

# **SAMPLE PROTOCOL**

American College for Advancement in Medicine

Institutional Review Board

## SAMPLE PROTOCOL

Title of Study: Chelation Therapy for Arteriosclerotic Disease

Principal Investigator: Eleazar M. Kadile, M.D.

1. What is the purpose of this Study?

The purpose of this study is to accumulate evidence to demonstrate the effectiveness and safety of chelation therapy for arteriosclerotic disease. Morbidity, mortality, health costs and quality of life will be analyzed every 5 years.

2. Selection of subject to be studied.

Patients with arteriosclerotic or vascular diseases will be introduced to the idea of EDTA and Magnesium versus other forms of therapy and will self-select according to their understanding of the benefits and the risks.

Choices will include:

- 1) No therapy at all
- 2) Nutrition: Fresh food freshly prepared without preservatives or additives if possible.  
Vitamins, Minerals, EFA, AA, Glutathione
- 3) Exercise, weight control
- 4) Combination of 2) and 3)
- 5) Medications: CA channel blockers  
B Blockers  
ACE inhibitors  
Diuretics
- 6) EDTA and MgC12  
Plus - Nutritional replacement of minerals. oral or IV  
Plus - Vitamins  
(ACAM Protocol)

3. Controls

Patient may be his/her own control based upon previous history, previous therapy and previous results. Patients choosing surgery or PTCA will also serve as controls to establish levels of allowable morbidity and mortality.

4. Compensation

No compensation will be paid to any subject in this study.

5. Procedure

Each patient will have a complete history and physical exam completed and documented in his chart. Appropriate studies may include CBC, U/A, Chem Panel Na, K, RBC mineral analysis, for trace and toxic minerals, TSH, Chest X-ray, EKG, Treadmill EKG. Patients with angina may elect to have angiograms performed, and this will be done by cardiologists at \* Hospital. A clinical evaluation will also be performed. Patients with claudication or evidence of pvd will have either angiograms or a vascular surgeon's evaluation of peripheral vascular competence, and also will be evaluated clinically. Patients with cerebral AS or carotid artery disease, will be evaluated both clinically and with carotid dopplar studies. Carotid/cerebral angiograms may or may not be included. After the foregoing appropriate workup, patients will be given information on the advantages/disadvantages of bypass surgery and the advantages/disadvantages of chelation therapy. They will then self select into one of the categories listed under "selection" (2. above). Those patients choosing EDTA chelation with magnesium chloride will be treated according to the ACAM Protocol dated 2/1/89 and as amended on 8/1/93 (attached).

6. Potential risks and benefits:

Risks of chelation therapy with the condition of the patients:

Patients with CHF - cautions re: Fluid overload

Patients with renal failure - Cautions re: CFR as measured by creatinine clearance

Patients with diabetes - Cautions re: Hypoglycemia

Patients with convulsive disorder - Cautions re: Hypocalcemia

Patients with hypoparathyroidism - Cautions re: Hypocalcemia

Patients with lead toxicity - Cautions re: CFR

All patients may risk thrombophlebitis of IV site

Benefits hopefully would include:

- increased ability to exercise
- decreased chest pain
- increased distance walking
- increased mental clarity

6.a. How would benefits be measured? This would depend upon the presenting symptoms:

**Presenting Symptoms:**

**Measure Improvement By:**

Angina of exertion . . . . .	Decreasing frequency and severity of attacks of angina Decreased need of medication Increasing treadmill time Improved EKG Criteria Improved lifestyle factors – energy, outlook, potency, etc. Improved coronary angiograms Increased survival time
Claudication . . . . .	Improved echocardiogram findings Distance walked before cramping Objective measurement of BP in legs Improvement in color of feet Decrease in gangrene if present Decrease in foot/leg pain Angiogram changes
Cerebrovascular . . . . . Insufficiency	Increased mental clarity Improved memory Improved carotid artery angiograms Improved lifestyle changes; i.e., ability to care for self, etc.

7. What alternatives are available that may benefit the participant?

See under paragraphs 2. and 3. above

8. Will there be any costs to the participant and/or insurer as a result of participation?

Costs to participating subjects include the usual charges for a complete history and physical exam, appropriate lab, x-ray and ancillary study charges, and office visits. Charges to insurance companies will depend upon the patient's coverage, noting that many insurance companies do not cover treatments that are considered "experimental."

9. See under paragraph 6. above

10. Adverse reaction or problem

I am available at all times, since I carry a pager and can usually return a call within 1-10 minutes. My pager number is (556-8512). Any medical emergency can be met by dialing 911 or going directly to the St. Vincent Hospital Emergency room. My office answering machine also gives patients specific instructions: telephone number is (468-9442).

11. Confidentiality of data

Confidentiality of data will be maintained as I usually do in my office practice. No information will be released without an adequately signed release of information.

12. I anticipate that I will be the primary physician in all patients. Reports may be generated to other physicians on an individual basis as appropriate.

13. Results of prior investigations

Prior studies support the conclusion that it is reasonably safe to begin the study.

Many references are noted after each chapter in ACAM's *A Textbook on EDTA Chelation Therapy*, edited by Elmer M. Cranton, MD. I have been an active member of ACAM since 1985 and have attended at least one ACAM meeting each year. Statistics provided by L. Terry Chappell, MD at the 1993 ACAM convention indicate good results in a meta-analysis of about 90% of all cases in a cohort study involving over 3000 patients. A compilation of references by ACAM in which over 3500 abstracts attest to the efficacy and validity of EDTA chelation therapy also is noted.

14. Laboratory facilities

Clinical laboratory facilities are available in a nearby building (100 feet away) and stat results are available. My office also has facilities for drawing blood and sending samples out to clinical laboratories.

Safety of the subject is assured by:

- a) Adequate evaluation by clinical and lab studies before chelation is started
- b) Maintaining surveillance by myself and my staff
- c) Appropriate clinical and lab studies at intervals of every 3 to 8 chelation treatments

15. Record keeping

At the initial evaluation, the diagnosis, with supporting lab, EKG and other data will be summarized and treatment outlined. Periodic updates of this data, along with periodic clinical and lab evaluations will be recorded. These records will be sent to the IRB periodically (annually). Samples of reporting forms enclosed.

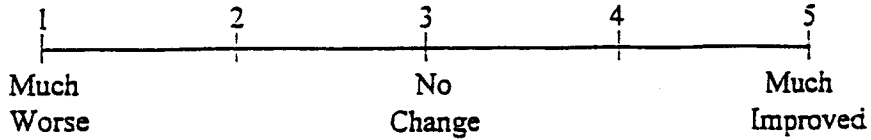
16. Informed consent enclosed.

**EDTA CHELATION OUTCOME RECORD**

Name: \_\_\_\_\_

Date: \_\_\_\_\_

Rate each item under "Symptom" (below) using the following scale:



**DATES OF CLINICAL EVALUATION**  
(Fill in date)

**SYMPTOM**

Overall

Chest Pain/Tightness  
Chest Discomfort

Palpitations/Arrhythmia

Leg Pain

Claudication

Sleep

Anxiety/Depression

Drugs #On

EKG

Stress Test

Angiography/PET  
Doppler/SPECT

Stress

Nutrition/Diet

Exercise

Supplements

DATES OF CLINICAL EVALUATION (Fill in date)				
SYMPTOM				
Overall				
Chest Pain/Tightness Chest Discomfort				
Palpitations/Arrhythmia				
Leg Pain				
Claudication				
Sleep				
Anxiety/Depression				
Drugs #On				
EKG				
Stress Test				
Angiography/PET Doppler/SPECT				
Stress				
Nutrition/Diet				
Exercise				
Supplements				

**INFORMED CONSENT, DISCLOSURE AND  
ACKNOWLEDGEMENT FORM FOR CHELATION THERAPY STUDY**

at the office of:

Name Eleazar M. Kadile, M.D.

Address 1538 Bellevue Street  
Green Bay, WI 54311

Patient's Name \_\_\_\_\_

(1) Title of Project - Chelation Therapy for Arteriosclerotic Disease

I am, by my signature on this document, indicating as a patient of Dr. E. Kadile my desire to participate in a treatment program involving the use of EDTA. (Ethylenediamine tetraacetic acid). This program in my case will involve the usage of this chelating agent for the treatment of arteriosclerosis. This treatment program will be conducted and supervised by Dr. E. Kadile.

(2) Purpose of Study

I understand that this project is conducted under the aegis of the Institutional Review Board ("IRB") of the American College for Advancement in Medicine ("ACAM"), for the purpose of establishing the effectiveness of treatment of arteriosclerotic diseases by intravenous ("IV") administration of EDTA with magnesium, according to protocol. The study will continue until this therapy is approved by the Food and Drug Administration. EDTA chelation therapy is a standard therapy approved by the FDA for treatment of heavy metal toxicities, hypercalcemia, and the control of ventricular arrhythmias secondary to digitalis intoxication. Its usage, however, is considered controversial for the generalized treatment of arteriosclerosis or atherosclerosis, and the view that it is of benefit in the treatment of such disorders is accepted by a minority of the medical community, but is considered "experimental" by most physicians. I am advised that my treating physician believes that chelation therapy does have positive clinical benefit.

(3) I understand that Dr. E. Kadile's program for chelation therapy includes:

1. A complete history and physical exam.
2. Appropriate x-ray, EKG, blood, urine, and U/S studies and may include exercise thallium treadmill studies, echocardiograms, and vascular evaluations, etc.
3. Treatment consists of a series of intravenous solutions (fluid flowing into my veins through a needle) and which contains EDTA (a synthetic amino acid), magnesium, and may also contain potassium, Vitamin C, and other vitamins and minerals which will contain between 250cc and 1000cc of solution which will require about 30 treatments, each treatment session taking about 1 1/2 to 3 hours, depending on the dose, for a basic course of treatment, at intervals of about 1-3 times per week. I will be required to take oral vitamins and minerals daily to replace those that are removed by this solution. Additional treatments may be advisable and this will be discussed with my physician at the conclusion of the initial treatment series, and other dietary and lifestyle changes may be advised.

4. Dr. \_\_\_\_\_'s monitoring of progress and results as the program proceeds, collating lab studies and clinical observations, collecting further information, keeping records, etc.

(4) The following are known potential risks or side effects to chelation therapy:

1. Kidney

While serious kidney problems or the risk of renal failure should not be significant with proper monitoring of my renal function during treatment, I realize that there is some risk of this developing, especially if I have suffered from any previous kidney diseases. I agree to execute a medical release so that all previously identified medical records of mine may be obtained from previous treating physicians, and I have disclosed openly any known previous kidney disorders. I agree to continued monitoring of kidney function by laboratory testing.

2. Thrombophlebitis

There is some possibility currently believed to occur in less than one percent of patients undergoing chelation therapy, that I may suffer from thrombophlebitis or a soreness or redness over the vein which could proceed to an inflamed red streak going up and down the vein or inflammation of my veins.

3. Lowering of Blood Sugar Levels

There is definite likelihood that my blood sugar may drop during intravenous chelation treatment, and that if I am diabetic this requires extra careful monitoring of my condition during treatment. I agree to cooperate in such monitoring if I am in fact diabetic.

4. Generalized Complaints

I understand that in what is estimated as one percent of patients undergoing chelation therapy there may be some generalized bothersome though not serious complications. These include the following: lowering of blood pressure and a resultant risk of feeling faint and weak immediately after treatment, nausea, diarrhea, numbness and cramping, headaches, low grade fever, skin rashes.

5. Mineral Loss

I understand that out of some concern that I may experience during chelation therapy some lowering of basic mineral levels such as zinc, copper, manganese and chromium, I will be monitored during therapy for reasonable levels of these minerals and supplements will be prescribed if deemed necessary by my physician.

6. Benefits

The benefits that I hope will occur include relief of chest pain, relief of leg pain on exercise, or \_\_\_\_\_

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(5) Alternatives to This Treatment

I understand that there are alternative treatments and/or procedures for treatment of arteriosclerosis or atherosclerosis which may be appropriate and available depending upon my individualized condition. These alternatives include:

1. No treatment at all.

2. Conservative lifestyle changes only.

This program would consist of dietary changes, dietary supplementation, an exercise program tailored to my needs, the cessation of all usage of tobacco and alcohol and attempts to deal with excessive levels of stress in my life.

3. Drug Therapy

Instead of chelation therapy, a common medical treatment is long-term drug therapy. Various drugs are available to deal with the effects of decreased bloodflow to and from the human heart (arteriosclerotic). These can include long-term use of a long-acting nitrate (to dilate blood vessels) or propranolol, a beta blocker, or the use of aspirin or the currently experimental and unproven usage of drugs such as persantin, which are currently believed to assist in decreasing blood clotting and other complications of arteriosclerosis. Other vasodilator drugs such as Pavabid (papavarine), Arlidin, Vasodilan, and others are available. If I desire further information about these types of drug therapy, I will ask my physician.

4. Surgery

There are various kinds of vascular surgical procedures, and if I am interested in these I will ask my physician to explain them to me and if necessary ask for referral to a surgeon who specializes in these types of surgical techniques. I understand that all these therapies have certain risks about which I should ask my physician if I am interested. Additionally, there may be substantial risk in my individual case of doing absolutely nothing at all about my condition, and I have discussed this particular risk with my physician.

- (6) Dr. \_\_\_\_\_ will answer my questions at times that are mutually agreeable. I may contact him through his office ( \_\_\_\_\_ ), answering phone ( \_\_\_\_\_ ) or pager ( \_\_\_\_\_ ). In the event that I experience any injury as a participant in this study, I understand that I should immediately contact Dr. \_\_\_\_\_ or go to \_\_\_\_\_ Hospital Emergency Room for emergencies.
- (7) I understand that it is my option to stop at any time this treatment protocol without reprisal or condition and to incur no further expense after I have directed that such treatment be stopped.
- (8) I understand that no compensation for participation in this study will be provided by Dr. \_\_\_\_\_, his office, ACAM or the IRB, and I also understand that neither ACAM nor the IRB has a policy to medically treat or compensate for physical injuries incurred as a result of participating in biomedical or behavioral research. I understand and agree that ACAM is not a participant in the study and that the IRB merely serves as a reviewer and collator of the data produced under this study. I expressly agree, as a condition of my participation in this study, that ACAM and the IRB shall not in any manner be responsible for any physical injuries incurred as a result of my participation in the study and I waive, in advance, any claims against either and both of them.
- (9) I understand that the confidentiality of my records will be protected and that the IRB has the authority to inspect all records and to utilize them for all statistical purposes. Any changes in the use of the information obtained other than that to which I have consented will first be presented to me for approval.
- (10) Costs to participating patients include the usual charges for a complete history and physical exam, appropriate lab, x-ray, and ancillary study charges, office visits, and other appropriate usual charges. IV chelation therapy will be charged at IV treatment bottle rates. Charges to insurance companies will depend upon my coverage, noting that many insurance companies do not cover treatment that are considered "experimental."



- (11) I understand that I will receive a copy of this signed consent form.
- (12) In the event that the results of the project are published as a study, I grant permission to be included, provided that my identity is protected.

**PATIENT'S AGREEMENT TO TESTING AND TREATMENT**

As a patient of the above-named physician, I have had the information in this disclosure and release form explained to me, and I have had the opportunity to ask any questions of my physician as they relate to the details of this document, the study, and all procedures to be utilized.

I have reviewed and considered the information contained in this document and the information provided to me through my conversations with my treating physician and I understand that there are no warranties or guarantees of successful treatment.

Patient's Name \_\_\_\_\_ Date \_\_\_\_\_  
(Typed name)

Patient's Signature \_\_\_\_\_ Date \_\_\_\_\_

Witness \_\_\_\_\_ Date \_\_\_\_\_  
(Typed name)

Witness Signature \_\_\_\_\_ Date \_\_\_\_\_

**ADDENDUM TO THE ACAM PROTOCOL FOR THE SAFE  
AND EFFECTIVE ADMINISTRATION OF  
EDTA CHELATION THERAPY**

The recommended dose of EDTA cited in the protocol is 50 mg. per kg. of lean body weight, administered over at least three hours and adjusted for lower than normal kidney function as determined by creatinine clearance. This yields an accepted safe rate of administration of 16.7 mg. per kg. per hour.

Some physicians have found that a lower dose (as low as one half of the above dose) has been effective in the treatment of vascular disease and have administered this lower dose over a proportionately shorter time. Since there is no exact amount of EDTA that has been determined to be the ideal for all patients, the protocol is hereby modified to allow for variation depending on the judgement and experience of the physician caring for the patient.

However, the accepted rate of administration for safety is still considered to be 16.7 mg. per kg. per hour, adjusted for creatinine clearance. Infusion rates in excess of 16.7 mg./kg./hr. do not at this time have an established safety record.

ACAM does not monitor physicians practicing chelation therapy and is not in a position to approve or disapprove of their treatment methods or the management of their patients. However, the Board of Directors and the Scientific Advisory Committee have not endorsed the safety or efficacy of any rate of administration above 16.7 mg. per kg. per hour or any specific protocol dose.

It is unacceptable for any physician to claim that his or her treatment method, if it differs from the above, is approved by the Board of Directors of ACAM.

August 1, 1993