

# History of EDTA Chelation and Review of the Published Literature

By Stuart H. Freedenfeld, MD

1930's Franz Munz, in attempting to decrease Nazi Germany's reliance on foreign imports, developed EDTA (ethylene-diamine-tetraacetic acid, a synthetic amino acid) as an alternative to citric acid which was imported from England and used to prevent stains by permanent dyes in the textile industry.

1930's Frederick Bersworth synthesized EDTA at Clark University in Worcester, Mass. Using a different production technique, he was able to obtain his own US patent in 1945.

1947: EDTA was approved by the FDA as a safe food additive. Medical experimentation began that year with unsuccessful attempts to treat breast cancer and kidney stones.

1950's Mark Rubin at Georgetown University demonstrated that EDTA would chelate plasma calcium.

1951: MgEDTA (the same form used in modern day chelation treatments) was used experimentally to chelate calcium and the released magnesium was found to lower blood pressure.

1952: CaEDTA began being used to treat lead poisoning. Practitioners reported dramatic improvement in elderly lead toxic patients with coexisting atherosclerotic cardiovascular disease. Multiple researchers also reported resolution of angina and arrhythmia due to digitalis toxicity.

1956 (Am J Med Sci 232:654-666). Norman Clark reported on 20 patients with documented angina whose symptoms improved or cleared after chelation treatments.

1957: A. J. Boyle demonstrated the reversal of atherosclerosis in man using EDTA.

1960 (Am J Card 6:233-236) H Ray Evers reported on his experience with 3000 patients in clinical private hospital settings using EDTA for atherosclerosis. In his conclusion he states "we will unequivocally state the it is our opinion that every patient with this disease in any part of the body should be given a therapeutic trial before any type of vascular surgery is performed." In a subsequent paper about the same 3000 patients he stated "We find in all cases of angina [that] the patient [has] no need for vasodilators (*medicines used to dilate arteries*) after about the fifth infusion... and that ninety percent of these problems in the lower extremities make significant gains including regaining the ability to walk long distances comfortably, freedom from claudication (*painful cramps due to blocked arteries*), and evidence of improved distal circulation."

1961 (Am J Med Sci 242:51-57) Meltzer, Kitchell and Palmon published a comprehensive clinical toxicity study involving 2000 consecutive EDTA chelation treatments in 81 patients with **coronary artery disease (CAD)**. Their conclusion was that no serious side effects occurred and that EDTA "can be used without danger over prolonged periods."

1963 (Am J Card 11:501-506) L E Meltzer reported on 38 very high risk patients with CAD treated with EDTA. Findings showed that 66% improved their angina after 3 months and 40% had EKG improvements. After 18 months 64% had increased exercise tolerance with no further treatments, dietary intervention or risk factor modification. Most of these patients had only 20 treatments!

1964 (Angiology 15:379-394) Carlos Lamar reported on 15 diabetic patients with **peripheral vascular disease (PVD)** (blocked leg arteries) and 3 with **diabetic retinopathy** (artery disease in eyes of

diabetics). All showed dramatic subjective and objective improvement. Seven had persistent decrease in insulin needs.

1968 (Proc Soc Exp Biol Med 128(1):1137-1145) Olwin and Koppel reported on 34 patients (14 diabetics) with lipid abnormalities. After EDTA chelation all **lipid parameters** improved including cholesterol and LDL.

1969 (International Congress of Angiology in Prague) Langhof et al reported that EDTA treatments in 12 patients with atherosclerosis gave good results after 6-8 weeks without side effects. Serum cholesterol improved.

**1969 Abbott's patent on EDTA ran out and there was no further commercial support of research in the US.**

1972 Nikitina and Abramova (Czechoslovakia) reported on 25 patients with CAD, 8 with **cerebrovascular disease (CVD)** involves arteries to the brain), and 7 with PVD all of whom had significant improvement. Their conclusion was that EDTA is the treatment of choice for atherosclerotic disease of arteries .

1976 Tamburino (IRCS Med Sci Libr Compendium 4:362) Reported that "**Osteoporosis** ...is reversed by EDTA, which initiates deposition of new bone matrix" due to induction of PTH and concomitant increase in osteoblastic/osteoclastic activity in bones.

1977 (J Mol Chem Cardiol 9:897-908) Peng et al reported data showing that "Abnormal mitochondrial oxidative phosphorylation of ischemic myocardium is reversed by calcium chelating agents."  
**Comment:** *This improves energy production in the heart muscles during angina or a heart attack and can protect the heart from damage.*

1980 (Environmental International 3:465-471) Blumer and Reich published findings of a 90% decrease incidence of **cancer** in 59 lead exposed individuals over a 10 year period compared to 231 untreated patients in the same lead exposed area. A follow up study in 1989 showed that after 18 years, only 1 of 59 (1.7%) treated patients died from cancer compared to 30 of 172 (17.6%) untreated patients.

1980's - mid 1990's McDonagh and Randolph published multiple papers on the beneficial effects of EDTA on lipids, CVD, Renal function, Diabetes, Serum calcium, fatigue, heart rate, blood pressure, bone density and chronic lung disorders.

1983 (J Holistic Med 5(1):3-15) Casdorff and Farr reported on the saving of 4 lower extremity limbs recommended for amputation by EDTA chelation.

1985 Schettler et al at the Univ. of Heidelberg in Germany performed a double blind placebo controlled study comparing EDTA to a platelet inhibitor called Fludilat. The study was sponsored by the manufacturer of Fludilat. The EDTA treated group showed a 250% increase in average walking distance compared to 64% for Fludilat. The EDTA patients continued to improve 30 days after treatment stopped while the Fludilat group all reverted to their pretreatment levels. ***This study was never published.***

1986 the US FDA granted an IND to study EDTA chelation in the treatment of claudicatory peripheral vascular disease. Unfortunately when the Persian Gulf War developed the medical personnel doing the study were transferred and funding was stopped. Thirty patients had completed the blinded study but

even those results have not been reported from Walter Reed Hospital where the study was being performed.

1988 (Medical Hypoth 27:41-49) E. Olszewer and James P Carter published results of a 28 month retrospective analysis of 2870 patients with documented atherosclerosis and other age-associated, degenerative diseases treated with EDTA showing marked improvement in 76.9% and good improvement in 17% of treated patients with ischemic CAD; marked improvement on 91% and good improvement in 8% of treated patients with PVD and claudication; and marked improvement in 24% and good improvement in 30% of patients with degenerative cerebral diseases. Overall nearly 90% of the patients showed good to excellent improvement as measured by walking distance, EKG and Doppler changes.

1988 (J Adv Med 1(4):182-190) D P Deucher published his observations on chelation therapy as an antioxidant strategy noting that 91% of patients with free radical associated diseases show good to excellent results.

1989 (J Adv Med 2(4):553-561) Rudolph and McDonagh reported on EDTA chelation in 38 patients with **chronic lung disorders**. After 30 infusions 30 of the 38 patients (79%) improved significantly in both FVC and FEV1 (important measures of lung function).

1989 (J Adv Med 2(4):563-566) Peter J van der Schaar reported on 111 patients after 25 EDTA treatments. Double- and triple-product measurements on treadmill testing improved in patients with CAD, PVD, and CVD.

1989 (J Adv Med 2(1,2) Rudolph and McDonagh studied 117 lower extremities in 77 elderly patients with documented occlusive PVD. After an average of 26 treatments ankle/brachial Doppler measurements demonstrated significant improvements in arterial blood flow.

1990 (J Nat Med Assoc 82(3):173-177) Effrain Olszewer, F C Sabbag, and James P Carter authored the first published double-blind placebo-controlled study detailing the effectiveness of EDTA chelation for PVD. Starting with 20 patients, half received EDTA chelation treatments and the others received placebo treatments. After 10 treatments half the patients were showing significant improvements in walking distances and ankle/brachial indices, so the investigators decided to break the code. All the improvements were in the treated group. For the next ten treatments both groups received EDTA. The original treatment group continued to improve and the previous control group began to show improvements similar to the first 10 treatments in the EDTA group

1990 (J Adv Med 3(1):5-11) Rudolph and McDonagh reported on a single patient with 98% occlusion of the right carotid artery. After 30 chelation treatments duplex scanning demonstrated the occlusion was reduced to 33%. The shear motion observed originally resolved to normal.

1991 (Am J Surg 162:122-125) J Sloth-Nielsen et al (a group of Danish vascular surgeons) published the first EDTA series whose conclusion was not supportive of the effectiveness of EDTA chelation. **Comment:** *This was supposed to be a double-blind, placebo-controlled study of 153 patients. For unclear reasons the authors only focused on 30 of the 153 patients. And even though 50-60% of the treated patients improved the placebo group had similar improvements and so there was no benefit over placebo. Subsequent reviewers of the study have criticized it on several grounds. The researchers did not use the accepted ACAM protocol for mixing the IV solution. In particular, there was no magnesium in the EDTA bottles which is required by the ACAM protocol for effectiveness. The patients were frequently left to start their own IV's after taking their own IV bottle off an unlabeled shelf. This along*

*with several reports of the patients themselves suggests that the two groups may have frequently taken the wrong bottle and so there was constant crossover between the two groups. This would explain the similarity of results in the two groups. This study has now been reviewed by the Danish Committee for the Investigation into Scientific Dishonesty and has been criticized in at least 4 different journals.*

1991 (J Adv Med 4:39-45) Rudolph and McDonagh demonstrated an average 17.5% reduction in serum iron level in 122 patients with various chronic degenerative diseases after 30 EDTA chelations. Interestingly, patients with abnormally high initial iron decreased 43% while those with initially low iron increased 41%. **Comment:** *Free iron radicals are powerful promoters of oxidative stress and degenerative disease. An unrelated study published in 1992 associated a 2.2 fold increased risk of MI in patients with ferritin over 200 mcg/l and a 4% increase risk for each 1% rise in serum ferritin levels.*

1991 (J Adv Med 4(3):157-168) Rudolph and McDonagh reported on 30 patients with severe stenosis of the internal carotid arteries. After 30 chelation treatments ultrasound imaging showed a 20.9% decrease in obstruction with the more severe arteries having the greater improvement.

1992 (J Adv Med 5(3):189-197) WJ Adams and C T McGee surveyed 54 patients who had completed a course of chelation treatments. Of the 50 patients (92.6%) who had initially improved, 92.6 % continued to report improvement and 36% were completely asymptomatic.

**1993 (J Adv Med 6(3):139-160) L Terry Chappell and John P Stahl published a sophisticated meta-analysis of nineteen published research studies meeting strict criteria for inclusion, with a total of 22,765 patients. Eighty seven percent of patients in the meta-analysis showed clinical improvement by objective testing.**

1993 (J Adv Med 6(3):161-170) C Hancke and K Flytjie published another Danish study but with markedly different results from those of the vascular surgeons. They treated 65 patients with chelation who were on the waiting list for bypass surgery for an average of 6 months. Eighty-nine percent of these patients were able to cancel their surgery because of symptomatic improvement. Similarly, they treated 27 patients who were recommended for amputations, and 24 limbs were saved. In total, of the 92 patients referred for surgery, only 10 required surgery after or during their treatment with EDTA chelation. **The study spanned a period of 6 years with no adverse side effects at a cost savings of \$3,000,000.**

1994 (J Adv Med 7:131-142) Chappell, Stahl and Evans in follow up to their previous meta-analysis they were concerned that excluding unpublished data might lead to a bias in the data (publication bias). They reviewed data on 1241 patients from 32 clinicians. Of these unpublished patients, 88% improved as measured by a variety of parameters including EKG, ankle/brachial index, walking distance, exercise tolerance, and Doppler testing.

1994 (N Z Med J 109:83) Andre M van Rij et al reported on 32 patients, 15 of which received 20 chelation treatments with all the vitamins and minerals that are part of the ACAM protocol. The other 17 patients received identical infusions missing only the EDTA. All patients had severe multi-vessel peripheral vascular disease at beginning of treatment. At the end of the 20 treatments 60% of patients in both groups had improved in walking distance and other parameters. **Comment:** *Their conclusion was that EDTA chelation had no benefit over placebo, but in fact the control group did not receive a placebo at all but an IV solution containing powerful agents designed to be part of an overall treatment program. Even so, at 3 months following treatment the EDTA group did show statistically significant results over the control group. None of the patients in the EDTA group worsened though this was not true for the control group. In the EDTA group 26% achieved a greater than 100% improvement in*

walking distance compared to only 12% of the control group. Among nonsmokers or those who stopped smoking, 66% of the EDTA group improved an average of 86% in walking distance compared to only 45% of the control patients who improved with an average of 56% increase in walking distance. In summary, this study was reported as a rebuttal of chelation, a reappraisal of the data suggested a different conclusion.

1994 Presentation at the American Chemical Society: M Rubin et al presented evidence of EDTA decalcification of coronary arteries documented by ultrafast CT scan.

1994 (J Adv Med 4(7):203-212) Rudolph, Samuels, and McDonagh documented reversal of **macular degeneration** by visual field testing and retinal photographs before and after EDTA chelation treatments.

1995 (Surgery and Surgeons 61(2):58-62) Escobar, Escobar, Ordonez and Gonzalez reported on 80 patients, 28 of whom were diabetic and 10 of whom had already had amputations, who were treated with EDTA chelation. Seventy-six (95%) had marked improvements in peripheral artery disease as measured by ankle/brachial indices and dorsalis pedis artery oscillography.

1996 (Townsend Letter for Physicians 157/58:92-94) Olszewer, Sabbage and Carter reported on a prospective evaluation of side effects from EDTA chelation treatments in Brazil where over 100,000 patients have received over 2 million chelation treatments. Their findings were:

Thrombophlebitis developed in 2 cases out of 200,000 infusions (0.001%). A burning sensation was mentioned by 16.5%.

Hypoglycemic symptoms were observed in 12 patient but only 2 actually had low blood sugar readings

Bone density was studied in 78 patients. Mild improvements were noted in Ward's triangle and in the lumbar spine. These did not rise to statistical significance.

Hypocalcemia was not observed in the 63 patients where serum calcium was evaluated before and after a chelation treatment.

Renal insufficiency was present in 36 patients prior to starting chelation treatments. Post treatment creatinine clearance improved an average of 14% in 78% of patients. Treatments were stopped in the remaining 22% because of worsening renal function tests.

1997 (J of Integrative Med 1(1):113-145 Majid Ali et al reported on 26 consecutive patients who presented with advanced ischemic heart disease and who had fared poorly after one or more coronary bypasses (5), one or more angioplasties (6), or who failed to respond to multiple drug therapies (15). All patients received at least 20 chelation treatments and follow up ranged from 15 months to 9 years. Evaluations showed excellent results (complete relief of significant symptoms and discontinuation of previous medications) in 61% of patients. Good results (75% reduction in symptoms) were achieved in 17% and fair results (50% reduction in symptoms) were achieved in 13%. The remaining 9% had 25% or less improvement in symptoms. No patient during the study period suffered an acute myocardial infarction or underwent coronary artery surgery or angioplasty.