outcome Measures The prespecified primary end point was a composite of total mortality, recurrent MI, stroke, coronary revascularization, or hospitalization for angina. This report describes the intention-to-treat comparison of EDTA chelation vs placebo. To account for multiple interim analyses, the significance threshold required at the final analysis was $P=.036$.

Results Qualifying previous MIs occurred a median of 4.6 years before enrollment. Median age was 65 years, 18% were female, 9% were nonwhite, and 31% were diabetic. The primary end point occurred in 222 (26%) of the chelation group and 261 (30%) of the placebo group (hazard ratio [HR], 0.82 [95% CI, 0.69-0.99]; $P=.035$). There was no effect on total mortality (chelation: 87 deaths [10%]; placebo, 93 deaths [11%]; HR, 0.93 [95% CI, 0.70-1.25]; $P=.64$), but the study was not powered for this comparison. The effect of EDTA chelation on the components of the primary end point other than death was of similar magnitude as its overall effect (MI: chelation, 6%; placebo, 8%; HR, 0.77 [95% CI, 0.54-1.11]; stroke: chelation, 1.2%; placebo, 1.5%; HR, 0.77 [95% CI, 0.34-1.76]; coronary revascularization: chelation, 15%; placebo, 18%; HR, 0.81 [95% CI, 0.64-1.02]; hospitalization for angina: chelation, 1.6%; placebo, 2.1%; HR, 0.72 [95% CI, 0.35-1.47]). Sensitivity analyses examining the effect of patient dropout and treatment adherence did not alter the results.

Conclusions and Relevance Among stable patients with a history of MI, use of an intravenous chelation regimen with disodium EDTA, compared with placebo, modestly reduced the risk of adverse cardiovascular outcomes, many of which were revascularization procedures. These results provide evidence to guide further research but are not sufficient to support the routine use of chelation therapy for treatment of patients who have had an MI.

Trial Registration clinicaltrials.gov Identifier: NCT00044213

JAMA. 2013;309(12):1241-1250 www.jama.com

Author Affiliations are listed at the end of this article.
A complete list of the TACT Investigators appears in the eAppendix.

Corresponding Author: Gervasio A. Lamas, MD, Columbia University Division of Cardiology, Mount Sinai Medical Center, 4300 Alton Rd, Miami Beach, FL 33140 (gervasio.lamas@msmc.com).

Conclusions

Patients with post-MI diabetes mellitus aged ≥50 years on evidence-based medications demonstrated a marked reduction in cardiovascular events, including total mortality in the unadjusted analyses, with EDTA-based chelation therapy. These findings support the initiation of clinical trials in patients with diabetes mellitus and vascular disease to replicate these findings and define the mechanisms of benefit. However, they do not constitute sufficient evidence to indicate the routine use of chelation therapy for all patients with post-MI diabetes mellitus.

- Jorge Bordenave MD
- Integrative, Functional Cardiology
- 305 - 446-2444
- Drbordenave.com

Thank you