Chelation Treatments - Uses and Abuses

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Occupational Medicine EFCOG Subgroup Meeting
20 April 2007
Albuquerque, NM

Chelation Agents

- DMSA – dimercaptosuccinic acid (succimer, Chemet)
- DMPS – dimercaptopropanesulfonic acid (unithiol, Dimaval)
- DTPA – diethylenetriaminepentaacetate (pentetic acid)
- EDTA – ethylenediaminetetraacetic acid (edetate, versenate, edathamil)
- Dimercaprol – 2,3-dimercaptopropanol (British antilewisite – BAL)
- Deferoximine – (Desferal, Desferin)
- D-penicillamine – 3-mercapto-D-valine
- Dithiocarb – diethyldithiocarbamate (DDC, Imuthiol)

Chelation for Metal Poisoning

- DMSA – **Pb**. Sb, As, Bi, Hg
- DMPS – **As, Hg**. Cr, Co, Cu, Au, Pb, Hg, Po, Ag, SbH_3
- DTPA – **Pu, Am, Bk, Cm, Cf**
- EDTA – **Cd, Co.** Zn
- BAL – **As, Hg (inorganic), Au.** Pb, Sb, Bi, Cr, Ni, W
- Deferoximine – **Fe.** Al
- D-penicillamine – **Cu.** Pb, As
- Dithiocarb – **Ni(CO)$_4$.** Cu

Chelation Agents – pitfalls and contraindications

- DMSA – sulfur odor, Pb rebound after D/C
- DMPS – childhood Pb (use DMSA instead)
- DTPA – Ur, Np poisoning. Use Zn-DTPA
- EDTA – Na_2EDTA. Pb poisoning (renal redistribution). Atherosclerosis
- BAL – Cd, Fe, Se, Te, organoHg poisoning (enhanced tissue uptake and redistribution)
- Deferoximine – renal impairment
- D-penicillamine – PCN allergy, SLE, renal failure
- Dithiocarb – Ni, Tl, Cd poisoning (redistribution to brain), disulfram-like rxn

EDTA

- Chelate named from Greek *chele* for claw-like chemical structure

- Binds di- and tri- valent metallic ions

- Chelates only water soluble metal ions

- Strongest binding with iron, weakest with calcium

- Non-selective binding of Hg, Cd, Pb, Al. Fe, Cu, Ni, Co, Zn, Mg, Mn, Ca

EDTA Chemical Structure
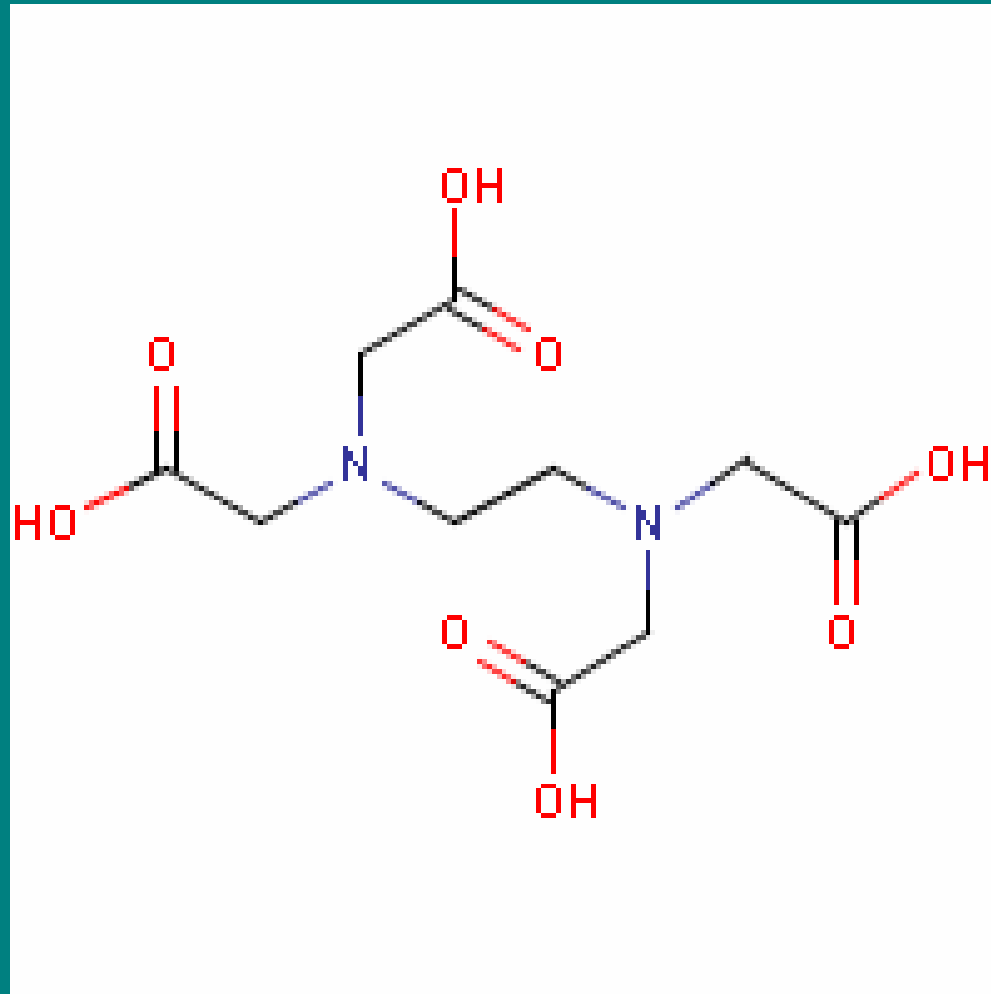
Hypotheses of EDTA and Atherosclerosis

- "Roto-rooter" – removing Ca in plaques would cause them to disintegrate
- Parathyroid hormone (PTH) – induced change in Ca balance from bone triggered activation of PTH
- Blocks production of free radicals – damage to arterial walls averted
- Prevents mutation – atheromas are benign tumors prevented by chelation

Placebo Controlled Studies of EDTA and Atherosclerosis

- Guldager, et al, EDTA treatment of intermittent claudication: A double-blind, placebo-controlled study. Journal of Internal Medicine, 1992.

- Knudson, et al, Chelation therapy for ischemic heart disease: a randomized, controlled trial. JAMA, 2002.

Case presentation

- 39 y/o male, "corrosion specialist" for pipeline Co. Changed Hg out of pressure meters. Hg spills in meter housing shacks.
- 7 yr. hx of generalized joint pain, extremity paresthesias, fasciculations
- "Kinesiology" tests suggested Hg poisoning
- Urine tests indicated Hg poisoning
- DMPS and supplements started
- No change in symptoms after 2 mos of tx
- Toxicology exam – stocking-glove hypesthesias, hyperreflexia, sustained ankle clonus. No tremor, mental status change, dermatitis/stomatitis or constitutional symptoms
- Had normal occupational exposure monitoring results.
- 24 hour Urine Hg and beta 2 microglobulins: WNL

POTENTIALLY TOXIC METALS

METALS	RESULT µg/g CREAT	REFERENCE RANGE	WITHIN REFERENCE RANGE	ELEVATED	VERY ELEVATED
Aluminum	< dl	< 35			
Antimony	0.2	< 5			
Arsenic	45	< 100			
Beryllium	< dl	< 0.5			
Bismuth	0.09	< 30			
Cadmium	0.2	< 2			
Lead	3.5	< 15			
Mercury	6.2	< 3			
Nickel	0.6	< 12			
Platinum	< dl	< 2			
Thallium	0.1	< 14			
Thorium	< dl	< 12			
Tin	5.7	< 6			
Tungsten	0.04	< 23			
Uranium	0.04	< 1			

CREATININE

	RESULT mg/dL	REFERENCE RANGE	2SD LOW	1SD LOW	MEAN	1SD HIGH	2SD HIGH
Creatinine	130	75- 200					

SPECIMEN DATA

Comments:
Date Collected: 4/16/2003
Date Received: 4/18/2003
Date Completed: 4/21/2003

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

Collection Period: timed: 12 hours
Volume:
Provocation: POST

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

PATIENT NOTIFIED
DATE: 04/24/03
BY: _illegible handwriting_

Discussed

Elevated Mercury. Orders

Chelation "Therapy" Case

- 5 y/o male with autism, brought from England to PA for treatment
- Treated by ENT specializing in environmental medicine
- IV Na_2EDTA
- Cardiac arrest in office
- Autopsy: hypocalcemia (<5 mg/dl, normal 8.8 to 10.1 mg/dl)
- CDC review results – wrong drug used

Discussion Points

- Do no harm vs. Do no good
    - Newer agents relatively safe
    - Non-selective nature of chelation
    - "Supplements" used during chelation tx
    - Results of long duration use unstudied