Jeffrey Morrison, MD

The use of CaEDTA and NaEDTA in Clinical Practice

About the lecture:

The word chelation is derived from the Greek word chele meaning claw, such as the claw of a crab. In practice, the mechanism by which chelation works is by creating a firm grasp or bond between a chemical (i.e., EDTA) to a metal or mineral ion. A more complete definition is "the molecular incorporation of a mineral ion or cation into a heterocyclic ring structure by an organic molecule, the chelating agent." EDTA (EthyleneDiameneTetraAcetic acid) is currently approved for use as a chelating agent in the United States by the FDA for lead poisoning, hypercalcemia, and for the control of ventricular Arrhythmias associated with Digitalis Toxicity. During this lecture we will discuss the basic biochemistry by which chelation therapy works as well as the rational for approved and off label use of this agent.

About Dr. Morrison:

Dr. Jeffrey Morrison is an award-winning medical doctor who champions a nutritional approach to healthcare, focusing on preventing and reversing degenerative and chronic diseases. Dr. Morrison's specific treatments are aimed at enhancing the body's ability to heal and detoxify itself. In 2001, Dr. Morrison was on the medical staff at the Atkins Center for Complementary and Alternative Medicine in New York City, where he worked under the late Dr. Robert Atkins. He then went on to become the medical director of the Wellness Medical Center of Integrative Medicine in New York City. In 2002, Dr. Morrison opened The Morrison Center, where he has used his successful integrative medicine and nutritional approach for patients with arthritis, high blood pressure, hormone imbalance, obesity, diabetes, chronic fatigue, anxiety, depression, heavy metal poisoning, and many other ailments. His areas of expertise also include fibromyalgia, irritable bowel syndrome, hypertension, and mercury poisoning. He also has extensive experience with intravenous therapies including toxic metal chelation, food and hormone allergy testing using P/N (Provocation/Neutralization), prolotherapy, natural hormone replacement therapy and herbal remedies. Dr. Morrison has an undergraduate degree from the University of Rochester and received his medical doctorate from Jefferson Medical College in Philadelphia. He is trained and Board Certified in Family Practice and has completed additional training in Environmental Medicine. Dr. Morrison is a member of the American Academy of Environmental Medicine (AAEM) as well as a lecturer and Board Member for the American College for the Advancement in Medicine (ACAM). Dr. Morrison has made many television appearances, written journal articles, chapters for textbooks, and has lectured throughout the country in the field of integrative and complementary medicine. See his web sites: www.TheMorrisonCenter.com and www.DailyBenefit.com.

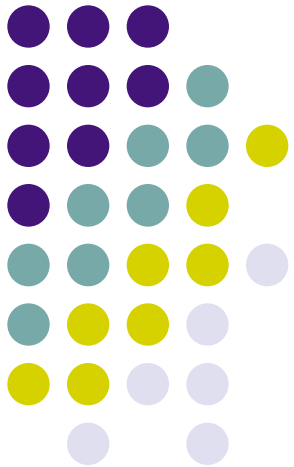
Contacting Dr. Morrison:

103 Fifth Ave., 6th Floor
New York, NY 10003

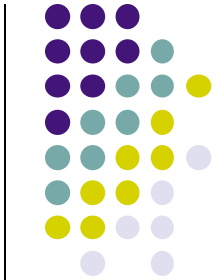
212.989.9828 - Office

CaEDTA / NaEDTA – Basic Biochemistry, Indications for On and Off label use

Jeffrey A. Morrison, M.D., C.N.S.
103 Fifth Avenue, 6th Floor
New York, NY 10003

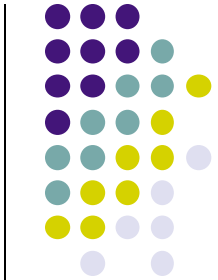


The following table summarizes chelating agents, the heavy metals they are used to treat, their route of administration, and their brand name.



Chelating Agent	Toxin	Route	Drug
Dimercaprol (BAL)	Arsenic Lead Mercury (inorganic)	i.m.	Dimercaptol Injection B.P. BAL in Oil
Dimercaptosiccinic acid (DMSA, Succimer)	Arsenic Lead Mercury	p.o.	Chemet
Dimercaptopropane-sulfonate (DMPS)	Arsenic Mercury	p.o. i.v.	Bulk form (for compounding by pharmacists)
D-pencillamine	Arsenic Mercury Lead	p.o.	Metalcaptase Pencillamine Cuprimine Depen
Ethylenediamintetra-acetic acid (EDTA) (Edetate disodium)	**Iron Lead Cadmium Aluminum**	**IV**	**Chealamide Versenate**

EDTA – Basic Biochemistry, Indications for On and Off label use

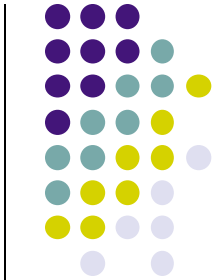


- During this lecture you will learn:
  1. The terminology and basic biochemistry of CaEDTA and NaEDTA chelation therapy
  2. The on and off label uses of chelation therapy.
  3. How to use EDTA chelation therapy in clinical practice
  4. The potential benefits and adverse reactions of chelation therapy.
  5. Case studies

What is EDTA Chelation Therapy?

- EDTA chelation therapy is an Intravenous treatment used for:
  - FDA approved uses:
    - Removing heavy metals (lead) - CaEDTA
    - Treating hypercalcemia - NaEDTA
    - Controling ventricular arrhythmias secondary to digitalis toxicity - NaEDTA
  - Non-FDA approved uses:
    - As an anti-oxidant by controlling lipid peroxidation
    - Reducing platelet stickiness in the management of atherosclerosis

The Definition of Chelation



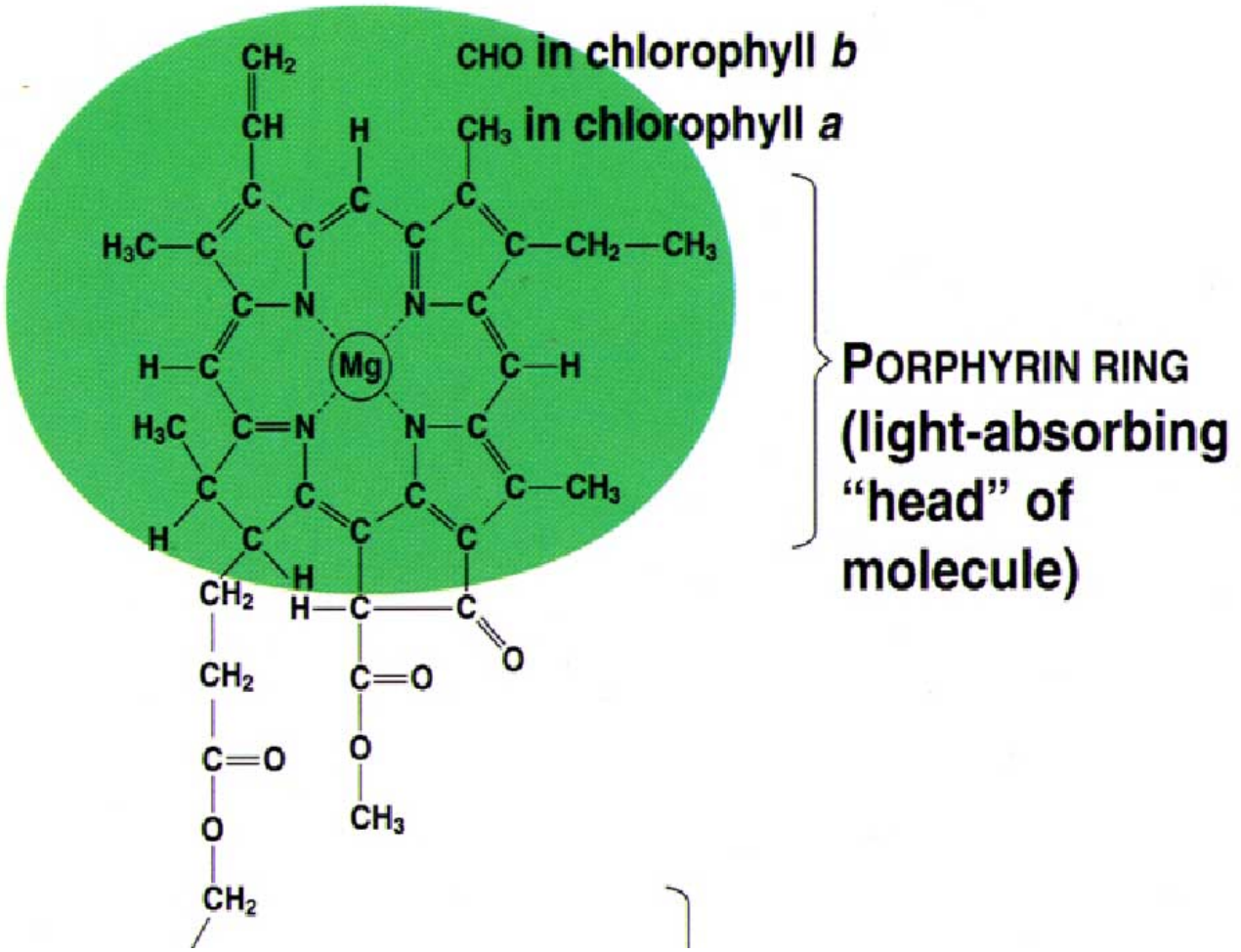
- The work ***chelate*** is derived from the Greek word ***chele***, which refers to the claw of a crab, implying the firm binding action of a chemical to a metal ion.
- **Morgan** and **Drew** defined the term chelation in 1920 as - the incorporation of a **metal ion** into a **Heterocyclic Ring Structure**

Basic Biochemistry
Heterocyclic Ring Structure

Chlorophyll

is a chelate of

Magnesium

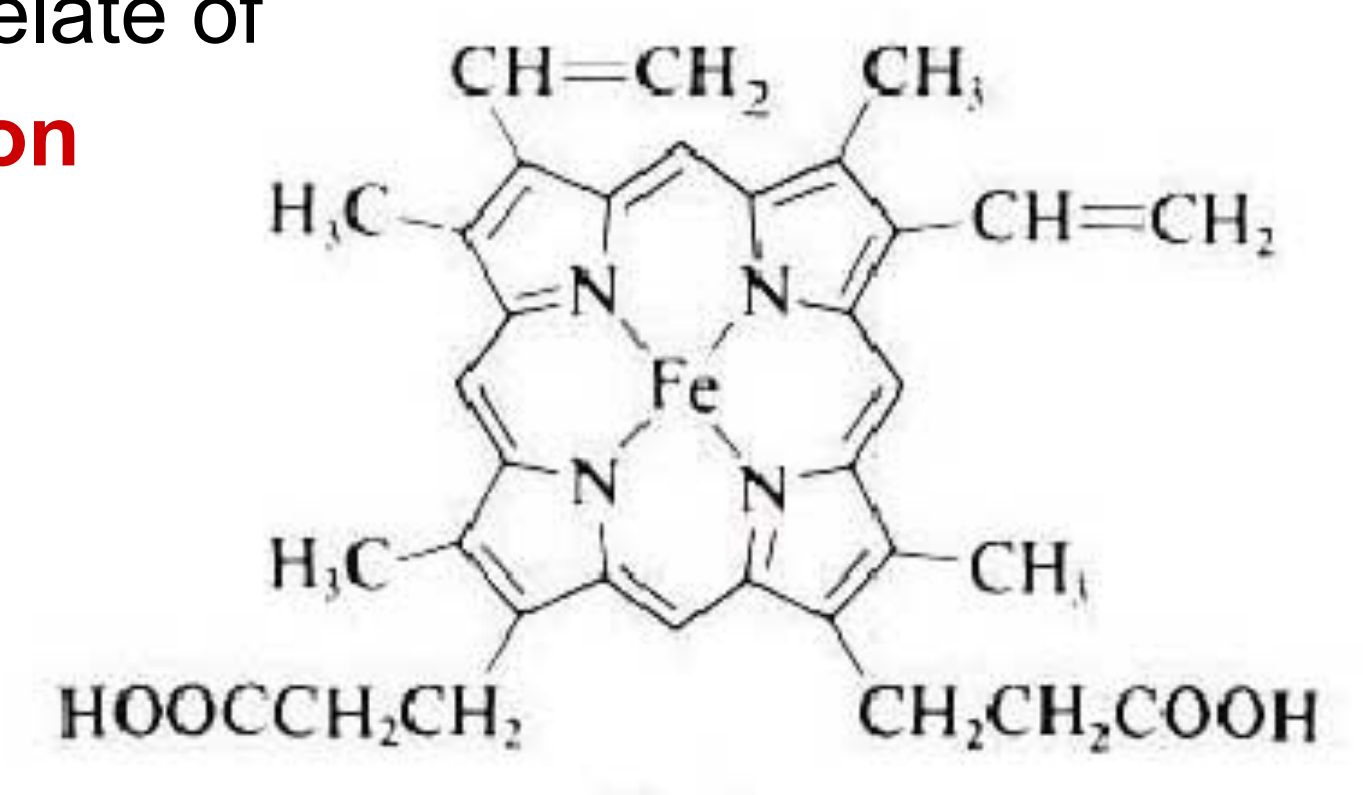


Basic Biochemistry
Heterocyclic Ring Structure

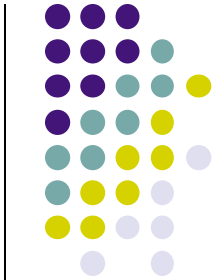
Hemoglobin

is a chelate of

Iron



Chelation Terminology



- Ion
  - A charged Particle
- Cation
  - Positively charged ion (Ca^{++})
  - Metals are positively-charged ions (cations)
- Anion
  - Negatively charged ion (Cl^{-})
  - Metal cations react to surround themselves with Anions

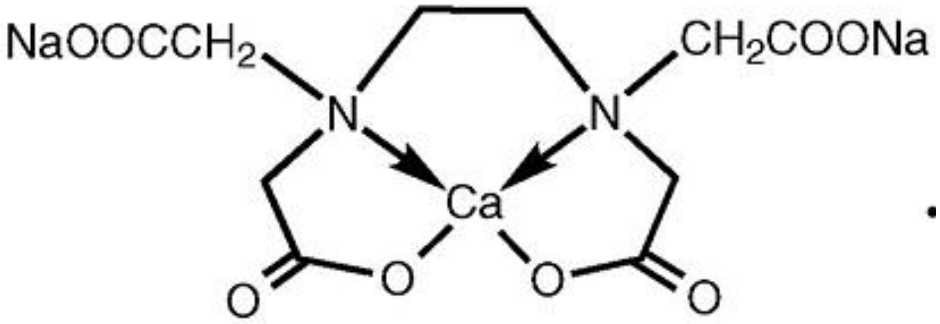
EDTA

(EthyleneDiamineTetraacetic Acid)

Octahedral structure:

- The EDTA molecule binds to a mineral or metal cation by donating up to 6 electron groups.
- By binding at these positions, a cation is surrounded by the EDTA molecule to form an **8 sided (octahedral) structure.**

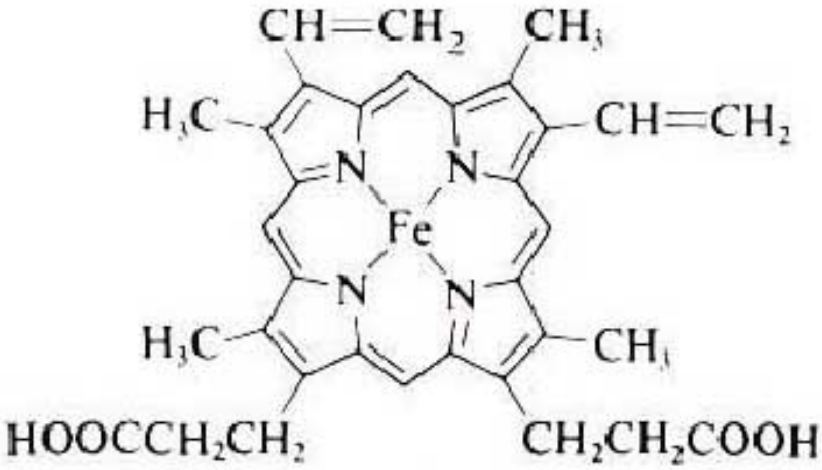
Calcium DiSodium EDTA



$C_{10}H_{12}CaN_2Na_2O_8 \bullet x\ H_2O$

Molecular weight 374.27 (anhydrous)

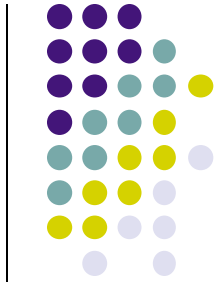
Hemoglobin



In Vitro Factors that determine the structure of EDTA complex

- **pH** - In low pH (more acidic), EDTA chelates become less stable and will release its ion more easily.
- **Binding Constant** - The higher the *binding constant*, the stronger a cation is bound to EDTA.
- **Concentration** - The higher the *concentration* of a cation, the more likely it is to bind to EDTA.

In Vitro Binding Constants



Metal Cation	Log K	Metal Cation	Log K
Cr^{++} (Chromium)	????	Cd^{++} (Cadmium)	16.5
Fe^{+++} (Iron)	25.1	Co^{++} (Cobalt)	16.3
Hg^{++} (Mercury)	21.8	Al^{+++} (Aluminum)	16.1
Cu^{++} (Copper)	18.8	Fe^{++} (Iron)	14.3
Pb^{++} (Lead)	18.5	Mn^{++} (Manganese)	13.7
Ni^{++} (Nickle)	18.0	Ca^{++} (Calcium)	10.7
Zn^{++} (Zinc)	16.5	Mg^{++} (Magnesium)	8.7

In Vivo binding constants
Special considerations

- **pH** - is not as much a factor in clinical practice due the tight regulation of physiologic buffers.
  - High pH (basic pH) in vitro is associated with greater binding stability
  - It is still important to encourage an alkaline diet as part of the chelation protocol to optimize outcomes

In Vivo binding constants
Special considerations

- **Concentration of Metals**
  - Through mass action – a high concentration of lower binding constant metals can displace metals of greater stability when they are present in low concentrations.
  - For example, **Calcium** is low in the stability constant table, however, a great deal of it is chelated by NaEDTA, because of its relative high concentration in the plasma.
    - This is why a patient may become hypocalcemic and it is unsafe to infuse NaEDTA quickly.

In Vivo binding constants
Special considerations

- **Concentration of Metals**
  - Although the binding constant for **zinc** is in the moderate range, great quantities of **Zinc** are removed with EDTA because of the relatively high concentration of **Zinc** in the body.

Important

  - This is why **Zinc** must be replenished when a patient undergoes a course of EDTA chelation therapy.

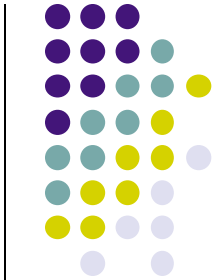
In Vivo binding constants
Special considerations

- **Binding constants** help direct treatment plan
  - **Fe+++** (ferric iron) has a high binding constant and is **easily removed with EDTA**.
    - This is good for patients with iron overload (hemochromatosis)
    - This may be bad for patients with iron deficiency anemia

In Vivo binding constants
Special considerations

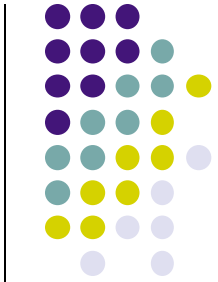
- The binding of **Mercury (Hg)** to EDTA **In Vivo** is not consistent with it's binding constant
  - Although **mercury** has a relatively high binding constant **In Vitro**, EDTA does not extract much **mercury** out of the tissues **In Vivo**.
  - This is because **mercury** is extremely tightly bound to organic Sulfhydral groups in tissues.

Additional Points



- The addition of Magnesium to a bottle of DiSodium EDTA prior to administration produces **Magnesium DiSodium EDTA**. However, because Mg^{++} has a low binding constant, the complex is not very stable and Mg^{++} is easily replaced by any of the metals with higher binding constants like **lead** or **cadmium**

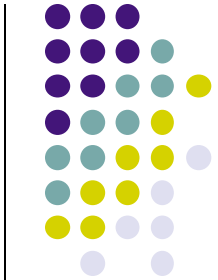
Selecting Patients



May Decrease MI and Stroke

- **Blood lead level** was significantly associated with both MI and stroke mortality in a nationally representative sample of 13,946 adult participants of the Third National Health and Nutrition Examination Survey recruited in 1988 to 1994 and followed up for up to 12 years for all-cause and cause-specific mortality. The association was evident at levels >0.10 μmol/L (>2 μg/dL)
  - Low-Level Enviromental Exposure to Lead Unmasked as Silent Killer, Circulation, Sept 26, 2006;114(13):1347-49.
  - Blood Lead Below 0.48 μmol/L (10 μg/dL) and Mortality Among US Adults, Circulation, Sept 26, 2006;114:1388-94.

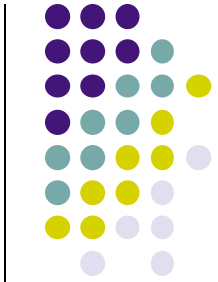
Selecting Patients



May Help Reverse Hypertenstion

- The improvement of Hypertension with EDTA chelation therapy may be due to the binding of heavy metals like Pb^{++} (lead) and Cd^{++} (Cadmium), both of which have been found to increase blood pressure.
  - JAMA 2003; 289: 1523-1532. – Lead stored in women's bones and released when they reach menopause multiplies their risk of potentially fatal high blood pressure (study of over 2000 women aged 40-59)
  - JAMA 1996, 275: 1171-1176. – Lead accumulation may be an independent risk factor for developing hypertension in men.
- Magnesium in NaMgEDTA may lower BP by decreasing vasospasm

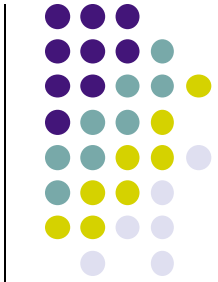
Selecting Patients



EDTA may improve Bone Mineral Density

- DisodiumEDTA binds with circulating unbound serum Calcium to form a Ca-EDTA complex. As a result of lowering serum Calcium levels, the body's homeostatic mechanisms are stimulated to release Parathyroid hormone (PTH). With repeated treatments, the pulsatile stimulation of PTH stimulates Osteoblastic bone activity, thereby recalcifying demineralized bone.
  - J Ad Med 1988: 1(2); 79-85. - …edta therapy might enhance bone growth in patients with osteoporosis and has no negative effect on patients with normal bone density readings.

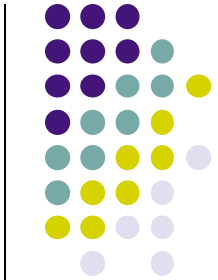
Selecting Patients



EDTA may improve kidney function

- Low-level environmental **Pb^{++} (lead)** exposure may accelerate progressive renal insufficiency in non-diabetic adults who have chronic renal disease. Repeated chelation therapy may improve renal function and slow the progression of renal insufficiency by lowering **Pb^{++}** levels.
  - NEJM 2003; 348: 277-286.

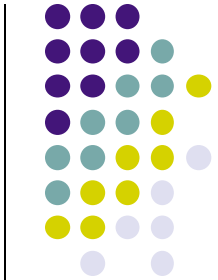
Selecting Patients



EDTA may improve degenerative processes

- EDTA is responsible for the reduction of intracellular heavy metals that impair enzyme reactions and block metabolic pathways.
- Heavy metal accumulation has been associated with:
  - Alzheimers disease
  - Parkinsons disease
    - Int J Occup Med Environ Health 2001; 14(3): 209-218. – Lead, mercury, manganese and copper have been implicated in ALS and Parkinsons disease. There is elevated risk for Alzheimers disease in areas where aluminum is in the drinking water
  - Cardiac Arrhythmias
    - Am J Card 1998; 82(5): 594-599. – Cumulative exposure to lead, even at low levels, may depress cardiac conduction.

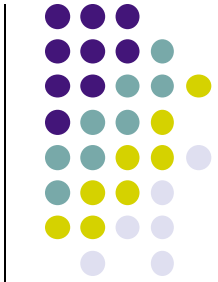
Selecting Patients



EDTA may improve circulation

- EDTA stimulates improved capillary bed perfusion and a decrease in basement membrane thickening. This subsequently causes a decrease in peripheral resistance with a secondary increase in peripheral flow, particularly in the Diabetic patient.
  - J Cardiovasc Nurs 1996; 10(3): 78-96. – Edta chelation is a valuable therapuetic option for vascular disease, either alone or in conjucntion with standard treatment protocols.

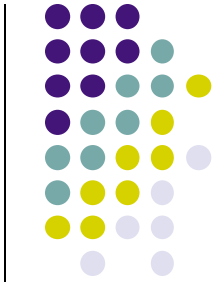
Selecting Patients



Other possible benefits

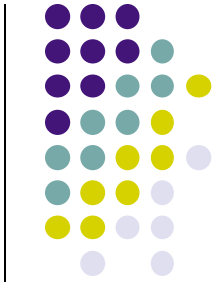
- May protect against cirrhosis
  - Zhongguo Zhong Xi Yi Jie He Za Zhi 2000; 20(12): 890-892. De-copper therapy with EDTA and / or DMPS could improve liver cirrhosis and liver function.
- May improve Glucose metabolism in diabetics
  - Diabetologia 1967; 3(5): 449-452. EDTA and insulin. A study of the effect of salts of EDTA upon insulin action in vivo and in vitro.
- May improve collagen disease processes (i.e. Rheumatoid Arthritis)
  - Clin Endocrinol (Oxf) 1990; 32(3): 323-328. A high intracellular calcium content is associated with inflammatory disease.
- May remove Calcium from plaque formation in blood vessels
  - Clarke N, et al. Am J Med Sci 1955;229:142. The “in vivo” dissolution of metastatic calcium: An approach to atherosclerosis.

List of diseases that may benefit with chelation therapy (off label use):



Coronary artery disease
Atherosclerosis
Cerebral vascular disease
Peripheral vascular disease
Cardiac Arrhythmias
Collagen vascular disease
(Lupus, Arthritis, etc)
Alzheimers disease
Parkinsons disease
Type I and Type II DM
Heavy Metal Toxicity
Osteoarthritis
Venous stasis disorders
Peripheral neuropathy
Fibromyalgia
Kidney disease
Osteoporosis

Commercial preparations of EDTA



IMPORTANT

- *DiSodium EDTA* (NaEDTA) – approved by the FDA for use in:
  - Hypercalcemia
  - Ventricular Arrhythmias associated with Digitalis Toxicity
- *Calcium DiSodium EDTA* (CaEDTA) – approved by the FDA for use in:
  - Removal of lead and other heavy metals
    - It is excreted primarily by the kidney with about 50% excreted in one hour and over 95% excreted within 24 hours.
    - Almost none of the compound is metabolized
    - Only about 5% is absorbed from oral administration

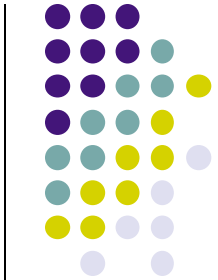
Commercial preparations of EDTA

WARNING

NaEDTA must only be given by the intravenous (IV) route. If it is administered intramuscularly (IM), the patient will experience severe pain associated with tissue sloughing at the injection site.

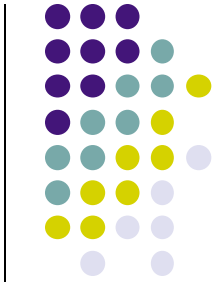
NaEDTA must only be given by slow IV infusion at 1gm / hour (16mg/min) or less.

Precautions for using EDTA:



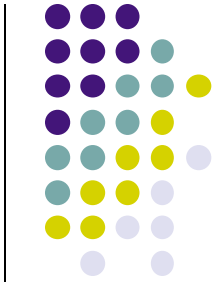
- **Drug Interactions:** None Known
- **Pregnancy:** Category B (however, EDTA should **NOT** be used during pregnancy!)
- **Nursing Mothers:** It is unknown whether CaEDTA is excreted in mother's milk. Caution should be exercised if it is used.
- **Pediatric Use:** Since lead poisoning occurs in children and adults, but is more severe in children, CaEDTA is used in all ages.

Precautions for using EDTA:



- **Contraindications:** Severe allergy to EDTA, pregnancy, anuria or acute lead encephalopathy.
- **Relative Contraindications:** Renal dialysis
- **Possible Side Effects:**
  - Nephrotoxicity – very rare if infused at proper rate, dose and frequency
    - Minimize this risk by re-checking kidney function tests every 5 to 10 treatments and adjust EDTA dose based on creatinine clearance

Precautions for using EDTA:

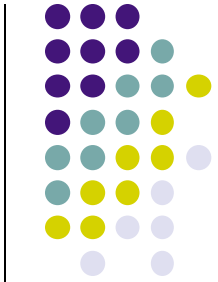


- **Possible Side Effects:**
  - Hypocalcemia – Occurs if infused too rapidly or in excessive doses
    - Watch for muscle cramps, numbness and tingling
    - May be reversed with IV Calcium gluconate
  - Allergy – True allergy to EDTA is rare
    - Allergic symptoms more likely from an admixture ingredient or preservative
    - Typically allergy to lidocaine or B-vitamin
    - Try to get preservative free ingredients

Precautions for using EDTA:

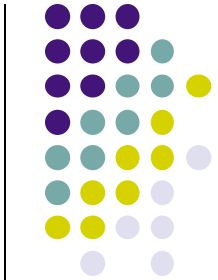
- **Possible Side Effects:**
  - Thrombophlebitis – From local irritation at the infusion site
  - **Prevention** of thrombophlebitis:
    - Use Heparin 1000iu to 5000iu in infusion mixture
    - Buffer to physiologic pH with Bicarbonate
    - Use a larger vein
    - Reduce the rate of infusion
  - **Treatment** – topical moist heat, NSAIDS, arnica, bromelain

Precautions for using EDTA:



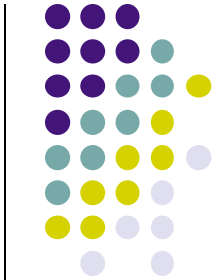
- **Possible Side Effects:**
  - Congestive Heart Failure – In patients with cardiovascular disease, the increased fluid load of the chelation may aggravate CHF.
    - Weigh cardiac patients each visit
    - Continue diuretic use and increase dose if needed
    - Decrease sodium content of infusion (IV Vit C contains 11% sodium by weight)
    - Slow the infusion rate
    - Decrease the calculated therapeutic dose of EDTA in proportionally less fluid

Precautions for using EDTA:



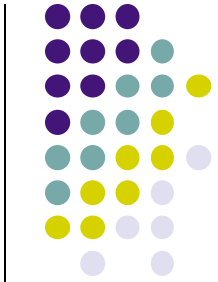
- **Possible Side Effects:**
  - Hypoglycemia – Blood glucose may fall during an EDTA IV
    - Ensure adequate protein intake before and during IV
    - Patients should bring a fruit snack
    - A 50% dextrose solution for IV use should be readily available.
  - Fatigue – patients may complain of feeling "washed out" for 24-48hrs after a single treatment
    - Use IV nutritional infusions without EDTA in between chelation treatments
    - Increase interval between treatments

Before initiating chelation therapy always:



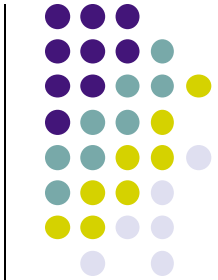
- Perform an H&P on your patient.
- Check
  - **Liver function tests**
  - **BUN / Cr, UA and Creatinine clearance**
  - CBC with Dif, electrolytes, EKG
  - Whole blood lead and provoked urine lead levels
  - condition specific work-up.
- Inform patient of risks and benefits of NaEDTA:
  - Pain / bleeding at infusion site
  - Hypoglycemia
  - Renal toxicity
  - Zinc deficiency

IV Na EDTA Chelation Protocol – 50mg/kg/day at 1gm/hour



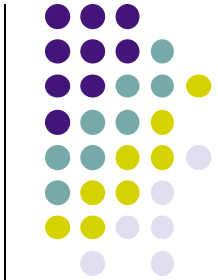
250cc – 500cc	Sterile Water
2.0cc	Vitamin B6 (100mg/cc)
1.0cc	B complex 100
20cc	Sodium Bicarbonate 1mEq/ml
5cc	Procaine
1.0cc	Vitamin B5 (250mg/cc)
10.0cc	Vitamin C (500mg/cc)
5.0cc	Magnesium Sulphate
1.0cc	Potassium Chloride 2Meq/cc)
10 - 20cc	DiSodium EDTA (150mg/cc) adjust per Cackcroft Gault Formula
2.5cc	Heparin (5000U/cc)

IV Ca EDTA Chelation Protocol



100cc	Normal Saline
1.0cc	Vitamin B6 (100mg/cc)
0.25cc	Vitamin B1 (100mg/cc)
0.25cc	B complex 100
1.0cc	Vitamin B12 (1000mcg/cc)
2.0cc	Vitamin B5 (250mg/cc)
3.0cc	Vitamin C (500mg/cc)
2.0cc	Magnesium Chloride (200mg/cc)
1.0cc	Potassium Chloride (2Meq/cc)
5 – 10cc	Calcium DiSodium EDTA (300mg/cc) adjust per Cackcroft Gault Formula
0.1cc	Heparin (5000U/cc)

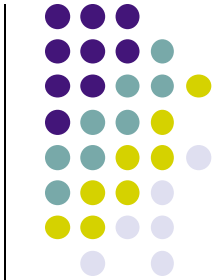
Minimize Pain



Use Magnesium

- Reduce the discomfort of the infusion by releasing the heat in the bottle instead of the patient.
  - The combination of NaEDTA with Magnesium in the infusion bottle prior to administration releases eight (8) kcal of heat in an Exothermic reaction.

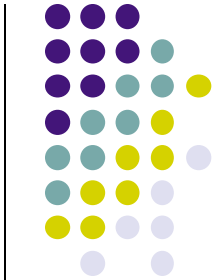
Minimize Pain



Alkinalize the solution

- Pain at the infusion site can be due to **acidity** of the solution. The EDTA solution becomes acidic due to the release of Hydrogen ions when Mg^{++} is added to the EDTA. (As the Mg^{++} is chelated by EDTA in the bottle, H^{+} (hydrogen ions) are released).
  - The carrier solution can be made more alkaline by adding **Sodium Bicarbonate**

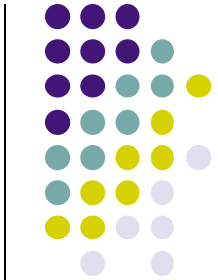
Minimize Pain



Create an **Isotonic** solution

- Care must be taken to choose the ingredients for the carrier solution to balance the osmolarity. Pain will occur if the solution is Hypertonic (too concentrated) or Hypotonic (too dilute) in relation to the normal osmolarity of blood.
  - An isotonic solution has a similar concentration to blood.

Calculating dose of EDTA



- **Acquire computer program to calculate dose**

or

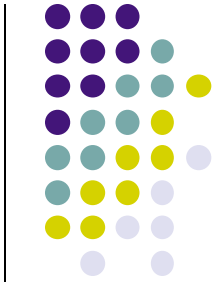
- 50 mg EDTA per Kg (LBW X 1.33) X (CrCl/ 100)

Glomerular Filtration Rate Computation

$$CrCl = \frac{(140 - Age) \times (LBW \times 1.33)}{(72 \times Cr)}$$

  - CrCl = computed Creatinine Clearance, approximating renal glomerular filtration rate in ml/min
  - Age =patient's age
  - LBW = computed lean body weight in Kg.
  - Cr = serum creatinine in mg/dL
    - For CrCl in women, multiply the above result by 0.85

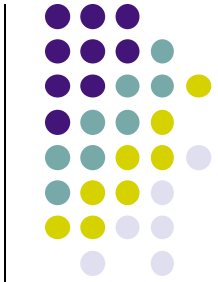
Calculating dose of EDTA cont'd…



LEAN BODY WEIGHT (LBW) IN KG AS USED IN ABOVE COMPUTATIONS

- Lean body weight for males is computed at 50 kg plus 2.3 kg for each inch of height over 5 feet.
- Lean body weight for females is computed at 45.5 kg plus 2.3 kg for every inch of height over 5 feet.
- Actual weight is used whenever actual weight is less than computed lean body weight.

Calculating dose of EDTA cont'd…

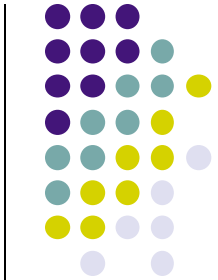


- The dose is usually limited to a maximum of 3.0 grams (widely accepted as the fully effective dose).
  - Correct for CrCl/100 only if computed creatinine clearance is less than 100 ml/min.
- Maximum rate of infusion is limited in NaEDTA to 1gm per hour.

Case Study CaEDTA: Mr D.

- 81 year old male in good state of health presents with concerns about fatigue and memory changes. (He has trouble remembering names.)
- Pmhx – CAD, MI, hypercholesterolemia
- Pshx – CABG x3 - Dec. 1984
- Meds – ASA, Atenolol, Plavix
- Occupation – Supervisor at Bear Sterns
- Requests chelation therapy

Mr D cont'd…



- Ht: 5' 3"
- Wt: 162lbs
- Cr: 1.2
- Blood lead: 4 mcg/dl (ref range <10)
- EDTA dose calculated to be >3.0gm
- Provoked tests done with 1.5gm CaEDTA
- Treatment done with 2.0gm CaEDTA

Mr D. cont'd…

URINE TOXIC METALS

DOCTOR'S DATA INC

LAB#: U070823-0635-1
PATIENT:
SEX: Male
AGE: 81

CLIENT#: 25128
DOCTOR: Jeff A. Morrison, MD

103 5th Ave 6th Floor
New York, NY 10003

POTENTIALLY TOXIC METALS

METALS	RESULT µg/g CREAT	REFERENCE RANGE	WITHIN REFERENCE RANGE / ELEVATED / VERY ELEVATED
Aluminum	82	< 25	
Antimony	< dl	< 0.6	
Arsenic	61	< 120	
Beryllium	< dl	< 0.5	
Bismuth	< dl	< 10	
Cadmium	2.6	< 2	
Lead	44	< 5	
Mercury	< dl	< 3	
Nickel	7.4	< 10	
Platinum	< dl	< 1	
Thallium	0.1	< 0.7	
Thorium	< dl	< 0.3	
Tin	1.3	< 9	
Tungsten	< dl	< 0.7	
Uranium	< dl	< 0.1	

CREATININE

	RESULT mg/dL	REFERENCE RANGE	2SD LOW 1SD LOW MEAN 1SD HIGH 2SD HIGH
Creatinine	24	45- 225	

SPECIMEN DATA

Comments:
Date Collected: 8/21/2007
Date Received: 8/23/2007
Date Completed: 8/29/2007

Method: ICP-MS
<dl: less than detection limit
Provoking Agent: CA EDTA

Collection Period: timed: 6 hours
Volume: 1850 ml
Provocation: POST PROVOCATIVE

Toxic metals are reported as µg/g creatinine to account for urine dilution variations. **Reference ranges are representative of a healthy population under non-challenge or non-provoked conditions.** No safe reference levels for toxic metals have been established.

V10.00

Mr D

After 10 CaEDTA tx

- Improved
  - Memory
  - Energy

URINE TOXIC METALS

DOCTOR'S DATA INC

LAB#: U071218-0283-1
PATIENT: [redacted]
SEX: Male
AGE: 81

CLIENT#: 25128
DOCTOR: Jeff A. Morrison, MD

103 5th Ave 6th Floor
New York, NY 10003

POTENTIALLY TOXIC METALS

METALS	RESULT µg/g CREAT	REFERENCE RANGE	WITHIN REFERENCE RANGE / ELEVATED / VERY ELEVATED
Aluminum	100	< 25	
Antimony	< dl	< 0.6	
Arsenic	8.4	< 120	
Beryllium	< dl	< 0.5	
Bismuth	< dl	< 10	
Cadmium	2.1	< 2	
Lead	12	< 5	
Mercury	0.9	< 3	
Nickel	5.6	< 10	
Platinum	< dl	< 1	
Thallium	0.2	< 0.7	
Thorium	< dl	< 0.3	
Tin	1.8	< 9	
Tungsten	< dl	< 0.7	
Uranium	0.1	< 0.1	

CREATININE

	RESULT mg/dL	REFERENCE RANGE	2SD LOW 1SD LOW MEAN 1SD HIGH 2SD HIGH
Creatinine	38	45- 225	

SPECIMEN DATA

Comments:
Date Collected: 12/13/2007
Date Received: 12/18/2007
Date Completed: 12/20/2007

Method: ICP-MS
<dl: less than detection limit
Provoking Agent: CAEDTA

Collection Period: timed: 6 hours
Volume: 800 ml
Provocation: POST PROVOCATIVE

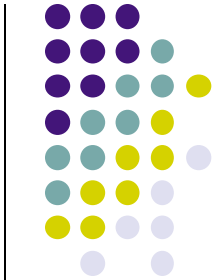
Toxic metals are reported as µg/g creatinine to account for urine dilution variations. **Reference ranges are representative of a healthy population under non-challenge or non-provoked conditions.** No safe reference levels for toxic metals have been established.

V10.00

Rec'd apt 1/10/08.

Case Study NaEDTA: Mrs B

- 78 y.o. Female patient present for second opinion on Carotid Endarterectomy, s/p R retinal artery branch occlusion and Carotid Doppler showing B/L Internal carotid artery 50-59% stenosis.
- Patient complained of fatigue, change in vision right eye
- EKG, Holter monitor and Echo showed no source for embolisation.
- Refused TEE
- Refused Carotid Endarterectomy



- Evaluation from Cardiologist #1 4/28/2005
  - Recommendations:
    - TEE
    - Urgent consultation with vascular surgeon for carotid endarterctomy
    - Medical treatment:
      - ACE inhibitor, statin medication, ASA
    - Patient refused all treatment

RICHARD L. MUELLER, MD, FACC, FACP
CARDIOVASCULAR DIAGNOSTICS, PC
MEDICAL ASSOCIATES OF NEW YORK
401 EAST 56th STREET
NEW YORK, NY 10022-4103

Tel: 212.593.9800

Fax: 212.593.5757
Fax: 212.319.1577

Richard L. Mueller, MD, FACC, FACP — Cardiovascular Diseases
Inna Bukharovich, MD, CBNC — Cardiovascular Diseases
Jason T. Slyer, RN, MS, FNP, BC — Cardiac Nurse Practitioner
Brian S. Hoch, MD — Internal Medicine / Nephrology
Yelena Karasina, MD — Internal Medicine
Markos I. Koutsos, MD — Gastroenterology

4/26/05

Susan Klein, MD
120 E. 79 St.
New York, NY 10021

Re: Ms.

Dear Dr. Klein: Susan

Thank you for referring Ms. for cardiologic evaluation. As you know, she is a 78 year old woman who recently suffered sudden right visual loss, due to a retinal artery branch occlusion supplying the right upper retinal field; this was, as you know, evaluated expertly by Dr. Levitsky. She was started on aspirin by you, and I suggested increasing it to 325 mg/d pending completion of evaluation.

She denies any cardiac symptoms, including chest pain, dyspnea, palpitations, syncope, edema, other neurologic symptoms, or claudication.

As her past medical history is well known to you, I will not recite it here. Her father had an MI at age 73.

Physical examination reveals blood pressure of 132/70 and pulse of 88 and regular. The remainder of the cardiopulmonary examination reveals only a pectus excavatum; the remainder is normal.

ECG reveals sinus rhythm at 60-70 bpm, with frequent APC's, and minimal (1/4 mm) usploping ST depressions in V5 and V6.

Recent cardiac testing has been forwarded to you; carotid Doppler revealed 50-60% bilateral internal carotid stenosis; echocardiography was a technically difficult study, but did not reveal an obvious source of embolism and had no major abnormalities; Holter monitor did not reveal atrial fibrillation or flutter. Limited additional echo today, performed due to technically difficult echo imaging due to closely spaced ribs and pectus deformity, revealed significant aortic arch and abdominal aortic atherosclerotic plaque, with possible small emboli in transit apparently visualized.

After lengthy discussions today and on 4/24/06 regarding the evaluation of stroke and all diagnostic and therapeutic implications, she has declined to undergo recommended transesophageal echocardiography. She is also reluctant to add a statin and ACEI as I have strongly advised.

The exact cause of Ms. ' retinal stroke (permanent / persistent visual defect at this point) is not fully certain, but it could clearly be explained by embolization from her moderate stenosis of the right internal carotid artery. Likewise, it could be explained by the apparent significant aortic arch plaque (with apparent embolic signals detected in transit during imaging). Other theoretic causes cannot be fully ruled out, due to the patient's refusal of TEE.

4

Recommended therapy for symptomatic carotid stenosis of > 50% narrowing would be carotid endarterectomy, aspirin, statin, and ACE inhibitor. Urgent consultation with a vascular surgeon of your choice was advised, but she declines both surgery and even a vascular surgery consultation at present, based on our discussions. Recommended therapy for embolism from aortic plaque is not fully defined, but both coumadin and statins have been advocated; no definite prospective studies or guidelines consensus are available.

As for the report of a positive IgM anticardiolipid antibody, I doubt it would affect therapy, given the probable source of embolism from the carotid artery and/or aortic arch.

The full differential diagnosis of stroke and embolism, as well as all diagnostic and therapeutic implications of findings to date, were discussed in great detail with Ms. ——. She declines TEE, agrees to continue aspirin at 325 mg/d with food, and is non committal about my recommendation to add a statin (regardless of LDL level) and altace. She also declines to see a vascular surgeon as I advised her to do. She understands the serious risk of stroke, embolism, disability, blindness, and death. She is non committal about whether she wants me to just perform cardiovascular testing only for her, or whether she wishes for me to join in her care. It appears for now that she wishes that I perform the tests only, and that she will follow up with you and with Dr. Levitsky. Follow up carotid Doppler in 1 year, and echocardiography in about 2 years, was advised. Given her frequent APC's, TSH should be checked, if not already done. BP should be well controlled; she states her BP is always normal, and lower than it was here today.

Given diffuse atherosclerotic disease and minimal non specific repolarization changes on ECG, an exercise myoview stress test was recommended, which she declined. Ms. — requested that I would only see her as needed, and for future cardiovascular testing.

Thank you again for referring Ms. as always, you have my warmest personal regards.

Best wishes,

Richard L. Mueller, MD, FACC, FACP, FASE
RM/jm
cc: Dr. Levitsky

4/27/06

ICANL
Nuclear Cardiology
Accredited Nuclear Cardiology Laboratory

04/24/2006 08:12 2125935757 MEDICAL ASSOCIATES

PID: 562407
04/18/2006

CEREBROVASCULAR DUPLEX SCAN

HP 2000

Name: DOB: 8/24/27 Sex: Female Date: 4/18/06 Tape: 21

Referral Source: Dr. Mueller

C.C.:

Risk Factors

Smoking: Angina/MI: No Hypercholesterolemia: COPD: No

Hypertension: No Family History: No Diabetes: No

Indications

Weakness: Syncope: Yes Dysphasia: No Memory Loss: No Dizziness: Yes

Previous CVA: Paresthesias: Paresis: Previous Bruit: No High Risk Patient: No

Previous TIA: Numbness: Head Trauma: No Pre-op Evaluation: No Amaurosis:

Subarachnoid Hemorrhage/Vasospasm: No Previous Carotid Stenosis: No Right: % Left: %

Previous Right Carotid Endarterectomy: No Date: Previous Left Carotid Endarterectomy: No Date:

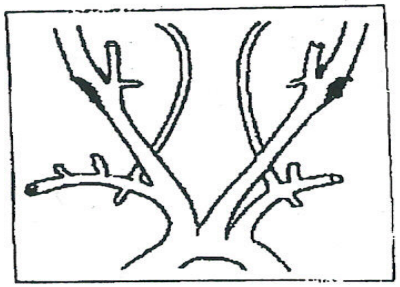
CAT Scan: No data

Other: No data

Results

RIGHT				LEFT		
Brachial BP: / Bruit: No				Brachial BP: / Bruit: No		
Systole	Diastole	% Stenosis	Velocity in cm/sec	Systole	Diastole	% Stenosis
127	29	50-59%	Proximal ICA	145	38	50-59%
160	36	50-59%	Distal ICA	126	33	50-59%
154	27		Proximal CCA			
			Distal CCA	127	27	
111	11		Bulb			
			Ext. Carotid Artery	93	8	
			Subclavian			
			Vertebral Artery			
1.0			ICA/CCA Ratio	1.1		
0.8			Resistance Index	0.7		
Prograde			Vertebral Flow	Prograde		
heterogeneous			Plaque Composition	heterogeneous		
smooth			Plaque Surface	smooth		

Carotid Artery Map:



Conclusions

RIGHT: Plaque formation is present at proximal internal carotid artery, causing 50-59% stenosis on this side. Normal common and external carotid arteries.

LEFT: Plaque formation is present at proximal internal carotid artery, causing 50-59% stenosis on this side. Normal common and external carotid arteries.

Interpreting Physician: Demetrios Georgiou MD

Technologist:

Lin

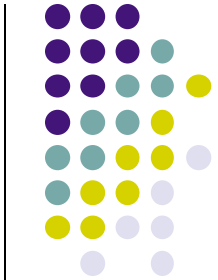
Medical Associates Of New York
401 East 55th St. ; NY, NY 10022-4103.tel# 212-593-9800

4/24/06

4

Document max

Evaluation by me on 6/2006



- 78 yo Female patient c/o fatigue and recent change in R visual field s/p R Retinal artery branch occlusion.
- PE – WNL except noticeable pale skin color and malaise
- Lab work WNL
- NaEDTA 3.0 gm qwk x 40 treatments
- After chelation, refer to new cardiologist for second opinion and retesting when complete course of treatment

ANTHONY J. PEPE, M.D., F.A.C.C.
CARDIOVASCULAR DISEASES

425 W. 59TH STREET, SUITE 8B
NEW YORK, NY 10019
TELEPHONE (212) 376-3180
FAX (212) 376-3190

30 March 2007

Jeffrey Morrison, M.D.
103 5TH Ave.—6th Fl.
N.Y. N.Y. 10003

RE: MS.

Dear Jeff,

Thank you for referring Ms. for cardiac evaluation. She has suffered a right retinal embolic event in 2005, although a definite cardiac source was not identified. There was no evidence of serious arrhythmia, atrial fibrillation, or intra-cardiac embolic sources. She has had several trans-thoracic echocardiograms, but has steadfastly refused trans-esophageal echo exams. There was no evidence of an atrial septal defect nor patent foramen ovale on one of her trans-thoracic studies. Of note is the presence of 50-60 % bilateral carotid disease, and some aortic arch and abdominal aortic atherosclerotic disease. The proximal aortic plaques may have shown evidence of embolization during one of her echo tests. She is currently undergoing chelation therapy under your guidance, and is taking an organic "platelet inhibitor" instead of aspirin; she has refused COUMADIN therapy. Her physical examination in my office showed no evidence of active vascular disease, and her BP was 130/70, with a regular pulse. Office ECG showed only APC'S.

After extensive discussion with the patient, she has agreed to undergo a trans-esophageal echocardiogram, which will be done at the Cardiology Division at Roosevelt Hosp. (her main concern was gagging during the procedure). Although the results of the TEE will not alter treatment, it may localize a probable source of the emboli. As far as treatment is concerned, she continues to refuse COUMADIN, but will re-consider ASA treatment, and high dose STATIN therapy. I discussed the importance of PLAQUE STABILIZATION with the patient, as well as possible plaque reversal with STATIN treatment. In addition, it is important to repeat her CAROTID DOPPLER examination, (the last being 4/06), especially after completing a course of chelation therapy.

I will send you the results of the TEE as they become available; thank you again for your kind referral. Best regards for a happy Spring !

Very truly yours,

Tony

Anthony J. Pepe, M.D.,F.A.C.C.

ap Enclosure

Evaluation from Cardiologist #2

- Recommendation for:
  - TEE
  - Medical treatment:
    - ACE inhibitor, statin medication, ASA
  - Repeat B/L carotid artery doppler

Columbus Cardiology Associates
425W 59th Street
Suite 8B
New York, NY 10019
Tel. (212) 376-3180

Date: 4/10/2007

Patient:
DOB: 8/24/1927

Referring Physician: Dr. Anthony Pepe, MD

Duplex Ultrasound Evaluation of the Carotid Arteries

Evaluation of both carotid arteries was performed using a HP 5000 HDI ultrasound machine. All vessels were evaluated using color Doppler as well as gray scale imaging.
Transverse and sagittal views were obtained and Doppler flow measurements performed in the proximal, mid and distal common carotid artery and proximal mid and distal internal carotid artery.
Direction of flow was determined for the vertebral arteries and evaluation of the external carotid arteries including assessment of stenosis in these vessels was performed.
Color Doppler images were recorded where appropriate.

Findings:

Carotid Arteries

Right side: The velocity measurement and ultrasound images are consistent with a **20-39%** stenosis. Moderate calcified plaque was seen in the right internal carotid artery. Mild plaque was seen in the right common carotid artery.

Left side: The velocity measurement and ultrasound images are consistent with a **20-39%** stenosis. Moderate calcified plaque was seen in the left internal carotid artery. Mild plaque was seen in the left common carotid artery.

Vertebral Arteries: Antegrade flow bilaterally.

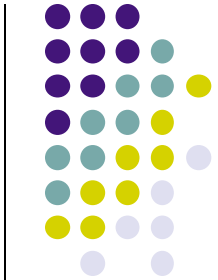
Impression: **20-39%** stenosis of the Right ICA
20-39% stenosis of the Left ICA

Olivier Frankenberger, MD

Last Evaluation of Mrs B by Dr Morrison

- After completion of 40 IV NaEDTA chelation treatments patient reported increased energy and had a visible improvement in color of skin.
- Patient is on maintenance IV NaEDTA 3.0gm 1x/month and still doing well.

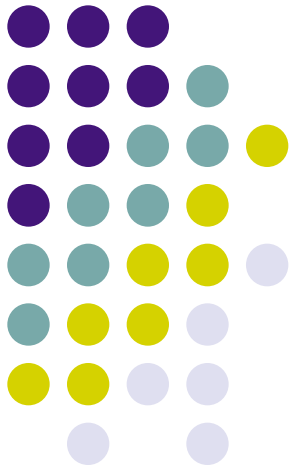
Summary



- By understanding how EDTA chelation works you can safely and effectively administer treatment
  - Remember – first do no harm and be prepared
  - Replace minerals in between treatments
    - Zinc and Iron if needed
  - Be prepared for side effects
    - Low blood sugar, vein irritation, change in kidney function
  - Decrease pain during administration

The Science Behind Chelation Therapy

Jeffrey A. Morrison, M.D.
103 Fifth Avenue, 6th Floor
New York, NY 10003



Jeffrey A. Morrison, M.D.
Chelation Therapy
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INFORMED CONSENT FOR Mg EDTA or Ca EDTA CHELATION THERAPY

I _____, hereby give consent to Dr._____, his associates, employees or staff, to perform intravenous EDTA chelation therapy ("Chelation Therapy") for the purpose of treatment of atherosclerotic disease and /or heavy metal toxicity, and /or prevention of treatment of degenerative diseases. I understand that Chelation Therapy is a standard therapy widely approved for the treatment of heavy metal toxicity , however, its usage is considered controversial for the generalized treatment of atherosclerotic vascular disease and other degenerative diseases, and the view that it is of benefit in the treatment of such disorders is accepted by a minority of the medical community and it is considered "experimental" by most physician, I am advised that my treating physician believes that Chelation Therapy does have positive clinical benefit. I have been informed that other treatment approaches have been used in these conditions, including but not limited to bypass surgery or angioplasty and these alternatives have been explained to my full satisfaction. As with any other medical procedure, a small percentage of patients do not respond to this therapy.

I understand that the benefits of Chelation Therapy are much greater if I follow a healthy lifestyle (non-smoking, weight control, proper exercise, proper diet, and nutritional supplementation). I understand that an initial series of treatment are anticipated, and that these treatments may be extended over a number of months. I have been informed that Chelation Therapy may need to be repeated from time to time in the future in order to maintain the benefits. I understand that it is my option to stop at any time this treatment protocol without incurring any further expenses after I have directed that such treatment be stopped.

I have been informed of possible risks and side effects including but not limited to discomfort at the injection site, thrombophelebitis, hypocalcemia, fatigue, muscle cramps, kidney problems including nephrotoxicity, allergic reaction, congestive heart failure, liver disease, anticoagulation, lower blood sugar levels and / or hypoglycemia, mineral loss and generalized complaints. If I have suffered from any previous kidney disease, I agree to execute a medical release so that all previous identified medical records of mine may be obtained from previous physicians, and I have disclosed openly any known previous disorders. I understand that this therapy should not be used if I am pregnant unless I have a severe life threatening disease. I understand that if I have a history of tuberculosis, Chelation Therapy may reactivate arrested tuberculosis and I agree to inform my physician of any occurrence of this disease. I understand the nature of the proposed procedure and the risks and dangers have been explained to me to my full satisfaction.

While I understand that there have been no warranties, assurances or guarantees of successful treatment made to me, I desire to undergo this treatment after having considered the information contained in this document, the information provided to me through my conversations with my treating physician and though materials provided to me by the office to educate me about the treatment. I acknowledge that I have had the opportunity to ask any questions of my physician with respect to the proposed therapy and the procedures to be utilized and all my questions have been answered to my full satisfaction. My Signature on this agreement will constitute a full and final release of any legal responsibility resulting from the administration of Chelation Therapy in my case and/or any other medical treatment that may be necessary as a result thereof.

I agree to have lab work performed and available to Dr. _____ when requested. I agree to schedule regular office visits with Dr. _____ at the requested intervals in order to continue my Chelation treatments and maintain an up-to-date health history and working relationship with physician.

Patient Name: _____ Date: _____

(Signature)

Patient Name: _____ Dr: _____

(Print or Typed Name)

INFORMED CONSENT FOR INTRAVENOUS DMPS THERAPY

I_____, hereby give consent to Dr _____, his associates, employees or staff, to perform Intravenous dimercapo-l-propanesulfonic acid sodium hereafter known as DMPS therapy for the purpose of treatment or prevention of Toxic Metal Accumulation.

I understand that intravenous DMPS therapy is not standard therapy widely approved or accepted for this/those purpose(s) and the view that it is of benefit in treatment of such disorders is accepted by a minority of the medical community and is considered "experimental" by most physicians. I am advised that my treating physician believes that intravenous DMPS therapy does have a positive clinical benefit. I have been informed that other treatment approaches have been used in these conditions, including but not limited to prescription medication and over- the-counter drugs and these alternatives have been explained to me in full satisfaction. As with any other medical procedure, a small percentage of patients do not respond to this therapy.

I understand that the benefits of intravenous DMPS therapy are much greater if I fellow a health lifestyle (non-smoking, weight control, proper exercise, proper diet, and nutritional supplementation). I understand that an initial series of treatment are anticipated and that these treatments may be extended over a number of months. I understand that it is my option to stop at anytime with this treatment protocol without incurring any further expense after I have directed that such treatment be stopped.

I have been informed of possible risks and side effects including but not limited to discomfort at the injection site, thrombophlebitis, of the arm, fatigue, allergic reaction, fever, chills and generalized complaints. I understand that this treatment should not be used if I am pregnant unless I have a severe life threatening disease. I understand the nature of the proposed procedure and the risks and dangers have been explained to me in full satisfaction.

While I understand that there have been no warranties, assurances or guarantees of successful treatment made to me, I desire to undergo this treatment after having considered the information contained in this document, the information provided to me through my conversations with my treating physician and through materials provided to me by the office to educate me about the treatment. I acknowledge that I have had the opportunity to ask questions of my physician with respect to the proposed therapy and the procedures to be utilized and all of my questions have been answered to my full satisfaction. My signature on this agreement will constitute a full and final release of any legal responsibility resulting from the administration of intravenous DMPS therapy in my case and/or any other medical treatment that may be necessary as a result thereof.

_____ Date: _____
PATIENT'S NAME (signature)

_____
PATIENT'S NAME (print or type name)

_____
Doctor

Heavy Metal Toxicity Scale

Score each symptom on a scale of 0 – 10 and calculate a total for each column to provide a number that will be entered in the total row. This flow sheet can be used to follow the progression or regression of a patient's treatment.

Symptoms:		**date**	**date**	**date**	**date**
1.	Unexplained irritability				
2.	Constant or very frequent periods of depression				
3.	Numbness and tingling in extremities				
4.	Frequent urination during the night				
5.	Unexplained chronic fatigue				
6.	Cold hands and feet, even in moderate weather				
7.	Bloated feeling				
8.	Poor memory or Brain fog				
9.	Sudden, unexplained anger				
10.	Constipation				
11.	Difficulty making decisions				
12.	Tremors or shakes of hands, feet, head, etc.				
13.	Muscle twitches				
14.	Frequent leg cramps				
15.	Ringing in ears				
16.	Get out of breath easily				
17.	Heartburn				
18.	Excessive itching				
19.	Unexplained rashes, skin irritation				
20.	Metallic taste in mouth				
21.	Jumpy, Jittery, Nervous				
22.	Suicidal thoughts				
23.	Insomnia				
24.	Unexplained chest pains				
25.	Constant or frequent pain in joints				
26.	Rapid heart rate				
27.	Unexplained fluid retention				
28.	Burning sensation on the tongue				
29.	Headaches after eating				
30.	Frequent diarrhea				
Total:					

Adopted from: Huggins, HA, It's All in Your Head, Avery Publishing Group, NY, 1993, pg. 54.

Score <30 – Low likelihood of metal toxicity
Score >30 – Significant likelihood of metal toxicity – recommend further evaluation