

# Questions & Answers: The NIH Trial of EDTA Chelation Therapy for Coronary Artery Disease

## **Introduction**

The National Center for Complementary and Alternative Medicine (NCCAM) and the National Heart, Lung, and Blood Institute (NHLBI), both components of the National Institutes of Health (NIH), have launched the Trial To Assess Chelation Therapy (TACT). TACT is the first large-scale, multicenter study to determine the safety and efficacy of EDTA chelation therapy for individuals with coronary artery disease. The questions and answers below provide additional information on coronary artery disease, EDTA chelation therapy, and the study.

## **1. What is coronary artery disease?**

Coronary artery disease (CAD) is the most common form of heart disease. In CAD, the coronary arteries, the vessels that bring oxygen-rich blood to the tissues of the heart, become blocked by deposits of a fatty substance called plaque. As plaque builds, the arteries become narrower and less oxygen and nutrients are transported to the heart. This condition can lead to serious problems, such as angina (pain caused by not enough oxygen-carrying blood reaching the heart) and heart attack. In a heart attack, or myocardial infarction, there is such poor oxygen supply to the heart that part of the heart muscle dies. If a sufficiently large portion of the heart is affected, it may no longer be able to pump blood efficiently to the rest of the body, resulting in death or chronic heart failure.

Approximately 7 million Americans suffer from CAD. It is the leading cause of death among American men and women; more than 500,000 Americans die of CAD-related heart attacks each year.

There are several factors that can each increase the risk of developing CAD:

- High blood pressure
- High cholesterol levels
- Smoking
- Obesity
- Physical inactivity
- Diabetes
- Family history of CAD
- Gender
- Age

A person with CAD may or may not have symptoms. Symptoms can include chest pain from angina, shortness of breath, lightheadedness, cold sweats, or nausea.

## **2. How is CAD diagnosed and treated?**

Because the severity of CAD and its symptoms can vary from person to person, the way the disease is diagnosed and treated can also vary. CAD is often diagnosed through a series of tests that can include blood tests to see if protein has been released into the bloodstream from damaged heart tissues, electrocardiograms (EKG) to check the heart's electrical activity, "stress" tests to record the heartbeat during exercise, nuclear scanning to check for damaged areas of the heart, and angiography to see how blood flows.

Treatment of CAD depends on many factors, such as the patient's age, heart function, and overall health.

Often, treatment begins with focusing on lifestyle--stopping smoking for patients who smoke, reducing fat in the diet, and engaging in a prescribed exercise program. Medications may also be prescribed, such as aspirin to prevent additional heart attacks, medications that decrease the workload on the heart, or medicines to reduce high blood cholesterol levels or high blood pressure. If these efforts are not effective, a patient may need to have the narrowed or blocked arteries re-opened through a procedure called balloon angioplasty, or bypassed through surgery. Balloon angioplasty involves threading a thin tube into the artery and expanding a balloon-like apparatus as a way to increase the size of the artery so more blood can flow. Bypass surgery is used to treat severe blockages by using veins or arteries from other areas of the body to divert blood flow around the blocked coronary arteries.

## **3. What is EDTA chelation therapy?**

Chelation is a chemical process in which a substance is used to bind molecules, such as metals or minerals, and hold them tightly so that they can be removed from a system, such as the body. In medicine, chelation has been scientifically proven to rid the body of excess or toxic metals. For example, a person who has lead poisoning may be given chelation therapy in order to bind and remove excess lead from the body before it can cause damage.

In the case of EDTA chelation therapy, the substance that binds and removes metals and minerals is EDTA (ethylene diamine tetra-acetic acid), a synthetic, or man-made, amino acid that is delivered intravenously

(through the veins). EDTA was first used in the 1940s for the treatment of heavy metal poisoning. EDTA chelation removes heavy metals and minerals from the blood, such as lead, iron, copper, and calcium, and is approved by the U.S. Food and Drug Administration (FDA) for use in treating lead poisoning and toxicity from other heavy metals. Although it is not approved by the FDA to treat CAD, some physicians and alternative medicine practitioners have recommended EDTA chelation as a way to treat this disorder.

#### **4. Does EDTA chelation therapy have side effects?**

When used as approved by the FDA (at the appropriate dose and infusion rate) for treatment of heavy metal poisoning, chelation with EDTA has a low occurrence of side effects. The most common side effect is a burning sensation experienced at the site where the EDTA is delivered into the veins. Rare side effects can include fever, hypotension (a sudden drop in blood pressure), hypocalcemia (abnormally low calcium levels in the blood), headache, nausea, vomiting, and bone marrow depression (meaning that blood cell counts fall). Injury to the kidneys has been reported with EDTA chelation therapy, but it is rare. Other serious side effects can occur if EDTA is not administered by a trained health professional.

#### **5. How might EDTA chelation therapy work to clear blocked arteries?**

Several theories have been suggested by those who recommend this form of treatment. One theory suggests that EDTA chelation might work by directly removing calcium found in fatty plaques that block the arteries, causing the plaques to break up. Another is that the process of chelation may stimulate the release of a hormone that in turn causes calcium to be removed from the plaques or causes a lowering of cholesterol levels. A third theory is that EDTA chelation therapy may work by reducing the damaging effects of oxygen ions (oxidative stress) on the walls of the blood vessels. Reducing oxidative stress could reduce inflammation in the arteries and improve blood vessel function. None of these theories has been well tested in scientific studies.

#### **6. Is there evidence that EDTA chelation therapy works for CAD?**

There is a lack of adequate prior research to verify EDTA chelation therapy's safety and effectiveness for CAD. The bulk of the evidence supporting the use of EDTA chelation therapy is in the form of case reports and case series. Some patients who have undergone chelation therapy and the physicians who prescribed it claim improvement in CAD. In addition, there are approximately 12 published descriptive studies and 5 randomized controlled clinical trials regarding the use of EDTA chelation for CAD. Although each descriptive study did report a reduction in angina, they were uncontrolled clinical observations or retrospective data, typically with a small number of participants. Of the five clinical trials in which patients were randomly selected to receive chelation therapy or a placebo (a dummy solution), the most rigorous way of assessing a new treatment, three trials involved so few people that only a dramatic improvement could have been detected. Studies need a larger number of participants to detect more mild benefits of a treatment. The fourth study was never published in final form, so its conclusions are uncertain. Finally, the fifth study reported that EDTA chelation was associated with an improvement in ability to exercise, but it had only 10 participants.

#### **7. How frequently is EDTA chelation therapy used?**

It is estimated by the American College for Advancement in Medicine (ACAM), a professional association that supports the use of chelation therapy, that more than 800,000 visits for chelation therapy were made in the United States in 1997 alone.

#### **8. Why did NCCAM and NHLBI decide to study this therapy?**

CAD is the leading cause of death among men and women in the United States. In spite of effective standard therapies, such as lifestyle modifications, medications, and surgical procedures, some patients with CAD seek out EDTA chelation therapy as a treatment option.

Therefore, NCCAM and NHLBI saw a public health need to conduct a large-scale, well-designed clinical trial that could determine more clearly whether EDTA chelation therapy is indeed an effective and safe alternative for treating CAD. However, there are professional organizations that are of the opinion that a large study of EDTA chelation therapy should not be carried out because of the lack of scientific evidence supporting its effectiveness.

#### **9. How will the NIH study be conducted?**

This placebo-controlled, double-blind study will recruit 2,372 participants aged 50 years and older with a prior myocardial infarction (heart attack) to test whether EDTA chelation therapy and/or high-dose vitamin therapy is effective for the treatment of CAD. This study, with a total cost of approximately \$30 million, is over 20 times larger than any previous study of chelation therapy. It is designed to be large enough to detect if there are any mild or moderate benefits or risks associated with the therapy.

EDTA chelation therapy, as practiced in the community, often includes administration of high-doses of antioxidant vitamin and mineral supplements. Thus, it is possible that effects of the therapy could be connected to these supplements. In order to test whether some of the therapy's effect may be attributable to vitamin/mineral supplements, or to the EDTA solution itself, the investigators will first randomly assign

participants to receive either EDTA chelation solution or placebo. Then the patients in these two groups (about 1,186 in each) will again be randomly selected to receive either low-dose or high-dose vitamin/mineral supplements.

The EDTA chelation therapy or placebo solution will be delivered through 40 intravenous infusions that are administered over a 28-month course of treatment. The first 30 infusions will be delivered on a weekly basis and the last 10 will be delivered bimonthly. Following the infusion phase, participants will have contact with study staff at 3-month intervals until the study is complete.

The protocol for the trial was developed using a model protocol for EDTA chelation therapy endorsed by the American College for Advancement in Medicine (ACAM). The ACAM protocol is used worldwide by chelation practitioners. It is the intent of this study to ensure that the most widely practiced method of delivering EDTA chelation is rigorously tested.

#### **10. What will the study determine?**

Overall, the investigators will assess whether EDTA chelation therapy and/or high-dose vitamin/mineral supplements are safe and effective in treating individuals with CAD. Specifically, they will determine if EDTA chelation and/or high-dose vitamin supplements improve event-free survival (length of time without another heart attack, etc.), are safe for use, improve quality of life, and are cost effective.

The investigators will look at several markers of improvement, or endpoints, to make these determinations. The primary endpoint in the trial will be a composite of:

- All causes of death
- Heart attack
- Stroke
- Hospitalization for angina
- Coronary revascularization.

Secondary endpoints will include:

- Cardiac death, or nonfatal heart attack, or nonfatal stroke
- The individual components of the primary endpoint
- The safety of the therapy
- Health-related quality of life
- Cost effectiveness.

#### **11. Who is the study's principal investigator?**

The principal investigator for the trial is Gervasio A. Lamas, M.D., director of cardiovascular research and academic affairs at Mount Sinai Medical Center-Miami Heart Institute, Miami Beach, Florida. Dr. Lamas is a board-certified cardiologist and an associate professor of medicine at University of Miami School of Medicine. He has extensive experience in the design, conduct, and analysis of randomized, multicenter trials of the treatment and management of cardiac diseases, including CAD.

#### **12. What types of participants will be recruited?**

Participants must be 50 years of age or older, have had a heart attack at least 6 weeks prior to evaluation, and have not had chelation therapy within the past 5 years. Other exclusion criteria include:

- History of allergic reactions to EDTA or any of the therapy's components
- Coronary or carotid revascularization procedures within the past 6 months or a scheduled revascularization
- History of cigarette smoking within the last 3 months
- Childbearing potential
- History of liver disease
- Diagnoses of additional medical conditions that could otherwise limit patient survival, such as cancer.

The goal is to recruit a patient study population of both men and women that is fairly typical of people with CAD. The study investigators also will recruit participants whose ethnic and racial makeup reflects the diversity of the United States population.

#### **13. Where will the study take place?**

The study will take place at more than 100 research sites located across the country. The research sites will represent a mix of clinical settings--university or teaching hospitals, clinical practices or cardiology research

centers, or chelation practices. The sites will be selected based on a thorough review of qualifications by the study team and require approval of the study by their local institutional (ethical) review boards.

**14. How long will it take to complete the study?**

Over the next several months, additional study sites will be identified. The investigators enrolled the first participants in September 2003. The study will take approximately 5 years to complete.

**15. How can I learn more about the study?**

Information about the study, locations, and enrollment will be available from the NCCAM Information Clearinghouse at 1-888-644-6226, NCCAM's Web site, and from [ClinicalTrials.gov](http://ClinicalTrials.gov), the NIH Web site for clinical trials information.

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