Heavy metals and chronic diseases: what therapeutic approaches?

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www.tierversuchsfreie-medizin.de

Calcium

- Calcium is the most abundant metal in the human body.
- The average adult body contains about 1 kg.
- Calcium is important for structure and function of the human body.

Structure

- 99% Calcium in the bones and teeth

Function

- secondary messenger
- energy metabolism
- neuromuscular junction

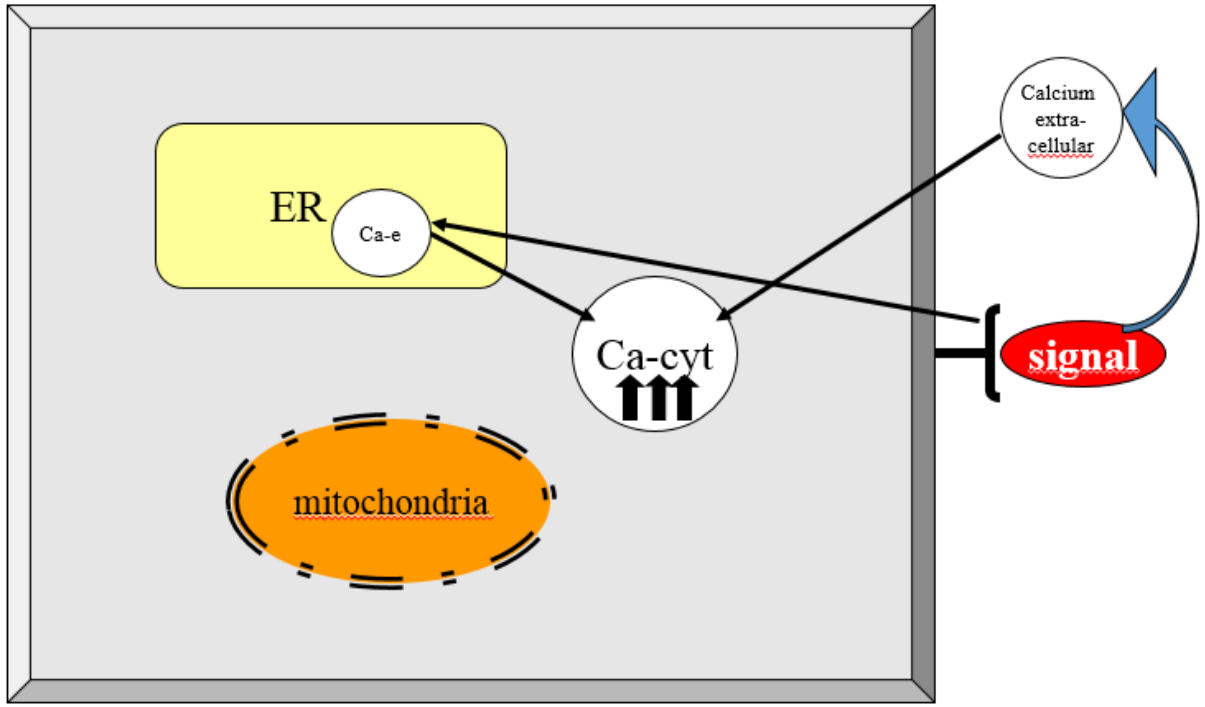
Calcium - a secondary messenger

As a secondary messenger calcium is important for the cell-regulation by hormons and transmitters

This is important for:

- muscle contraction
- synthesis and secretion of neurotransmitters / hormones
- gene-expression
- regulation of enzyme activity
- regulation of ion pumps

Calcium - a secondary messenger

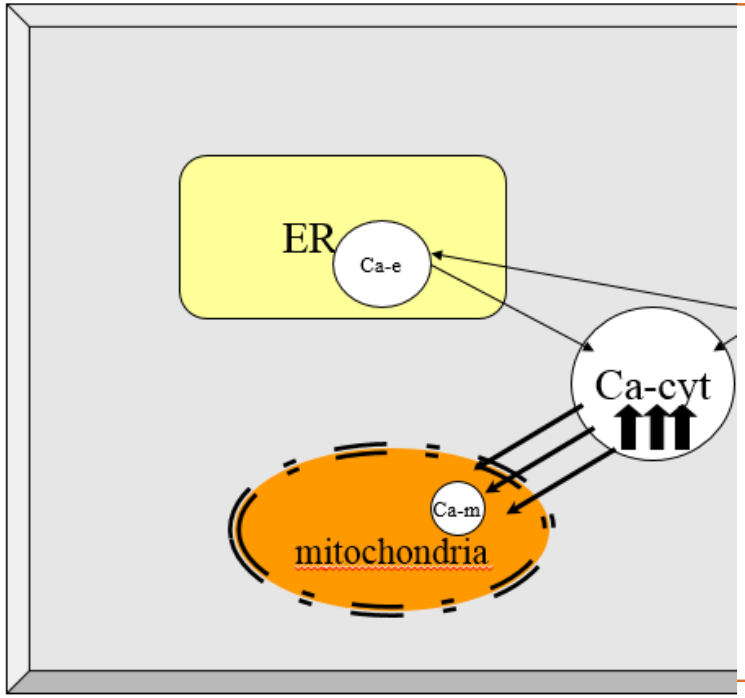


Hormons and transmitters change membrane receptors

opens plasma membrane calcium channels

stimulate the release of calcium ions (Ca2+) from intracellular stores (>the endoplasmic reticulum)

Calcium uptake in mitochondria



The Ca(2+) uptake can be divided into the following three steps:

1.- Ca(2+) movement from the endoplasmic reticulum to the outer mitochondrial membrane (OMM)

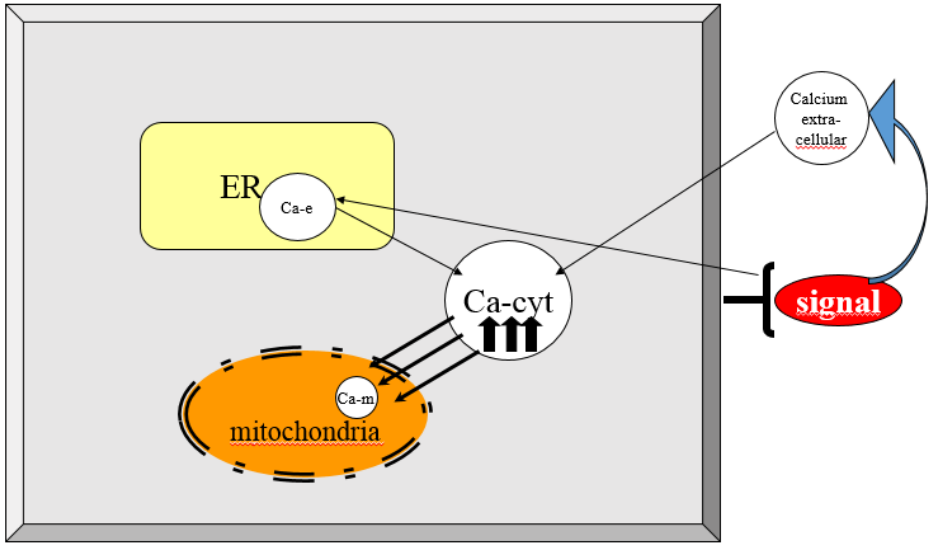
2. - Ca(2+) transport through the OMM

3. - Ca(2+) transport through the inner mitochondrial membrane (IMM)

Cell Calcium (Scotland) Nov-Dec 2002, 32(5-6) p363-77

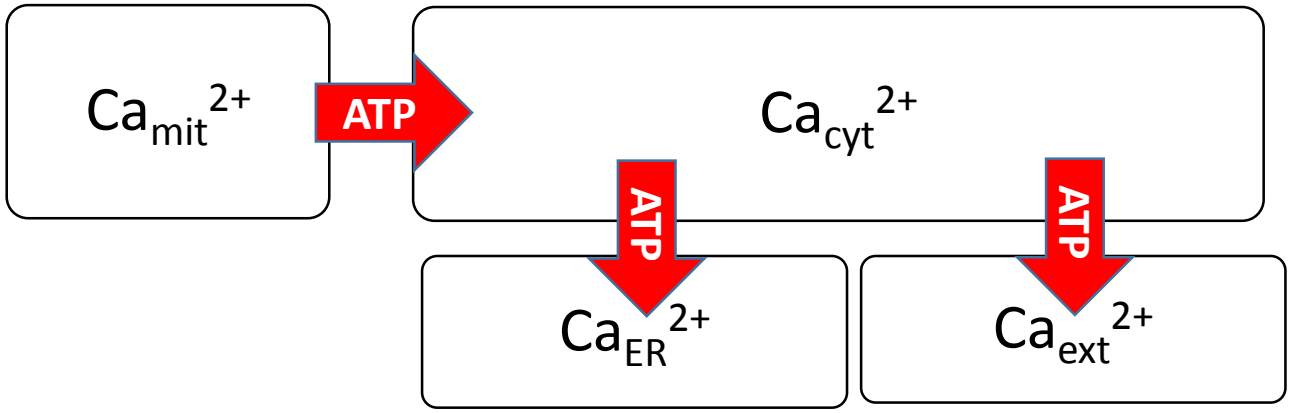
The intramitochondrial Ca(2+) controls the ATP production by oxidative phosphorylation

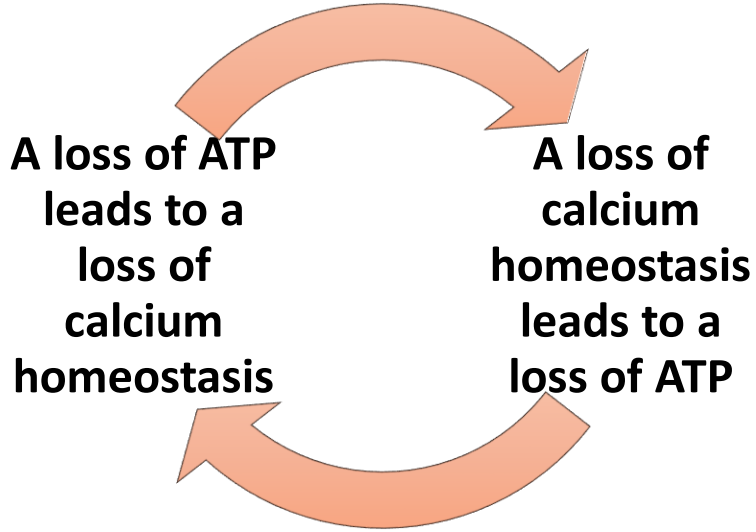
Cell-signals are linked with the ATP production via the Ca(2+) oscillations

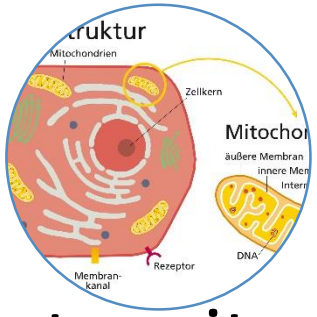


Energized mitochondria must expend a significant amount of energy to transport Ca(2+) against its electrochemical gradient from the matrix space to the external space.

Am J Physiol (United States), May 1990, 258(5 Pt 1) pC755-86







Accumulation of calcium into mitochondria play a key role as a trigger to mitochondrial pathology,

especially when the calcium uptake is accompanied by another stressor, in particular ROS or RNS

Duchen MR. Diabetes. 2004 Feb;53 Suppl 1:S96-102.

EMF causes altering of intracellular Ca^{2+} homeostasis

This mode of action was further supported by hundreds of studies showing microwave changes in calcium fluxes and intracellular calcium [Ca2+]i signaling.

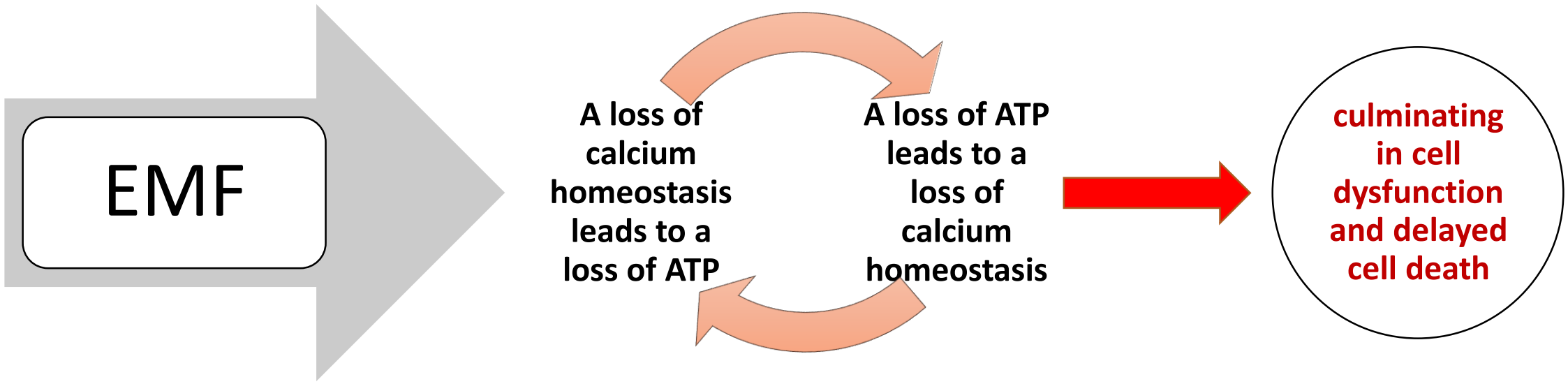
Pall M. Rev Environ Health. 2015 Apr 16

Extremely low-frequency electromagnetic fields (ELF-EMF) causes various biological effects through altering intracellular calcium homeostasis.

Cui Y, Liu X, Yang T, Mei YA, Hu C. Cell Calcium. 2014 Jan;55(1):48-58.

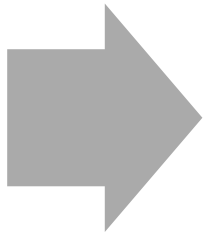
Together, these findings indicate that ELF-EMF exposure specifically influences the intracellular calcium dynamics of neurons via a calcium channel-independent mechanism.

Luo FL, Yang N, He C, Li HL, Li C, Chen F, Xiong JX, Hu ZA, Zhang J. Environ Res. 2014 Nov;135:236-46


EMF
A loss of calcium homeostasis leads to a loss of ATP
A loss of ATP leads to a loss of calcium homeostasis
culminating in cell dysfunction and delayed cell death

Mimicry of toxic metals

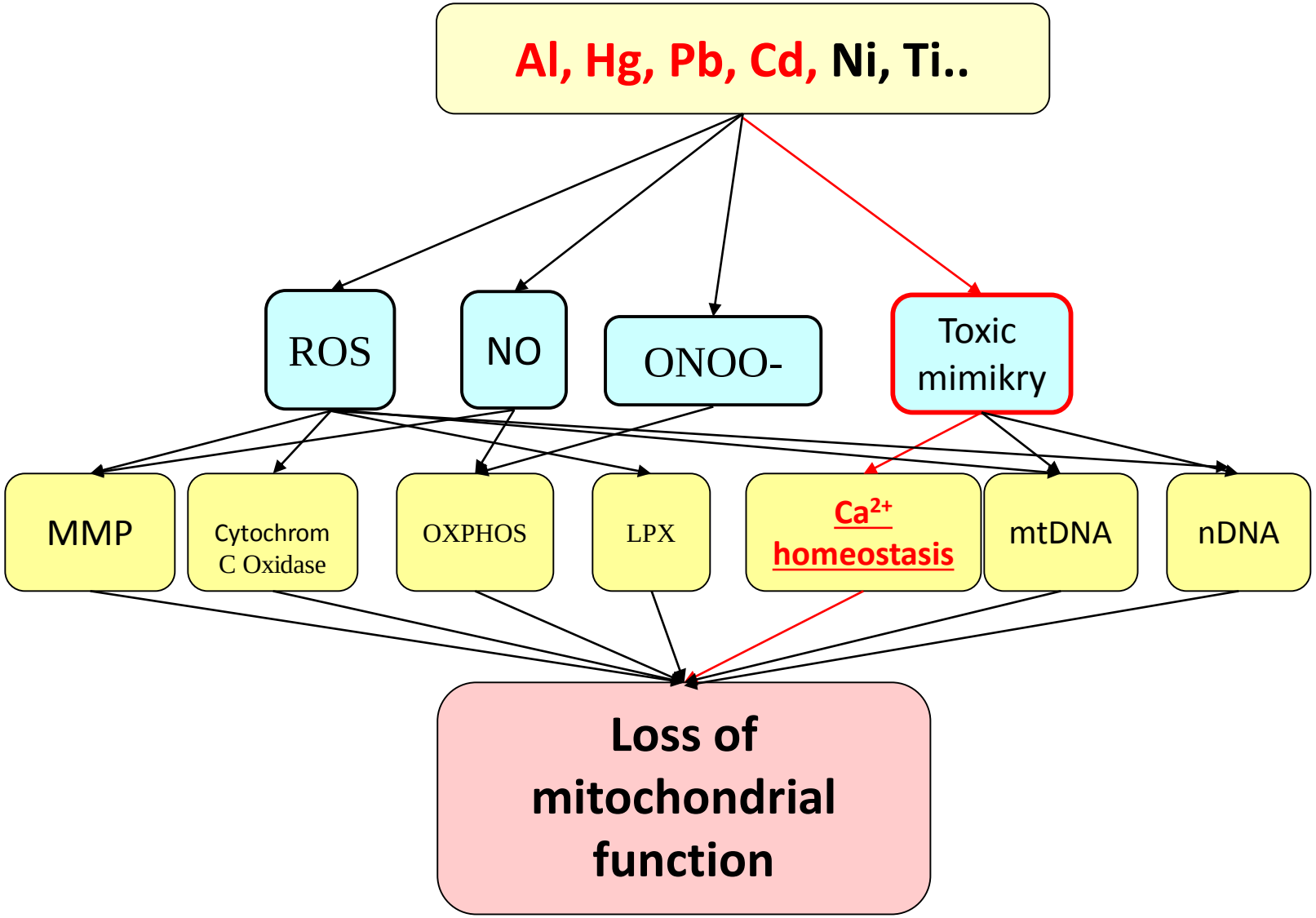
Toxic metals (Al,As,Cd,Hg,Pb,..) can displace essential metals (Mg,Ca,Fe and Zn)

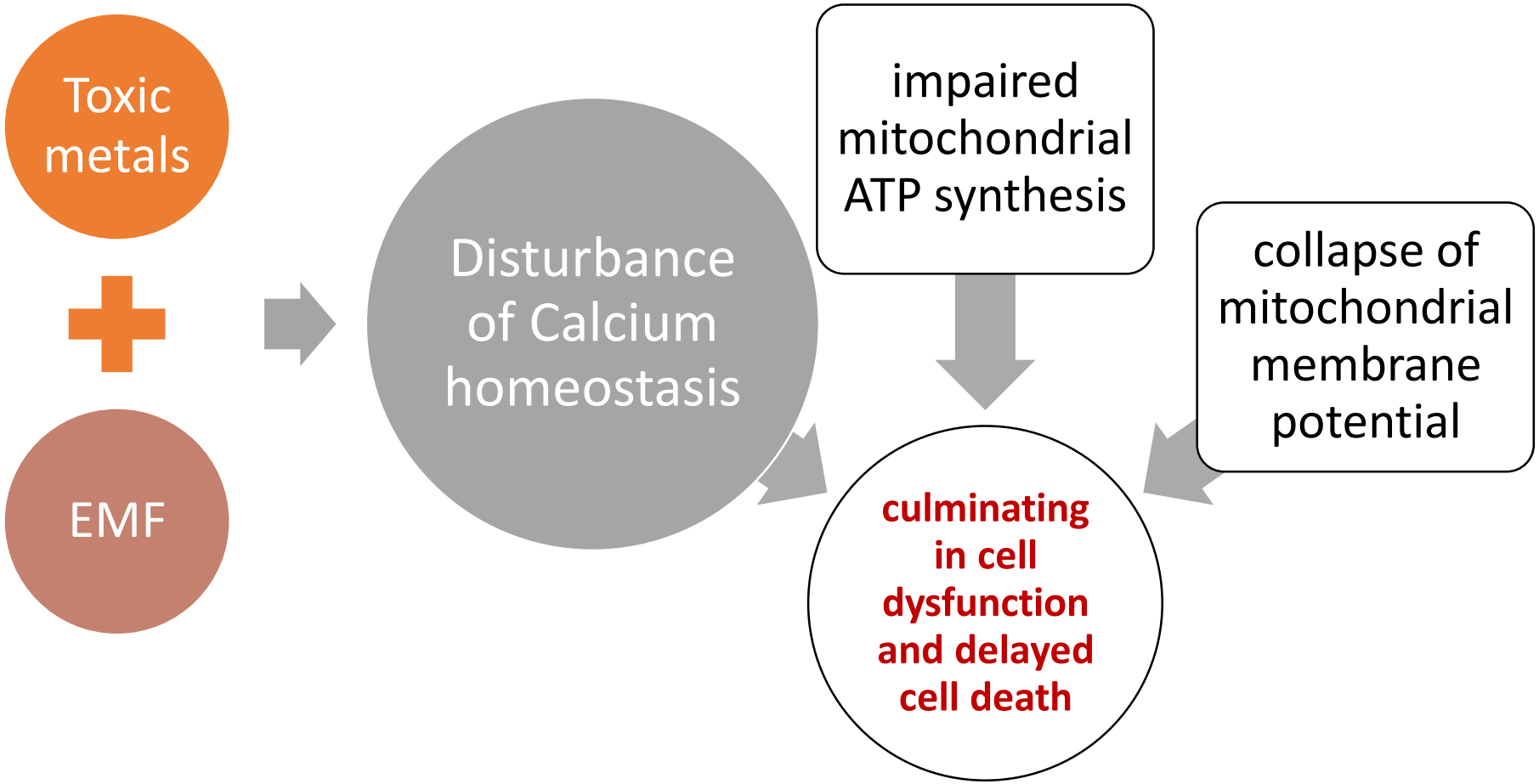


The consequence is a loss of function from small molecules, enzymes and nucleic acids.

Jennette KW. Environ Health Perspect, Aug 1981, 40 p233-52

Ballatori N. Environ Health Perspect, Oct 2002, 110 Suppl 5 p689-94


Al, Hg, Pb, Cd, Ni, Ti..
ROS
NO
ONOO-
Toxic mimikry
MMP
Cytochrom C Oxidase
OXPHOS
LPX
Ca2+ homeostasis
mtDNA
nDNA
Loss of mitochondrial function


Toxic metals
EMF
Disturbance of Calcium homeostasis
impaired mitochondrial ATP synthesis
collapse of mitochondrial membrane potential
culminating in cell dysfunction and delayed cell death

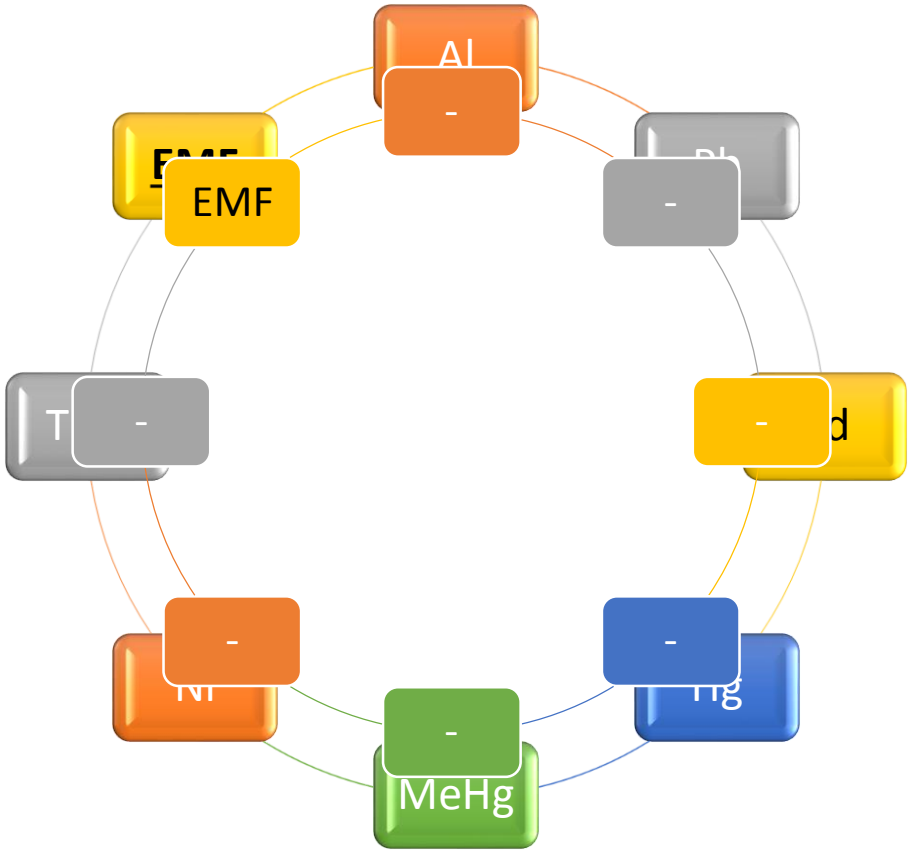
Working hypothesis:

The dysregulation of CH is a comined effect of toxic metals and EMF

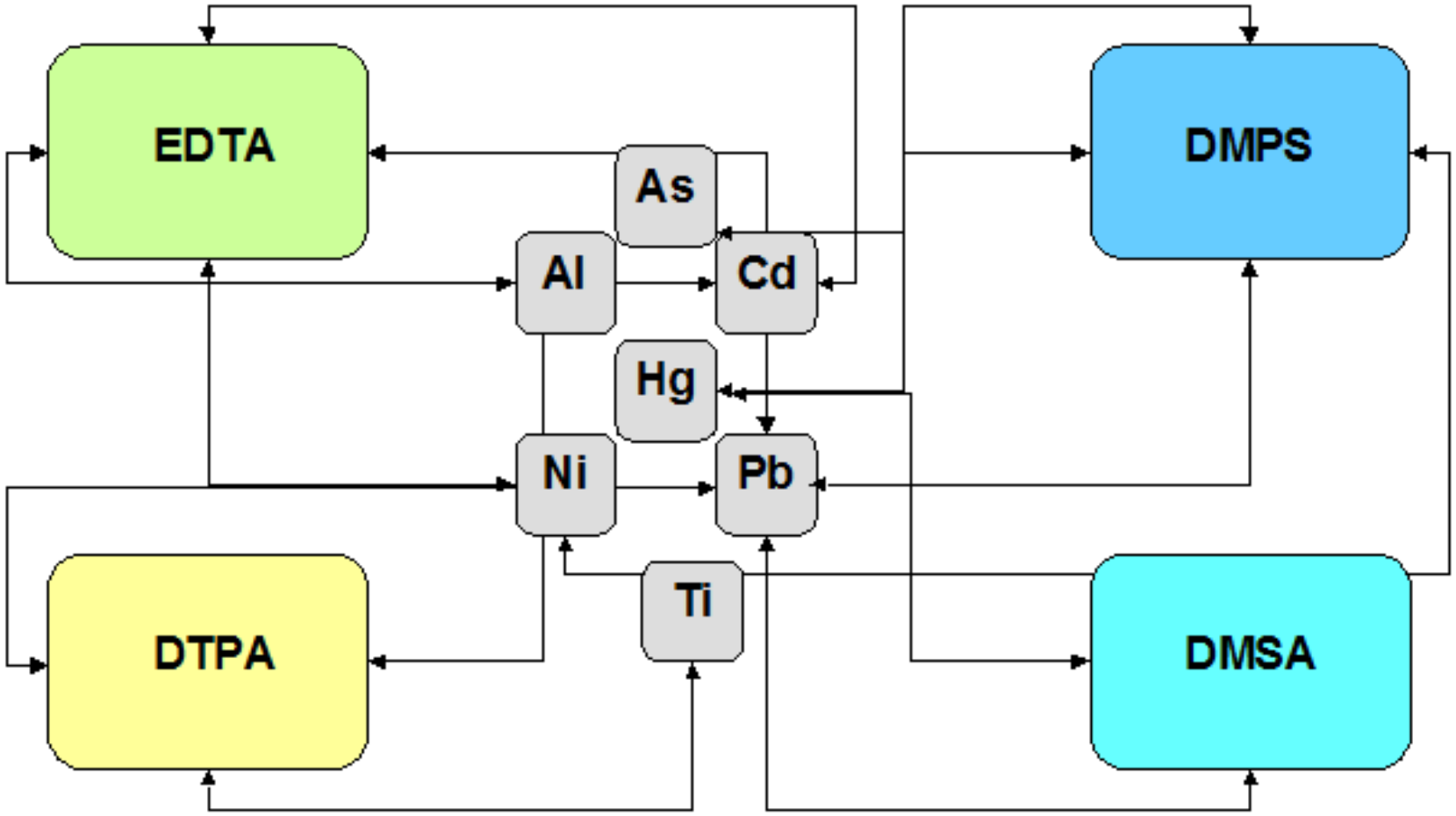
Reduction of concentrations of toxic metals

Reduction of CH-dysregulation

If You reduce the concentration of TM, you reduce the EMF effects on cells



Metal-binding agents



Secondary mitochondrial disease caused by toxic metals

40 year old female

- Severe CFS
- Loss of memory and of cognitive function
- Dermatitis
- Diminished ability to perform activities of daily living (ADL)

Challenge Test with Chelating agents i.v

(zinc trisodium diethylenetriaminepentaacetate - ZnDTPA)
(dimercaptopropanesulfonate - DMPS)

Potentially Toxic Metal	Test Result (mcg/g Creatin)	Normal Range (unprovoked)
Aluminum	**62,69**	< 17
Cadmium	1,56	< 0,5
Lead	**44,49**	< 1
Mercury	17,61	< 1
Nickel	11,44	< 2,1

ATP intracellular: 0,69 µM (reference value: > 2µM)

Secondary mitochondrial disease caused by toxic metals

Therapy :

- **11 x DMPS/ ZnDTPA i.v.**
- **28 x 3gr Na_2Mg-EDTA i.v.**
- **7 x 200mg DMSA i.v.**
- **4 x DMPS i.v.**
- HOT/UVB

Therapy of a lea

Inte ar therapy

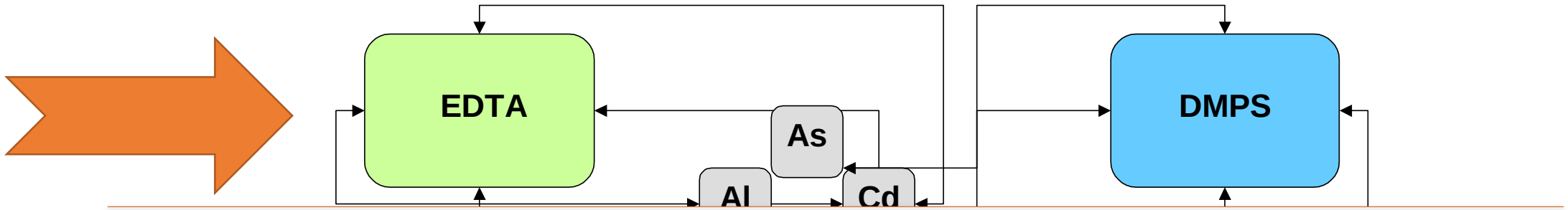
Sym ms of therapy:

- function
- ement to perform activities of daily living (ADL)
- Improvement in quality of life
- Opening a practice for psychotherapy

6 years later her condition is still good

ATP intracellular: 2,01 µM (reference value: > 2µM)

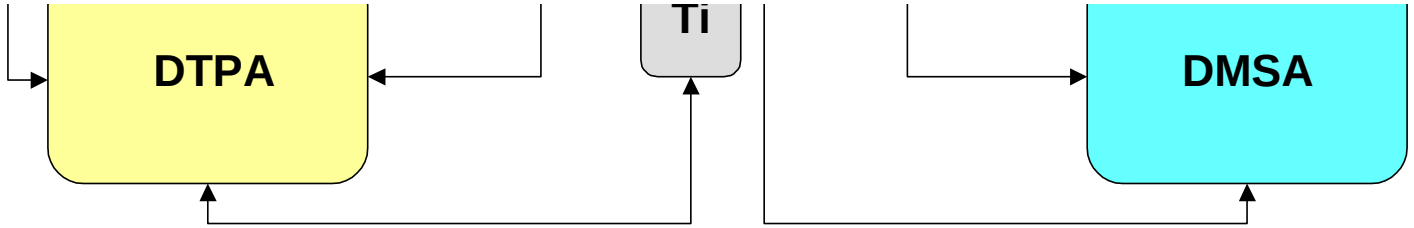
Metal-binding agents



Standard medical treatment:

Use for acute metal intoxication

Not used for the treatment of chronic metal burden from the environment



ClinicalTrials.gov

A service of the U.S. National Institutes of Health

TACT – Trial to Access Chelation Therapy

- The Trial to Assess Chelation Therapy (TACT) is a randomized, double blind, placebo-controlled, 2×2 factorial clinical trial which is sponsored by the National Institute of Health (NIH).
- It was designed to determine the safety and efficacy of EDTA chelation therapy for individuals with coronary artery disease (CAD) and prior myocardial infarction (MI).
- **IMPORTANCE:**
- Chelation therapy with disodium EDTA has been used for more than 50 years to treat atherosclerosis without proof of efficacy.
- **OBJECTIVE:**
- To determine if an EDTA-based chelation regimen reduces cardiovascular events.

ClinicalTrials.gov A service of the U.S. National Institutes of Health	TACT – Trial to Access Chelation Therapy

CONCLUSIONS AND RELEVANCE:

Among stable patients with a history of MI, use of an intravenous chelation regimen with disodium EDTA, compared with placebo, **modestly reduced the risk of adverse cardiovascular outcomes**, many of which were revascularization procedures. These results provide evidence to guide further research but are not sufficient to support the routine use of chelation therapy for treatment of patients who have had an MI.

Lamas GA, et al. JAMA 2013 Mar 27;309(12):1241-50.

EDTA

- Al, Cd, Pb, Ca, Fe, Mg, Co, Cu, Mn, Zn

EDTA binds no mercury and no arsenic

Hindawi Publishing Corporation
ISRN Hypertension
Volume 2013, Article ID 234034, 15 pages
http://dx.doi.org/10.5402/2013/234034

Hindawi

Review Article

The Influence of Arsenic, Lead, and Mercury on the Development of Cardiovascular Diseases

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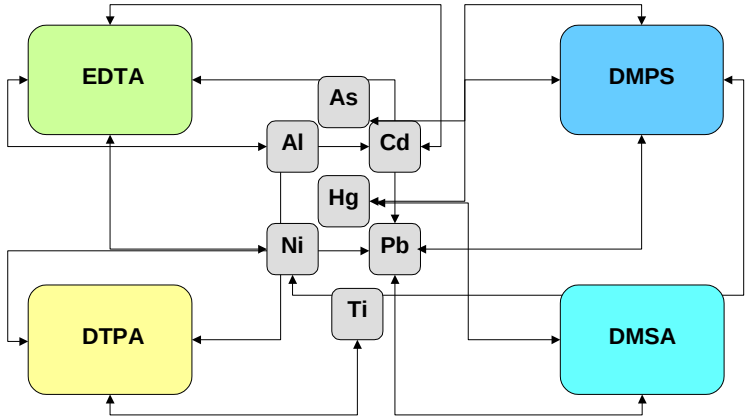
„The cardiovascular effects of arsenic, lead and mercury exposure and its impact on cardiovascular mortality need to be included in the diagnosis and the treatment of CVD.“

It can be assumed that patients who participated the TACT and had an arsenic and / or mercury load would have benefited from a combination of EDTA and DMPS or DMSA.

Nevertheless, the TACT is a milestone in the recognition of the therapeutic use of chelating substances beyond the treatment of acute metal poisoning.

The use of metal-binding agents should be recognized as necessary for the treatment of diseases which are linked with chronic metal burden from the environment.



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CONCLUSION:

The use of chelating substances for the treatment of chronic metal intoxication is a novel therapeutic approach for patients with CFS, MCS and EHS.