

# Questions and Answers: The NIH Trial of EDTA Chelation Therapy for Coronary Heart Disease

Results from the Trial to Assess Chelation Therapy will be published in the Journal of the American Medical Association on March 27, 2013. The questions and answers below provide information on the purpose of the study, what EDTA chelation is, and key results of the trial, as well as more general information about coronary heart disease.

## About the Study

### What is the Trial to Assess Chelation Therapy (TACT)?

TACT is the first large-scale, multicenter study designed to determine the efficacy of a specific form of chelation therapy using disodium ethylene diamine tetra-acetic acid (EDTA) for individuals who suffered prior heart attacks. The National Institutes of Health's National Heart, Lung, and Blood Institute (NHLBI) and National Center for Complementary and Alternative Medicine (NCCAM) co-sponsored TACT. This study is more than 20 times larger than any previous study of chelation therapy. It was designed to be large enough to detect if there are any moderate benefits or risks associated with the therapy.

### What were the key results of the study?

The researchers concluded that:

- TACT provides evidence that a regimen of 40 infusions of disodium EDTA modestly reduced the risk of some cardiovascular events in adults who have previously had a heart attack. This treatment effect lasted during the 5-year follow-up period and in patients that were on evidence-based medicines (or medicines known to be effective in patients with a history of heart attacks)
- Overall, those receiving chelation had an 18 percent reduced risk of subsequent cardiovascular events such as heart attack, stroke, hospitalization for angina, or coronary revascularization or death from any cause. A cardiovascular event occurred in 222 (26 percent) of the chelation group and 261 (30 percent) of the placebo group.
- Two subgroups of participants had a greater reduction in risk for cardiovascular events. Those with diabetes had a 39 percent reduction in risk and those who had experienced a specific type of heart attack, called an anterior myocardial infarction, had a 37 percent reduction in risk.
- Since this is the first clinical trial to show a benefit, these results are not, by themselves, sufficient to support the routine use of chelation as post-heart attack therapy.

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

In addition to effective standard therapies, such as lifestyle modifications, medications, and surgical procedures, some patients with coronary heart disease (CHD) seek out EDTA chelation therapy as a treatment option based on anecdotal reports of improved symptoms in patients with heart disease.

In fact, between 2002 and 2007, use of chelation therapy to treat heart disease and other diseases grew in the United States by nearly 68 percent to 111,000 people, according to the 2008 National Health Statistics Report.

Prior to TACT, the evidence cited in the support of using EDTA chelation therapy was in the form of case reports and case series. It was important to conduct a large-scale, well-designed clinical trial that looked at whether EDTA chelation therapy is safe and effective in patients with a history of a heart attack.

### **How commonly is EDTA chelation therapy used?**

The 2008 National Health Interview Survey, conducted by the Centers for Disease Control and Prevention, found that 111,000 adults 18 years of age and older used chelation therapy as a form of complementary medicine in the previous 12 months.

### **What was the purpose of the study?**

The purpose of the study was to determine the safety and efficacy of EDTA chelation therapy for treating CHD. TACT was designed to see whether EDTA chelation therapy and/or high-dose vitamin/mineral supplements are safe and effective in treating individuals with prior heart attacks. Specifically, they sought to determine if EDTA chelation and/or high-dose supplements improved event-free survival (length of time without a cardiovascular event, such as a heart attack).

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

- All causes of death
- Heart attack
- Stroke
- Hospitalization for angina (chest pains sometimes warning of an impending heart attack)
- Coronary revascularization (coronary stents or bypass surgery).

Secondary endpoints included:

- Cardiovascular 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

### **What was the basic design of the study?**

The study was a placebo-controlled, double-blind design that included 1,708 participants aged 50 years and older who had suffered a prior heart attack. Its purpose was to test whether EDTA chelation therapy and/or high-dose vitamin therapy is effective for treating CHD.

EDTA chelation therapy, as practiced in the community, often includes administration of high doses of antioxidant vitamin and mineral supplements. In order to test whether the therapy's effect may be attributable to vitamin/mineral supplements or to the EDTA solution itself, the investigators randomly assigned participants to receive either EDTA chelation solution or placebo. The patients in these two groups were also randomized to receive either low-dose or high-dose vitamin/mineral supplements.

The EDTA chelation therapy or placebo solution was delivered through 40 intravenous infusions (into the veins) that were administered during a 28-month course of treatment. The first 30 infusions were delivered on a weekly basis and

the last 10 were delivered every 2-8 weeks. Following the infusion phase, participants had contact with study staff at 3-month intervals until the study was complete.

### **What did TACT cost?**

TACT cost approximately \$31.6 million during the 10-year period it took to conduct it.

### **Study Background**

#### **What is coronary heart disease?**

[Coronary heart disease \(CHD\)](#) is the most common form of heart disease and is the leading cause of death among American men and women. Each year, nearly 380,000 Americans die from CHD. In CHD, the coronary arteries (the vessels that provide oxygen-rich blood to the tissues of the heart) become blocked by deposits of a waxy substance called plaque. As plaque builds, the arteries become narrower and less oxygen and nutrients are transported to the heart. CHD can lead to serious problems, such as heart attack and angina (pain caused by not enough oxygen-carrying blood reaching the heart). A heart attack occurs if the flow of oxygen-rich blood to a section of heart muscle is cut off. If blood flow is not restored quickly, the affected section of heart muscle begins to die. Without quick treatment, a heart attack can lead to death or serious health problems.

Factors that can increase the risk of developing CHD include

- High blood pressure
- High blood cholesterol levels
- Smoking
- Overweight or obesity
- Physical inactivity
- Diabetes
- Insulin resistance
- Metabolic syndrome
- Unhealthy diet
- Family history of CHD
- Older age

Symptoms of CHD can include chest pressure or tightness, shortness of breath, lightheadedness, cold sweats, or nausea, but not everyone with CHD has symptoms.

#### **How is CHD diagnosed and treated?**

Diagnosis of CHD is based on personal medical and family histories, risk factors for CHD, a physical exam, and the results from tests and procedures. Doctors who suspect CHD may recommend one or more tests, such as those that check levels of fats, cholesterol, and sugar; electrocardiograms (EKG) to check the heart's electrical activity; "stress" tests to test for ischemia (not enough oxygen getting to heart muscle) during exercise; nuclear scanning to check for ischemic or previously damaged areas of the heart; and/or angiography to see if there are blockages or narrowings in the blood vessels that feed the heart. Treatment of CHD includes lifestyle changes—stopping smoking for patients who smoke, reducing fat in the diet, and engaging in a prescribed exercise program. Medications also may be prescribed, such as aspirin to prevent heart attacks, medications that decrease the workload on the heart, or medicines that reduce blood cholesterol levels or blood pressure. If these efforts are not effective and patients continue to have symptoms, a patient may need to have the narrowed or blocked arteries re-opened through a procedure called percutaneous coronary intervention (PCI), or bypassed through surgery. PCI involves threading a thin tube into an 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.

To learn more about CHD and its diagnosis and treatment visit:

<http://www.nhlbi.nih.gov/health/health-topics/topics/cad/>.

### **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 calcium disodium EDTA, a chelation therapy in order to bind and remove 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 are the salts of EDTA (ethylene diamine tetra-acetic acid), a synthetic, or man-made, amino acid that is delivered intravenously. EDTA was first used in the 1950s for the treatment of heavy metal poisoning. Calcium disodium EDTA chelation also removes heavy metals and minerals from the blood, such as lead, iron, copper, and calcium, however unlike disodium EDTA, calcium disodium EDTA is approved by the U.S. Food and Drug Administration (FDA) for use in treating lead poisoning and toxicity from other heavy metals. Rather than testing calcium disodium EDTA, TACT used another salt, disodium EDTA, under an FDA license as an Investigational New Drug (IND). Although disodium EDTA it is not approved by the FDA to treat CHD, some physicians and alternative medicine practitioners have recommended its use in chelation as a way to treat CHD. Disodium EDTA is not approved by the FDA to treat any diseases at this time. However, it is produced by compounding pharmacies for individual patients, so people can still attain the treatment.

### **What did the chelation infusions contain?**

For TACT, the active, 10-component chelation solution was selected to match most closely the standard solution used by chelation practitioners. The solution contained up to 3 grams disodium EDTA; 7 grams of Vitamin C, ascorbic acid; 2 grams of magnesium chloride; 100 mg of procaine hydrochloride; 2500 U of unfractionated heparin; 2 mEq potassium chloride; 840 mg sodium bicarbonate B vitamins, 250 mg pantothenic acid, 100 mg thiamine, 100 mg pyridoxine; and sterile water to make up 500 mL of solution. The placebo solution consisted of 500 mL of normal saline and 1.2 percent dextrose.

The infusions for the study were prepared at a central pharmacy and then shipped to the study sites in refrigerated containers.

### **What are the possible side effects of EDTA chelation therapy?**

The most common side effect is a burning sensation at the site where EDTA is administered. Rare side effects can include fever, headache, nausea, and vomiting. Even more rare are serious and potentially fatal side effects that can include heart failure, a sudden drop in blood pressure, abnormally low calcium levels in the blood (hypocalcemia), permanent kidney damage, and bone marrow depression (meaning that blood cell counts fall). Hypocalcemia and death may occur particularly if disodium EDTA is infused too rapidly. Reversible injury to the kidneys, although infrequent, has been reported with EDTA chelation therapy. Other serious side effects can occur if EDTA is not administered by a trained health professional.

### **How was patient safety monitored?**

A number of safety mechanisms were in place, including a rigorous protocol with standard rates of infusions and doses of disodium EDTA based on kidney function. Oversight by a Clinical Coordinating Center ensured that the sites did not give infusions to patients for whom they might pose a risk because of their medical conditions or infuse faster than protocol requirements. An NIH-appointed Data and Safety Monitoring Board monitored the trial throughout its entirety, providing ongoing oversight and review of patient safety. In addition, the FDA provided oversight as is required for all drugs used under an IND.

### **Were there any adverse events reported?**

Overall, 38 people (16 percent) receiving chelation and 41 people (15 percent) receiving placebo cited an adverse event as the cause of discontinuing study infusions. There were four unexpected severe adverse events that were possibly or definitely attributed to study therapy—two in the chelation group (one death), and two in the placebo group (one death). Heart failure was reported in 57 (7 percent) chelation patients, and 71 (8 percent) placebo patients. A total of 55,222 infusions were given throughout the course of the study. Of those infusions, 330 (0.60 percent) were administered at least 30 minutes too rapidly. Hypocalcemia, prior to an infusion, was reported in 52 (6.2 percent) chelation patients and 30 (3.5 percent) placebo patients. One patient had hypocalcemia associated with muscle cramping that led to an emergency department visit.

### **Where did the study take place?**

The study was conducted at 134 research sites located across the United States and Canada. The research sites represented a mix of clinical settings—university or teaching hospitals, clinical practices or cardiology research centers, and chelation practices. Per standard clinical trial procedure, the sites were selected based on a thorough review of qualifications by the study team and required approval of the study by their local institutional (ethical) review boards. All sites received extensive training prior to the start of the trial and they were regularly monitored.

### **Who participated in TACT?**

During the course of the study 1,708 patients were randomized after signing informed consent—839 patients to chelation and 869 patients to placebo. The study recruited participants who were at least 50 years of age or older, had had a heart attack at least six weeks prior to evaluation, and had not had chelation therapy within the past five years. The participants also could not have:

- 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

On average, TACT participants were 65 years old. Eighteen percent of participants were women and 9 percent were minorities. Participants' heart attacks had, on average, occurred 4.6 years before enrollment. The study population had a high rate of diabetes (31%), prior coronary revascularizations (83%), and use of medications, such as aspirin (84%), beta-blocker (72%), and statins (73%).

### **For More Information**

**NHLBI Health Information Center**

The NHLBI Health Information Center provides information to health professionals, patients, and the public about the treatment, diagnosis, and prevention of heart, lung, and blood diseases and sleep disorders.

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