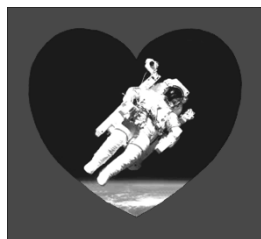


Historical Perspectives on the Development Of Various Chelation Therapies: EDTA – DMSA – DMPS

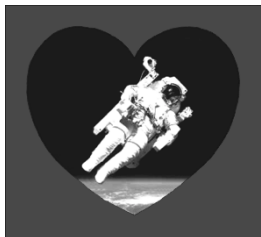
John Parks Trowbridge M. D., FACAM
Diplomate, American Board of Clinical Metal Toxicology



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History

- discernment of biases
 - intrigue of politics
- crescendo of achievement
- deepest pit of despair



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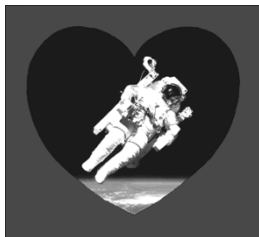
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History

- our responsibility to the future:

more free, more able, more aware

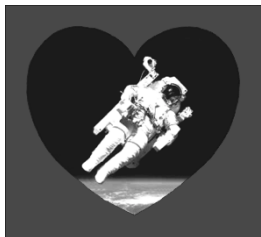
- people and the problems they faced



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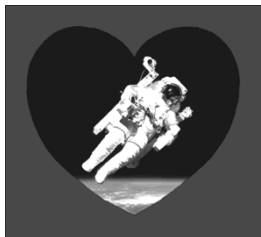
History is a *happening* thing!



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1893

Alfred Werner
proposed theory of
Metal-Ligand Binding
as a
ring formation

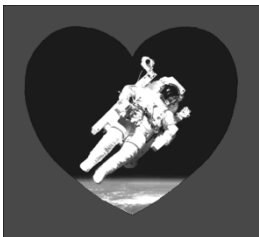


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1893

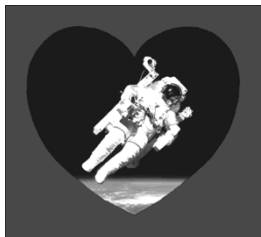
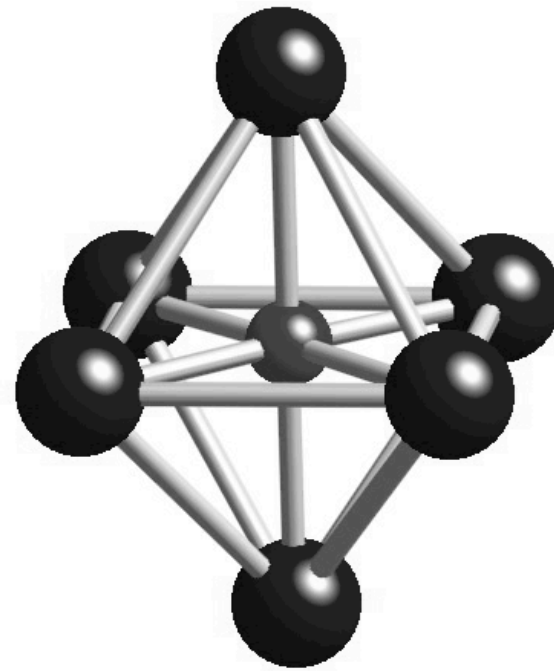
Alfred Werner
illustrated the
metal atom placed
at *center* of an
octahedron



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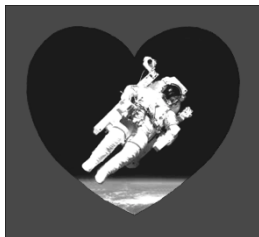
The atoms at the corners are ***covalently*** bonded and “cuddle” the divalent ion within by ***coordinate*** forces



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1913

Alfred Werner
received the Nobel Prize
for his discovery of
“complexion” chemistry
(metal-ligand *complexes*)

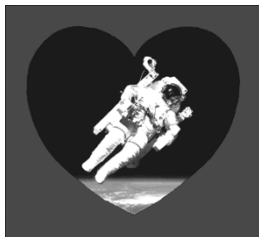


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1920

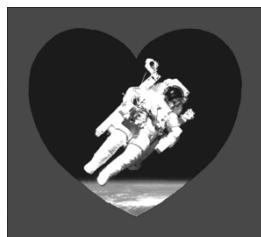
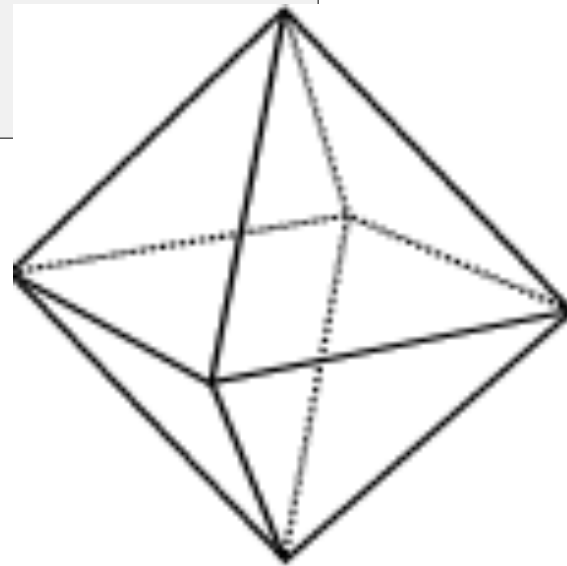
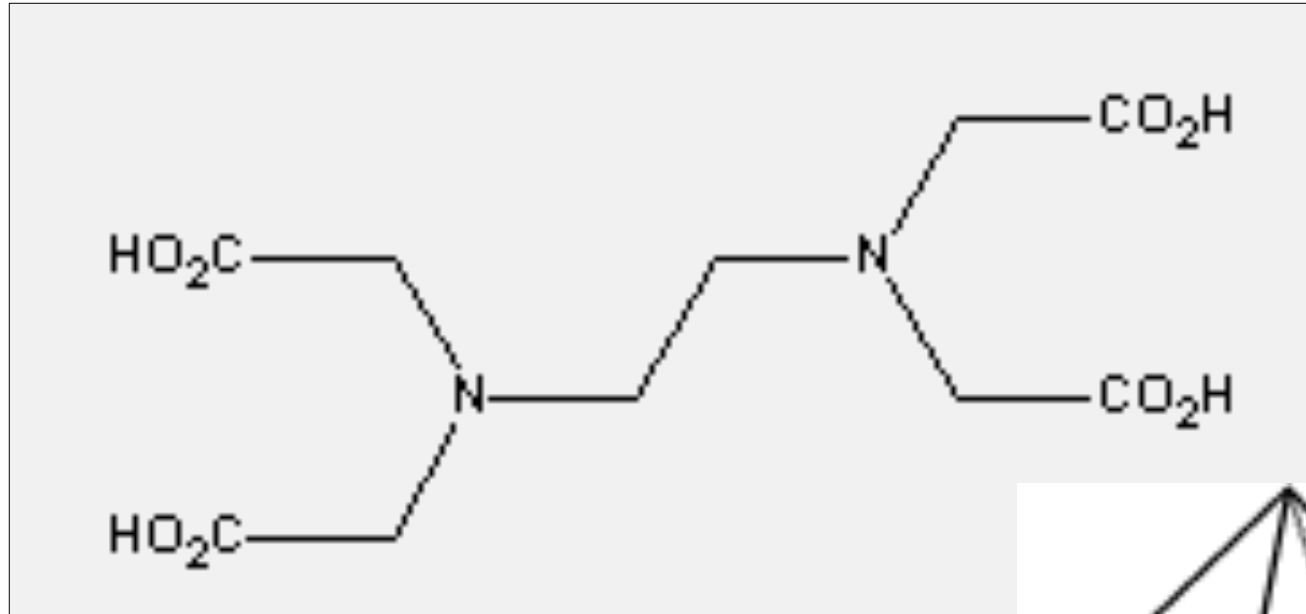
Morgan and Drew
defined “chelation”
as a metal ion
incorporated into a
heterocyclic *ring*

(Journal of the Chemical Society [London])



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mid -1930s

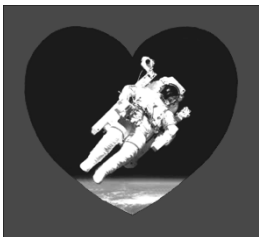
Franz Munz

first synthesized EDTA

(later called “Trilon-B”)

to substitute for citric acid

(process used ethylenediamine
with chloracetic acid)



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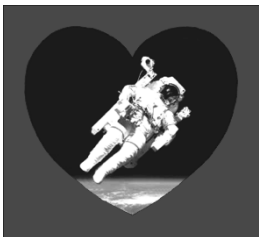
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1935

First patent for EDTA

filed in Nazi Germany (marketed as “Trilon-B”)

(salts of NTA -- nitrile triacetic acid --
were marketed as “Trilon-A”)

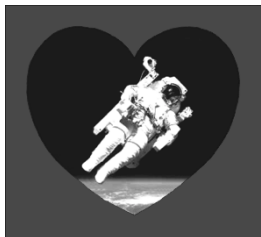


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1930s

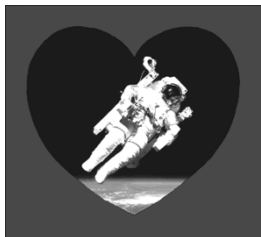
Frederick Berswerth
synthesized EDTA
(by a formaldehyde/cyanide process)
for American marketing
as “Versene”



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1941

Frederick Berswerth
filed first EDTA
patent application
for “Versene,”
finally granted in 1945

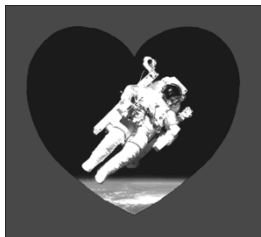


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early 1940s

World War II search
for antidotes to nerve gases

Arsenic = nerve toxin
= metal
= affinity for -SH groups
metal - (SH) - ligand = chelation



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1945

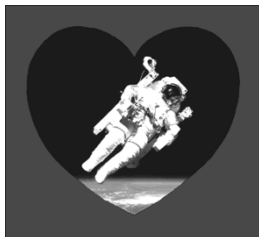
Peters, Stocken, and
Thompson

developed new chelator:

BAL

(Dimercaprol)

(Nature)



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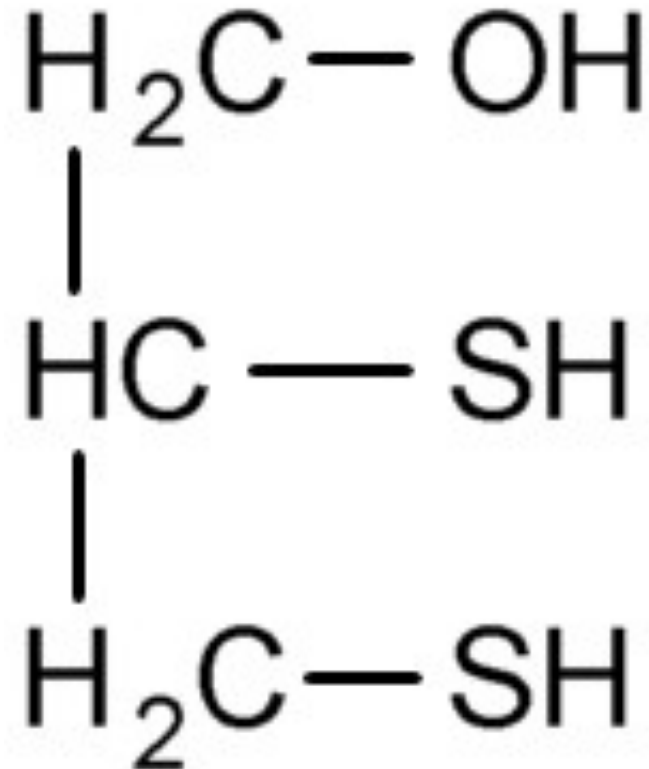
1945

BAL

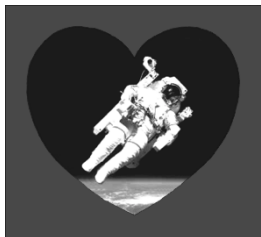
B = British

A = Anti-

L = Lewisite



“Lewisite” = a heavy metal toxin

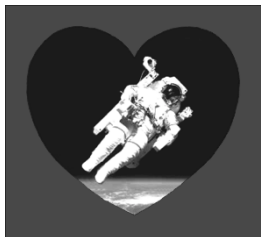
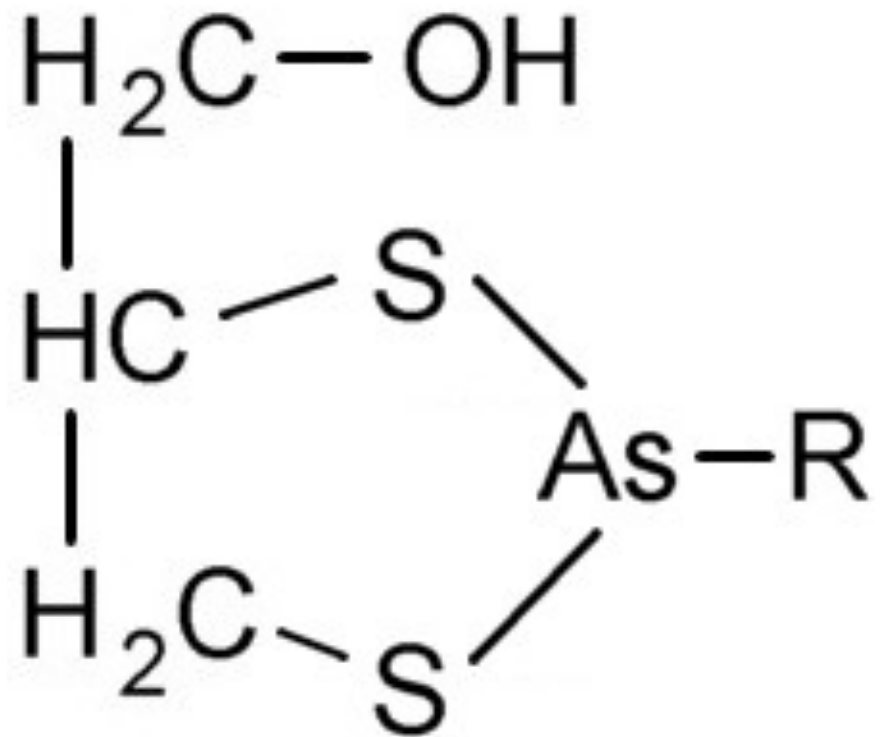


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1945

BAL illustrates
complexing
action of all
chelating
agents

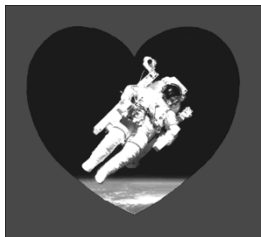


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1945

BAL

as the first drug treatment for
“heavy metal” exposures
marked beginning of the era:
chelation therapy

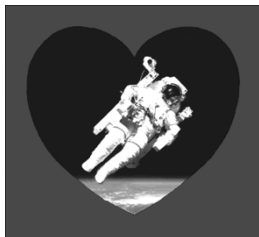


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1947

Martin Rubin
met Berswerth,
later explored EDTA for
calcium chelation
and anti-coagulation
(hematology “lavender-top tube”)

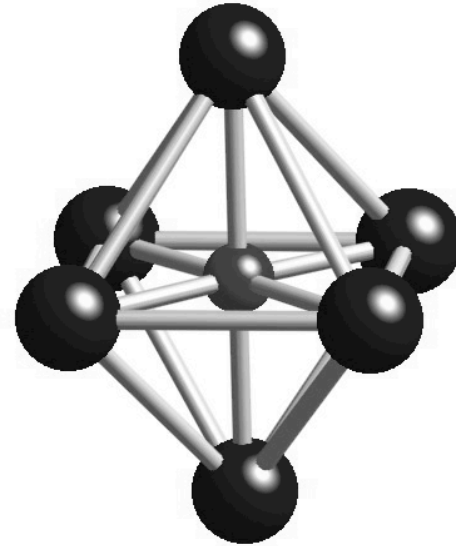
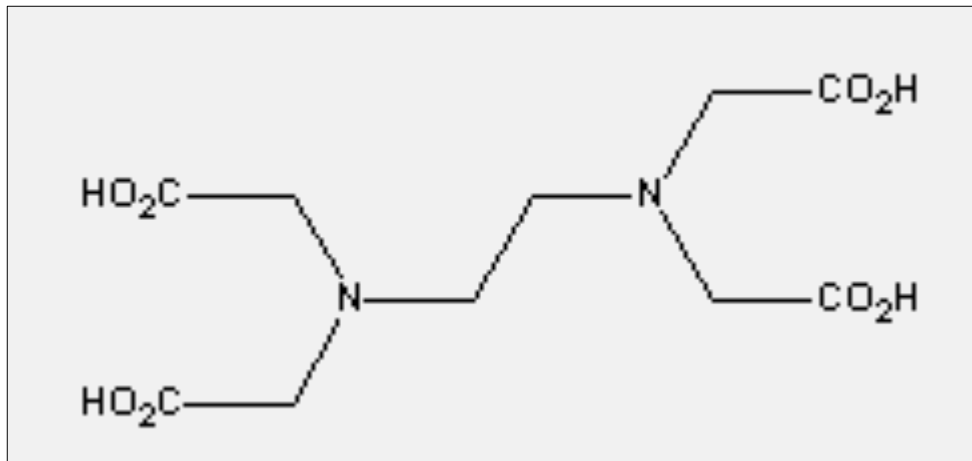
(Bulletin of the Georgetown University Medical Center)



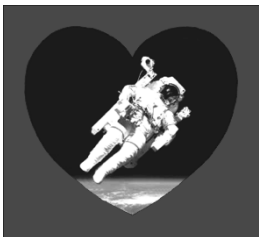
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EDTA



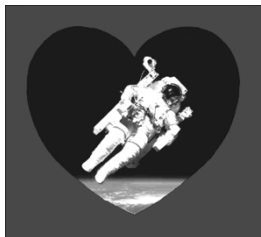
ethylene diamine
tetra-acetic acid



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1947

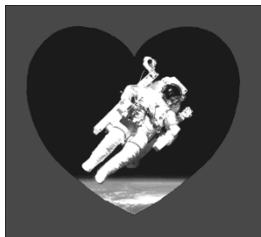
Charles Geschickter
was first physician to
administer (nickel)-EDTA
to a human being
(attempt to treat breast cancer)



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1947

Walter Reed
Army Medical Center
physicians
gave EDTA as attempt to
dissolve kidney
and bladder stones



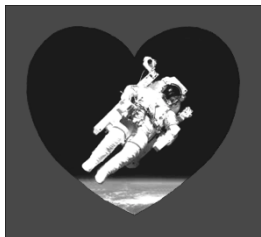
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1950

Rubin and colleagues
showed that iv-EDTA
would chelate plasma calcium
leading to hypocalcemia and urinary
excretion of calcium-EDTA

(Proceedings of the Society for
Experimental Biology and Medicine)



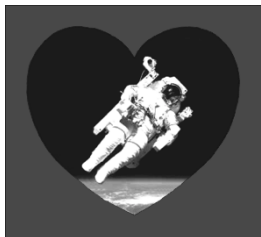
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1951

Rubin and Martell
proposed using
magnesium-EDTA
to lower blood pressure
-- clinicians *not* interested

(Bulletin of the Georgetown University Medical Center)



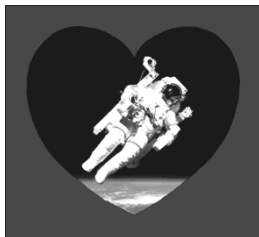
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1952

Rubin and colleagues
showed in vitro that
calcium-EDTA would
exchange with lead, forming
lead-EDTA

(Medical Annals, District of Columbia)



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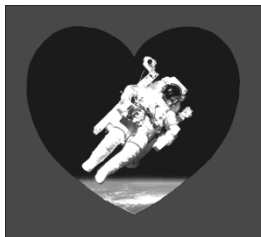
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1952

S. P. Bessman
used calcium-EDTA to
successfully treat a child with
acute lead poisoning

(“Experts” said: “It’ s ***not*** possible”)

(Medical Annals, District of Columbia)

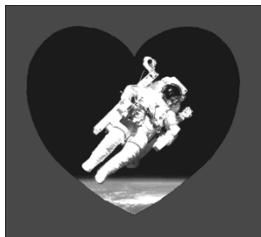


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early 1950s

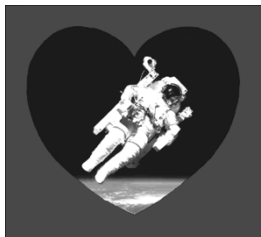
Elderly patients treated
with EDTA for lead poisoning
showed unexpected
dramatic improvements with
coexisting ASCVD



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1950s

Exciting era for
basic science and clinical
research into the properties
of EDTA as a medical
treatment

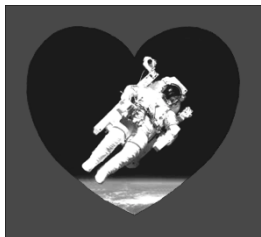


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1950s

“Endrate” brand of EDTA,
marketed by Abbott, used in
medical treatment:

Na₂-salt increases solubility
of the chelating agent



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1952

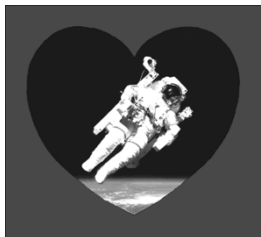
Herta Spencer

first treated

hypercalcemia

with EDTA

(marketed by Abbott as “Endrate”)



(Journal of Clinical Investigation)
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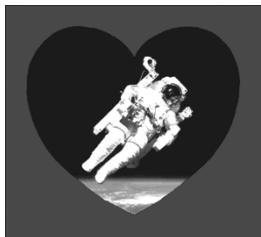
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1950s

Norman E. Clarke, Sr.
did pioneering clinical
studies on EDTA chelation
for ASCVD

at Providence Hospital, Detroit, Michigan



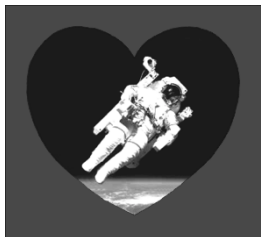
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1950s - 1960s

Norman E. Clarke, Sr.
reported clinical findings
in peer-reviewed journals

*“Father of EDTA Chelation Therapy
in America”*



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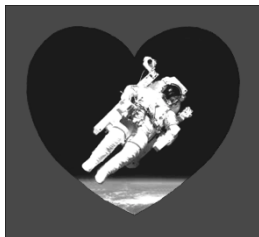
1955

Norman E. Clarke, Sr.

with Clarke and Mosher

first published findings on
effectiveness of EDTA in
treatment of ASCVD

(American Journal of Medical Sciences)

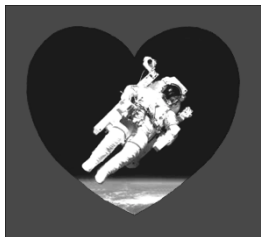


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1955

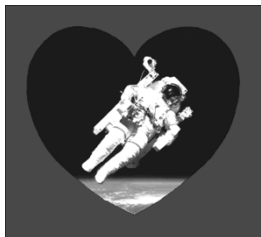
Use of EDTA for ASCVD
marked the acknowledged
beginning of chelation therapy
as a successful cardiovascular
intervention



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1955

Denham Harman
first proposed theory of
free radical damage
as a key factor
in aging and illness



(U. S. Atomic Energy Commission)

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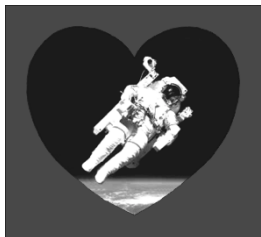
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1956

Clarke, Clarke, and
Mosher

published on 20 EDTA patients:
uniform improvement of
angina and EKG abnormalities

(American Journal of Medical Sciences)



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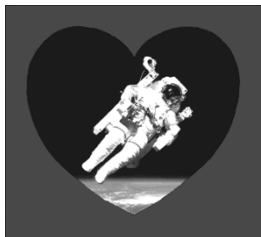
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1957

Denham Harman explained atherosclerosis:

- (1) oxidative polymerization
of serum lipoproteins
- (2) anchoring oxidized material
- (3) inflammatory reactions

(Journal of Gerontology)



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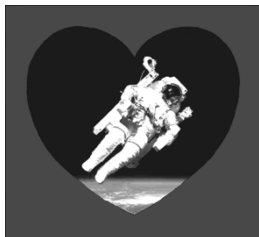
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1957

Gubner and Kallman described EDTA treatment of digitalis toxicity

(although credit is usually given to Surawicz, who
in 1959 - 1961 treated digitalis toxicity
along with relief of cardiac arrhythmias)

(American Journal of Medical Sciences)

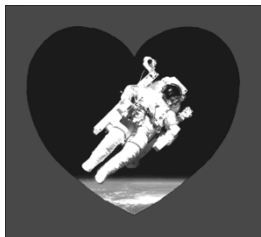


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late 1950s

Fertile years for discovery of
mechanisms and
toxicity of EDTA ...



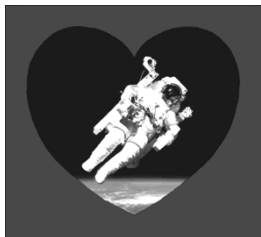
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late 1950s

Boyle -- reversal ASCVD

Perry -- B₆ deficiency,
urinary loss of zinc

Vogt and Cottier -- necrotizing
nephrosis



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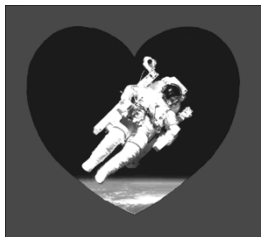
late 1950s

Moeschlin -- nephrosis

Perry -- urinary loss of
trace minerals

Cohen, Spritz, Lubash, and

Rubin -- arrhythmias



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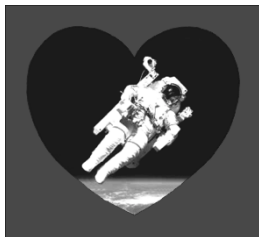
1959

Marvin Seven

hosted first symposium on
“*Metal-Binding in Medicine*”
at

Hahnemann Medical College

(Philadelphia, Pennsylvania)



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1960

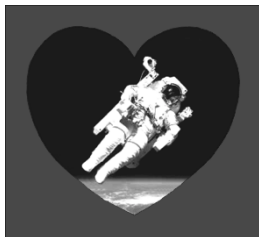
Marvin Seven

hosted second symposium

... then died in 1961

in car accident ...

chelation lost



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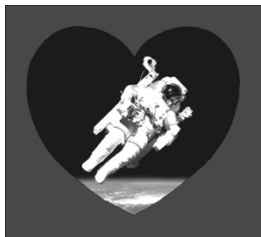
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1960s

H. Ray Evers

continued extensive EDTA
clinical treatment programs:
“Every ASCVD patient
deserves a
therapeutic trial”



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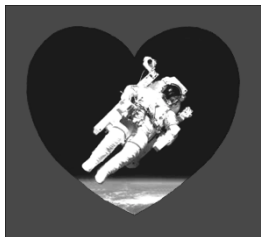
1960

Clarke and Mosher

reported on 283 patients treated with EDTA
for ASCVD over prior 4 years
with 87% improving

without significant clinical side effects

(American Journal of Cardiology)



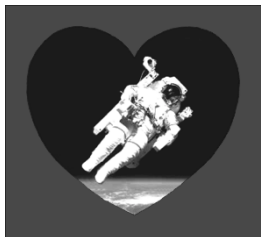
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1960

Meltzer, Ural, and Kitchell

reported on EDTA in 10 men
with CAD/angina:
delayed improvements in 90%,
no significant toxicity
(in *Metal-Binding in Medicine*)



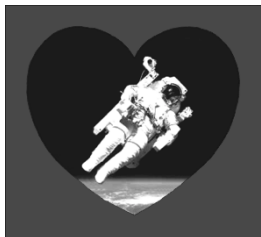
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1961

Meltzer, Kitchell, and Palmon

published comprehensive
clinical toxicology of EDTA
in 81 patients with CAD over 2 years:
“Used without danger”
(American Journal of Medical Sciences)



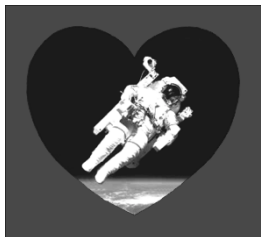
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1961

Catsch

reviewed various chelating agents
against various
radioactive metals

(Federation Proceedings)

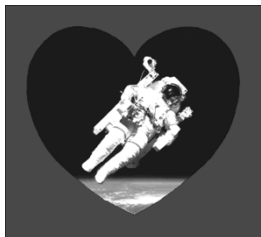


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1962

L. W. Wilder and colleagues
showed arterial calcium released
by EDTA perfused over plaque
was proportional to degree of
atherosclerosis present

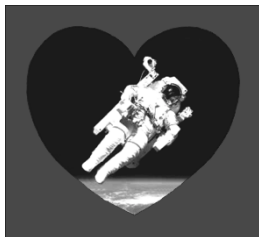
(Surgery)



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1964

Albert Soffer
edited monograph,
Chelation Therapy,
describing benefits of
EDTA in ASCVD



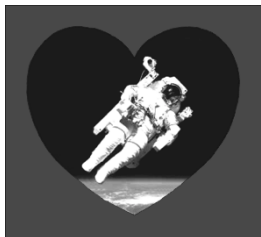
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1964

Carlos Lamar
coined term for EDTA as
“chemical endarterectomy”
and published on vascular
improvements in 15 diabetics

(Angiology and
Journal of American Geriatric Society)



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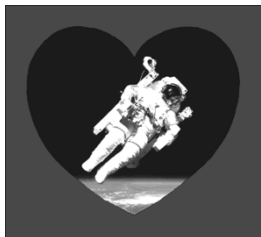
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late 1960s

Renewed research into
EDTA mechanisms ...

Wartman -- plaque reversal

Doolan and Schwartz --
pinocytosis in kidney



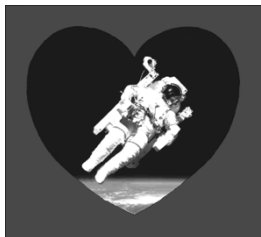
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late 1960s

Boyle and McCann --
raise parathyroid hormone

Olwin and Koppel --
lower plasma lipids

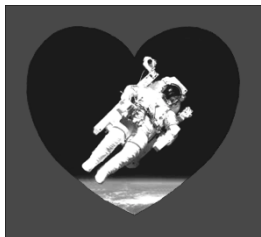
Langhof -- lower cholesterol



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1969

Abbott's patent expired
on EDTA, leaving it an
“orphan drug”
-- the final blow to
American chelation research

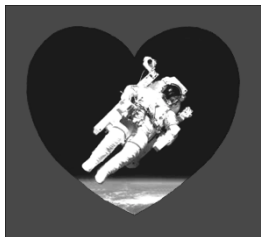


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1973

Harry Demopoulos
published on
free radicals
in vascular pathology

(Federation Proceedings)



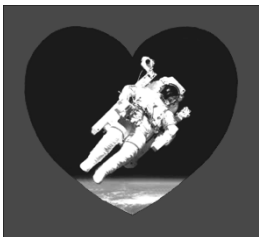
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1973

AAMP

American Academy of
Medical Preventics

-- Harold Harper
was first president



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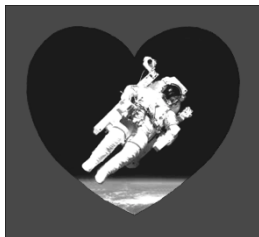
1976

W. A. Pryor

edited a series

of several volumes:

Free Radicals in Biology



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1976

Garry Gordon and Robert Vance

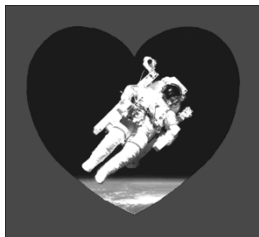
published extensively referenced article
on history and mechanisms
of EDTA chelation

(Osteopathic Annals)

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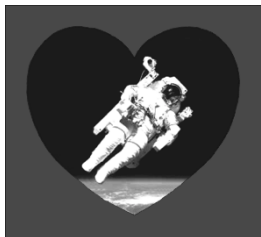
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1976

Tamburino and colleagues
reported osteoporosis is
reversed by EDTA, where
PTH
increases osteoblastic activity

(IRCS Medical Science Library Compendium)

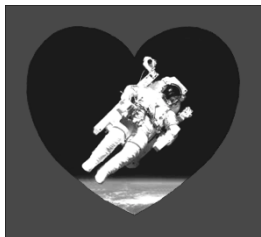


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1977

Peng and colleagues
showed EDTA improves
mitochondrial energy
production in ischemic
myocardium

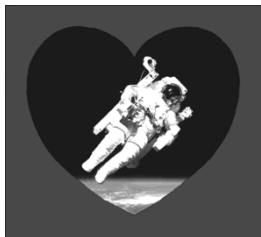
(Journal of Molecular and Chemical Cardiology)



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1978

H. Ray Evers
won on federal court appeal:
“Physician may vary the
conditions of drug use from
those approved on insert”



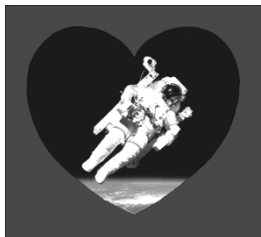
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1979

Hollander and
colleagues

reported reduction of aortic
atheromatous lesions
in *EHDP*-chelated rabbits

(Atherosclerosis)



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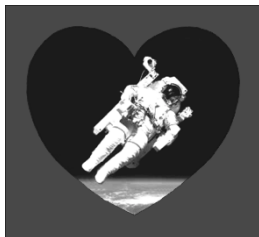
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1979

Bruce Halstead

published monograph,

*The Scientific Basis of
EDTA Chelation Therapy:*
“significant improvements”



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1980

Blumer and Reich

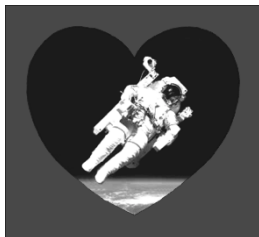
showed EDTA

reduced cancer *incidence*

by 90% in 59 patients

over *10* years

(Environmental International)



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1980

Walker

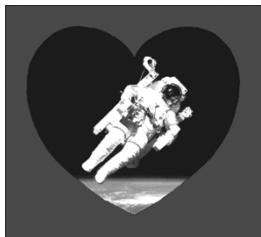
showed EDTA

removes calcium from

arteriosclerotic plaque

in rabbits

(Ph.D. thesis, Texas State University)



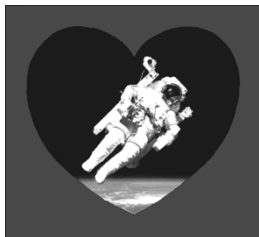
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1980

J. Bjorksten
published theories on
life extension potential
of EDTA chelation therapy

(Rejuvenation)



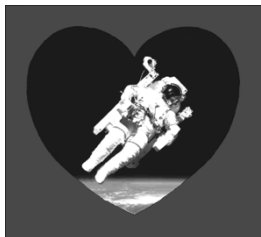
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early 1980s

H. Richard Casdorph

published key studies on
effectiveness of EDTA in
CAD, cerebrovascular, and
peripheral arterial disease



(Journal of Holistic Medicine 1981, 1983)

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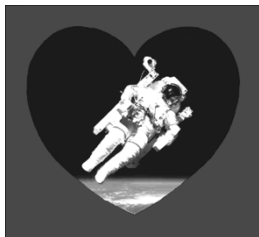
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1980s - early 1990s

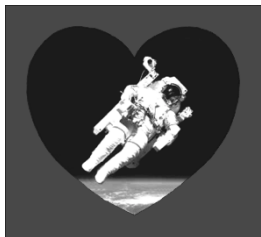
McDonagh, Rudolph,
Cheraskin, and colleagues
published a long series of
EDTA clinical studies
documenting improvements



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1980s - early 1990s

McDonagh, Rudolph, and
Cheraskin showed improvements with
HDL lipoproteins, blood cholesterol,
arterial stenosis, creatinine, BUN,
fasting serum calcium, glycohemoglobin,
fatigue, heart rate, systolic BP, “clinical
change,” vascular dynamics, bone density



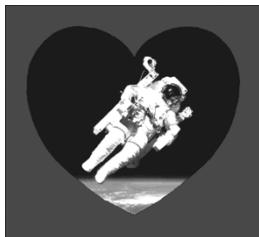
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1983

ABCT

American Board of
Chelation Therapy

-- Charles Farr
was first chair



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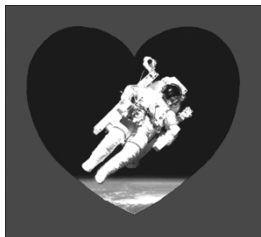
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1983

GLACM

Great Lakes Association
of Clinical Medicine

-- Jack Slingluff
was first president



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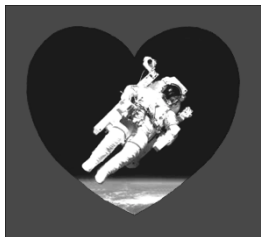
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1983

ISCT

International Society of
Chelation Technicians

-- Robert White
was first executive director



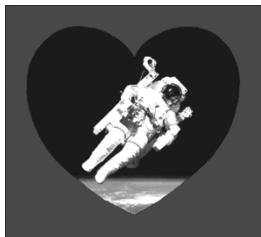
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1984

**Elmer Cranton and
James Frackelton**
published definitive review:
“Free Radical Pathology in
Age-Associated Diseases”

(Journal of Holistic Medicine)



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1985

A. Zechmeister

demonstrated in mini-pigs
arterial calcification patterns:
“macro” in cerebral
“macro + micro” in coronary
“micro” in peripheral

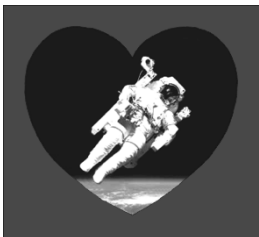
(Czechoslovakia)

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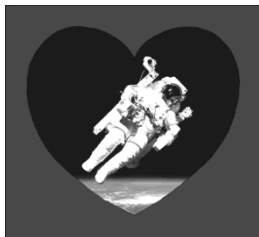
1986

FDA granted an IND

(Investigational New Drug)

**application authorizing the
study of EDTA
chelation therapy
in peripheral ASCVD**

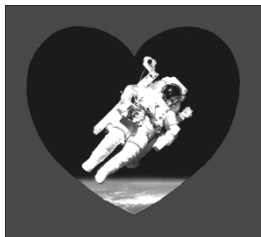
(#128.847)



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1986
AAMP
changed its name to
ACAM
American College for
Advancement in Medicine



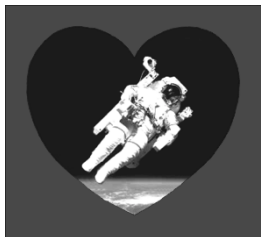
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1987

IBOM

International Bio-Oxidative
Medicine Foundation

-- Charles Farr
was first chair



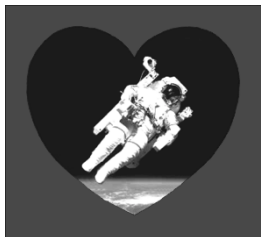
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1988

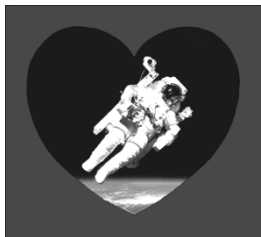
Olszewer and Carter
published on 2,870 patients:
77% markedly better with CAD,
91% markedly better with
peripheral ASCVD

(Medical Hypothesis)



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1988
JAM
Journal of
Advancement in Medicine
first published by ACAM
-- Elmer Cranton
was first editor



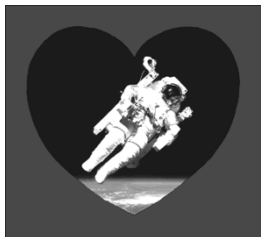
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1988

Deucher

published observations on
EDTA as antioxidant strategy:
good to excellent results in
91% of patients

(Journal of Advancement in Medicine)



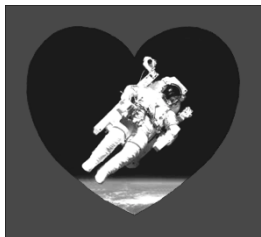
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1989

Cranton

edited a special edition of
Journal of Advancement in Medicine
detailing safe and effective
administration of EDTA

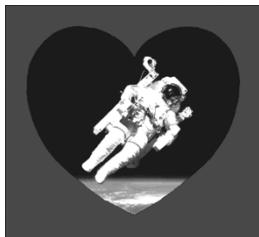


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1989

Cranton and Frackelton
reviewed current status of
EDTA chelation in ASCVD:
safe and effective,
less expensive than bypass

(Journal of Advancement in Medicine)

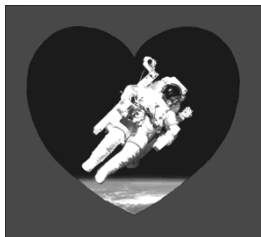


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1989

Blumer and Reich
showed EDTA
reduced cancer *deaths*
by 90% in 59 patients
over 18 years
(Journal of Advancement in Medicine)

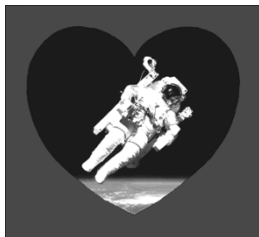


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1989
IRB
(Institutional Review Board)
founded by GLACM

(now ICIM)

-- L. Terry Chappell
was first chair



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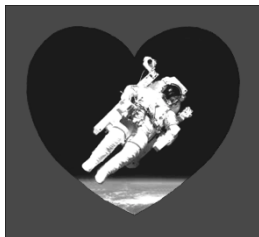
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1990

Olszewer, Sabbag,
and Carter

published first double-blind,
placebo-controlled EDTA study
in peer-reviewed journal

(Journal of the National Medical Association)



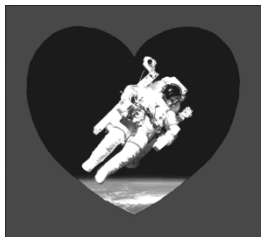
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1990

Olszewer, Sabbag, and Carter:

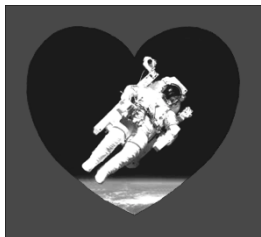
10 patients with claudication,
5 walked significantly better
after 10 treatments (of 1.5 g EDTA)
so code broken and all 10 then
showed treatment improvements with EDTA
(Journal of the National Medical Association)



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1990

Robert Rowen
persuaded Alaska State
Legislature to pass first law:
“freedom of choice
in health care”



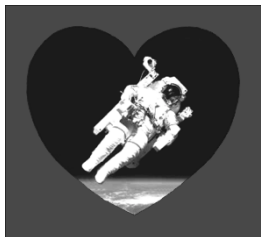
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1991

Rudolph, McDonagh, and Barber

published Doppler results

in 30 patients with carotid artery
stenosis, 30 treatments each:
21% plaque reduction



(Journal of Advancement in Medicine)
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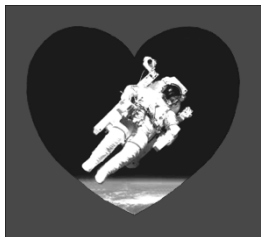
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1990 - 1992

FDA IND-study of EDTA

in peripheral ASCVD

ground to a halt as U. S. Army
medical personnel were
transferred to Operation
Desert Storm



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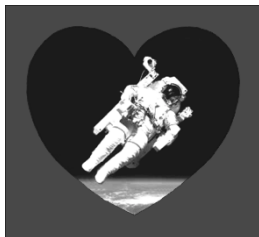
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1992

Salonen and colleagues
studied 1,931 asymptomatic
Finnish men for 3 years:
iron (as *ferritin*) showed
increasing risk for MI

(Circulation)

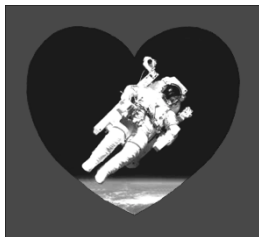


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1992

Salonen and colleagues
demonstrated that *ferritin*
is second strongest risk
factor for myocardial infarct,
following cigarette pack-years

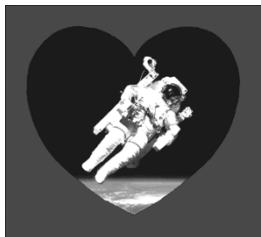
(Circulation)



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1992
APMA
American Preventive
Medical Association
-- Alexander Schauss
was first executive director



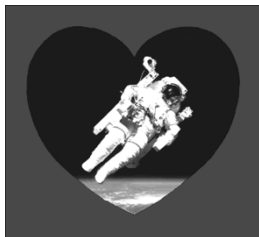
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1993

Chappell and Stahl
published meta-analysis of
19 EDTA studies -- 22,765 patients
with vascular disease:
87% improved

(0.88 correlation coefficient)

(Journal of Advancement in Medicine)



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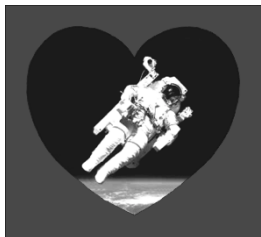
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1993

Hancke and Flytlie

published Danish *medical* study
of pre-surgery EDTA patients:
58 of 65 *cancel* planned CABG,
24 of 27 limbs *saved*

(Journal of Advancement in Medicine)



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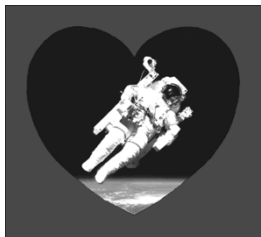
1993

IRB

(Institutional Review Board)

founded by ACAM

-- Stephen Elsassser
was first chair



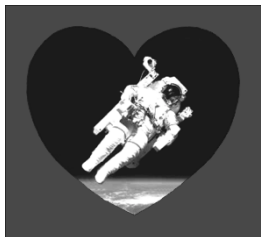
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1994

Rubin, Rozema,
Casdorph, and Scarchilli
presented ultrafast CT scans in
2 patients showing EDTA
decreased
coronary artery calcification

(American Chemical Society)



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1994

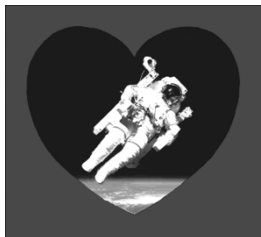
Denham Harman

reviewed functional life span:

“Aging is accumulation of
free radical changes ...

life span is determined by
rate of damage”

(Age)



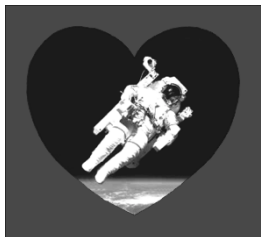
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1995

Escobar and colleagues
noted marked improvement in
76 of 80 patients treated
with EDTA for peripheral
ASCVD

(Surgery and Surgeons)



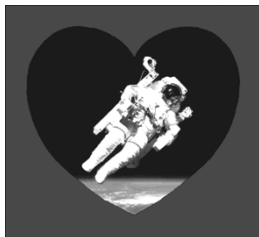
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1996

**Philip Hoekstra III
submitted results of
tele-thermography in
19,147 EDTA patients with
peripheral ASCVD showing
86% improved**

(pre-publication)



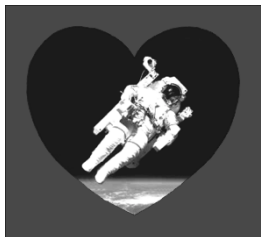
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100

1996

Chappell and Janson reported on history and current status of EDTA treatment in vascular disease

(Journal of Cardiovascular Nursing)



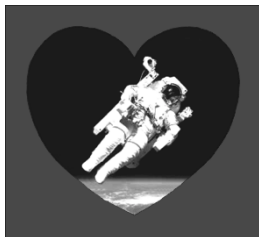
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1996

Michael Schachter published overview, history, and status of EDTA treatment for atherosclerosis

(Journal of Advancement in Medicine)



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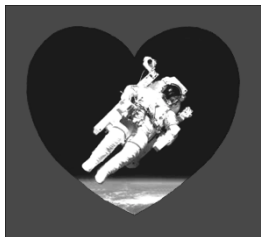
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1996

Olszewer, Sabbag, and Carter

reported Brazilian experience
with 100,000+ EDTA patients and
small prospective studies showing
minimal side effects

(Townsend Letter)



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1996

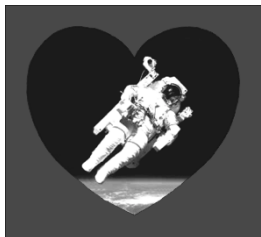
Martin Rubin

published “Magnesium
EDTA Chelation”

chapter in Messerli’ s

Cardiovascular Drug Therapy

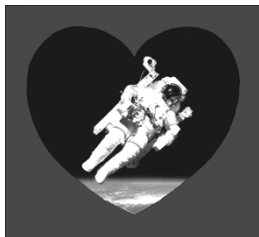
(second edition)



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1996
GLACM
changed its name to
GLCCM
Great Lakes College
of Clinical Medicine



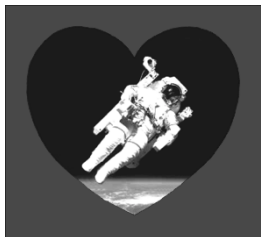
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1997

Bruce Halstead and Ted
Rozema

published updated edition of monograph,

*The Scientific Basis of
EDTA Chelation Therapy:*
still significant improvements



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late 1990' s

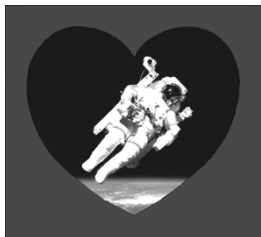
Rozema, Kindness, et al.

studied compounded

EDTA rectal suppositories

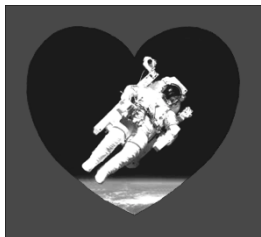
showing marked excretion of

lead in children



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2000
GLCCM
changed its name to
ICIM
International College
of Integrative Medicine

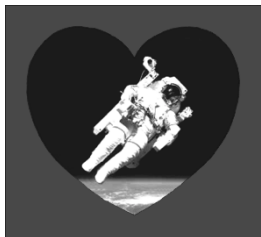


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2002

National Institutes of Health
announced \$35 million
for 5-year multi-center NIH

“TACT” study of EDTA
chelation
for coronary artery disease

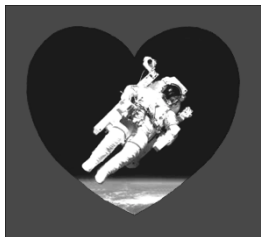


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2003

Lin, Lin-Tan et al.
reported EDTA chelation improves
progressive *non*-diabetic
renal insufficiency
that is otherwise accelerated
by low-level lead exposure

(NEJM)



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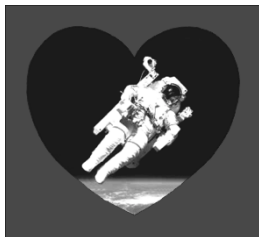
2003

ABCMT

American Board of Chelation Therapy
changes its name to

American Board of Clinical Metal Toxicology

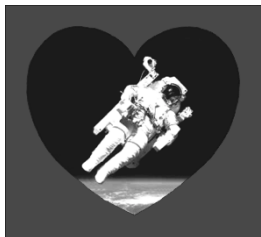
(Same for International Board as well)



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DMSA



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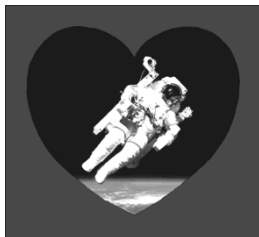
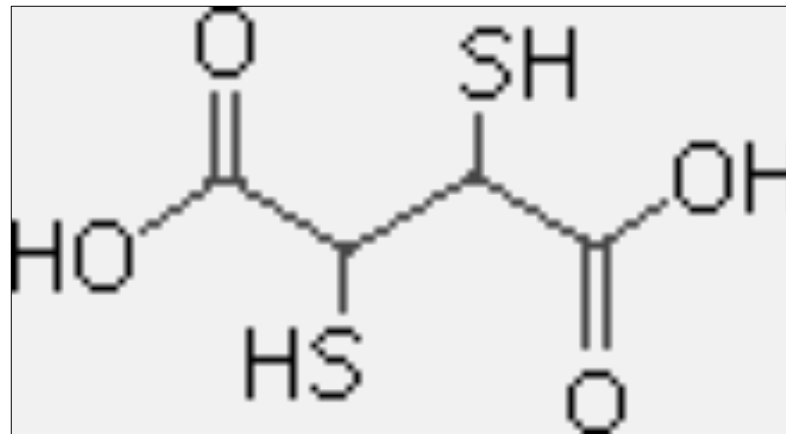
1950' s

DMSA

(meso 2,3-dimercaptosuccinic acid)

is a dithiol (two-SH groups)

analog of BAL,
lipid-soluble



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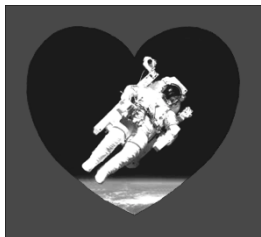
1954

DMSA

studied extensively in

Soviet Union

(Unithiol)



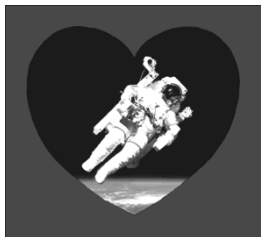
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1950' s

DMSA

(also known now as Chemet[®],
Succimer[®], or Captomer[®])

was extensively studied
in China (PRC) and Japan?
(for lead and other metals)

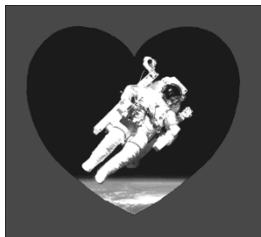


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1957

Prior to use of chelation for
lead intoxication, death rate
for lead encephalopathy
was about 60%

(Chisholm and Harrison, Pediatrics, 1957)

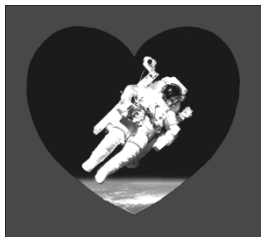


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1960' s

Lead encephalopathy
treated with chelation
lowered death rate
to 30%

(Chisholm, Pediatrics, 1974)

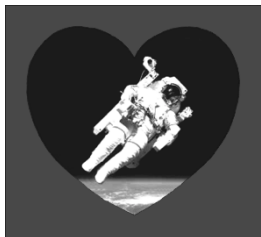


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1975

DMSA used in mercury
toxicity in 1970's
-- reported by Friedheim as
having low toxicity in mice

(J Pharm Pharmacol, 1975)



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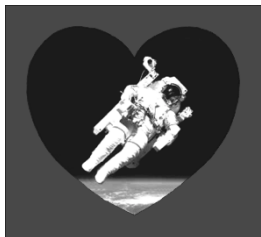
1978

**DMSA administration increases
urinary mercury excretion and
reduces blood and tissue
mercury concentration,
especially in brain**

(Aaseth and Friedheim, Acta Pharmacol Toxicol, 1978)

(Butterworth et al, Can J Neurol Sci, 1978)

(Kostyniak, J Toxicol Environ Health, 1983)



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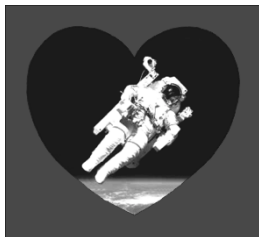
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1981

DMSA shown effective in treatment of arsenic poisoning

(Lenz et al, Acta Toxicol, 1981)

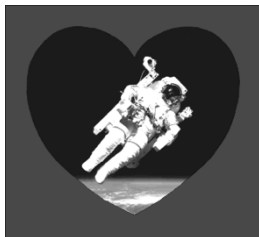


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1983

DMSA shown effective as heavy metal antidote by multiple routes of administration

(Aposhian, Ann Rev Pharmacol Toxicol, 1983)

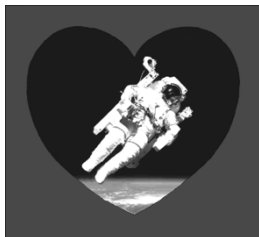


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1984

DMSA shown as effective
antidote for arsenic poisoning
and other heavy metals ...
but “orphan drug” and
difficult to obtain funding

(Aposhian et al, Fund & Appl Toxicol, 1984)

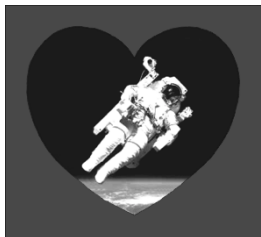


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1984

Provoked excretion (DMSA) of
mercury and other heavy
metals proposed as only way
to estimate
total body burden

(Zhang, Am J Indust Med, 1984)



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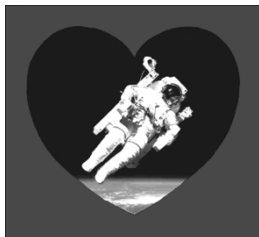
123

1985

DMSA shown to be
effective and safe chelator
for lead poisoning,
reducing blood levels by 35%

(Graziano et al, Clin Pharmacol Ther, 1985)

(Fournier et al, Med Toxicol Adv Drug Exp, 1988)



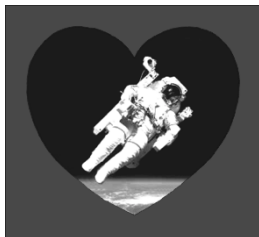
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1990

Effectiveness of lowering
blood lead levels
brings proposals to lower
blood levels for treatment

(Chisholm, Environ Health Perspect, 1990)

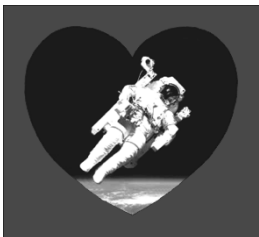


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1991

DMSA (as Chemet )
approved by FDA
as “orphan drug” for
treating lead poisoning
in children



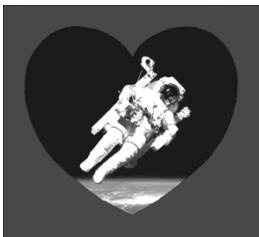
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1991

DMSA successfully used to treat mercury poisoning in exposed workers

(Roels et al, Br J Ind Med, 1991)

(Bluhm et al, Hum Exp Toxicol, 1992)



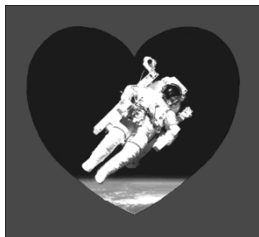
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2000

DMSA concluded
to provide optimal safety
and effectiveness for
treatment of lead poisoning
in children

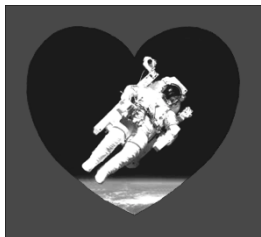
(Chisholm, J Toxicol – Clin Toxicol, 2000)



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DMPS



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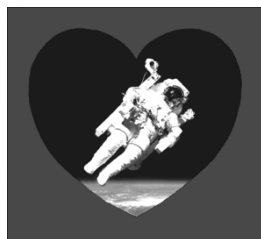
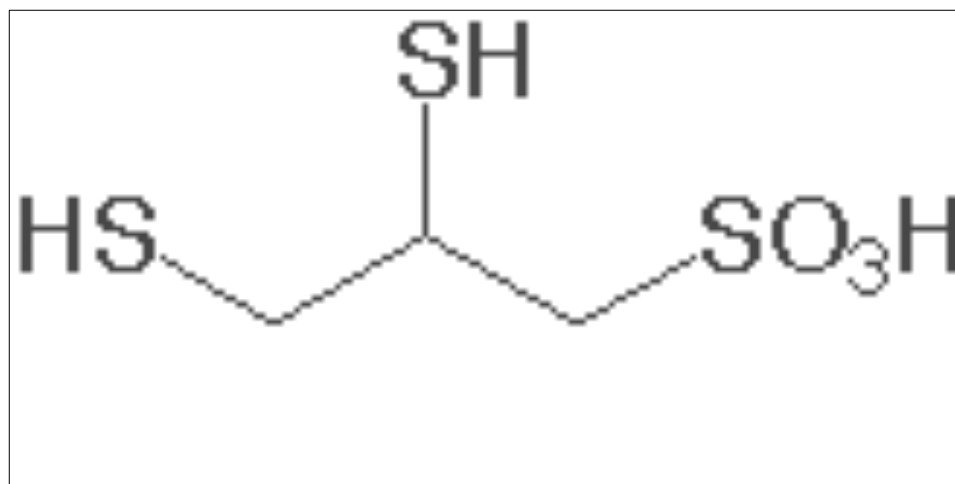
early 1940' s

DMPS

(2,3-[di]mercapto-propane-1-sulfonic acid)

is a dithiol (two-SH groups)

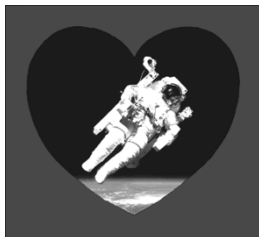
analog of BAL,
lipid-soluble
(Dimaval)



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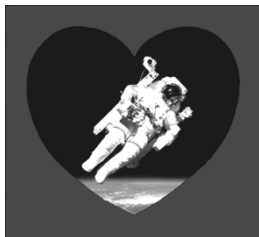
early 1940' s
Peters and Stocken
discovered DMPS
when searching for antidote
to use against arsenical
nerve gases (BAL)



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1945

Peters and Stocken
chose to concentrate on
BAL as arsenic antidote
due to ease of production
in large quantities

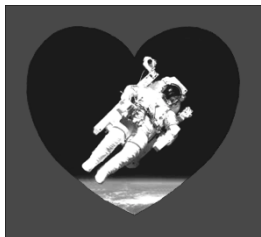


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1970' s

Soviet studies showed
DMPS to be effective in
treatment of various
heart and blood vessel
conditions

(Kurliandchikoc, Zapacnick)



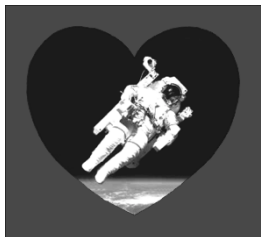
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1978

DMPS

available for research and
clinical use when produced
by German company, Heyl
(Dimeval)

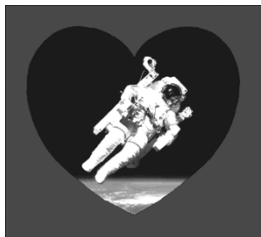


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1981

DMPS reported most effective
in removal of
methyl mercury
in Iraqi wheat
disaster in 1972

(Clarkson et al, J Pharmacol Exp Ther, 1981)



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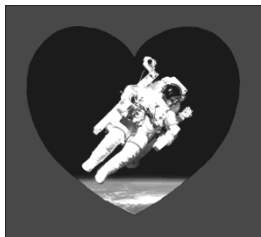
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1983

**Aposhian reported on
DMPS and DMSA
as water-soluble antidotes for
arsenic, lead, mercury, other
toxic heavy metals**

(Aposhian, Ann Rev Pharmacol Toxicol, 1983)



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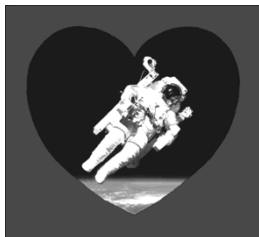
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1983

Hoover and Aposhian argued
that BAL – the “approved”
military chelator – is 300
times *more* toxic than DMPS
and causes redistribution to
brain tissue

(Hoover and Aposhian, Toxicol Applied Pharmacol, 1983)



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137

mid-1980' s

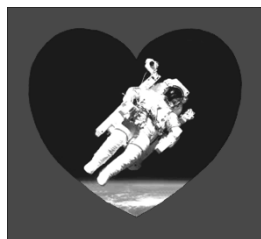
DMPS is used extensively in Europe to remove arsenic, lead, and mercury – only limited use in United States

(arsenic – Aposhian et al, Fund & Appl Toxicol, 1984)

(lead - Chisholm and Thomas, J Pharmacol Exp Ther, 1985)

(mercury - Campbell et al, J Am Med Assoc, 1986)

(mercury - Schiele et al, Occup Med Soc Med Prevent Med, 1989)



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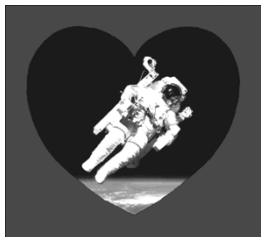
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1992

Aposhian showed mercury excretion provoked by DMPS correlated well with dental amalgam scores

(resting blood or urine levels show little correlation with
body burden in low-level chronic exposures)

(Aposhian et al, FASEB J, 1992)



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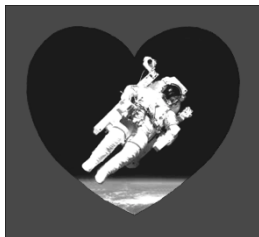
1995

Aposhian showed DMPS
(*unlike* BAL and EDTA)

does *not* cross blood-brain
barrier, does not redistribute
mercury into brain

(Aposhian et al, Toxicol, 1995)

(Aposhian et al, Toxicol, 1996)

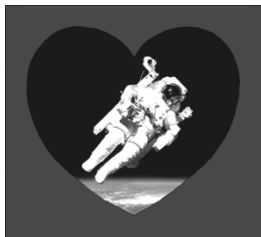


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1995

Aposhian proposes BAL and
CaNa₂EDTA are outmoded:
DMSA will be used for lead,
DMPS will be preferred for
lead, arsenic, and mercury

(Aposhian et al, Toxicol, 1995)

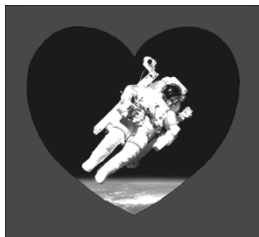


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1997

Ruprecht prepares Scientific Monograph, Dimaval (DMPS), extensively referencing European safety and efficacy literature

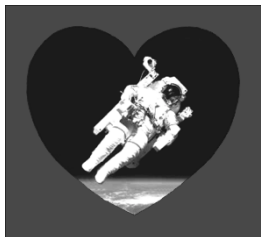
(Houston, Texas: Heyltex Corporation, 1997)



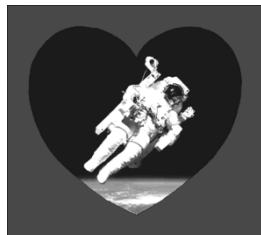
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Today and beyond
Look around *you* ...
Tomorrow's history
is being made today
by people you're looking at
right now ...



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