May 5th, 2014

To FACT Members:

The attached article entitled “Protocol Controversies for treating Cardiovascular Disease with EDTA Chelation Therapy”, is the newest report on EDTA chelation and the TACT trial, to be published in the May 2014 Townsend Newsletter. Here are my thoughts about this important TACT study, and the importance of oral chelation therapy.

EDTA chelation is thought to reverse cardiovascular disease by removing calcium from arterial plaques. I believe that this hypothesis should be expanded and revised as it is not the best approach to understanding what chelation therapy actually does. It would be more beneficial to look at the adverse effects of lead on health, the benefits of removing lead via EDTA, as well as the effects of EDTA on blood clotting.

Lead and heavy metal toxicity is the real problem in heart disease and cancer, and we are polluted from birth. Lead levels in patients are on average a 1,000 times greater than bone lead levels that were present 700 years ago. Higher bone lead levels increase risk of heart attack sixfold2. Lead in bones is also in equilibrium with body tissues including the eyes3, which Harvard has reported leads to the formation of cataracts. The American Heart Association Journal 'Circulation' published an article in 2006 entitled 'Low-Level Environmental Exposure to Lead Unmasked as Silent Killer'4, reporting bone lead levels have a relative risk factor of 8.8, which exceeds by far the relevance of all other commonly studied risk factors today, and shows that we all need more de-leading, not less. LOWERING LEAD DECREASES ALL CAUSES OF MORBIDITY AND MORTALITY. There is simply NO SAFE LEVEL of lead.

I believe lifetime detoxing is key, and daily oral chelation is an important part of my program. I have probably read more literature on EDTA that anyone alive today, and I have compiled a list of ‘307 References’ on EDTA, as well as two heavily referenced major chelation therapy articles supporting the effectiveness of oral chelation, available on my website at http://www.gordonresearch.com/infer.cfm?siteid=502&itemcategory=50864&prid=46753&pid=46753

For instance, Dr. Walter Blumer, M.D. of Switzerland has documented the results of CaEDTA heavy metal detoxification treatment for over 20 years. He showed that patients receiving a minimum of 30 treatments experienced an 85% reduction in cardiovascular events and a 90% reduction in new malignancies when compared to individuals in the same village who did not receive the treatments. Prof. Johan Bjorksten, creator of the crosslinkage theory of aging, estimated that the average human life span could be increased by 15 years as a result of chelation therapy. He surmised that removing heavy metals reduces the crosslinking that contributes to the aging phenomena.

Since my experience has led me to emphasize the detoxification aspect, and de-emphasize the potential of plaque reversal as the long-term outcome of intravenous chelation, I have chosen to help educate physicians in the use of Calcium EDTA. CaEDTA can be given much more affordably, rapidly and painlessly in a 5-minute IV push, saving patients needless hours sitting in a doctor’s office. Interestingly enough, the more rapid administration of the CaEDTA causes a greater lead excretion to occur, as shown by Doctors Data.

Oral chelation therapy has been shown to …

- Cleanse your system of heavy metal toxicity and harmful calcium deposits in the arteries
- Help thin the blood and prevent the formation of blood clots—and reduce your risk of heart attack or stroke
- Lower your blood pressure and cholesterol levels (One of my patients at Stanford University could not get her cholesterol below 500. Using my CaEDTA-based chelation formula, her cholesterol lowered to 200—a remarkable result.)
- Neutralize free-radicals … a major cause of atherosclerosis, as well as accelerated aging, cancer, and arthritis

Cardiologists Roy Heilbron, MD and Angelique Hart, MD recently released the movie “Unleaded”, about the $31 million double-blind NIH PACT & TACT studies on the effects of Chelation Therapy on heart disease, diabetes, and heart attacks. They actually took part in the TACT trial studies, and have chosen to speak the truth about the positive results... the results official reports in JAMA worked very hard to hide. Even so, the TACT trial did not run long enough to reveal the true benefits that I see continually in my patients. I have had NO fatal heart attacks or strokes year after year in high risk documented vascular disease patients who are on my preventative protocol. Chelation works, but we need more of it more consistently every day of life, unless you can stop the lead particulates that are everywhere!

By removing calcium from plaque in blood vessels, and reducing the amount of bone lead absorption, EDTA has the ability to make bones stronger which significantly reduces the incidence of osteoporosis. It stimulates bone growth through a complex action of the
parathyroid glands, which controls the amount of calcium in the blood and within the bones. When calcium levels are off, the parathyroid hormone signals increase blood calcium levels, by stimulating osteoclasts to break down bone and release calcium. So, the more chelation we give people, the less osteoporosis they have and the less age-related calcium accumulation there is in their blood vessels. The average 80-year-old man shows 140 times more calcium than he had at age 10. This means you're gradually turning to stone in all your arteries. We have documented that calcium accumulation in the artery is totally reversible by enough chelation.

But remember lead and calcium are chemically very similar, and the body will often mistake lead for calcium; picking it up, transporting it through the blood and into soft tissues and organs, eventually storing it in bones and teeth. Once stored, leaching from bone back to blood occurs slowly over the normal remodeling period, and it is especially amplified during times of physiologic stress, pregnancy and lactation, menopause, broken bones, and calcium imbalances or deficiency. Because bone in adults takes fifteen years on average to remodel, there is no chelation therapy, intravenous or oral, that will dramatically reduce the risk factors for heart disease unless it is used continuously for these many years, and ideally for life.

I find that years of DAILY continuous oral chelation with safe natural detoxifying substances such as Zeolite, Garlic, Fiber, EDTA, Vitamin C etc. is needed to effectively deal with bone lead accumulations, which are now known to date back to in-utero life, and bones can take 15+ years to remodel. IV CHELATION does not lower bone lead. I also advise some patients to add Nattokinase or Boloouke, when there is a history suggesting a hypercoagulable condition such as LEIDEN 5, which is present in 5% of the population.

Chelation doctors do a disservice to patients if they do not prescribe and keep them on a long-term deleading therapy. Not everyone can come in to the office 1-2 times a month for IV chelation, and the 507 study references listed on my website prove that oral chelation provides people with ample protection against daily exposures to lead and other metals. We have the obligation to warn patients that even after 30 IV treatments, their heart and kidneys and liver can all be largely delead, but the Harvard study shows that the bone lead will leach out and reach equilibrium within the organs and soft tissues again. Daily oral chelation is the only safe, effective, affordable and broadly accessible answer!

This is why I helped develop an oral chelation formula using CaEDTA, called Binding Cellular Impurities, or BCI. Working with Lester Morrison MD PhD, former Director of the Arteriosclerosis Research Institute, BCI is based upon his ten million dollar institute formula which documented a 91% reduction in fatal heart attacks. It was discovered that when we added CaEDTA to the formula, it significantly enhanced its anticoagulant and blood viscosity lowering effects, and as the work of Dr. Kenneth Kelsey has proven, blood viscosity and clotting is the primary problem in cardiovascular disease, not elevated cholesterol.

Common anti-clotting therapies like aspirin and Coumadin are effective against only about one-third of excessive platelet aggregation and coagulation ("sticky" blood and plaque formation. CaEDTA makes Heparin-like molecules work by mouth, replacing the need for many to use drugs like Coumadin. Aspirin has a well-known corrosive effect on the membrane of the stomach, causing a micro-hemorrhage right where the pill hits the stomach. CaEDTA on the other hand, appears to reduce all harmful clotting mechanisms, and combined with BC-1's powerful multiple mineral supplement with Resveratrol and Vitamin K2, it maintains soft arteries and hard bones, and provides much better cholesterol improvement than any statin drug.

I have also gained extensive experience with energy medicine therapies such as PEMF, and I am increasingly confident that most patients can be greatly helped without surgery. I generally postpone any major invasive heart treatment by first utilizing all the metabolic cardiological information I have obtained in my over 40 years of involvement with ACAM and the chelation movement.

I successfully continue, year after year, to hear of NO vascular related fatalities in any of my patients using my BCI, so increasingly I recommend against stents or other invasive vascular procedures including BYPASS. Daily continuous oral chelation to lower all tissue lead levels including bone, is more effective in lowering all causes of morbidity and mortality than most other therapies that excessively rely on lowering cholesterol, fasting blood sugar, blood pressure, homocysteine, or c-reactive proteins. I believe it is UNETHICAL to tell patients that ORAL CHELATION IS USELESS, as my personal and medical experiences and expertise, as well as the 507 references I have gathered of published papers on the effectiveness of oral EDTA and lead, have proven otherwise.

Sincerely,

Garry F. Gordon MD,DO,MD(H)

President, Gordon Research Institute

www.gordonresearch.com
Protocol Controversies for Treating Cardiovascular Disease with EDTA Chelation Therapy
by L. Terry Chappell, MD, and Jeanne A. Drisko, MD, CNS

Introduction
The Trial to Assess Chelation Therapy (TACT) is the only large, randomized clinical trial to provide statistically significant evidence that EDTA chelation therapy with high-dose multivitamins can reduce future cardiac events in patients with known cardiovascular disease.1,2 TACT utilized the published protocol that is used by organizations such as the American College for Advancement in Medicine (ACAM), the International College of Integrative Medicine (ICIM), the American Board of Clinical Metal Toxicology (ABCT), and the International Board of Clinical Metal Toxicology (IBCMT), all of which teach physicians how to administer the therapy and/or test them to provide certification.3

TACT used an intravenous dose of 3 g of disodium EDTA with magnesium, adjusted downward if kidney function was compromised, 7 g of vitamin C, 500 cc of sterile water, and several minor additives, all infused over a minimum of 3 hours.1,2 (See Table 1.) The published protocol is more flexible, allowing for 1.5 g to 3 g of disodium magnesium EDTA over no more than 1 g per hour and varying amounts of vitamin C, as long as the osmolality of the treatment solution is not hypotonic and not so hypertonic as to cause problems. Calcium EDTA has also been used in various forms with claims of effectiveness for vascular disease. The use of calcium EDTA, especially in the oral form, to treat cardiovascular disease has been criticized by the teaching organizations mentioned above. Concerns have also been raised about high doses of vitamin C, which becomes a prooxidant instead of an antioxidant at certain levels.4

The purpose of this article is to discuss the rationale, evidence, and experience of physicians who are acknowledged experts in the use of EDTA for treating cardiovascular disease. We hope to clarify whether calcium EDTA should be used to treat vascular disease and how much EDTA and vitamin C are effective and safe to use.

The Published Protocol
TACT used the 3 g basic dose of disodium EDTA with magnesium to treat patients who had a history of documented myocardial infarction. The basic protocol for TACT is shown in Table 1. The 3 g dose for disodium EDTA has been taught for years, and many doctors who provide intravenous chelation therapy use it routinely. However, there is evidence that a lesser dose might be just as effective.5 As a result, a substantial number of treating physicians use the lesser dose, based on these reports. Obviously, a lesser treatment time is more convenient for patients. Neither dose puts the kidneys at risk as long as the required rate of administration is followed. For patients with congestive heart failure, a lesser fluid volume for the treatment might be advantageous.

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
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<tbody>
<tr>
<td>Na2EDTA</td>
<td>3 g</td>
</tr>
<tr>
<td>Magnesium chloride</td>
<td>2 g</td>
</tr>
<tr>
<td>Procaine HCl</td>
<td>100 mg</td>
</tr>
<tr>
<td>Heparin</td>
<td>2500 units</td>
</tr>
<tr>
<td>Ascorbate (vitamin C)</td>
<td>7 g</td>
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<tr>
<td>KCl</td>
<td>2 mEq</td>
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<tr>
<td>Na bicarbonate</td>
<td>840 mg</td>
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<tr>
<td>Pantothenic acid</td>
<td>250 mg</td>
</tr>
<tr>
<td>Thiamine</td>
<td>100 mg</td>
</tr>
<tr>
<td>Pyridoxine</td>
<td>100 mg</td>
</tr>
<tr>
<td>Sterile water</td>
<td>To 500 mL</td>
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</table>

The mixture of components given in TACT was based on committee consensus between the TACT investigators and representatives of the chelating community. The agreed-upon solution was selected as the representative mixture that had been in use. The amount of EDTA administered to the trial participants was tailored to the individual renal function based on the Cockcroft-Gault equation.5-7

Chappell and Stahl performed a meta-analysis of studies showing objective improvement for patients with cardiovascular disease treated with intravenous EDTA chelation therapy.8 Nineteen published studies involving 22,765 patients met the inclusion criteria. All of these studies used the 3 g dose of EDTA with one exception. Olszewer and Carter treated 2482 patients with the 1.5 g dose, and 2379 improved.8 In the meta-analysis, 87% of patients improved, and there was a correlation coefficient of 0.88 between improvement in vascular function and treatment with EDTA. Patients of the physician who used the 1.5 g dose did as well as those from the other sites combined.
Chappell and associates did a follow-up meta-analysis of 32 unpublished reports on 1241 patients. Of these, 1086 or 88% showed measurable improvement. W7 patients were treated with the 1.5 g bottle. A comparison of the 1.5 g and 3 g doses in this study showed almost identical results.

Born and Geurink published a retrospective, randomized study comparing patients with peripheral artery disease treated with the 3 g dose of EDTA to those treated with the 1.5 g dose. Both treatment groups were given to 15 patients. Those with the lower dose were given using Doppler ultrasound by an average of 123%. The patients in the 3 g group improved by an average of 70%. The results were statistically significant. One patient treated with 1.5 g improved 715%. That patient was omitted from the study as an outlier.

Chappell and associates compared 220 vascular patients treated with a basic course and maintenance chelation with matched controls from the literature. An average of 58 treatments were given. Subsequent cardiac events were much less in the EDTA-treated group. The patients treated with the 1.5 g dose had virtually the same results as those with the 3 g dose.

An in vitro study published in Surgery in 1962 showed the mobilization of calcium from atherosclerotic plaque with EDTA in the laboratory. The results demonstrated that the longer the plaque is exposed to EDTA, the more calcium is removed. To our knowledge, this finding has not been confirmed in vivo. Blaurock-Busch observes that the German Chelation Society approves both a 2 g and 3 g dose. Gordon wrote the first American Academy of Medical Prevents (AAMP) chelation protocol in 1972, based on the work of such pioneers as Clark and Lamar. It was not published, but it was used in coursework for many years. He listed the EDTA dose of 50 mg/kg. Cranton's 1989 textbook refers to a maximum of 3 g dose, except for large patients who could receive up to 5 g at 50 mg/kg. The textbook was updated in 2001. Rozema's protocol for EDTA lists both a 3 g and 1.5 g dose, as does van der Schaars 2012 textbook. The latter has a maximum of 4 g for large patients. All of these protocols insist on an infusion rate of disodium EDTA not faster than 1 g per hour to avoid overloading the kidneys.

Because of TACT, the best evidence for treatment of vascular disease with intravenous disodium EDTA lies with the 3 g dose. However, the published studies cited above that compare the 3 g dose with the 1.5 g dose show the latter to be less effective. As noted, one study showed the 1.5 g dose to be more effective for peripheral vascular disease. Future large clinical trials will be necessary to determine the lowest amount of EDTA that can produce the best outcome in cardiovascular disease.

Mechanisms of action for EDTA

Proposed mechanisms of action for EDTA chelation therapy have been documented, but no consensus exists as to which mechanism(s) are most important to treat vascular disease. It is well known that both disodium EDTA and calcium EDTA can remove heavy metals. Such metals as lead, cadmium, and mercury increase the risk of vascular diseases by increasing free radical activity. Reduction of free radicals by EDTA infusions reduces inflammation, which might lessen the likelihood of the rupture of unstable plaques. The clot that occurs as a result of this rupture is the accepted mechanism for most myocardial infarctions and strokes. A small study by Chappell and Angus showed a reduction of brachial artery stiffness with chelation. Iron deposits have been found in macrophage foam cells, which further increase free radicals and inflammation. Excessive copper also increases free-radical activity. EDTA chelates both iron and copper.

Lowering blood calcium levels with intravenous boluses of disodium EDTA can inhibit platelet aggregation for weeks at a time. Intravenous EDTA has been proposed as a safer substitute for clopidogrel to prevent clotting after inserting drug-eluting stents. The anticoagulant effect is likely to be an important mechanism for chelation's cardiovascular benefits. Selye demonstrated harmful deposition of calcium in soft tissues when a sensitized individual is exposed to a new challenge after a suitable interval. The drop in serum calcium that occurs immediately upon IV infusion of disodium EDTA stimulates parathyroid activity. Parathormone mobilizes calcium from soft tissue deposits, but the effect is irregular. Although there are case reports of plaque can be reduced with disodium chelation, studies have not shown a predictable improvement in lumen size for arteries blocked with plaque. It is possible that the calcium reduction cascade stabilizes vulnerable plaques, but this also has not been proved.

High doses of magnesium are put into the intravenous treatment solution, which prevents adverse effects from the brief drop in calcium levels. Improved levels of intracellular magnesium might reduce irritable foci that cause arrhythmias and lower blood pressure. To prevent progressive calcium depletion, it is important that IV infusions of disodium EDTA be given no more often than 2 to 3 days per week, with at least 24 hours between treatments. With 60 years of use of intravenous disodium EDTA for vascular disease, no fatalities have been attributed to EDTA when the protocol has been followed. However, there have been isolated fatalities when disodium EDTA was administered by rapid IV push.

Nitric oxide (NO) is an important signaling molecule that is antiatherosclerotic. NO production declines with age and is worse with a high-fat diet. Lead inhibits NO
Protocol Controversies

formation. EDTA not only removes lead but also independently increases NO production.24 This might be an important mechanism for improved circulation for both disodium EDTA and calcium EDTA.

Vitamin K2 also might help remove metastatic calcium from arterial walls. It has been suggested as an oral supplement to augment the decalcifying effect of disodium EDTA.25 However, vitamin K2 is not currently included in the chelation therapy protocol.

Calcium EDTA

Intravenous calcium EDTA is approved for removing lead and is used to treat accumulations of other toxic metals. Since there is no reduction of serum calcium as is seen with disodium EDTA, certain mechanisms that are proposed for treating vascular problems do not apply. Specifically, metastatic calcium is not mobilized and platelets are not inhibited.

Oral, sublingual, transdermal, and rectal EDTA all consist of calcium EDTA. Oral EDTA is only about 5% absorbed. Rectal EDTA might be absorbed as much as 35% to 37%.26 Intravenous calcium EDTA is used widely as a challenge test and a treatment for toxic metals. It was used in a small study by Lin that showed that nondiabetic patients with moderate kidney disease might progress less rapidly with EDTA treatment than without.27 Chen and associates showed that diabetic nephropathy in the presence of high lead levels progressed at a slower rate than controls when their lead levels were reduced and kept under control with 1 g calcium EDTA treatments IV.28 High levels of lead have been shown to be associated with lower blood pressure and an increased risk of vascular disease.29 Reducing the lead burden might result in improved blood pressure and better circulation to the kidneys. However, without a drop in serum calcium, decalcification of the arterial wall is highly unlikely. The many published studies showing improvement in vascular disease, including TACT, all have used disodium EDTA with magnesium.

Gordon has proposed that calcium EDTA combined with lecithin and other nutrients improves blood viscosity, and he cites the work of Lowe and others.30 One might expect this to be the case since lavender-top tubes with EDTA are used to anticoagulate blood drawn from patients for testing. However, the EDTA used for that purpose is potassium EDTA (K2EDTA), not calcium EDTA. We were unable to find evidence that calcium EDTA reduces platelet activity directly. One mechanism for inhibition of platelet aggregation is a depletion of calcium ions. However, another probable mechanism that applies to calcium EDTA is its stimulation of the production of NO. Several oral nutrients that can lesson platelet aggregation, such as vitamin E and gingko, can be given orally along with calcium EDTA.

Cranton points out on his website a potential danger of oral chelation.31 Some toxic metals that are ingested might not be absorbed into the body if calcium EDTA is present, but many more essential minerals will also not be absorbed. Depletion of zinc, chromium, copper, manganese, and other minerals can reduce antioxidant defenses and endocrine function. Cranton stresses the importance of the rapid decrease in both toxic metals and calcium with disodium EDTA. This occurs extracellularly, since EDTA does not enter the cells. A reequilibration results so that calcium is mobilized as described above and toxic metals are brought out of storage in the bone, brain, and fat cells.

Calcium EDTA is widely sold and advertised as an ingredient in various nutritional supplements. Claims of effectiveness for calcium EDTA in treating vascular disease are often made based on research that was done for intravenous disodium EDTA. Calcium EDTA and disodium EDTA are two separate compounds that act on calcium differently in the body. Although useful mechanisms of action might apply for calcium EDTA, we did not find any clinical trials that support the use of calcium EDTA for treating vascular problems.

Van der Schaar's textbook describes many toxic metals and chelating agents,32 DMSA, DMPS, and the two forms of EDTA are commonly used in clinical practice at this time. DMSA is available orally and is used to chelate lead and mercury in adults and children. DMPS is a compounded substance for oral or IV use, mostly for lead and mercury, but it is not an FDA-approved medication. DFO is sometimes used parentally for iron overload, but serial phlebotomies are generally more effective. D-penicillamine can be helpful as a challenge test and occasional treatment. These medications can be used in combination if the prescribing physician is experienced. The two forms of EDTA are broader chelators and are especially effective for lead. EDTA has perhaps the weakest affinity for mercury. If mercury is elevated with a challenge test, it might be prudent to treat with DMSA or DMPS before prescribing intravenous EDTA. Maintaining good levels of beneficial minerals is important no matter what chelation agent(s) is/are prescribed. Treatment with DMSA or DMPS reduces free radical activity by binding and excreting heavy metals, which might be beneficial. However, we did not find any clinical trials that have studied either one as a treatment or preventative for vascular disease.

Vitamin C

As with any medical practice, whether conventional or alternative, different approaches and individualized styles of practice evolve. Some of the differences in approaches relate to experience and some are based on growing evidence from the scientific literature. And
so it is with EDTA chelation therapy with certain groups giving differing amounts of EDTA over varying times and by different routes of administration, while others advocate using different formulations and combinations of additives in the mix. One proposed change has been the recent suggestion that vitamin C or ascorbic acid be removed from EDTA chelation therapy because of its known action as a prooxidant in the extracellular space in living systems.13–14

Seminal findings regarding the unexpected prooxidant action of intravenous vitamin C were discovered in the National Institutes of Health (NIH) lab of Mark Levine, MD, along with his colleagues, Qi Chen, PhD, and others.11–12 Levine and colleagues clearly defined that oral vitamin C was a vitamin with tight physiologic control and antioxidant properties, while intravenous vitamin C administration bypassed tight control and through Fenton chemistry became prooxidative in the extracellular space.11 In people with normal G6PD status, the prooxidative nature of vitamin C does not occur in the vascular space.11

It is interesting that another well-known antioxidant, glutathione, does not behave like vitamin C when injected in high doses.16 Glutathione maintains its antioxidant properties even when injected at increasing concentrations and has led to the recommendation against adding IV vitamin C and IV glutathione together at the same setting.17 To date, other antioxidants such as alpha lipoic acid have not been evaluated in this manner to determine if they might exhibit a dual nature like vitamin C.

The prooxidative nature of intravenous vitamin C has led some to postulate that adding vitamin C to EDTA chelation therapy might have a deleterious effect on patients with already high oxidative burden, as seen in diabetes.18–20 The hypothesis is that patients with oxidative disease processes may not be able to tolerate the additional oxidative burst that briefly occurs after intravenous vitamin C. Roussel and colleagues conducted a small uncontrolled trial in 6 adults where EDTA chelation therapy was administered according to standard protocol except for elimination of the vitamin C from the infusate.18 In the reported trial, markers for oxidative damage were evaluated in the absence of added vitamin C and were found not to be present. The group concluded that EDTA chelation therapy without added vitamin C decreases oxidative stress. But as Roussel and colleagues clearly stated, the small trial was not designed to test

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the curative effects of the chelation therapy. They acknowledged they were focusing solely on antioxidative effects.

The Roussel trial is in contrast to TACT, wherein 1708 participants with known cardiovascular disease were enrolled. The sample size was chosen so that the effect of EDTA chelation therapy on cardiovascular outcomes could be evaluated. The standard accepted protocol was chosen and this included 7 g of vitamin C injected at each infusion. An unexpected and remarkable finding at the conclusion of TACT was the marked reduction in cardiovascular events in diabetic participants. This has prompted the NIH to ask researchers to focus on the positive effects in the standard EDTA infusate that may have promoted such beneficial outcomes. However, the belief that intravenous vitamin C is a harmful prooxidant has led other experienced practitioners of chelation therapy to abandon the addition of vitamin C to the mix. The trial findings with the small sample size and the concerns raised by Roussel and colleagues are contradicted by the positive outcomes of TACT.

What then is the effect that vitamin C plays in the chelation infusion? Is it related to the prooxidative burst? Is it related to other as yet undescribed effects, apart from Fenton chemistry? It is advisable to remember that in the vascular space, when there is normal G6PD status, there are no significant detectable levels of hydrogen peroxide and no detectable prooxidant effect. Any hydrogen peroxide that might be formed after infusion of vitamin C is quickly and effectively quenched in the vascular space, unlike what occurs in the extracellular space. Is it possible that vitamin C at increased concentrations has an effect on the endothelium? Or on the function of blood elements such as the red blood cells that are so critical for oxygen mobilization? Unpublished research carried out by the Levine team points to this possibility.

The epidemiology literature shows that vitamin C is critical for improvement of HbA1c and avoiding untoward effects in diabetics. However, it can easily be argued that this is a vitamin effect, not a pharmacologic effect. In the tobacco literature it has been shown that the prolonged and destructive exposure to tobacco smoke markedly reduces available vitamin C levels in vivo that are only replenished effectively with intravenous infusion. Functional effects on the microvascular bed can be reversed with IV vitamin C. It can be argued that tobacco smoking is a model for highly oxidative chronic diseases such as diabetes. Benefits of infused vitamin C could have positive effects on microvascular function. This would certainly be a good model for future research.

Other nonvascular effects of IV vitamin C also come into play, such as the effects of ascorbate in steroidogenesis, vascular tone, adrenal gland function during stress, and general well-being. Taking the narrow view that vitamin C acts as only a prooxidant or an antioxidant may result in the risk of excluding vitamin C with its various positive functions, both known and as yet unknown, in the beneficial treatment of cardiovascular disease with EDTA chelation therapy.

Conclusions

Scientific evidence, especially with TACT, supports intravenous disodium EDTA with magnesium, along with oral multivitamins, to treat vascular disease. Disodium EDTA can only be given by slow intravenous drip, at a rate not faster than 1 g per hour. Under no circumstances can this preparation be given by intravenous push because of its effect to rapidly lower serum calcium. Evidence supports treatment doses of 1.5 or 3.0 g of disodium EDTA. The dose should be reduced if kidney function is impaired. Kidney function should be monitored during the course of treatment. Treatments should be limited to no more than 2 or 3 days per week with at least 24 hours between treatments. 20 to 30 treatments are needed to complete a basic course of treatment for vascular disease. More treatments may be required in difficult cases. Most experts recommend monthly maintenance after the basic course is completed. If the published protocol is followed, safety is not an issue.

Disodium EDTA with magnesium effectively removes heavy metals from the body. Other likely mechanisms of action include reduced platelet aggregation, mobilization of metastatic calcium by parathormone, increased NO production, and antioxidant activity.

Calcium EDTA can be given intravenously or by other routes of administration to remove toxic metals. Oral absorption is only 5% and rectal absorption might be as high as 35% to 37%. Calcium EDTA does not have all the mechanisms of action that disodium EDTA does to reduce or prevent vascular disease. However, calcium EDTA with multivitamins increases NO production and decreases free radical activity. Moderately impaired kidney function might improve with IV calcium EDTA. Clinical trials have not been done to support calcium EDTA as a treatment for vascular disease at this time. Calcium EDTA should not be given on a continuing basis without being careful to avoid depletion of essential mineral nutrients. Optimal mineral balance might be difficult to accomplish with oral preparations given on a daily basis.

At this juncture because of the positive TACT outcomes, vitamin C should not be excluded from or reduced in the infusate. The hypothesis that IV vitamin C results in a significant deleterious oxidative burst has not been borne out and as part of the total chelation component seems to provide an additional benefit in patients with diabetes and cardiovascular disease.
As shown in other conditions with high oxidative environments, IV vitamin C can provide protection and vascular stability. Exciting research opportunities lie ahead in parses out the effect of the various chelation components in treating cardiovascular disease.

**Comments from a Few Experts**

**Ralph Miranda:** I suspect that the most consistently effective dose is the 3 grams of disodium-magnesium EDTA in the 500 ml bag/bottle infused over 3 hours. I believe that the attraction of metal ions and ligands causes enough of a shift in pools of metal ions, that previously inhibited enzymatic reactions are liberated from the effects of toxic metals and permitted to contribute to normal and desirable repair processes for which they are suited. Remove the poisons from the systems, and the systems work closer to their innate abilities, to clean up the damage inherent to everyday life.

Of course, some patients are too frail to withstand the higher dose or the greater fluid volumes, so the 1.5 g dose infused at the same rate over half the time or a bit longer suits them well. I’m convinced that the patients who get the “half dose” get far more than “half” the benefit. This dose also works well for patients who are not at liberty to spend as much time away from work, or in my office. Another reason to treat lightly would be patients on multiple pharmaceuticals or with multiple intertwined medical conditions.

I will also use the calcium disodium EDTA, especially when the sole focus of treatment is removal of specific toxic metals. I am not a fan of the rapid infusion of this mixture, even though many chelating doctors recommend the rapid push due to the absence of risk for hypercalcemia. I believe there is plenty of potential for disruption of physiologic levels of Zn, Mn, Cr, and other trace metals from too rapid an injection. Oral EDTA and rectal suppositories share the lack of significant absorption for purposes of CVD and reducing metals. These are the least effective choices, and I reserve them for those who cannot, for whatever reason, use the IV therapies.

**Michael Schachter:** I generally follow the ACAM protocol, using Cockgroft-Gault to calculate the proper dosage with a maximum of 3 grams of EDTA. My infusions are generally 3 hours. We have used catheters exclusively for many years to avoid butterflies’ tendency to come out of the vein when the patient moves around. If my primary goal is removing lead or cadmium, I use calcium EDTA instead of disodium EDTA and usually run the infusion over 20 to 30 minutes.

**Claus Hancke:** Since 1987 I have been using exactly the same protocol with great success and not one single mortality or serious side effect in nearly 100,000 infusions. Nothing is added that can be given as effectivley orally. My carrier solution is 250 cc of isotonic glucose. This does not create problems with diabetic patients and avoids a saline load for those with heart failure. Magnesium and bicarbonate avoid infusional pain and tremor. I use 3 g of EDTA and have recently reduced from 5 g to 2 g of vitamin C. My infusions last 3 hours.

We EDTA doctors of the world have been using the EDTA chelation protocol mainly unchanged from 1987. Now, after 25 years, we have succeeded against our opponents and can show the TACT study with significant results. So I don’t think it is politically wise to change the protocol right now. Let’s make serious trials to see the efficacy of different infusion modalities, but never give up what we have established.

**Ted Rozema:** Hans Seyle comments in his book Calciphylaxis about how PTH is a direct producer of calcium deposition in arterial walls. My personal take on the deposition of calcium in arterial walls leading to atherosclerosis is that as we age, the fundus of the stomach does not produce the gastric acid needed to embed a marker on the calcium molecule so it can be seen by the gut villi cells and be invited into the bloodstream. This will cause not enough calcium to be absorbed to maintain the tightly controlled calcium balance in the bloodstream. Over time, there is a miniscule parathyroid hormone release to take calcium from the bone to make up the shortfall. This produces the sensitization to put some of the calcium into arterial walls. Over many years, the clinical picture of early death and other vascular conditions result.

The issue of using calcium EDTA (instead of magnesium disodium EDTA to reduce metastatic calcium and treat vascular disease) is embedded in the use of magnesium disodium EDTA. Once the latter molecule hits the bloodstream, the magnesium is dropped for chelation of calcium. The resulting decrease in free serum calcium is what triggers the parathyroid action (and the platelet effect). The resulting calcium disodium EDTA will then do all the toxic metal binding that calcium disodium EDTA does when given as a short IV infusion.

**Joe Hickey:** I believe that mercury is chelated with EDTA. The resulting mercury EDTA rapidly vaporizes from urine and thus is difficult to measure. If one believes that neither CaNa2 EDTA nor MgNa2 EDTA effectively chelates mercury, then one must account for mercury with DMSA or DMPS. If urine and fecal measurements are done, the largest amount of heavy metals removed is by far mercury with lead a distant second place. If only urine is collected, lead is usually the highest excretion with mercury second, in my patients. Therefore, I also use DMSA if tolerable with either form of EDTA to account for mercury. I will give 10 mg/kg of DMSA for three days, starting on the day of the IV with EDTA. DMSA is less likely to vaporize in the stool.
Protocol Controversies

When treating primarily for vascular disease, I use MgNa2 EDTA 1.5 g over 1.5 hours with the addition of the DMSA. I have found this regimen to be successful in patients who have had recurrent angina, post bypass, and stent closure. I am rarely able to talk patients into consistently sitting for the 3 g/3-hour infusion. I believe that there is probably an additional effect for the 3-hour infusion in cases of calcific valvular disease and scleroderma, because of the parathyroid effect, but I am not convinced that the 3 g dose is the sole treatment for vascular disease. In younger patients with fibromyalgia or neuropathy, I will usually use CaNa2 EDTA in combination with DMSA. If DSMA is not tolerated, I will alternate with DMPS.

John Trowbridge: What are we trying to accomplish with chelation treatments? If a patient is substantially “loaded” with toxic metals, treatment goals will be different than those for one with high-grade blockage disease in critical arteries. Patients suffering with crippling inflammatory and/or autoimmune diseases might require a different approach.

Injectable and oral medication alternatives to EDTA should be considered, depending on a variety of factors. However, 60 years of beneficial and safe reports regarding EDTA would argue for that to be the basic IV chelator. Others could be added in ways that maximize their safety considerations as well, such as oral DMPS, DMSA, and d-penicillamine, as well as IM DFO.

With different stability constants and side effects, using two or more chelating agents at the same time poses potential risks to the patient. The simplest way to avoid such unpredictable interactions is to administer one chelating drug at a time. In 1993 I developed the idea of administering different chelating drugs on an intermittent, pulsatile schedule. This protocol avoids the potential of interaction of two or more chelation drugs but still allows for exploiting the “preferences” of each drug for different toxic metals. Extra physiologic minerals would, of course, be needed to handle the additional chelator load.

To minimize side effects, I have patients take 1 250 mg tablet each evening during the week. For example, a patient might be advised to take d-pen 250 mg each bedtime on days 1-7 of the month, then DMSA 250 mg each bedtime on days 8-14, then d-pen again on days 15-21 and DMSA again on days 22-28, with a “break” until day 1 of the next month. I do not mix IV EDTA with DFO, nor do I give d-penicillamine or DMSA within 4 to 6 hours of EDTA IV.

With the changing urinary elements test reports, a patient might be told to take just d-pen or DMSA every day of the month. Now that oral DMPS is readily available, it might be inserted into the “weekly” protocol as well, especially when mercury levels are substantially elevated on the test report.

By 1997, I had confirmed that our reduction of toxic heavy metal body burden – as measured by the d-Pen challenge urinary elements test – was proceeding at a rate at least one-third faster than with IV EDTA alone.

Two serious mistakes that beginning doctors often make when giving chelation therapy are insufficient attention to mineral depletion and too rapid reduction of cardiovascular medications. Ample minerals must be supplied, either orally or IV, and gradual reductions of meds are required in order for the body to “relearn” more normal functions.

Conrad Maulfair: With calcium being an important factor in the aging process and in the atherosclerotic disease process, we want to have the maximum benefit from its removal that is possible. I personally am a strong advocate of the 3-4 hour chelation treatment simply based on clinical experience.

Patients suffering from end-stage chronic degenerative diseases are misled when they are told that oral application of chelating agents and in particular EDTA can be an alternative to a comprehensive chelation therapy program including the parenteral administration of EDTA. A patient having significant end-stage disease opting to take an oral chelation product because it is cheaper and does not require a personal commitment of time and involvement is most assuredly going to experience a poor outcome. A practitioner who encourages a patient with significant disease to think that using oral chelation is better than doing nothing is being as irresponsible as allowing a patient uncontested to continue to smoke one pack of cigarettes a day because it is better than the two packs a day that he/she had previously smoked.

Garry Gordon: There are many articles and studies that support the use of calcium EDTA. A great number are listed on my website. I have listed 507 abstracts that document the usefulness of oral calcium EDTA to protect lead workers from toxic exposures. Patients who have leaky gut might benefit more from oral EDTA due to enhanced absorption. Blumer and Cranton’s classic article that was included in Cranton’s textbook showed a 90% reduction in the incidence of cancer for patients with high levels of lead who were treated with intravenous calcium EDTA.

The reported results with IV calcium EDTA for patients with kidney failure and/or diabetes are impressive. This alone should stimulate a flood of research to examine the benefits of calcium EDTA.
Notes

Protocol Controversies