Health concerns of the heavy metals and metalloids

Chris Cooksey

- Toxicity - acute and chronic
- Arsenic
- Mercury
- Lead
- Cadmium

Toxicity - acute and chronic

Acute - LD_{50}

Trevan, J. W., 'The error of determination of toxicity', Proc. Royal Soc., 1927, 101B, 483-514

LD50 (rat, oral) mg/kg

CdS	7080
NaCl	3000
As	763
HgCl	210
NaF	52
Tl_2SO_4	16
NaCN	6.4
$HgCl_2$	1

Hodge and Sterner Scale
(1943)

Toxicity Rating	Commonly used term	LD_{50} (rat, oral)
1	Extremely Toxic	<=1
2	Highly Toxic	1 - 50
3	Moderately Toxic	50 - 500
4	Slightly Toxic	500 - 5000
5	Practically Non-toxic	5000 - 15000
6	Relatively Harmless	>15000

GHS - CLP

LD_{50}	Category
<=5	1 Danger
5 - 50	2 Danger
50 - 300	3 Danger
300 - 2000	4 Warning

Globally Harmonised System of Classification and Labelling and Packaging of Chemicals
CLP-Regulation (EC) No 1272/2008

Toxicity - acute and chronic

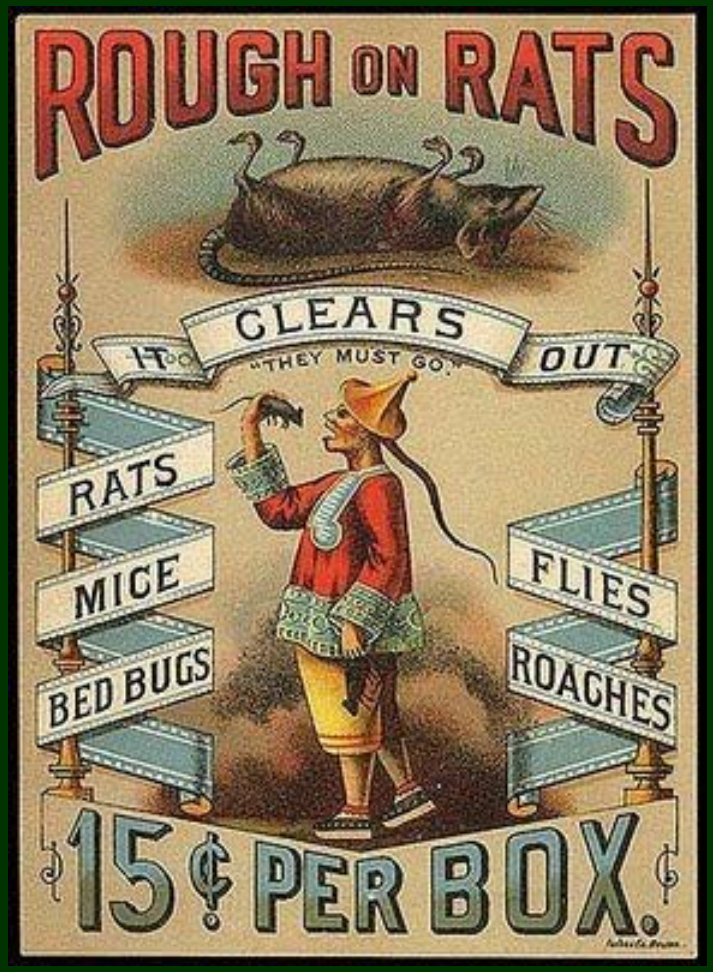
Chronic

The long-term effect of sub-lethal exposure

- Toxicity - acute and chronic
- Arsenic
- Mercury
- Lead
- Cadmium

Arsenic

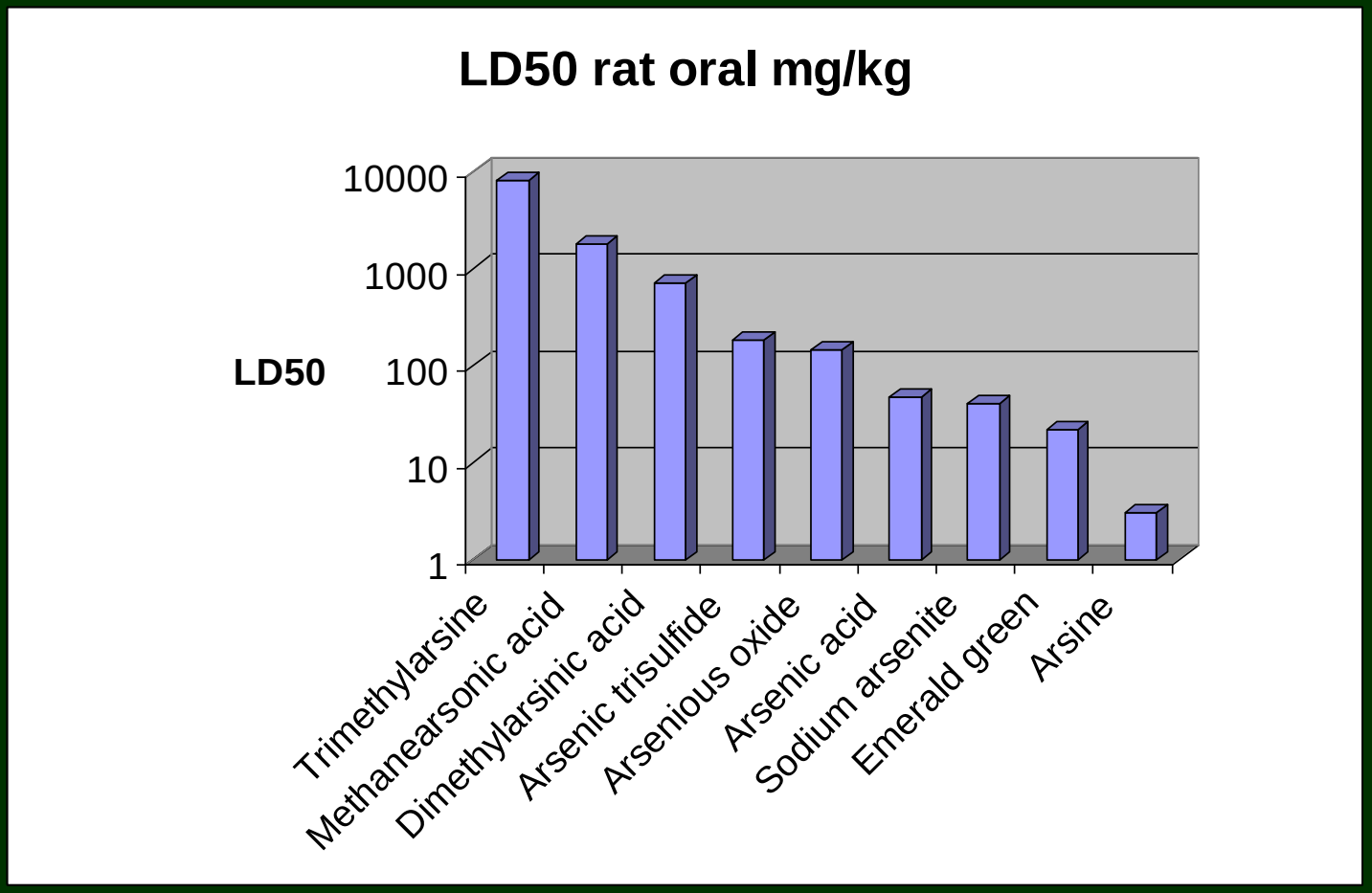
- Pesticide
  - Inheritance powder
- Taxidermy
- Herbicide
  - Agent Blue
- Pigments
- Therapeutic uses



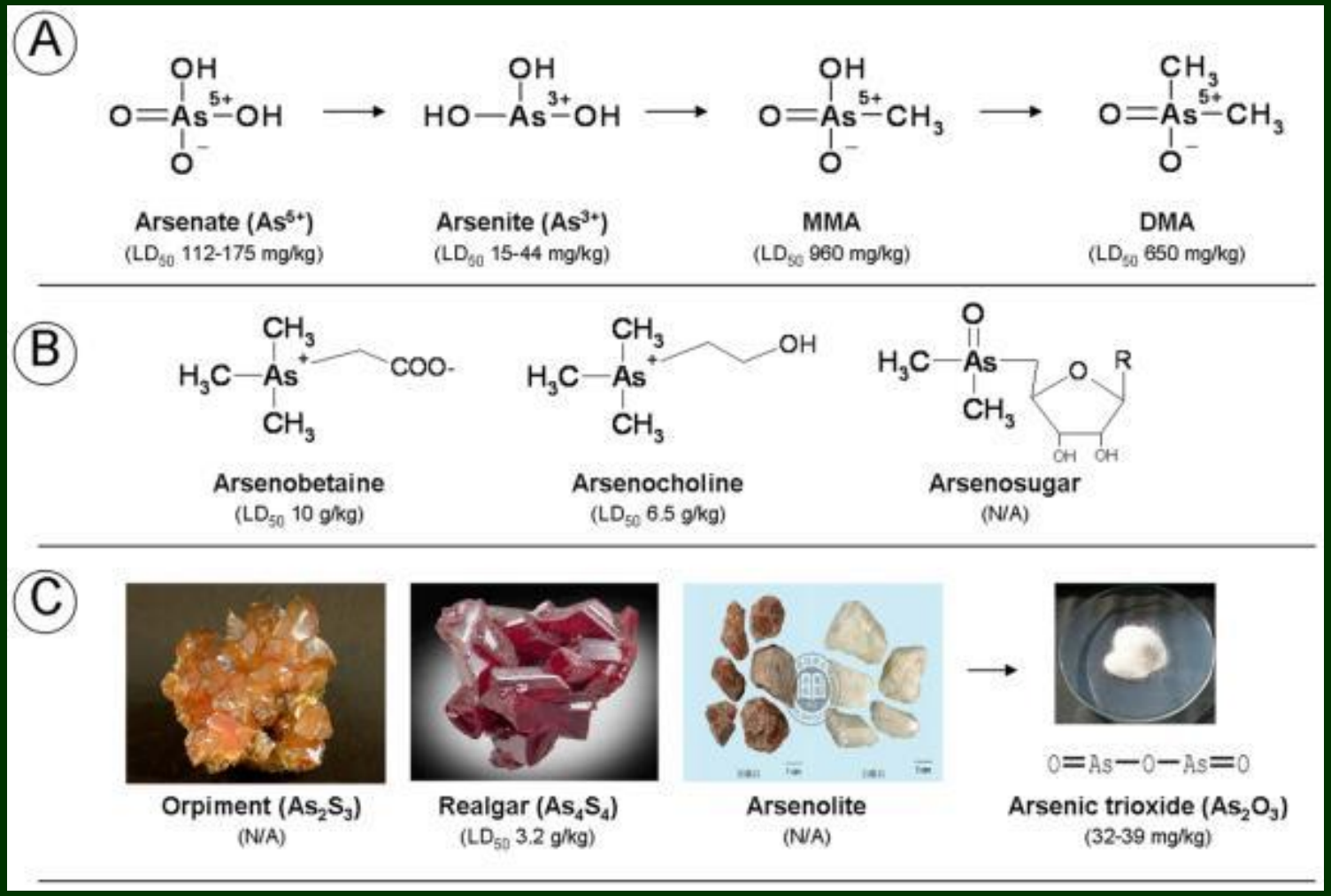
Inorganic arsenic poisoning kills by allosteric inhibition of essential metabolic enzymes, leading to death from multi-system organ failure.

Arsenicosis - chronic arsenic poisoning.

Arsenic


LD50 rat oral mg/kg
LD50
10000
1000
100
10
1
Trimethylarsine
Methanearsonic acid
Dimethylarsinic acid
Arsenic trisulfide
Arsenious oxide
Arsenic acid
Sodium arsenite
Emerald green
Arsine

Arsenic


A
Arsenate (As^{5+})
(LD_{50} 112-175 mg/kg)
Arsenite (As^{3+})
(LD_{50} 15-44 mg/kg)
MMA
(LD_{50} 960 mg/kg)
DMA
(LD_{50} 650 mg/kg)
B
Arsenobetaine
(LD_{50} 10 g/kg)
Arsenocholine
(LD_{50} 6.5 g/kg)
Arsenosugar
(N/A)
C
Orpiment (As_2S_3)
(N/A)
Realgar (As_4S_4)
(LD_{50} 3.2 g/kg)
Arsenolite
(N/A)
Arsenic trioxide (As_2O_3)
(32-39 mg/kg)

poisoning by volatile arsenic compounds from mouldy wall paper in damp rooms

- Gmelin (1839) toxic mould gas
- Selmi (1874) AsH_3
- Basedow (1846) cacodyl oxide
- Gosio (1893) alkyl arsine
- Biginelli (1893) Et_2AsH
- Klason (1914) Et_2AsO
- Challenger (1933) Me_3As
- McBride & Wolfe (1971) Me_2AsH

or is it really true ?

William R. Cullen, Ronald Bentley

The toxicity of trimethylarsine: an urban myth

J. Environ. Monit., 2004

- Odour threshold 2 ng/kg in water
- LD_{50} 7870 mg/kg

Arsenic

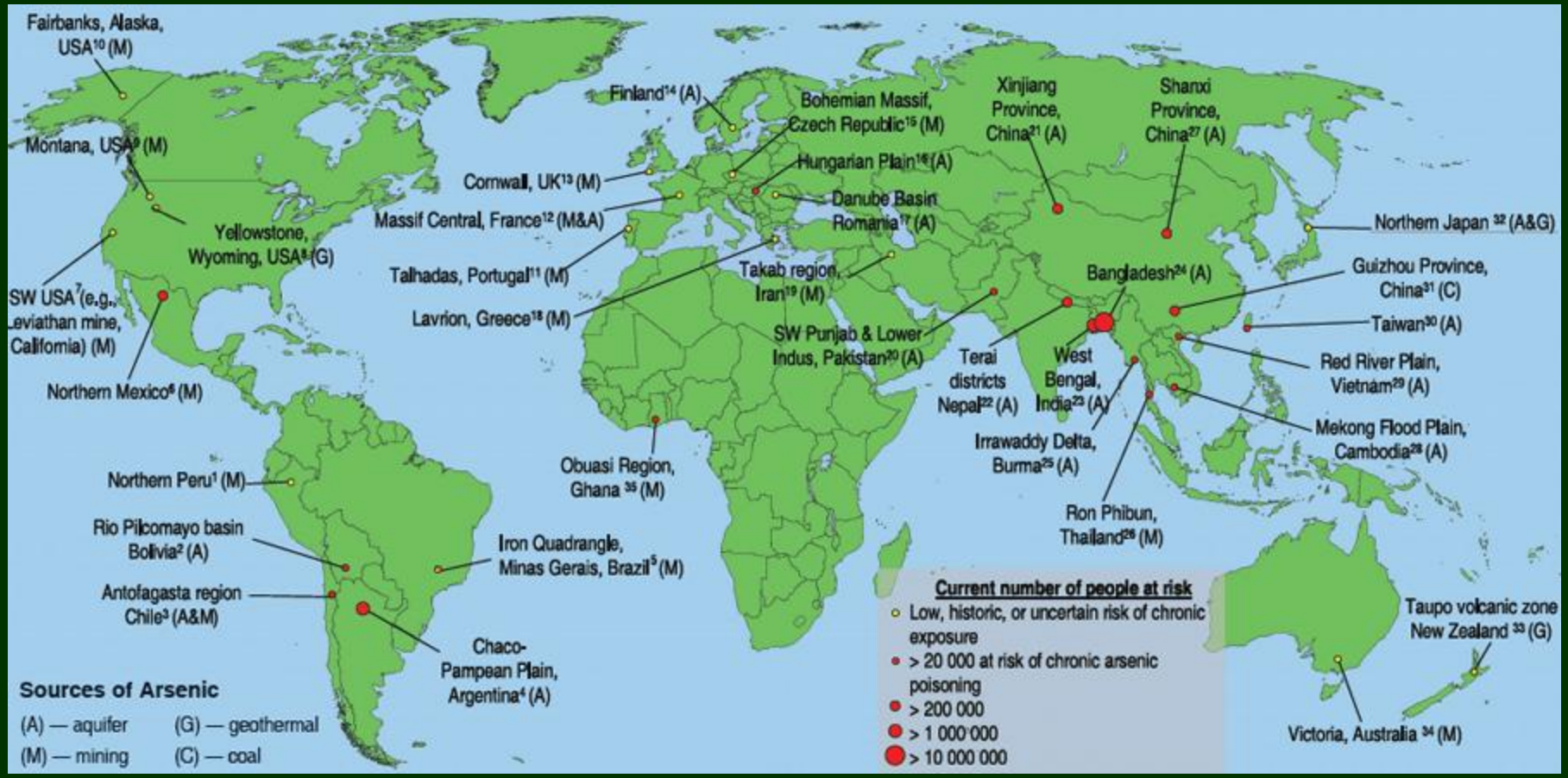
The toxicity of arsine and methyl arsines by inhalation arises because of the generation of radicals which cause DNA damage.

Arsenic

Chronic toxicity leading to skin cancers is caused by inorganic arsenic in drinking water

Hutchinson J (1887) Arsenic cancer. Br Med J, 2: 1280.

WHO: "the largest mass poisoning in history"; recommends <0.01 mg/L arsenic in drinking water.

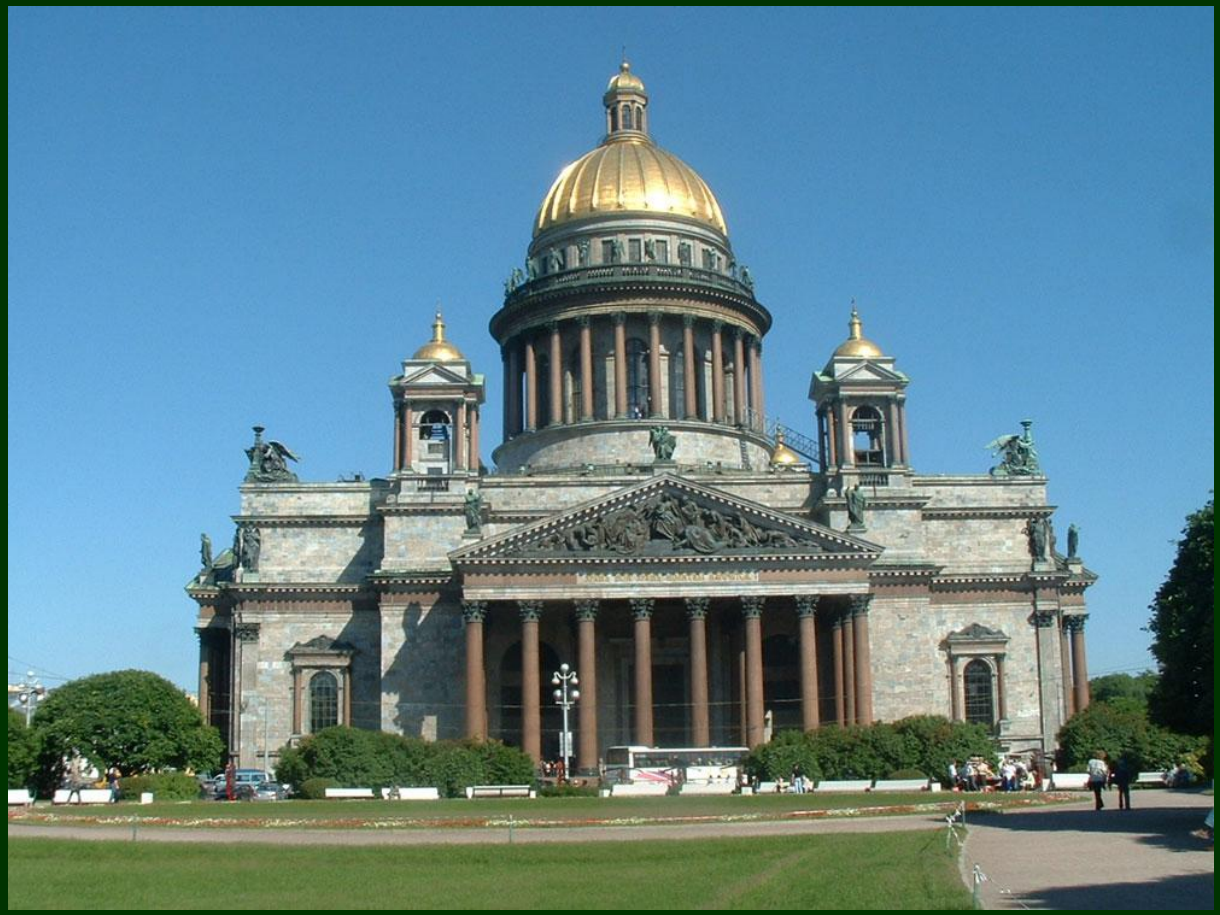

Fairbanks, Alaska, USA[10] (M)
Montana, USA[9] (M)
Yellowstone, Wyoming, USA[8] (G)
SW USA[7] (e.g., Leviathan mine, California) (M)
Northern Mexico[6] (M)
Northern Peru[1] (M)
Rio Pilcomayo basin Bolivia[2] (A)
Antofagasta region Chile[3] (A&M)
Chaco-Pampean Plain, Argentina[4] (A)
Iron Quadrangle, Minas Gerais, Brazil[5] (M)
Finland[14] (A)
Cornwall, UK[13] (M)
Massif Central, France[12] (M&A)
Talhadas, Portugal[11] (M)
Lavrion, Greece[18] (M)
Bohemian Massif, Czech Republic[15] (M)
Hungarian Plain[16] (A)
Danube Basin Romania[17] (A)
Takab region, Iran[19] (M)
SW Punjab & Lower Indus, Pakistan[20] (A)
Obuasi Region, Ghana[35] (M)
Xinjiang Province, China[21] (A)
Shanxi Province, China[27] (A)
Northern Japan[32] (A&G)
Bangladesh[24] (A)
Guizhou Province, China[31] (C)
Taiwan[30] (A)
Terai districts Nepal[22] (A)
West Bengal, India[23] (A)
Red River Plain, Vietnam[29] (A)
Mekong Flood Plain, Cambodia[28] (A)
Irrawaddy Delta, Burma[25] (A)
Ron Phibun, Thailand[26] (M)
Taupo volcanic zone New Zealand[33] (G)
Victoria, Australia[34] (M)
Sources of Arsenic
(A) — aquifer
(G) — geothermal
(M) — mining
(C) — coal
Current number of people at risk
Low, historic, or uncertain risk of chronic exposure
> 20 000 at risk of chronic arsenic poisoning
> 200 000
> 1 000 000
> 10 000 000

- Toxicity - acute and chronic
- Arsenic
- Mercury
- Lead
- Cadmium

Mercury

- Uses
  - Kastner-Kellner cells
  - Measuring instruments
  - Floating lighthouse mirrors
  - Gold extraction
  - Laxative
  - Dental fillings
    - Largest exposure to mercury vapour

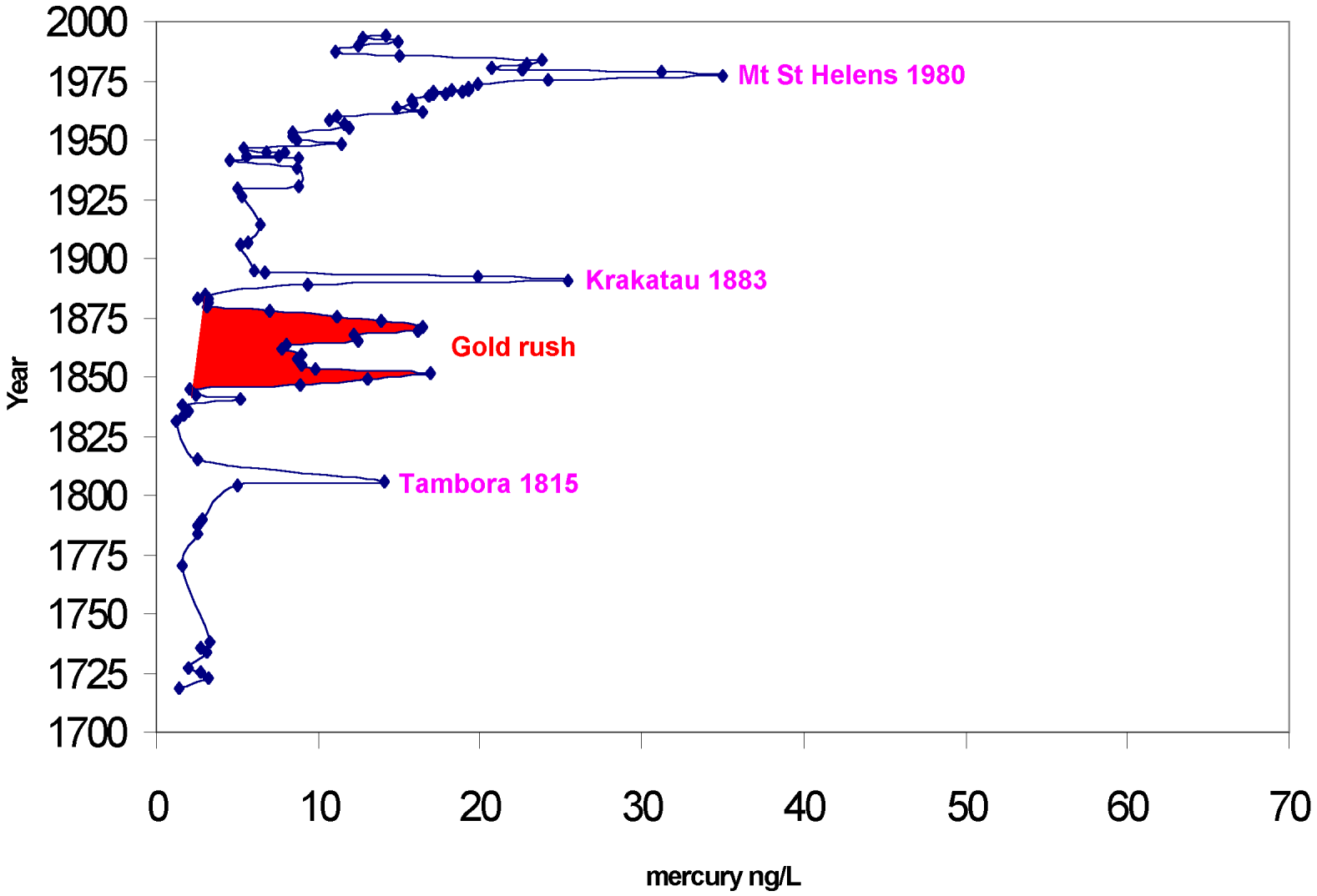
Mercury



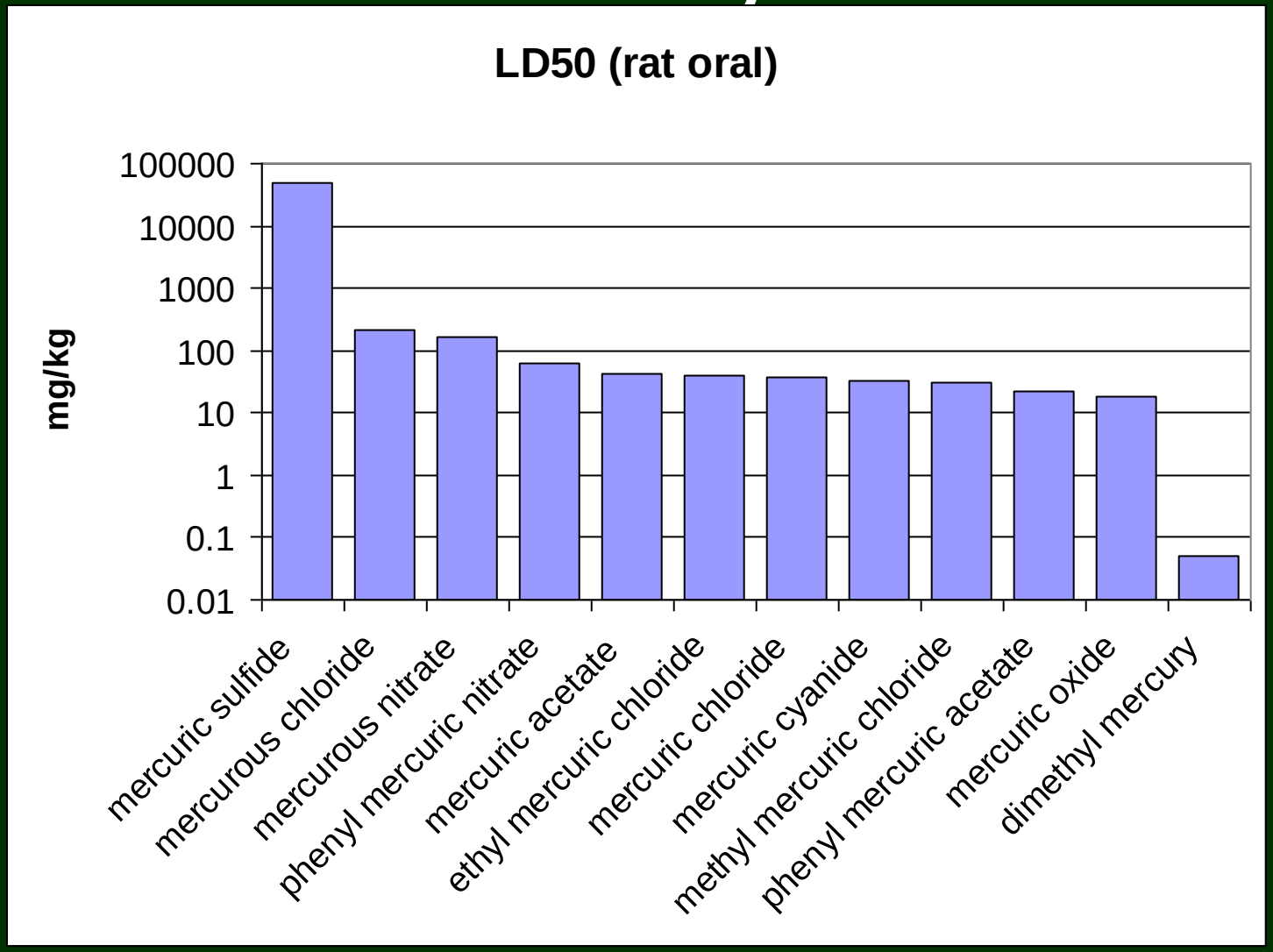
Mercury

- Sources
  - 65% coal fired power plants
  - 11% gold extraction
  - Cremation
    - 1300-2200 t in fillings (EU + EFTA, 2003)
  - volcanos

Mercury in the Fremont glacier



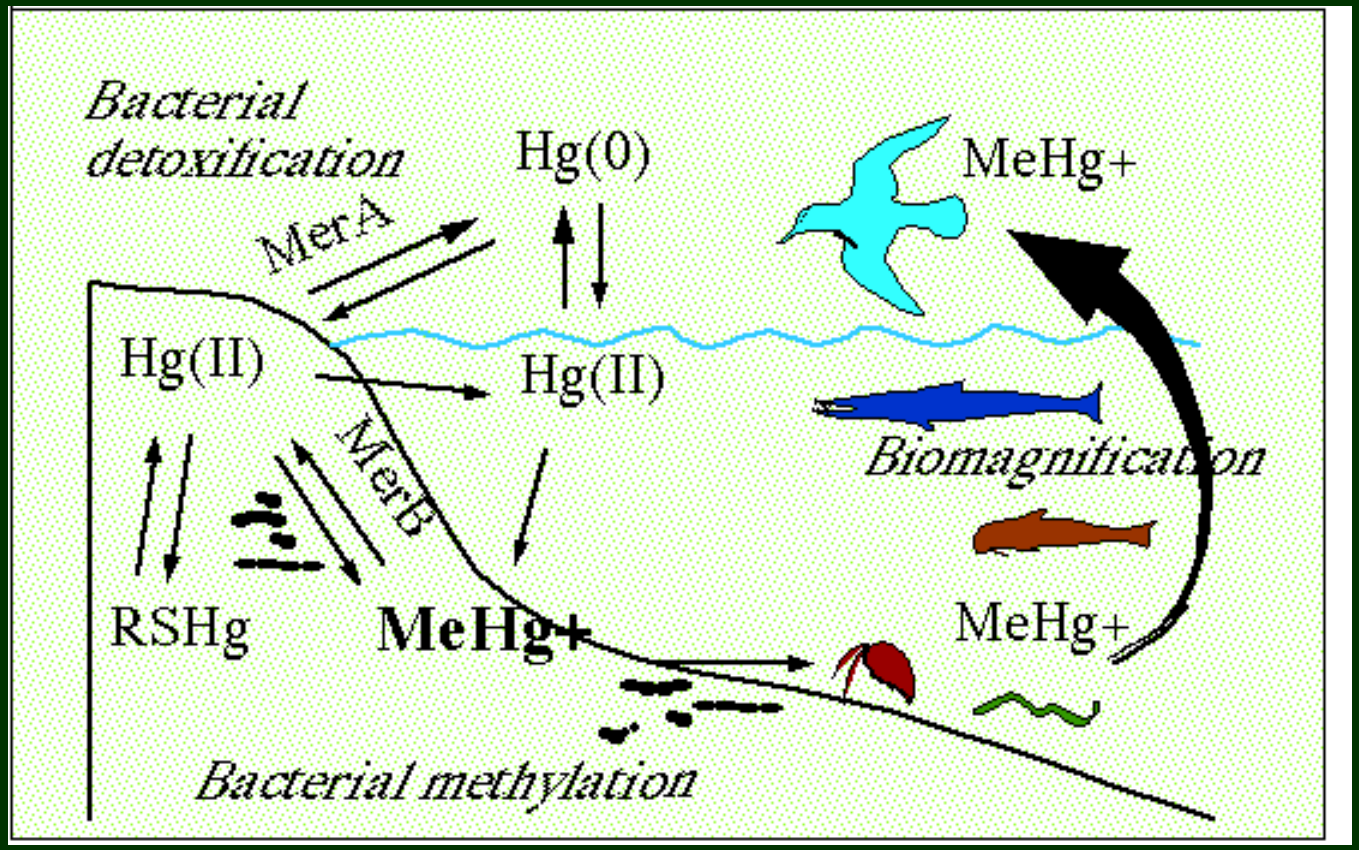
Mercury


LD50 (rat oral)
mg/kg
100000
10000
1000
100
10
1
0.1
0.01
mercuric sulfide
mercurous chloride
mercurous nitrate
phenyl mercuric nitrate
mercuric acetate
ethyl mercuric chloride
mercuric chloride
mercuric cyanide
methyl mercuric chloride
phenyl mercuric acetate
mercuric oxide
dimethyl mercury

Methyl mercury

- Japan Nitrogenous Fertilizer Company
  - Nihon Chisso Hiryo - Kabushiki Kaisha (1908)
  - Calcium carbide - cyanamide - calcium nitrate
  - Acetylene - acetaldehyde (Hg catalysed) (1932 - 1968)
    - Waste containing methyl mercury CH_3Hg^+ was discharged into the sea
  - Minamata

Mercury


Bacterial detoxification
Hg(0)
MeHg+
MerA
Hg(II)
Hg(II)
MerB
Biomagnification
RSHg
MeHg+
MeHg+
Bacterial methylation

Dimethyl mercury

- readily crosses the blood-brain barrier
- causes ataxia, sensory disturbance and changes in mental state, birth defects
- inhibits several stages of neurotransmission in the brain
- very slowly excreted from the body

Dimethyl mercury

- First published record of fatal occupational MeHg poisoning, Edwards 1865
- Report on organic mercury poisoning in acetaldehyde production workers, Koelsch 1937
- Official acknowledgment of MeHg as cause of Minamata disease 1968

Methylmercury

- Introduced as a fungicide for seeds 1914
  - Iraq in 1955–1956 and 1959–1960
  - Pakistan in 1961
  - Guatemala in 1965
  - Iraq in 1970–1971

Mercury

- Directive 2007/51/EC
  - mercury-in-glass thermometers banned
- Recommendation 2003/4 on Controlling the Dispersal of Mercury from Crematoria.

  - 50% reduction in emissions by 2012

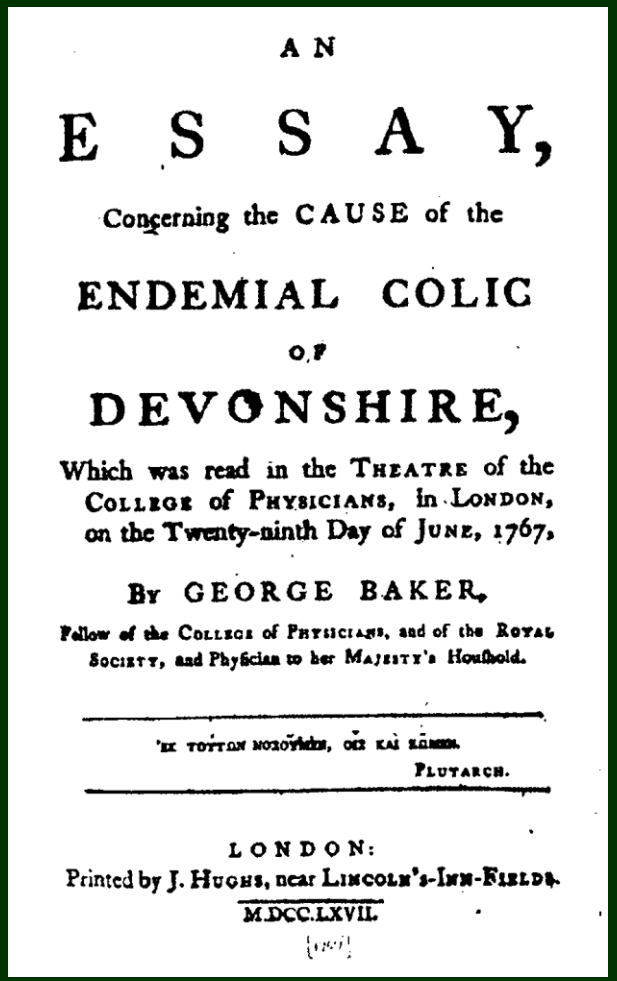
- Toxicity - acute and chronic
- Arsenic
- Mercury
- Lead
- Cadmium

Lead

While it is being melted, all the apertures in the vessel should be closed, otherwise a noxious vapour is discharged from the furnace, of a deadly nature, to dogs in particular.

Pliny XXXIV, 50

Lead



A N

E S S A Y,

Concerning the CAUSE of the

ENDEMIAL COLIC

OF

DEVONSHIRE,

Which was read in the THEATRE of the COLLEGE of PHYSICIANS, in LONDON, on the Twenty-ninth Day of JUNE, 1767,

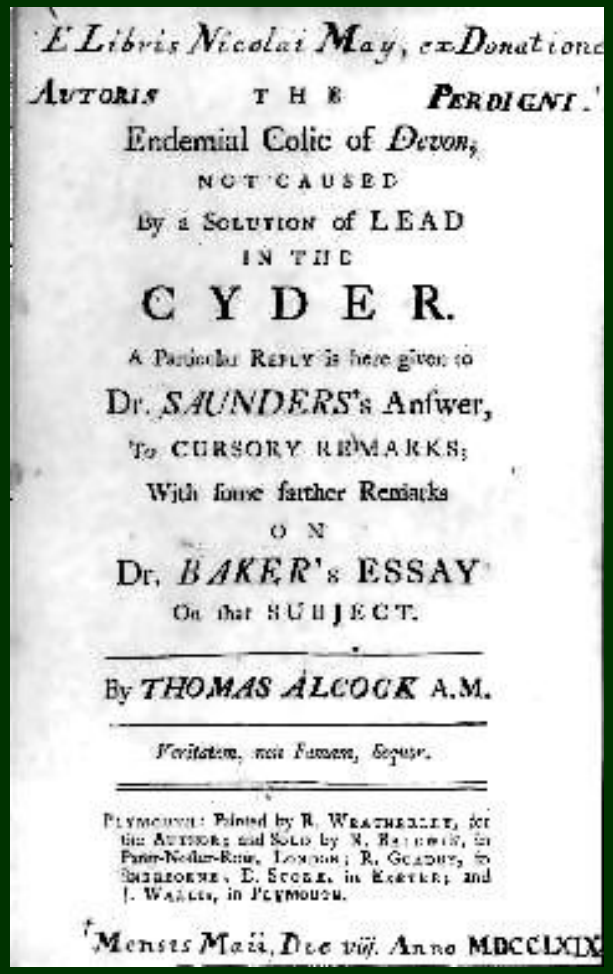
BY GEORGE BAKER,

Fellow of the COLLEGE of PHYSICIANS, and of the ROYAL SOCIETY, and Physician to her MAJESTY's Household.

΄ΕΚ ΤΟΥΤΩΝ ΝΟΣΟΥΣΙΝ, ΟΥΣ ΚΑΙ ΚΤΕΙΝΕΙ.

PLUTARCH.

LONDON:
Printed by J. HUGHS, near LINCOLN's-INN-FIELDS.
M.DCC.LXVII.



Ex Libris Nicolai May, ex Donatione
Autoris THE *Perdigni.*

Endemial Colic of *Devon*,
NOT CAUSED
By a SOLUTION of LEAD
IN THE
CYDER.

A Particular REPLY is here given to
Dr. *SAUNDERS*'s Answer,
To CURSORY REMARKS;
With some farther Remarks
ON
Dr. *BAKER*'s ESSAY
On that SUBJECT.

By *THOMAS ALCOCK* A.M.

Veritatem, non Famam, sequor.

PLYMOUTH: Printed by R. WEATHERLEY, for the AUTHOR; and Sold by R. BALDWIN, in Paternoster-Row, LONDON; R. GOADBY, in SHERBORNE; D. STOREY, in EXETER; and J. WALLIS, in PLYMOUTH.

Mensis Maii, Die viij. Anno MDCCLXIX

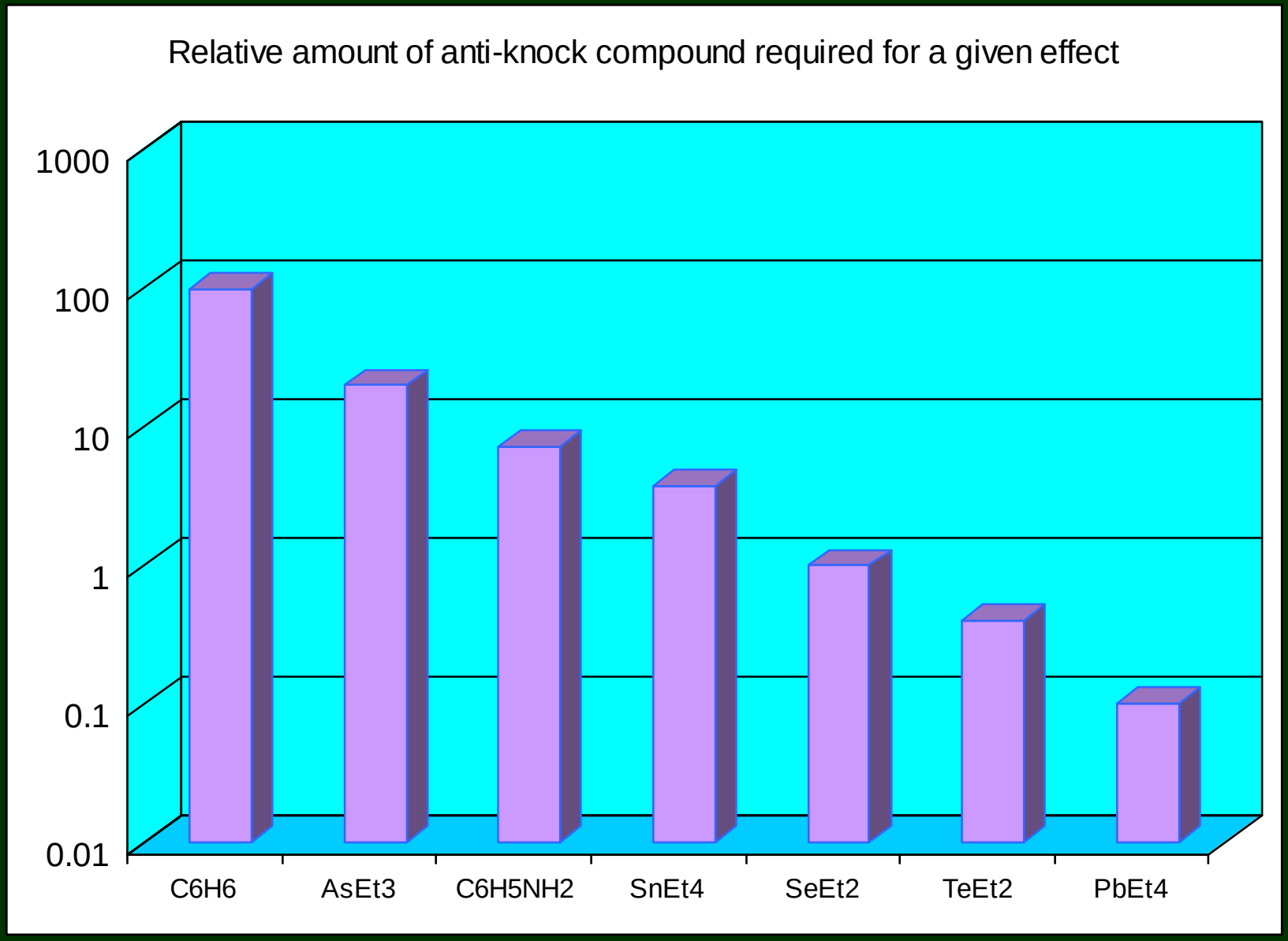
Lead

A Case of Lead Poisoning by Beer

E. Rice Morgan, BMJ, 1900, 1373

Tetraethyllead

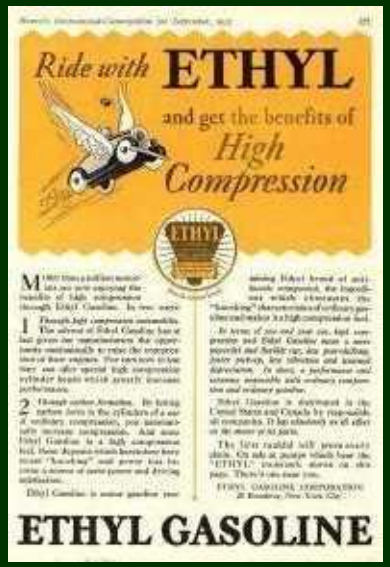
- Carl Jacob Löwig (1803 - 1890)
- Thomas Midgley (1889 - 1944)
- Clair Cameron Patterson (1922 - 1995)


Relative amount of anti-knock compound required for a given effect
1000
100
10
1
0.1
0.01
C6H6
AsEt3
C6H5NH2
SnEt4
SeEt2
TeEt2
PbEt4

Ethyl Gasoline Corporation

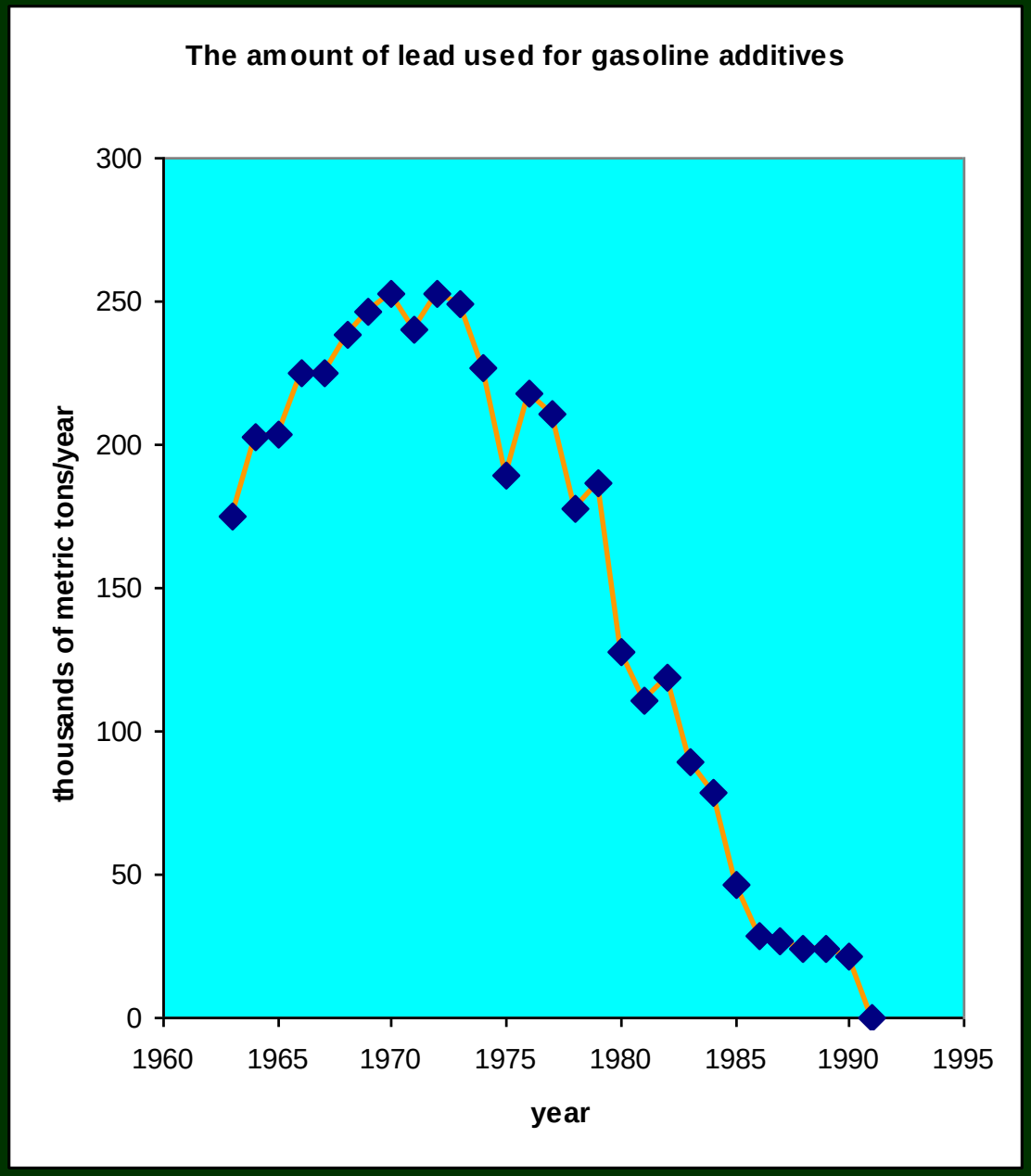
- 1 February 1923

Thomas Midgley, Jr.



Clair Patterson

- Measured U/Pb ratios in old rocks
- Concluded (1953) that the age of the Earth was 4550 my


The amount of lead used for gasoline additives
thousands of metric tons/year
300
250
200
150
100
50
0
1960
1965
1970
1975
1980
1985
1990
1995
year

- Toxicity - acute and chronic
- Arsenic
- Mercury
- Lead
- Cadmium

Cadmium

Cadmium is a recent discovery (1817)

Karl Samuel Leberecht Hermann (1765 – 1846)
Friedrich Stromeyer (1776 – 1835)

Cadmium

Sovet [poisoning caused by powder used in cleaning of silver ...]

Presse Med Belge 1858, **10**, 69-70

$CdCO_3$ dust inhalation

Cadmium

By the 1950s the hazards of working with cadmium were well established, causing

- Emphysema and proteinuria from inhalation

Cadmium

The first chronic poisoning was reported in 1940

Mancioli, G. (1940). Rass. Med. industr., 11, 632.

rhinitis and pharyngitis in plating workers

Cadmium

Jinzu River valley in Japan

Mitsui Mining & Smelting (1910)

First poisoning reported 1912

1939-1954 200 people affected by *itai-itai*, 100 died

- renal osteomalacia
- bone disease with fractures and severe pain

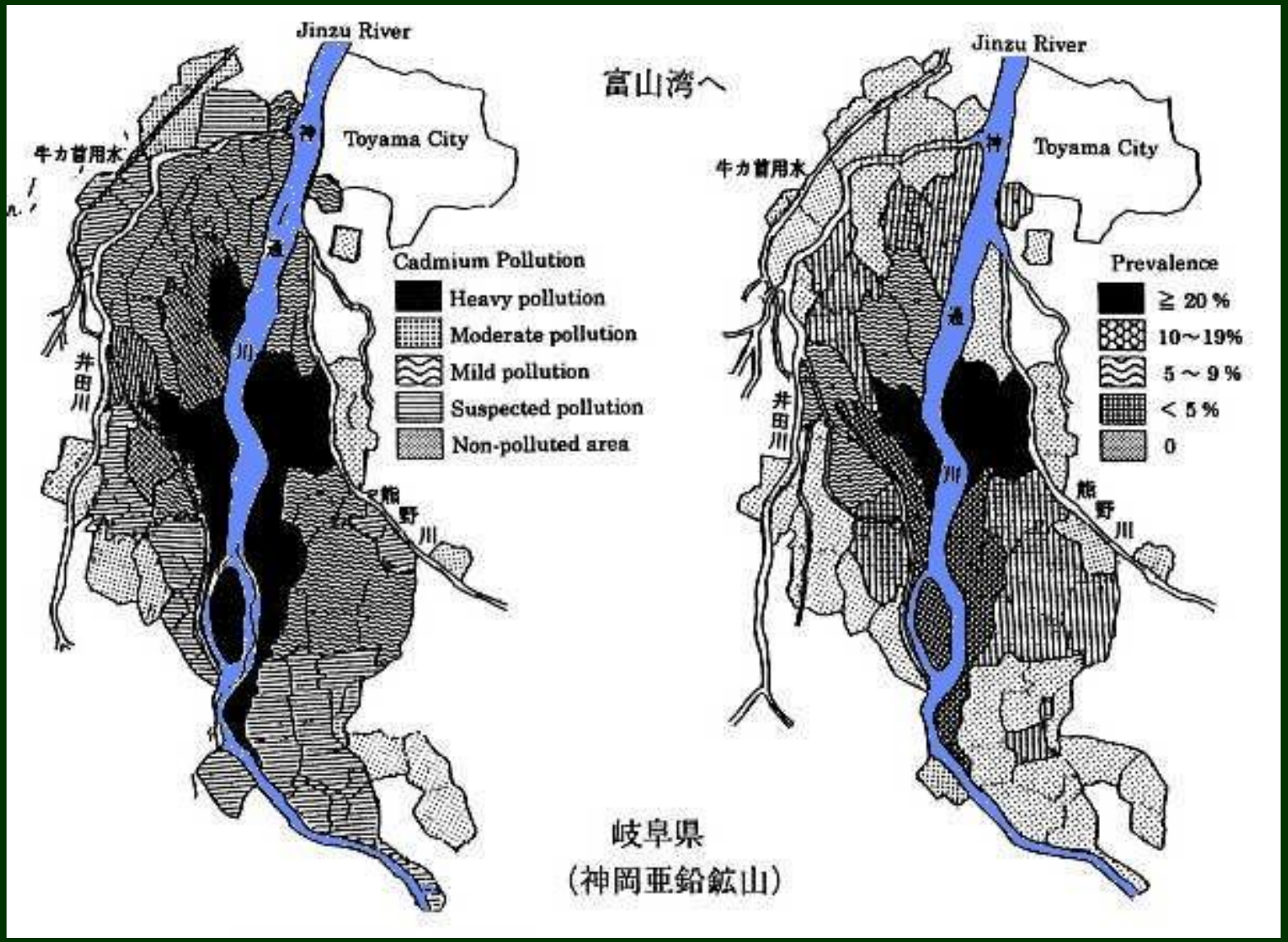
Cadmium

Dr Noboru Hagino (1957)

Suggests the cause is waste water from factories

(1961) Especially cadmium discharged during mining in Kamioka by Mitsui Mining Company

May 1968 the Ministry of Health and Welfare announced the disease was caused by cadmium poisoning


Jinzu River
Toyama City
牛カ首用水
井田川
熊野川
Cadmium Pollution
Heavy pollution
Moderate pollution
Mild pollution
Suspected pollution
Non-polluted area
富山湾へ
Jinzu River
Toyama City
牛カ首用水
井田川
熊野川
Prevalence
≧ 20 %
10～19%
5 ～ 9 %
< 5 %
0
岐阜県
(神岡亜鉛鉱山)

Jinzu River

River water containing 1 mg/kg Cd was used to irrigate rice fields

Patients with Itai Itai Disease

Cadmium

A drinking-water guideline value of

0.005 mg/litre has been set for cadmium (WHO, 1984)

- Toxicity - acute and chronic
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- Lead
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