Clinical aspects and management of poisonings with cyanide

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Introduction

- Cyanide : a potent intracellular poison, with attachment to the ferric form of necessary enzymes (cytochrome oxidase, succinic dehydrogenase, superoxide dismutase, …)
- It results in tissue hypoxia, acidosis, and death.

➡ Recognition of a non-classical situation of CN poisoning may be difficult.

➡ Laboratory diagnosis may take hours to days

➡ Early aggressive treatment with appropriate antidotes is essential

The spectrum of cyanide poisoning

- HCN (50 ppm,30 min; 200-400 ppm, 1-2 min)
- CN salts : CN Na
  CN K
  CN Hg, ...
  CN Au
  CN Br, CN Cl
- Nitriles : Acetonitrile: $CH_3CN \longrightarrow HCN + CH_2O$
  Propionitrile, ...
- Nitroprusside
- Cyanogenic plants
- Stored CN salts : CN $\longrightarrow$ CNO

Conditions resulting in exposure to cyanide or cyanogen compounds

- Household exposure: residential fires (pipe, furniture, organic, plastics)
- Industrial incidents: fumigation, photographic chemicals, metallurgy, electroplating, organic synthesis, fertilizers
- Individual or mass suicide
- Therapeutic exposure to drugs such as nitroprussiate and laetrile
- Dietary exposure to plants such as cassava
- Terrorist attack (non persistent lethal agent):
  - Contamination of water
  - Food containing cyanogen compounds
  - Dispersion of cyanide gas in a closed space
  - Vector facilitating skin penetration

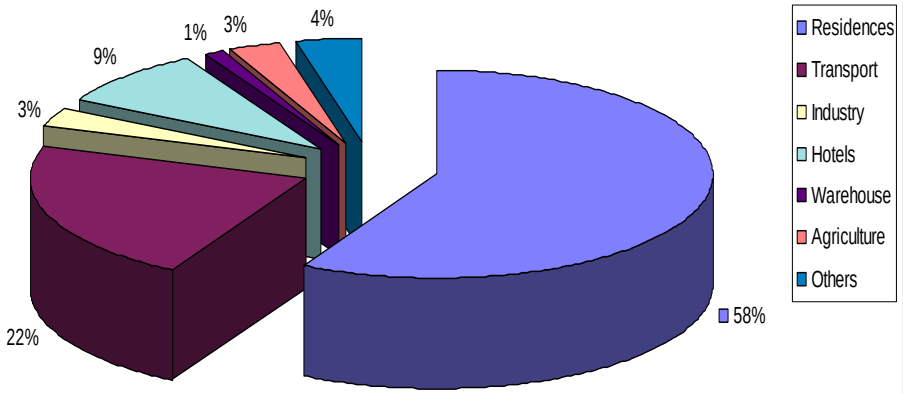
Smoke inhalation (1)

Each year in France :

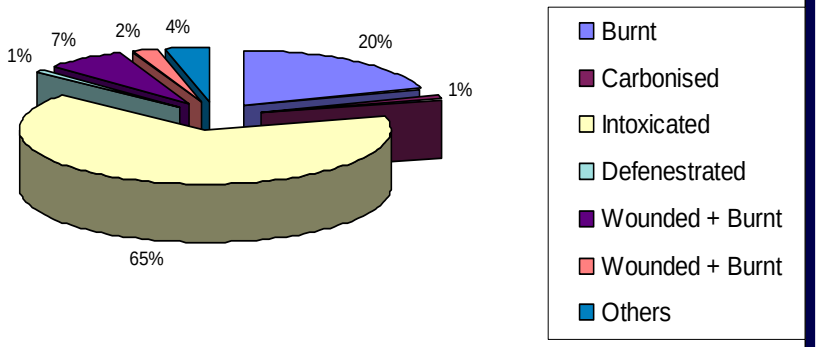
- 250,000 fires (58% residence fires)
- 4,000 victims (< 30% burnt)
- 400 deaths

In the US: Mortality rate : 0.98 deaths / 100 000 inhabitants

Nature of fires in France over a 20 year- period



Human injuries following fire exposition
in France over a 20 year-period



Smoke inhalation (2)

Fire may expose to 3 dangers:

- Thermal risk (flames, heated gases)
- Traumatic risk (blast, defenestration)
- Chemical risk

Smoke inhalation associates:

- Neurological and cardiac anoxic systemic injuries
- Ocular and respiratory irritant injuries

~ 80% of deaths are related to toxic smoke inhalation:

- Early death (*per* exposition) 80%
- Late death (*post*-exposition) 20%

Smoke composition

Polyintoxication: combustion or pyrolosis products in fire smokes

Compounds responsible of direct cellular anoxic toxicity :

- Carbon dioxide (CO_2)
- Carbon monoxide (CO)
- Hydrogen cyanide (HCN)
- Anhydro- derivates : sulfur dioxide, hydrogen sulfide
- Nitric oxide (NO)

Compounds responsible of mucous membrane irritant toxicity :

- Soot (particulates of polycyclic nitric and carbon compounds)
- Aldehydes : acrolein, formaldehyde, butyraldehyde, acetaldehyde, …
- Nitrous derivates : nitric oxide and ammonia, isocyanides and amines
- Mineral acids : hydrochloric, hydrofluoric, hydrobromic acids, …
- Carbon halogenated oxides : phosgene, chlorine
- Water vapors

Composition varies with environment

CN: residential fires, including pipe and furniture, organic materials, plastics (polyurethane), and melanine resines

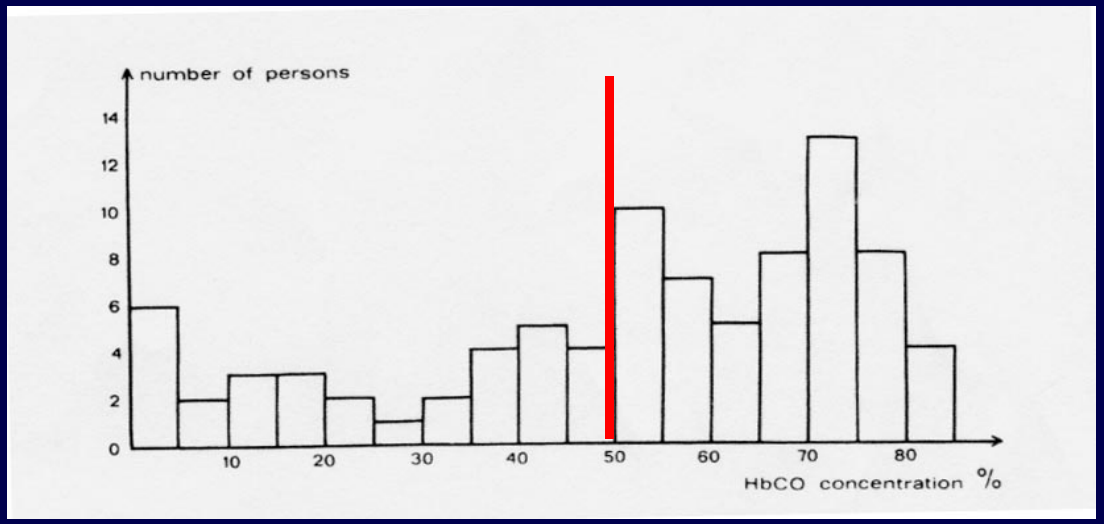
Smoke inhalation ≠ CO poisoning

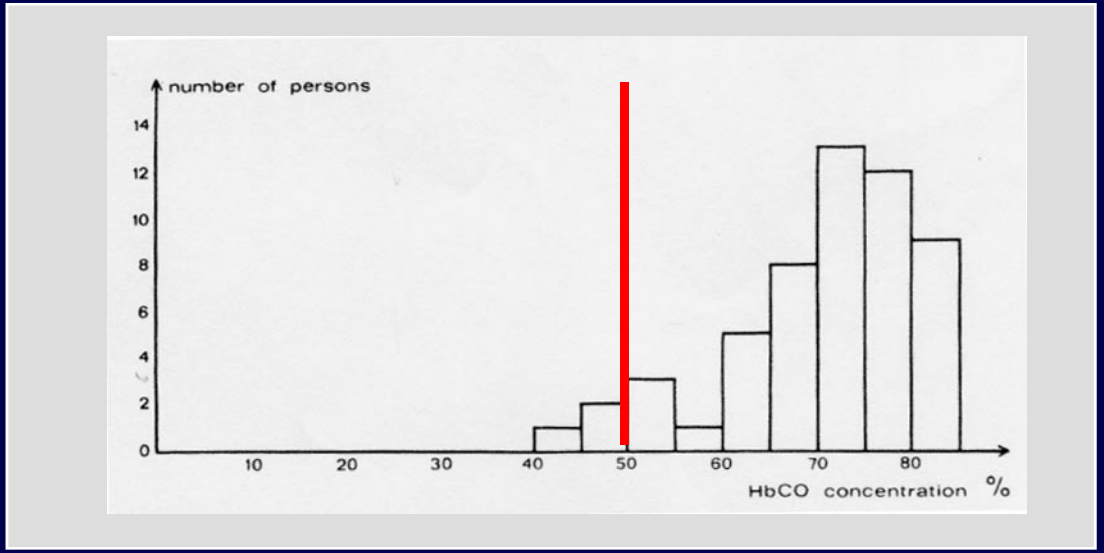
Post-mortem HbCO in 57 fire victims

Exposition duration: 30 min

Post-mortem HbCO in 54 cases of fatal CO poisoning

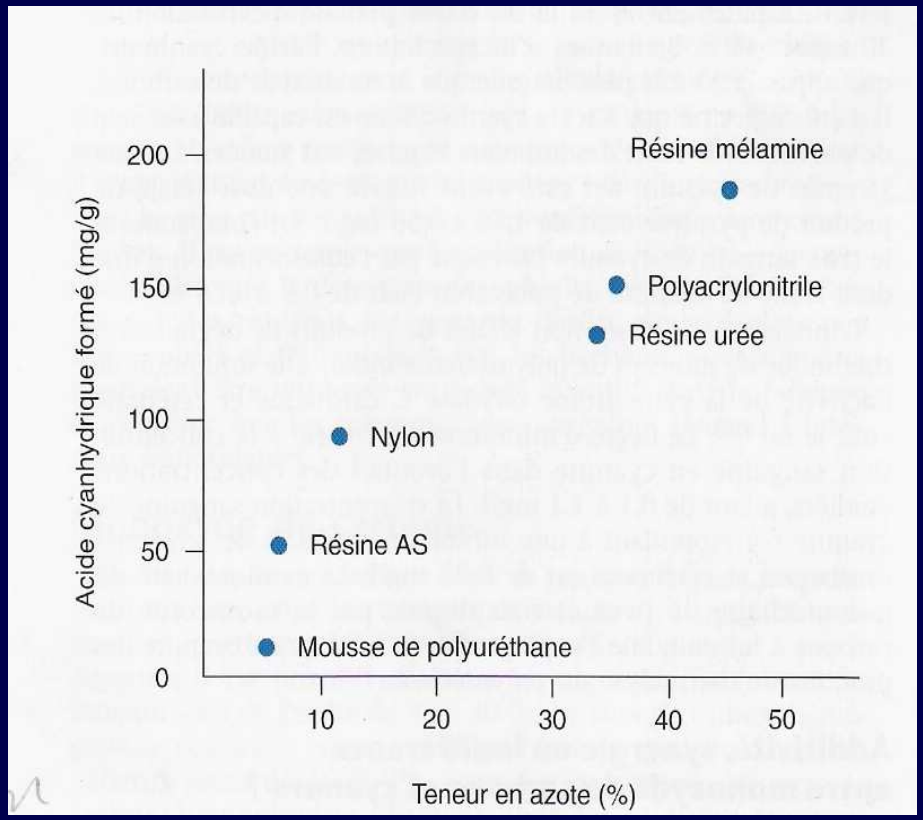
Exposition duration: 8 à 12 h





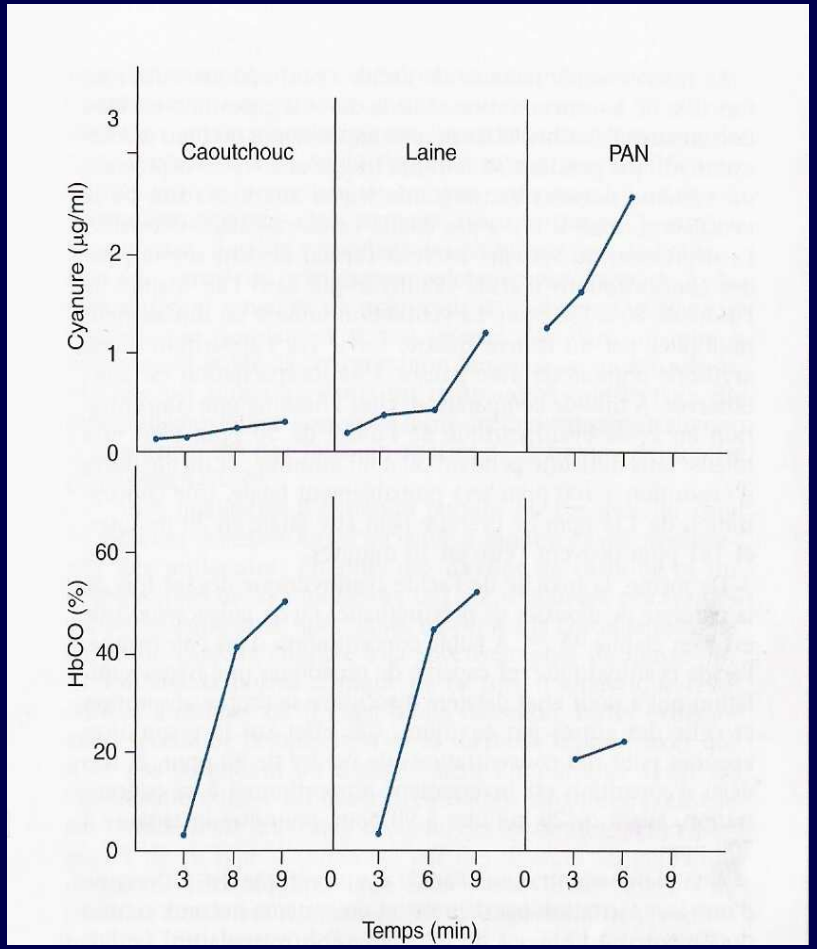
Teige et al. Z Rechtsmedizin 1977

Relationship between N content and CN production



Ballentyne B. Clinical and experimental toxicology of cyanides, 1987

Relationship in vivo between CN and HbCO

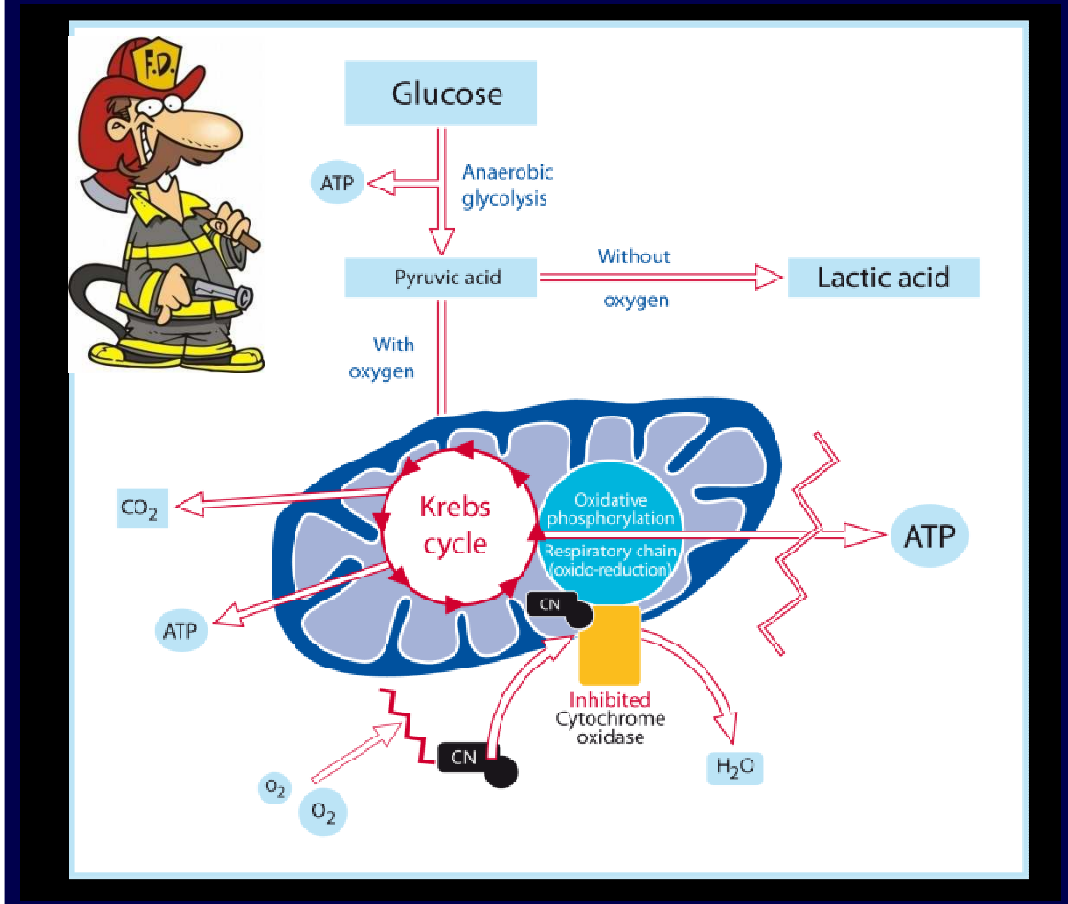


Bertol E. *Forens Sci Int* 1983

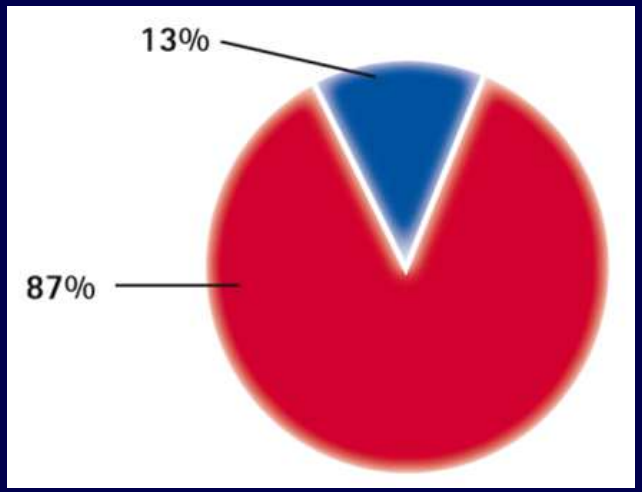
Pathways of cyanide toxicity

A potent intracellular poison, with attachment to the ferric form of necessary enzymes (cytochrome oxidase, succinic dehydrogenase, SOD)

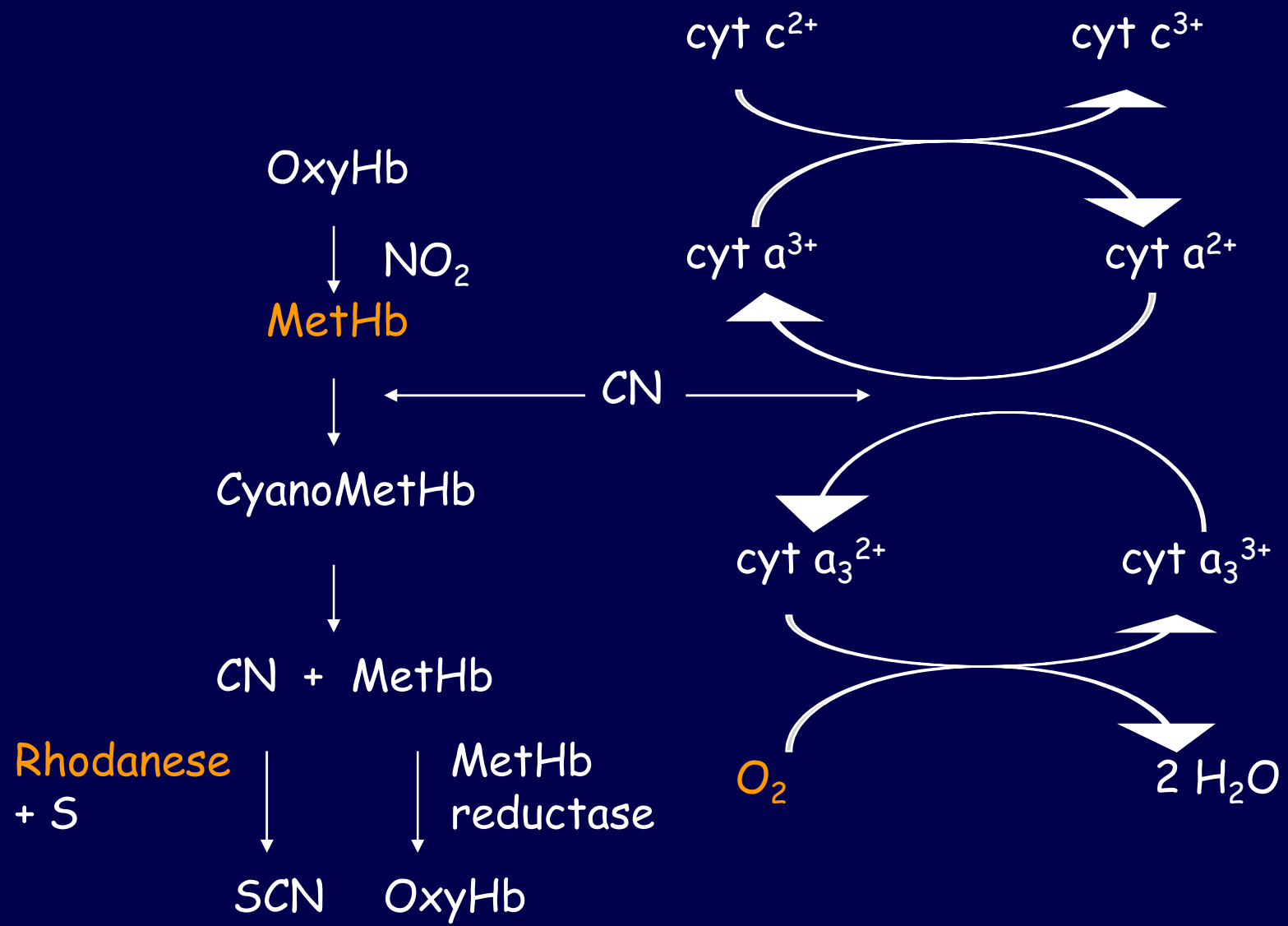
CN poisoning results in tissue hypoxia, acidosis and death.



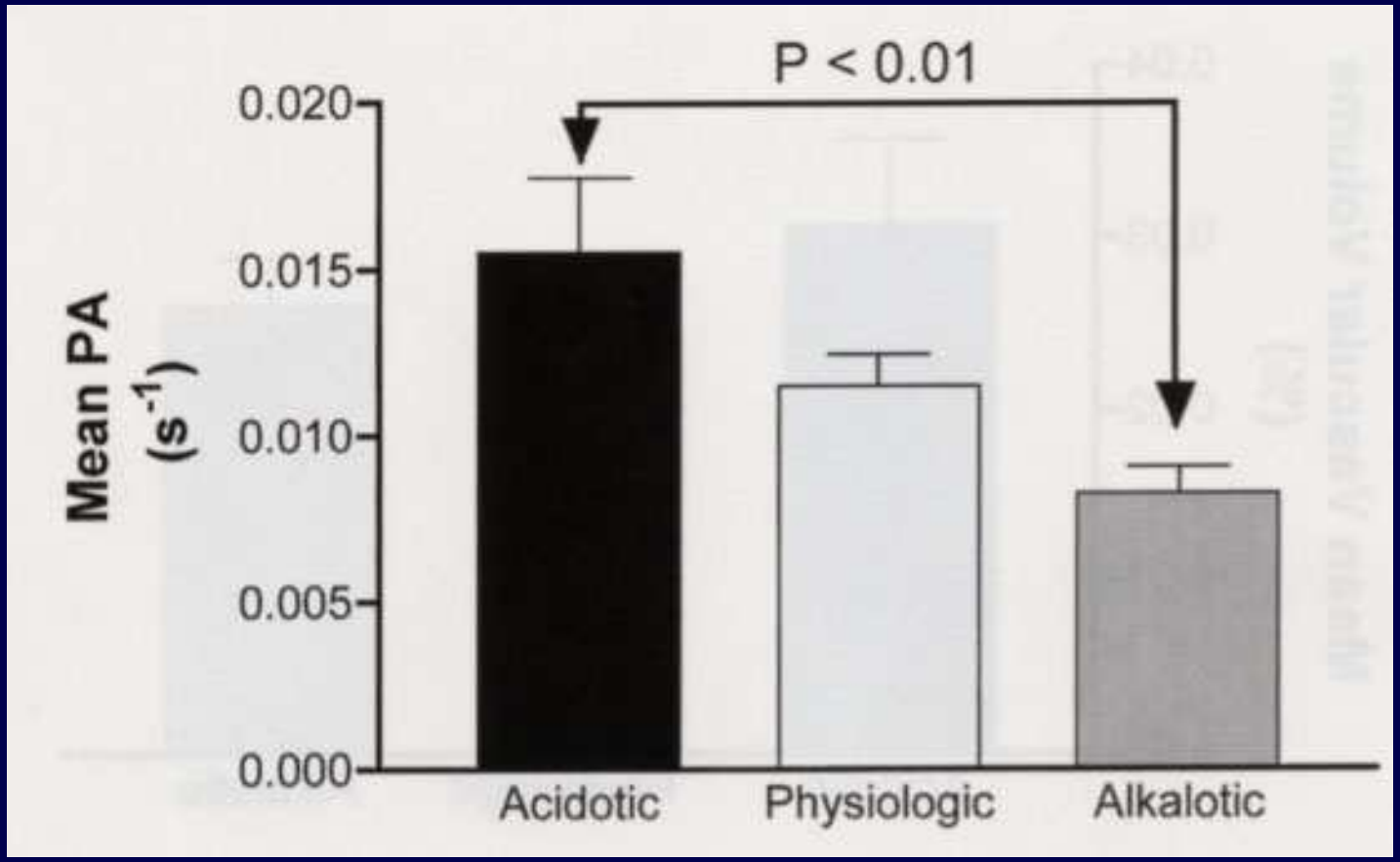
CN levels in fire-related deaths



Pathways of cyanide toxicity and detoxification



Increase of CN distribution into the brain with acidosis



Djerad A. *Tox Sci* 2001

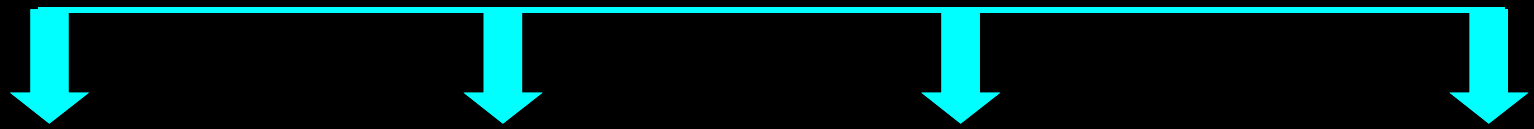
Clinical presentation
Delay in onset of clinical manifestations

Seconds : HCN

Minutes : CN salts

Hours : Cyanogenic compounds :
Nitriles
Nitroprusside

Clinical presentation



Neurological

Dizziness
Restlessness
Anxiety
↓
Confusion
↓
Coma
+
Seizures

Respiratory

Hyperpnea
↓
Central apnea
±
Pulmonary edema

Cardiovascular

HTA
↓
Shock
↓
Cardiac arrest

Metabolic

↗ Blood glucose
↗ Lactate
Metabolic acidosis
Rhabdomyolysis
Renal failure

Positive diagnosis

Smoke inhalation

The two fundamental signs are :

1)- **Soot in the airways** (nostrils, mouth, throats)

2)- **Neurological impairment** (Headaches, dizziness, confusion, seizures, changes in mental status, coma)

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Carbon monoxide intoxication	83	63	43	92
Cyanide intoxication	98	56	28	99

Vital signs in pure CO poisoning

Symptoms	*CO (mmol/l)*	*SBP (mmHg)*	*HR (/min)*	RR (/min)	Lactates (mmol/1)
Severe (n= 54)	2.87 ± 2.15	124 ± 19	88 ± 15	19 ± 4	3.2 ± 1.7
Moderate (n= 12)	0.84 ± 0.82	126 ± 18	85 ± 20	19 ± 3	2.3 ± 1.2
Mild (n= 65)	0.43 ± 0.56	125 ± 18	82 ± 13	19 ± 5	1.9 ± 0.9
Asymptomatic (n=15)	0.38 ± 0.45	128 ± 19	80 ± 6	17 ± 4	1.9 ± 0.7
p value		0.9	0.07	0.6	< 0.0001

Benaissa ML. *Intensive Care Med* 2003

Diagnosis of cyanide poisoning

1- Cardiovascular impairment

Hypotension, collapse, shock, or cardiac arrest
Transient reversible cardiomyopathy

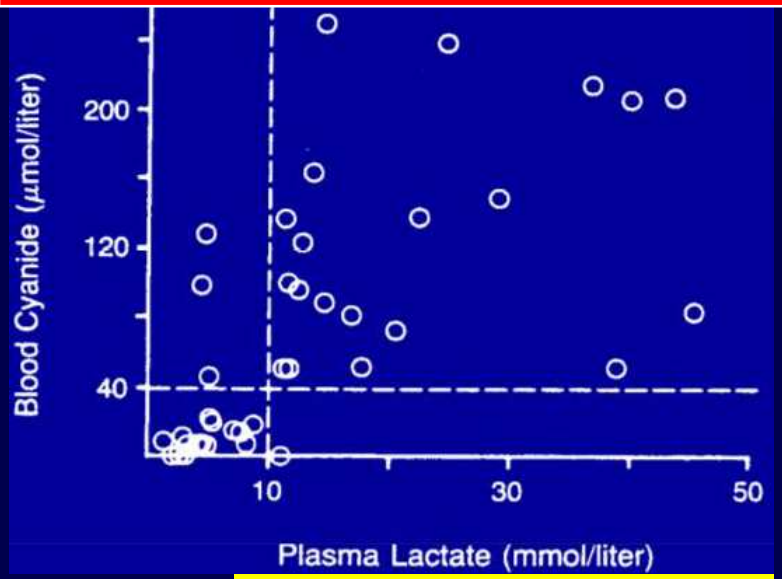
2- Abnormal respiratory pattern

Polypnea, wide ventilation, hypopnea or apnea

3- Metabolic impairment

Lactate concentration > 10 mmol/l in the presence of smoke inhalation without severe burns is strongly suggestive of CN (≥ 40 µmol/l) intoxication.

Se: 87 % - Spe: 94 % - PPV: 95 %



Baud FJ. *NEJM* 1991

Occurrence of signs and symptoms in cases of CO and CN poisonings

Signs and symptoms	CO (%)	CN (%)
Headache	64	6
Dizziness	56	6
Gastro-intestinal	43	33
Altered mental status	15	13
Loss of consciousness	31	NR
Coma	25	70
Dilated pupils	6	77
Seizures	3	34
Abnormal respiratory pattern	23	95
Pulmonary oedema	6	6
Hypotension/shock	7	61
Plasma lactate (mM) + coma	2.8	13.4

Clinical symptoms among 36 cyanide intoxications* admitted to the Toxicological Intensive Care Unit at Fernand Widal Hospital in Paris, France

Symptom	N =	%
Asymptomatic	8	22
Cardiovascular collapse	10	28
Coma	13	36
Convulsions	6	17
Respiratory arrest	8	22
Metabolic acidosis	18	50
Post-anoxic coma and death	5	14
Psychomotor retardation	6	17

* Intoxications by ingestion or inhalation, excluding smoke inhalation victims

Type of Poison, Blood Cyanide and Plasma Lactate Concentrations, Clinical Status at the Time of Presentation, and Final Outcome in 11 Cases of Acute Cyanide Poisoning

	Type of Cyanide	Blood Cyanide (µmol/L)	Plasma Lactate (mmol/L)	Systolic Blood Pressure (mm Hg)	Respiratory Rate (b/min)	Glasgow Coma Score	Outcome
1	KCN	256	53.0	40	0	3	Fatal
2	KCN	239	47.7	40	0	3	Fatal
3	$Hg(CN)_2$	217	19.6	60	ND	15	Survival
4	CN salt	196	21.0	0	0	3	Fatal
5	KCN	158	8.6	160	25	15	Survival
6	KCN	154	13.6	110	8	12	Survival
7	KCN	150	17.7	95	0	3	Fatal
8	KCN	125	24.6	70	ND	15	Survival
9	$Au(CN)_2$ - KCN	44	4.8	120	ND	15	Survival
10	BrCN*	13	5.1	130	18	15	Survival
11	KCN	ND*	ND*	80	0	3	Survival

Baud F. *Crit Care Med* 2002

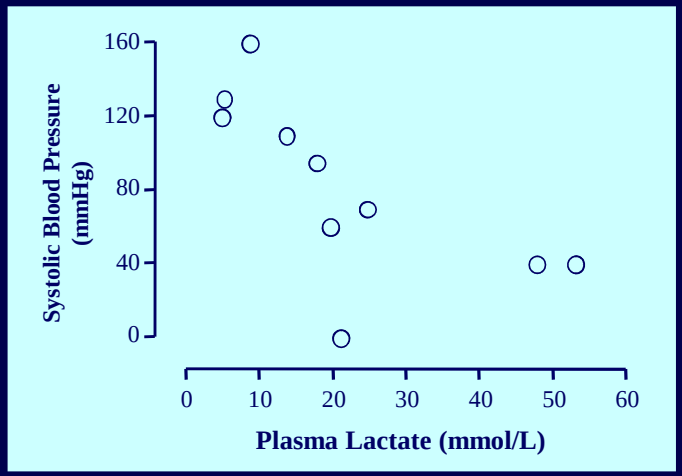
Arterial Gases in 11 Cases of Acute Cyanide Poisonings

Patients	Arterial pH	Arterial PaCO2 (mm Hg)	Arterial PaO2 (mm Hg)	Anion Gap (mmol/L)
1	7.16	24.2	446.6	39.0
2	7.22	53.6	84.0	37.5
3	7.33	37.2	131.3	32.4
4	7.24	19.4	513.8	49.8
5	7.36	37.4	102.8	26.4
6	7.27	18.7	169.7	19.3
7	7.38	27.0	491.3	29.3
8	ND	ND	ND	ND
9	7.38	48.0	65.3	21.7
10	7.57	22.8	94.2	21.4
11	ND	ND	ND	ND

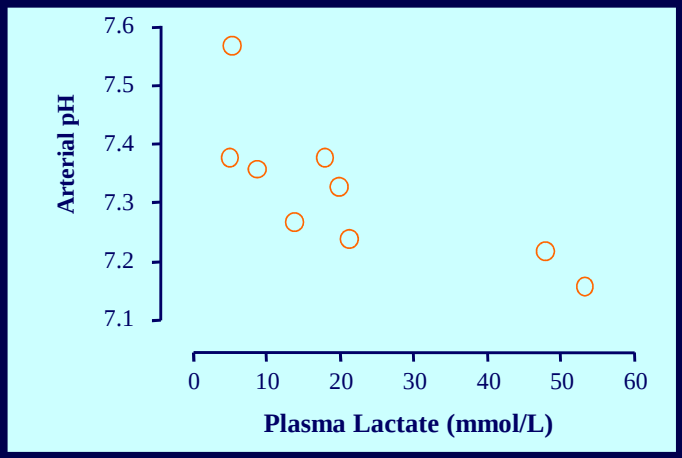
ND : denotes not determined.

Baud F. *Crit Care Med* 2002

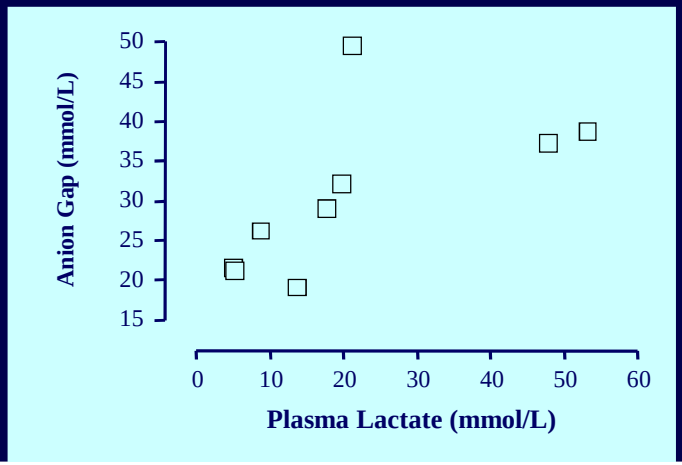
Correlation between the plasma lactate concentrations and the systolic blood pressure, the arterial pH, and the anion gap before antidotal treatment



r = 0.87
p = 0.002



r = 0.87
p = 0.0004



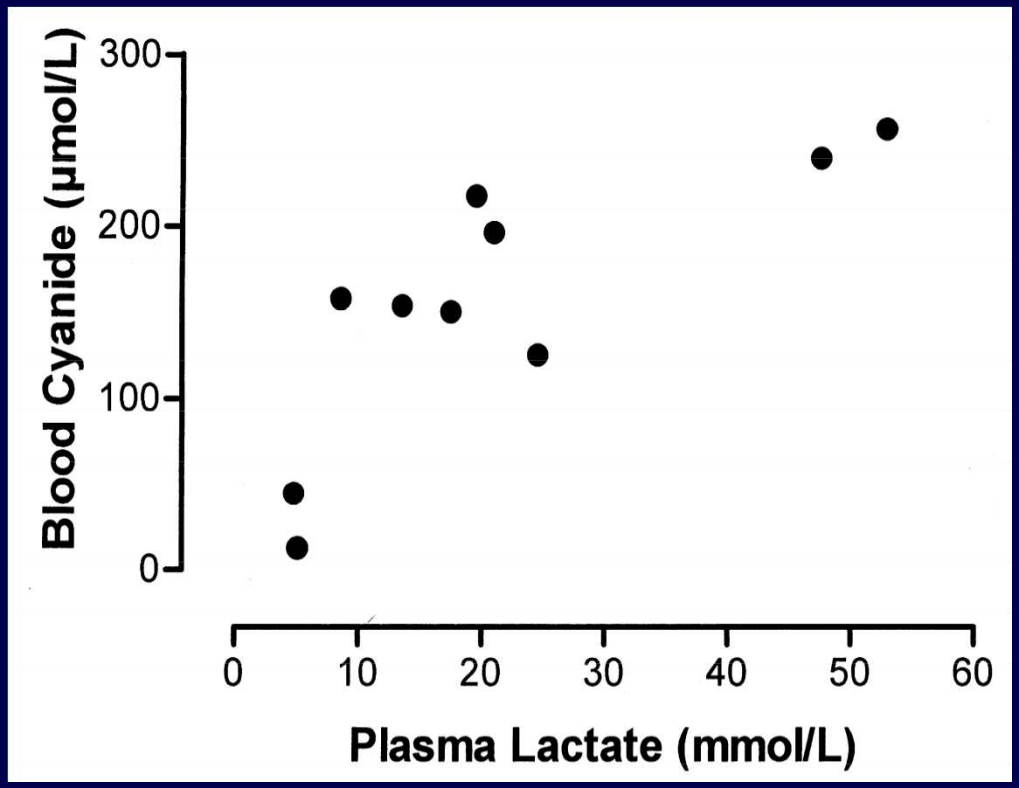
r = 0.83
p = 0.008

Baud F. *Crit Care Med* 2002

Correlation of blood cyanide and plasma lactate before antidotal treatment

Before antidotal treatment :

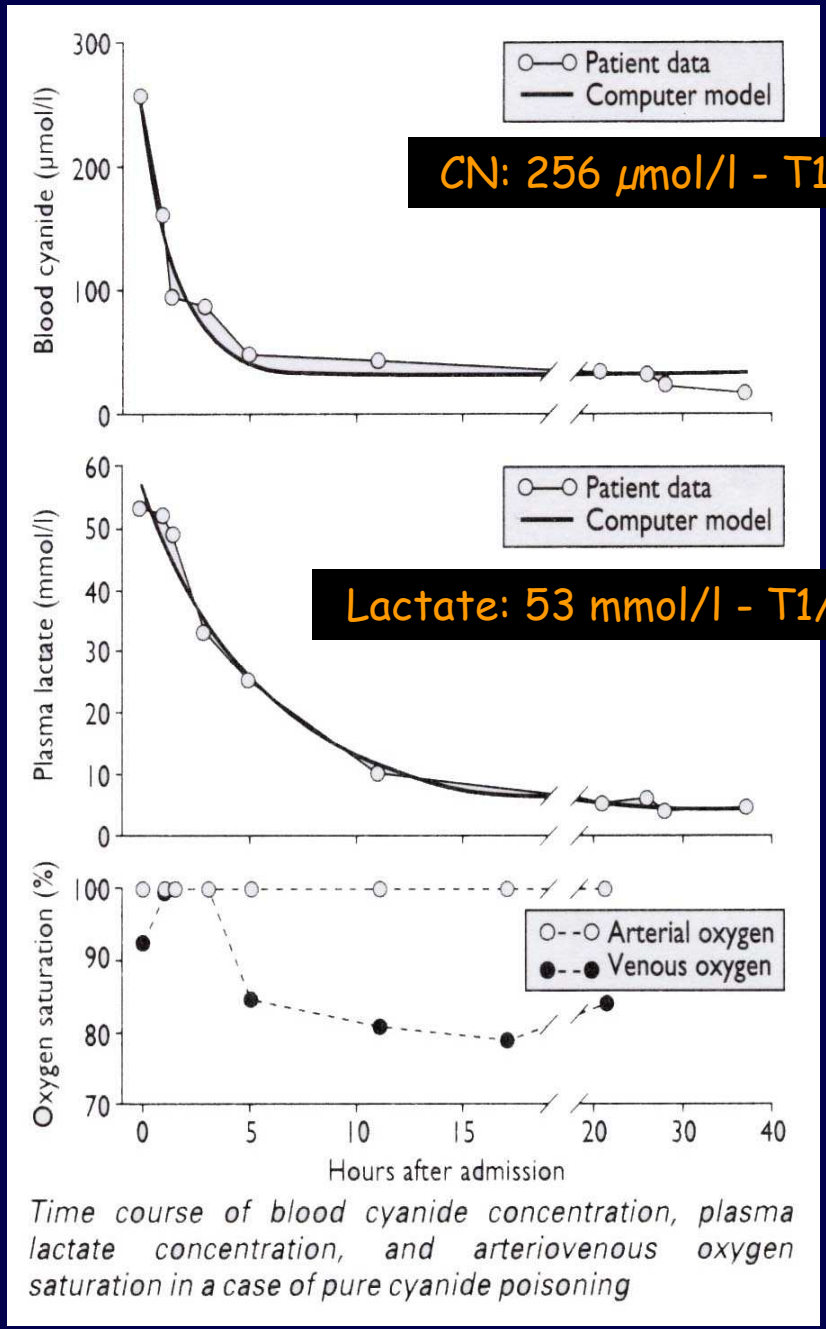
- The median plasma lactate concentration was 18.6 mmol/L
- The median blood cyanide concentration was 155.9 µmol/L.



r = 0.74
p = 0.017

Baud F. *Crit Care Med* 2002

Relationship of plasma lactate concentrations to blood CN levels in a patient with pure acute CN poisoning



Time course of blood cyanide concentration, plasma lactate concentration, and arteriovenous oxygen saturation in a case of pure cyanide poisoning

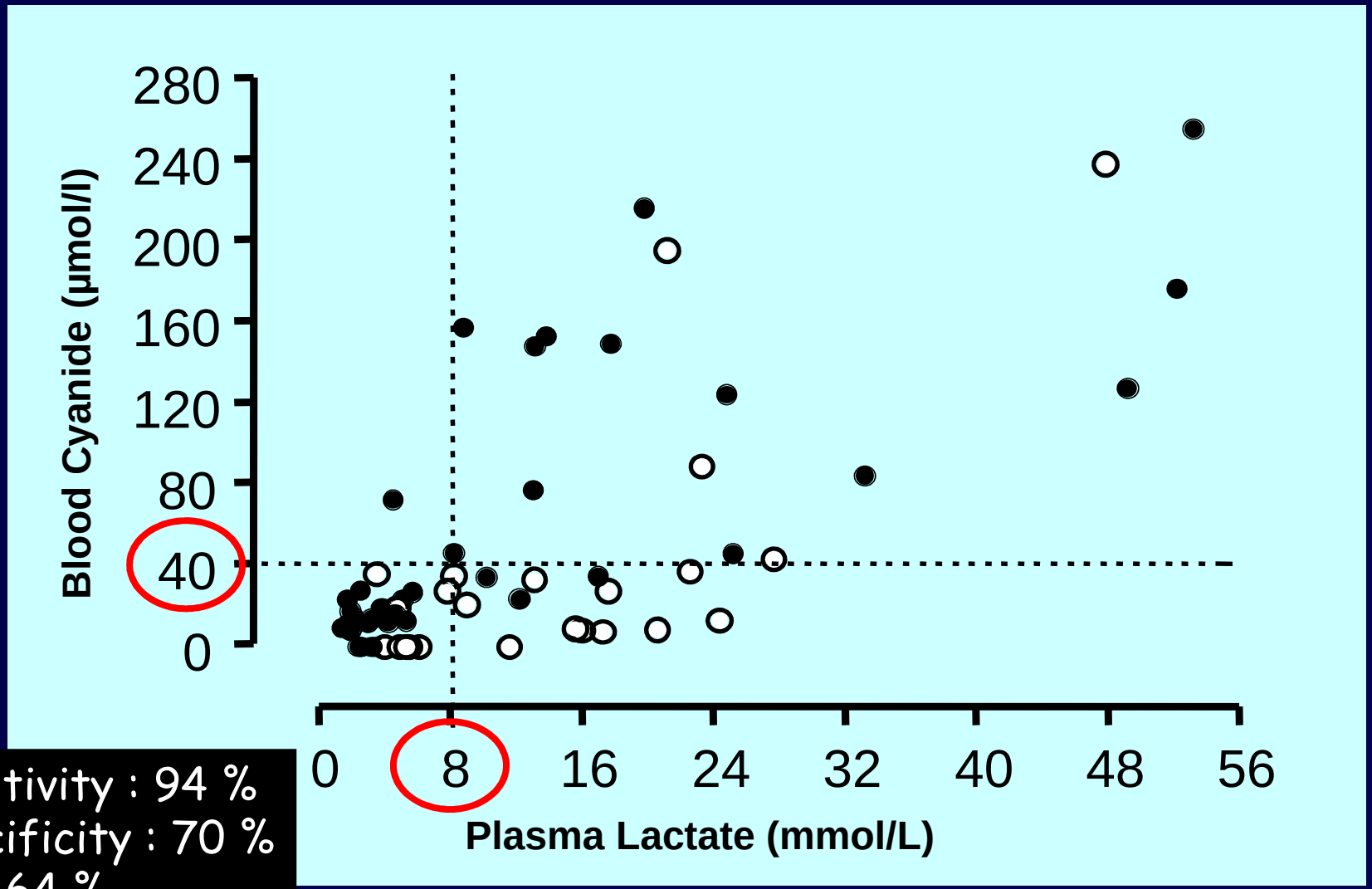
Baud F. *BMJ* 1996

Origin of lactate in poisonings ?

- Lactic acidosis is not specific. Various toxicants can induce lactic acidosis : CO, Azide, H_2S, …

- Several factors can contribute to lactic acidosis :
  - Cardiovascular failure
  - Apnea
  - Seizures
  - Acute liver failure
  - Catecholamine rush
  - Mitochondrial dysfunction

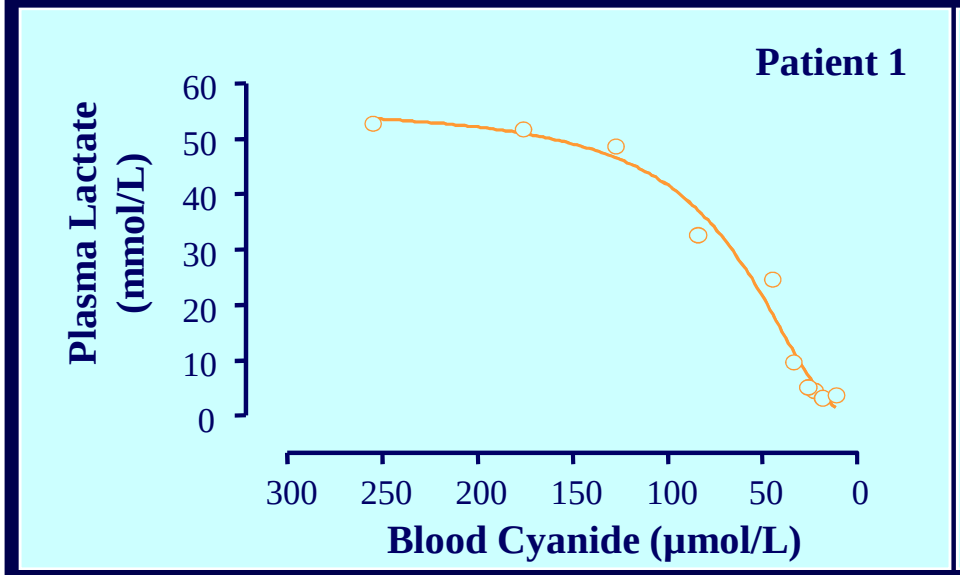
Interest of lactate measurement in cyanide poisoning

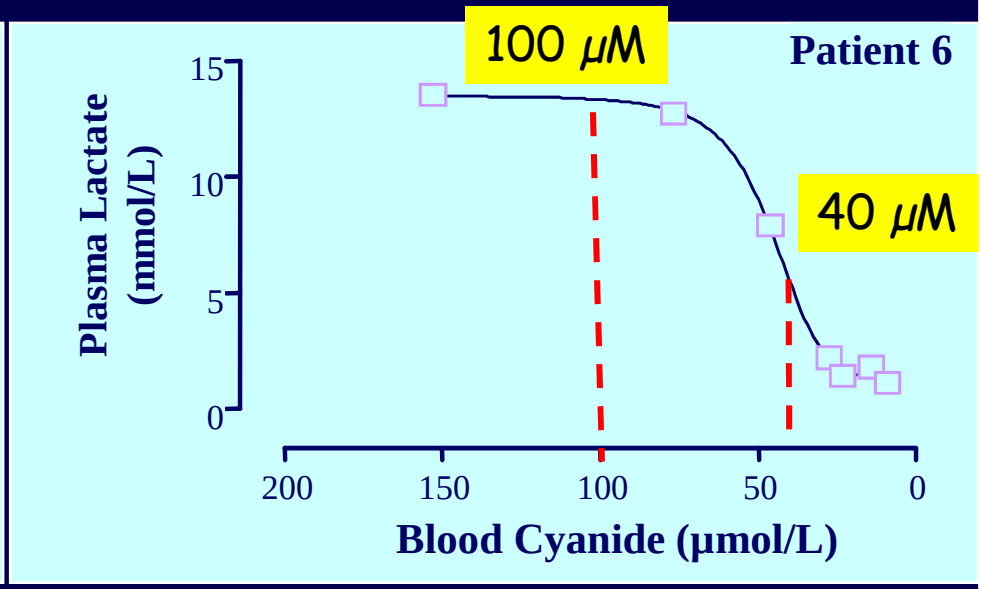


Sensitivity : 94 %
Specificity : 70 %
PPV: 64 %
NPV: 98 %

Baud F. *Crit Care Med* 2002

TK-TD relationships in 2 cases of CN poisoning





Patients	E0 (mmol/L)	Emax (mmol/L)	C50 (µmol/L)	N	R^2
1	0.3 (4.2)	55.7 (7.9)	62.6 (8.6)	2.2 (0.6)	0.981
6	1.4 (0.2)	12.1 (0.4)	45.5 (1.1)	5.4 (0.9)	0.998

$$E = Emax * C^n / [C_{50}^n + C^n] + E_0$$

Baud F. *Crit Care Med* 2002

Does Cyanide toxidrome exist ?

Most frequent presentation = Rapid onset of (N = 86)

Neurological symptoms	73 %
Mydriasis	71 %
Seizures	30 %
Cardiovascular symptoms	
Tachycardia	99 ± 33 / min
Reduction in SBP	103 ± 30 mmHg
Abnormal respiratory pattern	92 %
without pulmonary edema	94 %
Metabolic acidosis	7.20 ± 0.24
lactate increase	16.9 ± 11 mmol/l
SvO_2 arteriolization	89.5 ± 6.2%
Cardiac arrest (10 %), death (24 %)	

Conventional treatment of CN poisoning

Conventional treatment of cyanide poisoning includes

- Decontamination
- Supportive treatment
- Specific treatment: antidotes

Decontamination

- Decontamination attempts to decrease the bioavailability of cyanide.
- Decontamination should be adapted to the conditions of cyanide poisoning.
- Does decontamination improves the prognostic of this poisoning ?

Decontamination should be performed but never postpone supportive treatment.

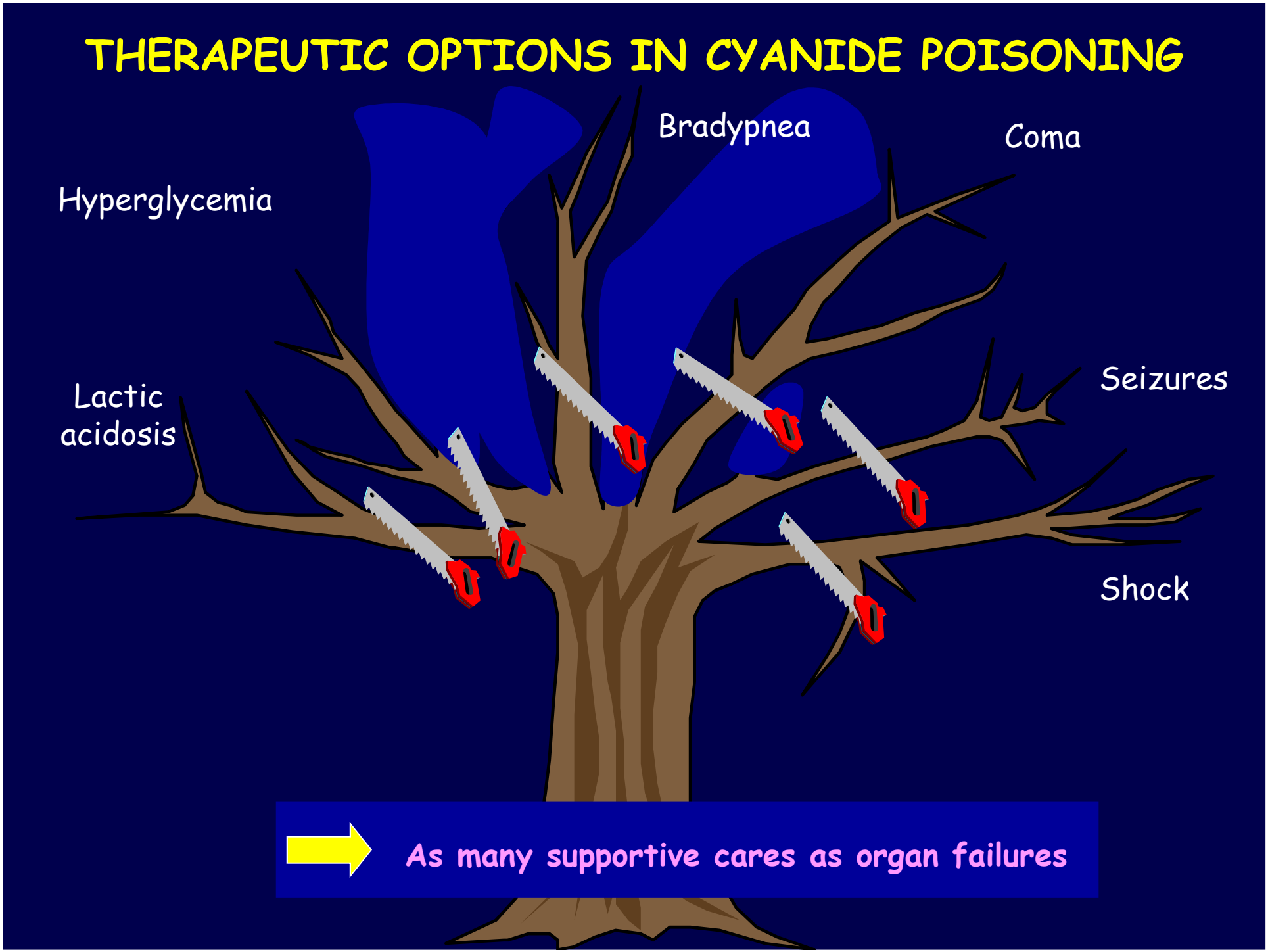
Supportive treatment

- Basic life-support of CN poisoning includes :
  1- Immediate administration of high flow of oxygen,
  2- Protection of the airways,
  3- Cardiopulmonary resuscitation.

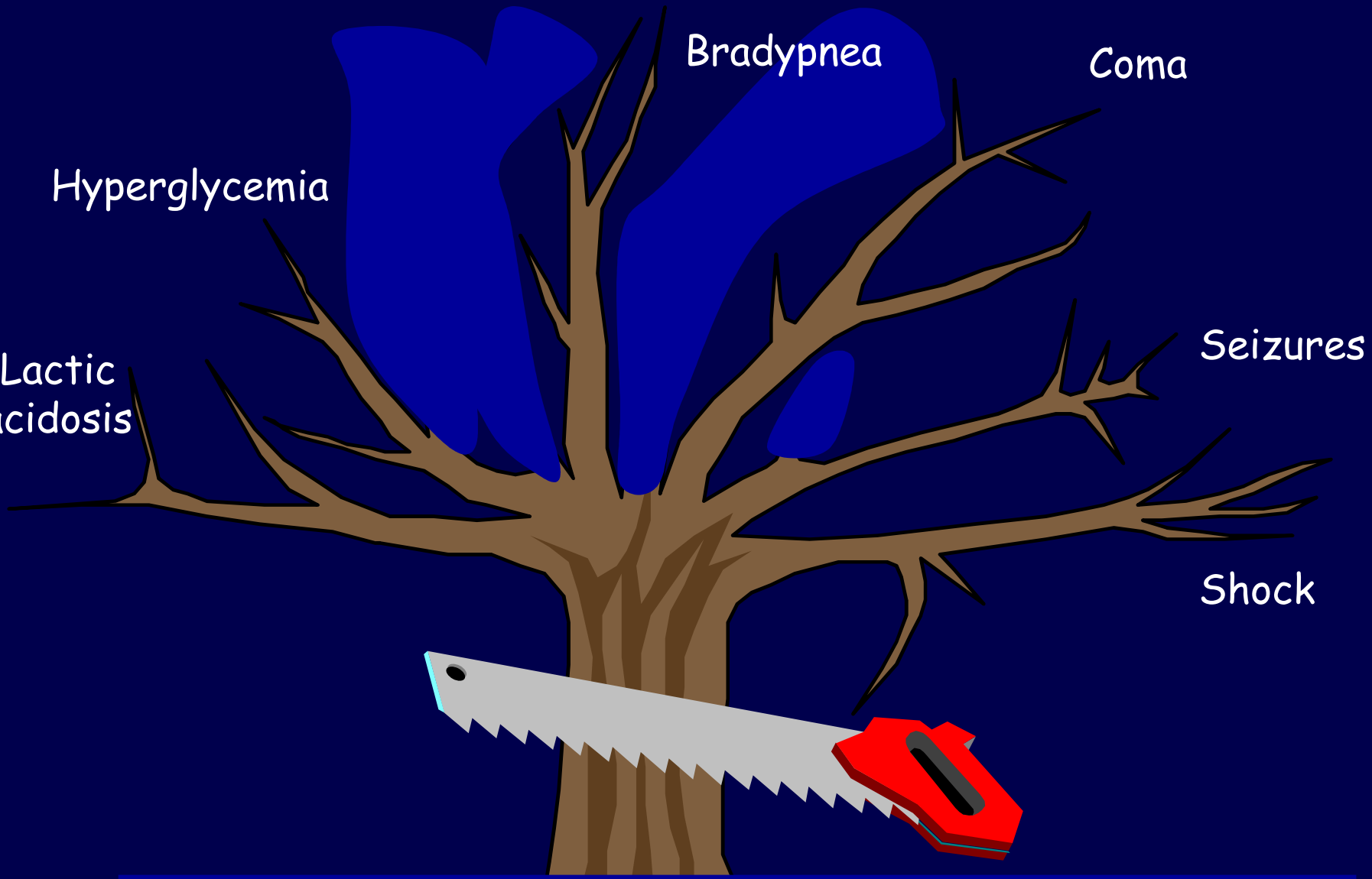
- Advanced life support includes:
  1- Endotracheal intubation in comatose patients
  2- Anti-epileptic drugs in case of seizures,
  3- Epinephrine infusion to correct cardiovascular collapse,
  4- Sodium bicarbonate to correct deep metabolic acidosis.

- Supportive treatment is efficient in pure CN poisoning.

THERAPEUTIC OPTIONS IN CYANIDE POISONING



THERAPEUTIC OPTIONS IN CYANIDE POISONING



Oxygen + hydroxocobalamin ± sodium thiosulfate
A combination treatment for all symptoms

Therapeutic strategies of this rare poisoning

- should take into account for the most common cause of cyanide poisoning in western countries, i.e. smoke inhalation which always results in a poly-intoxication involving CO.

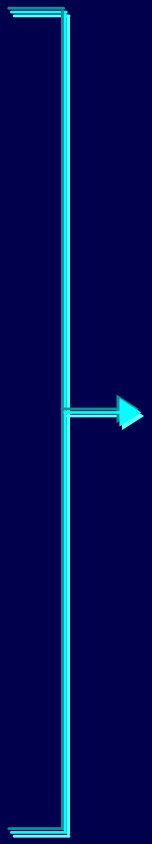
An emergency antidote is an available drug

allowing a right to error = safety first + proven efficiency

The list of antidotes to cyanide

Toxicodynamic treatment

- **Oxygen**
- **Methaemoglobin forming agents**
  - Nitrites
  - DMAP (dimethylaminophenol)
- **Cobalt compounds**
  - Dicobalt EDTA
  - Hydroxocobalamin
- **Sulfur donors**
  - Thiosulfate



Toxicokinetic treatments

The only available FDA-approved antidote in the US until 6 years ago was the Pharmaceutical Cyanide Antidote Kit

Contains 3 components:

- **Amyl nitrite pearls:**
  In the absence of IV access, gauze sponge[illegible] 30 sec each min
  or held between the O_2 source and the[illegible]

- **A solution of 3% sodium nitrite:**
  10 ml (0.33 ml/kg) IV 2-4[illegible] 100-150 ml solution
  Repeat at half the initial[illegible] absence of response
  Produce 30% Met[illegible]
  + Vasopressor[illegible], vasodilatation)

- **25% sodium thiosulfate:**
  50 ml (1.65 ml/kg)

I do not use it

$$Fe^{3+}metHb + CN\text{-}Fe^{3+}Cytaa_3 \longrightarrow CN\text{-}metHb$$

Dicobalt EDTA (Kelocyanor®)

I do not use it

- Currently used in Europe but not av… USA
- Dose: 300-600 mg IV ov…
- Repeat dose in … rovement
- **Adverse eff…** tachypnea, cardiovascular and hemdynamic instability, seizures, gastrointestinal symptoms, angioedema, allergic manifestations

Marrs TC. *Clin Tox* 2016

Thiosulfate

I exceptionally use it

- Rhodanese, a sulfur transferase locat… chondria: irreversible transfer of a sulfane… hiosulfate to CN
- Large doses required, si… ntracellular penetration. Limited interest in a… since slow detoxification ($t_{1/2}$:26 h)
- Dose: 8 - 16… infusion, after initial bolus.
- Us… ile poisoning (CN hepatic production).

$$CN\text{-}Fe^{3+}Cyt.Ox\ a3 + Na_2SO_3 \longrightarrow \text{Thiocyanates}$$

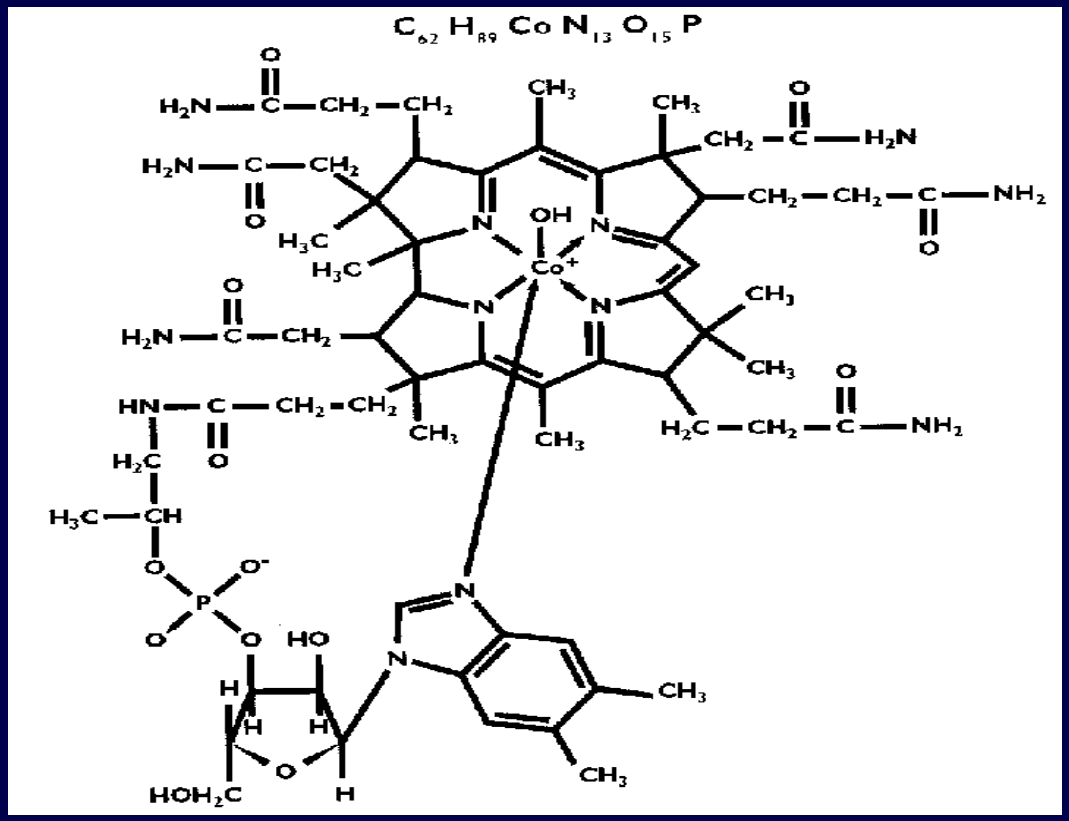
Hydroxocobalamin (Cyano

I systematically use it

- Currently used in Europe and rece A
- 50 g of hydroxycobalamin t N
- Dose: 5 g (70 mg/kg 5g) IV (15 min), repeated according to seriousness (g).
- Ability to ne blood-brain barrier
- Ad reddish discoloration of the skin and urine, allergic

Borron SW. *Ann Emerg Med* 2007

Hydroxocobalamin molecule



OH

CN-Fe^{3+}Cyt.Ox a3 +

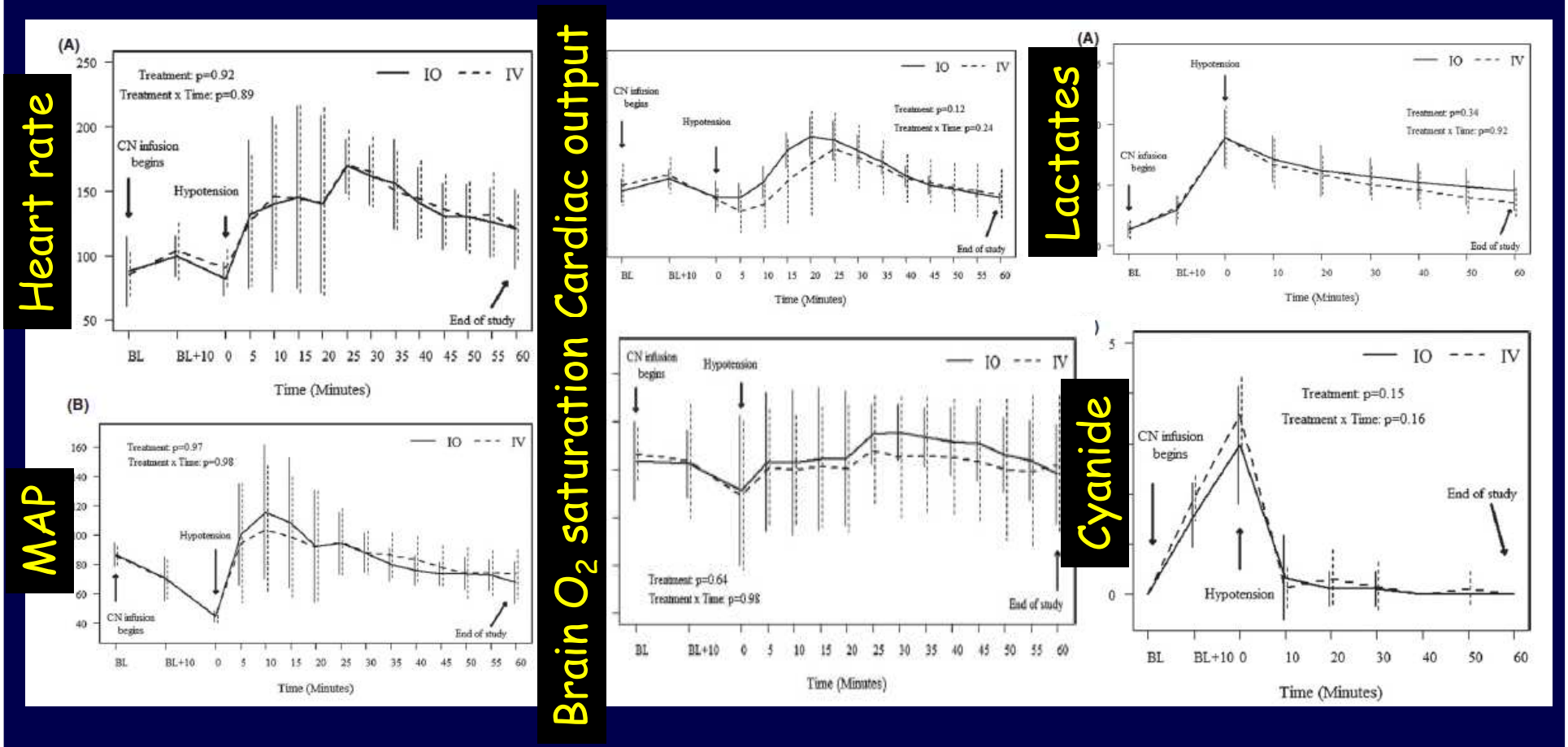
CN

+ Fe^{3+}-Cyt. Ox a3

Hydroxocobalamine

Cyanocobalamine

Intraosseous vs. intravenous infusion of hydroxocobalamin to treat acute severe cyanide toxicity in a swine model

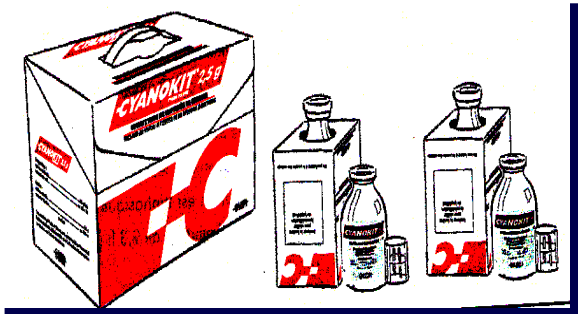


Bebarta VS. Acad Emerg Med 2014

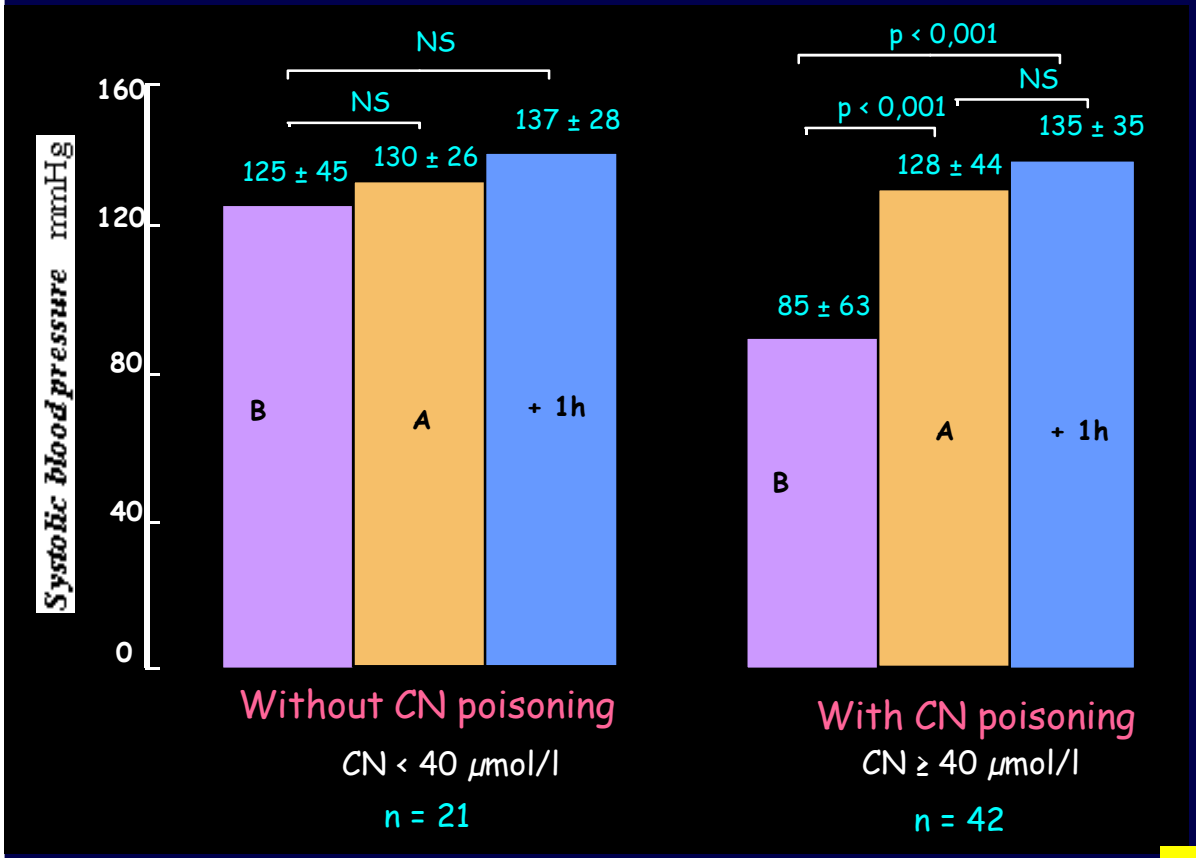
Assessment of hydroxocobalamin efficiency in experimental studies of cyanide poisoning

Fifty-four beagle dogs were poisoned by IV administration of a potentially lethal dose of potassium cyanide.

Borron SW. *Clin Tox* 2006



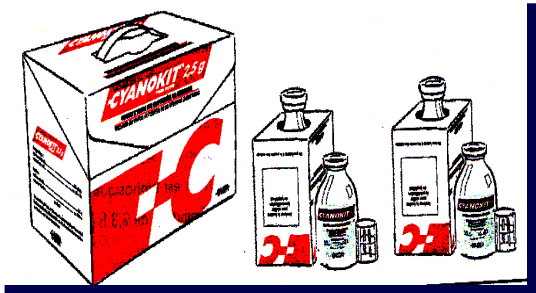
Prospective study of fire victims treated with empiric hydroxocobalamin



67% survivors among the 42 patients confirmed *a posteriori* to have had CN poisoning.

Well-tolerated treatment irrespective of the presence of CN poisoning.

Borron SW. Ann Emerg Med 2007



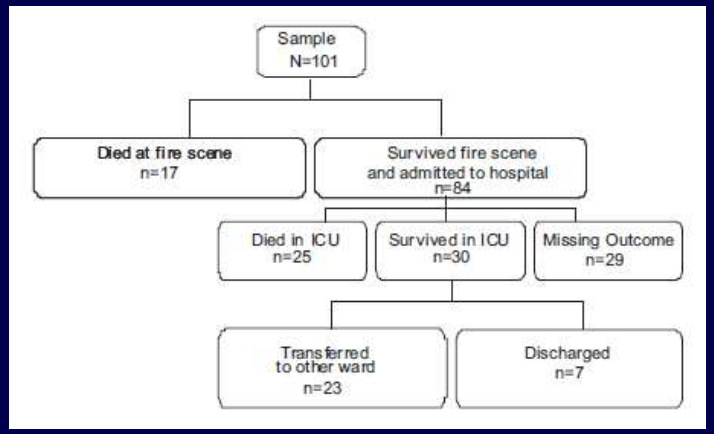
Utility and outcomes of hydroxocobalamin use in smoke inhalation patients

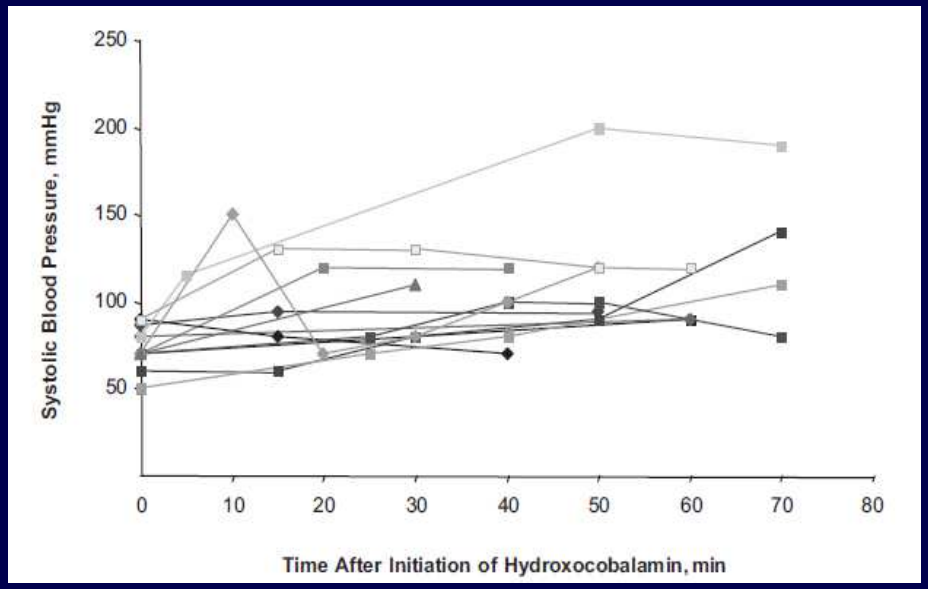
	Overall (n = 273)	Hydroxocobalamin (n = 138)	No hydroxocobalamin (n = 135)	p
7 day creatinine difference (mg/dL), median (IQR)	0.09 (−0.05 to 0.29)	0.09 (−0.04 to 0.24)	0.08 (−0.50 to 2.81)	0.95
Pneumonia, n (%)	97 (35.5)	31 (22.5)	66 (48.9)	<0.01
Ventilator days*, median (IQR)	5.0 (2–13)	4.0 (1–10)	7.0 (3–16)	<0.01
Vent-free days (VFD)†, median (IQR)	15.0 (0–25)	20.0 (0–26)	11.0 (0–24)	0.02
ICU LOS, days, median (IQR)	6.0 (2–15)	6.0 (2–13)	10 (4–20)	0.03
HLOS, days, median (IQR)	10.0 (3–20)	7.0 (3–18)	11.0 (5–24)	0.06
Mortality, n (%)	78 (28.6)	40 (29.0)	38 (28.1)	0.89

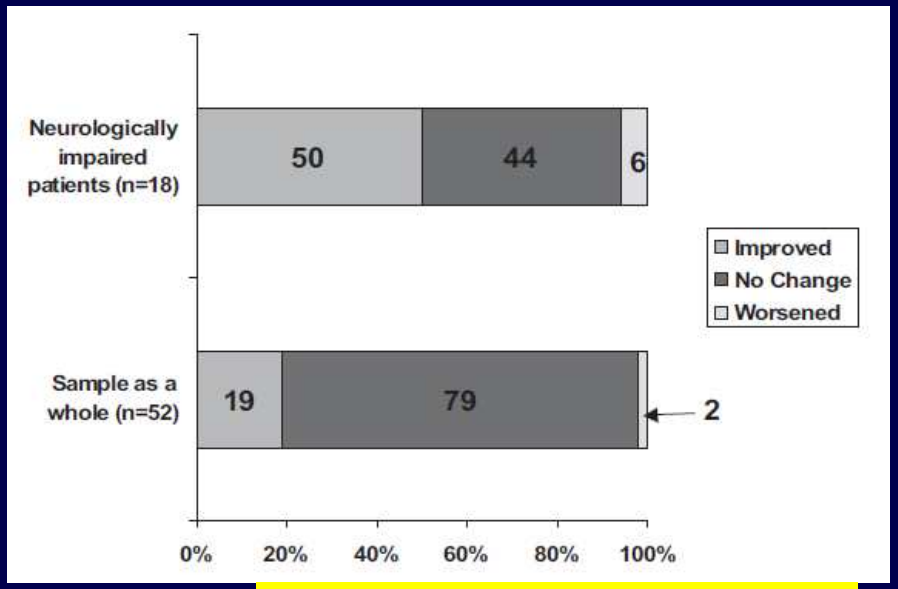
Routine administration was associated with lower rate of pneumonia, faster liberation from the ventilator, and reductions in ICU stay

Nguyen L. Burns 2017

Prehospital administration of hydroxocobalamin for smoke inhalation-associated CN Poisoning: 8 years of experience in the Paris Fire Brigade



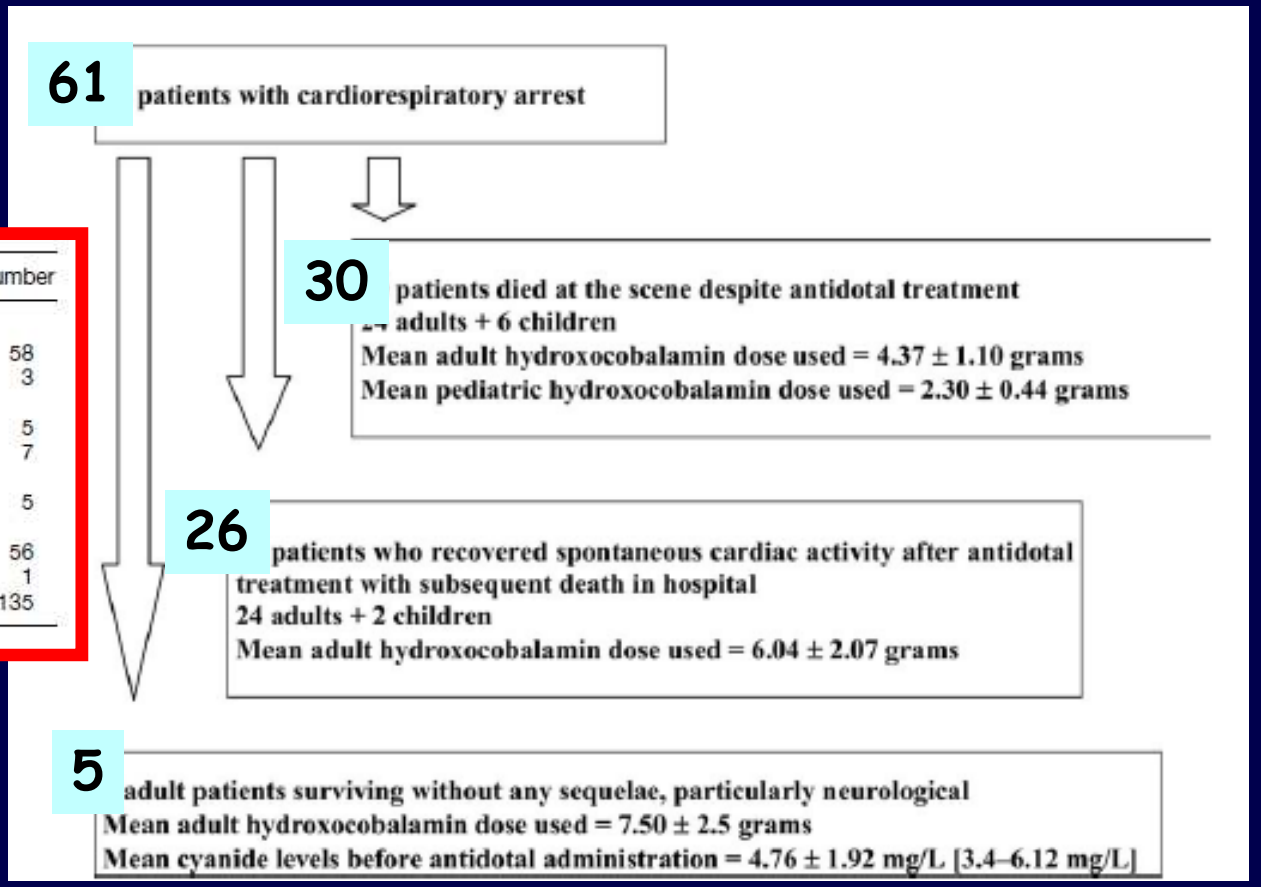




Fortin JL. Clin Toxicol 2007

Cardiac disorders in smoke inhalation-associated CN poisoning

Cardiac Disorder	Number
Cardiocirculatory arrest	
Asystole	58
Ventricular fibrillation	3
Repolarization disorders	
Myocardial ischemia	5
Subendocardial lesion	7
Conduction disorders	
Intracardiac	5
Rhythm disorders	
Supraventricular tachycardia	56
Ventricular tachycardia	1
Total	135



Fortin JL. J Emerg Med 2010

Pre-hospital algorithm

EuSEM guidelines 2012

Smoke inhalation incident

Evaluate:
- Fire in an enclosed space
- Duration of exposure
- Nimber of victims

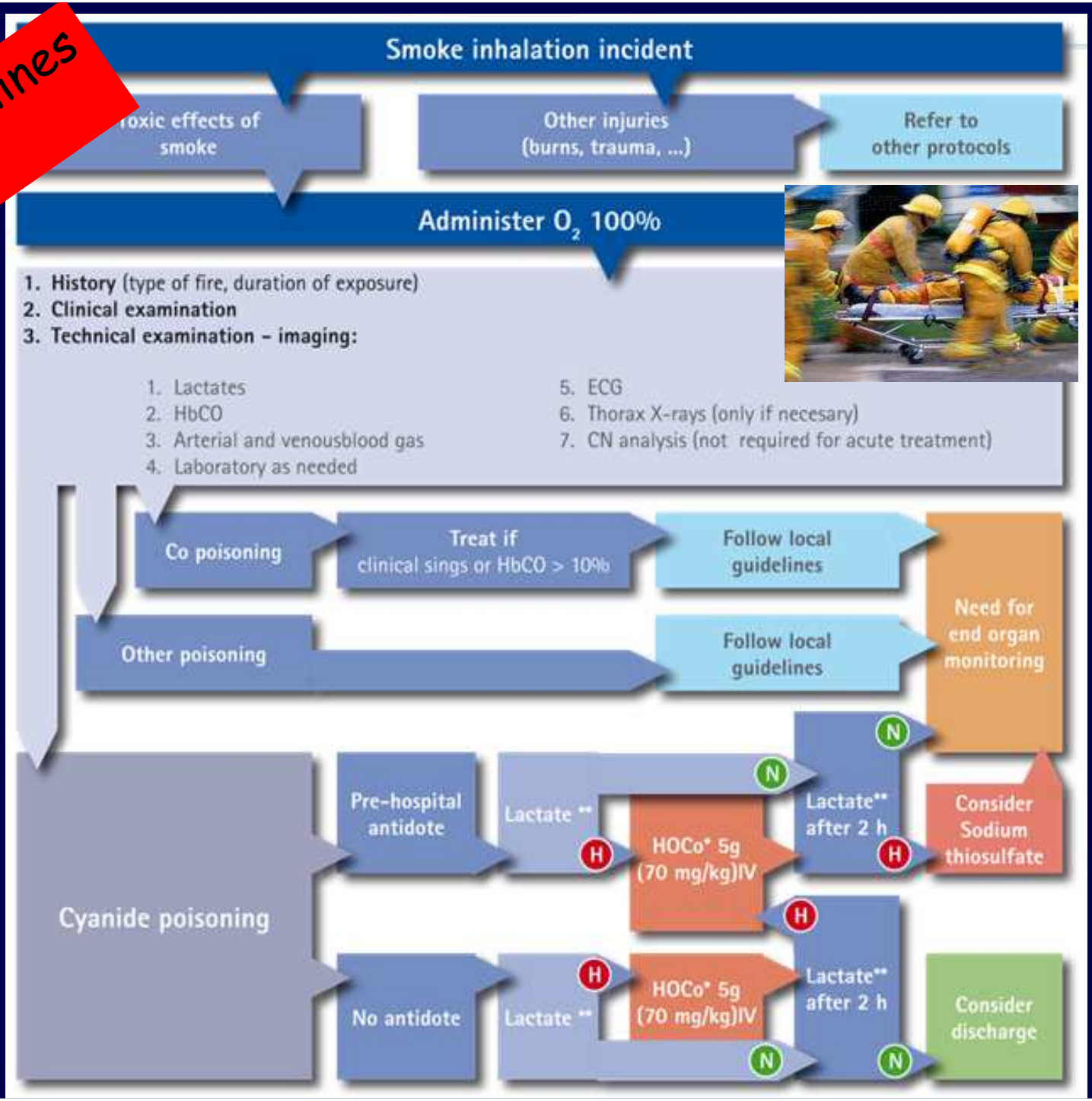
Administer O_2 100%

Severe poisoning GCS ≤ 9	Intermediate poisoning GCS 10-13 and/or abnormal ABC	No neurological and/or hemodynamic symptoms GCS ≥14
Collect blood samples, if possible		
Hydroxocobalamin 5g (70 mg/kg)*	Hydroxocobalamin 5g (70 mg/kg)**	Monitoring

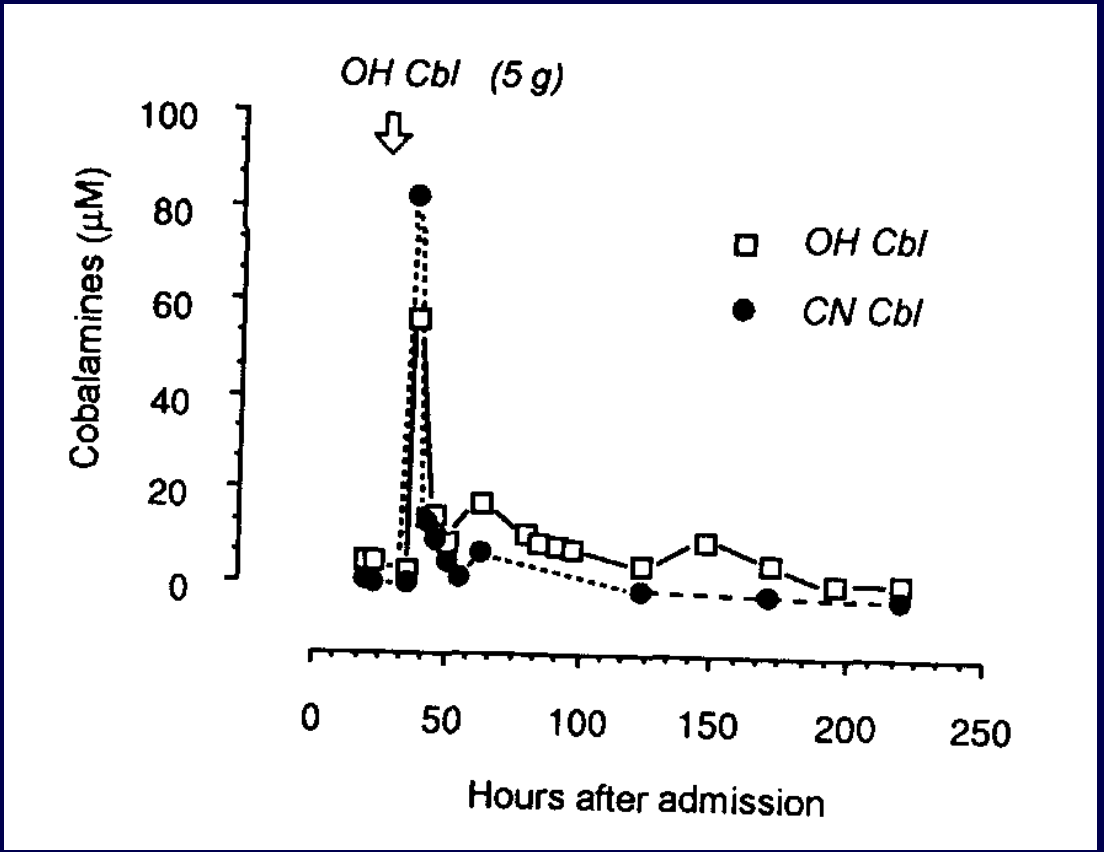
Transfer to hospital

EuSEM guidelines 2012

Hospital algorithm



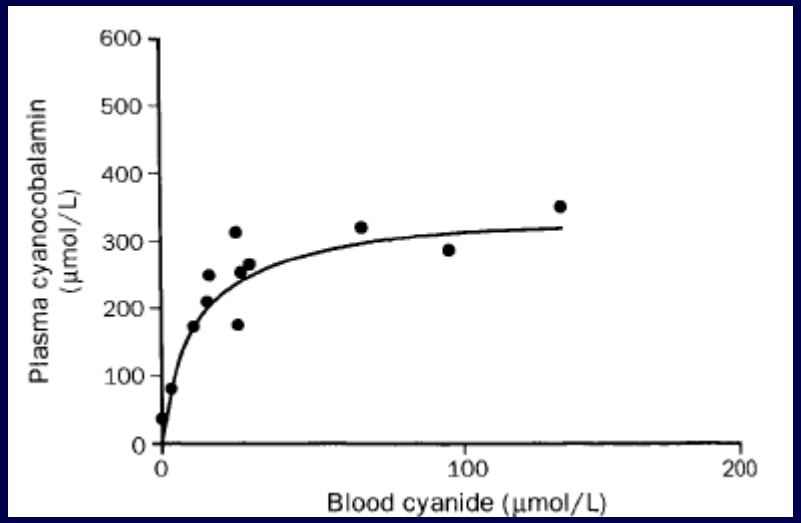
Hydroxocobalamin pharmacokinetics

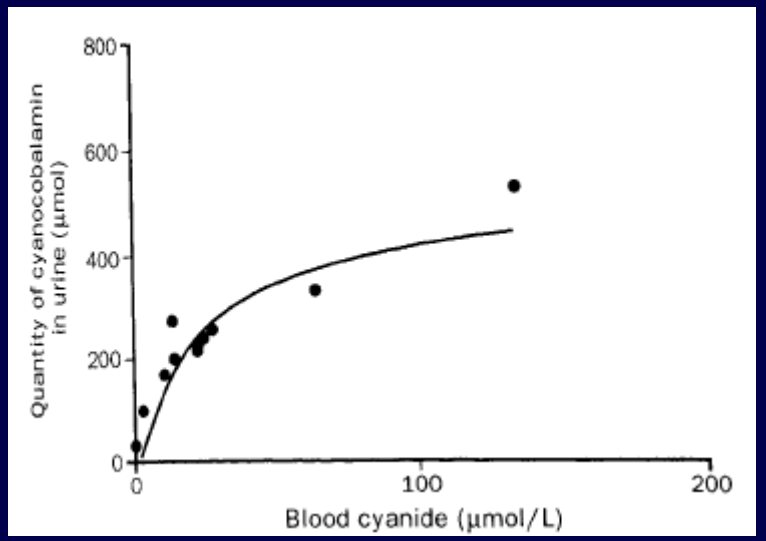


Typical PK profile from a severely CN poisoned patient treated with a 5-g hydroxocobalamin (OHCbl). The initial cyanide level was 128 µM. Formation of cyanocobalamin (CNCbl) was immediately obseved, indicating the rapid complexation of cyanide by OHCbl, followed by the elimination of the excess OHCbl and the formed CNCbl

Astier A. *Chromatogr* 1995

Relation of blood CN to plasma cyanocobalamin concentration after a fixed dose of hydroxocobalamin





- Hydroxocobalamin 5 g can bind all available CN for CN up to 40 µM.
- A cut-off of 300 µmol/L is the maximum amount of cyanocobalamin able to be formed after hydroxocobalamin 5 g dose.
- Urinary cyanocobalamin correlateq linearly with the initial blood CN for those patients with blood CN < 40 µM.

Houeto P. Lancet 1995

Interactions with other drugs

- HOCo mixed with $S_2O_3Na_2$

  → unefficient thiosulphato-cobalamin

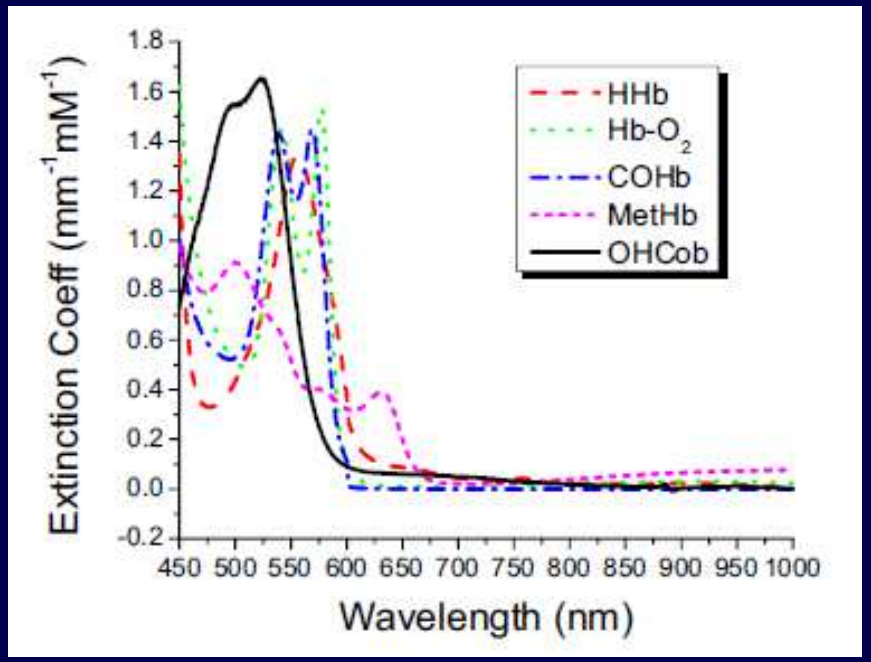
  Evans CL. Br J Pharmacol 1964

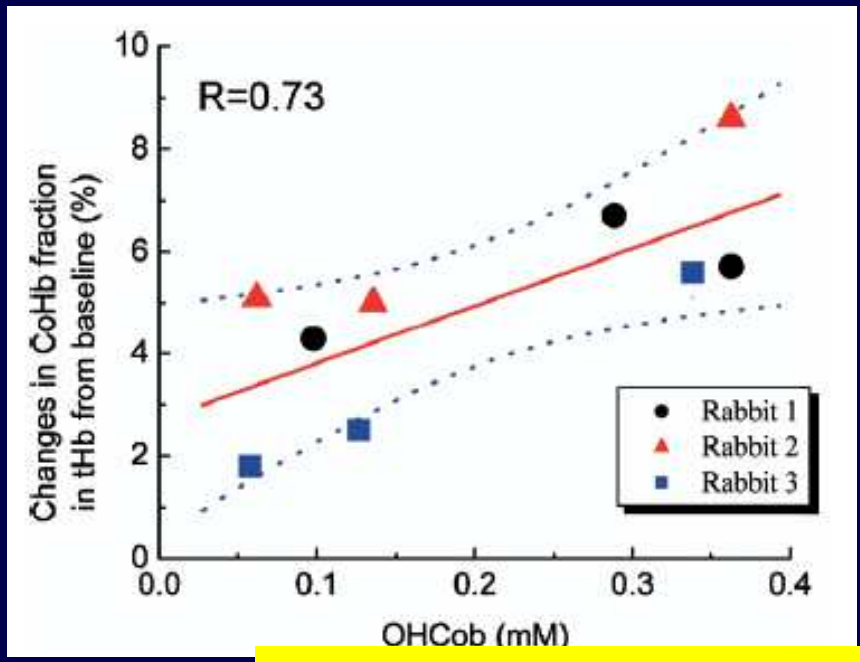
- HOCo is a chelating agent of NO

  Rajanayagam et al. Br J Pharmacol.1993

Potential interference by hydroxocobalamin

Cooximetry hemoglobin measurement





Lee J. Ann Emerg Med 2007

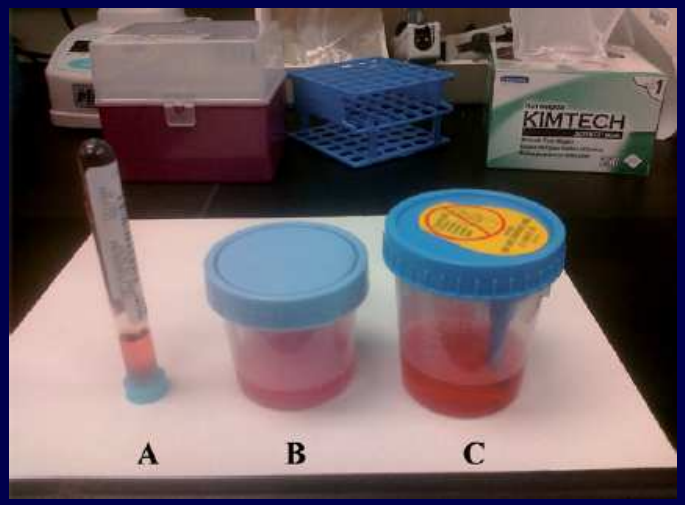
Spectrophotometric assays on the Beckman Coulter DxC and AU680 analyzers : ALT, amylase, total bilirubin, cholesterol, creatine kinase, creatinine, magnesium, uric acid.

+ On the DxC; direct bilirubin, iron, phosphate, protein and triglycerides

Ranjitkar P, Acta Clin Chem 2015

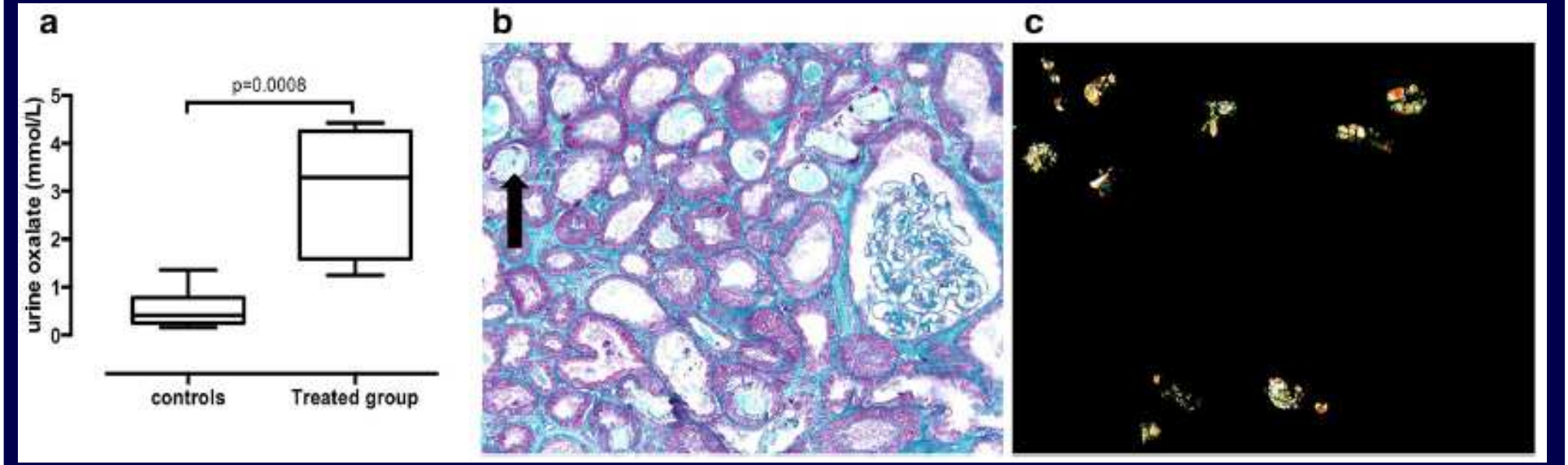
Blood leak alarm interference by hydoxocobalamin is hemodialysis machine dependent

Dialysis machine	Manufacturer	Is Pseudo-blood leak likely to happen with hydroxocobalamin use?
Althin	Baxter	No
C3	Cobe/Gambro	No
DBB 06	Nikkiso	Yes
DCS-6	Nipro	Unknown
Dialog Plus	B-Braun	Yes
Diapact	B-Braun	Yes
Diamax	Nipro	Unknown
Formula 2000 Plus	Bellco	No
Formula 2000 Domus Plus	Bellco	No
Fresenius 2008K	Fresenius	Yes
MDS 101	Asahi	No
MR100B	C-THME	Unknown
NCU-8	Nipro	Unknown
NxStage	NxStage	No
Phoenix	Gambro	No
Prismaflex	Gambro	No



Sutter ME. Clin Tox 2012
Avila J. *Clin Nephrol* 2012

Risk of oxalate nephropathy with the use of hydroxocobalamin in critically ill burn patients



The patients treated with hydroxocobalamin (n = 19) had an increased risk of AKI (OR: 5.8 [1.6–20.7]) and RRT (OR: 4.3 [1.09–17]. Association between AKI and hydroxocobalamin remained after adjusting for abbreviated burn severity index, SAPSII, and lactate on admission.

Legrand M. Intensive Care Med 2016
Megarbane B. *Intensive Care Med* 2016

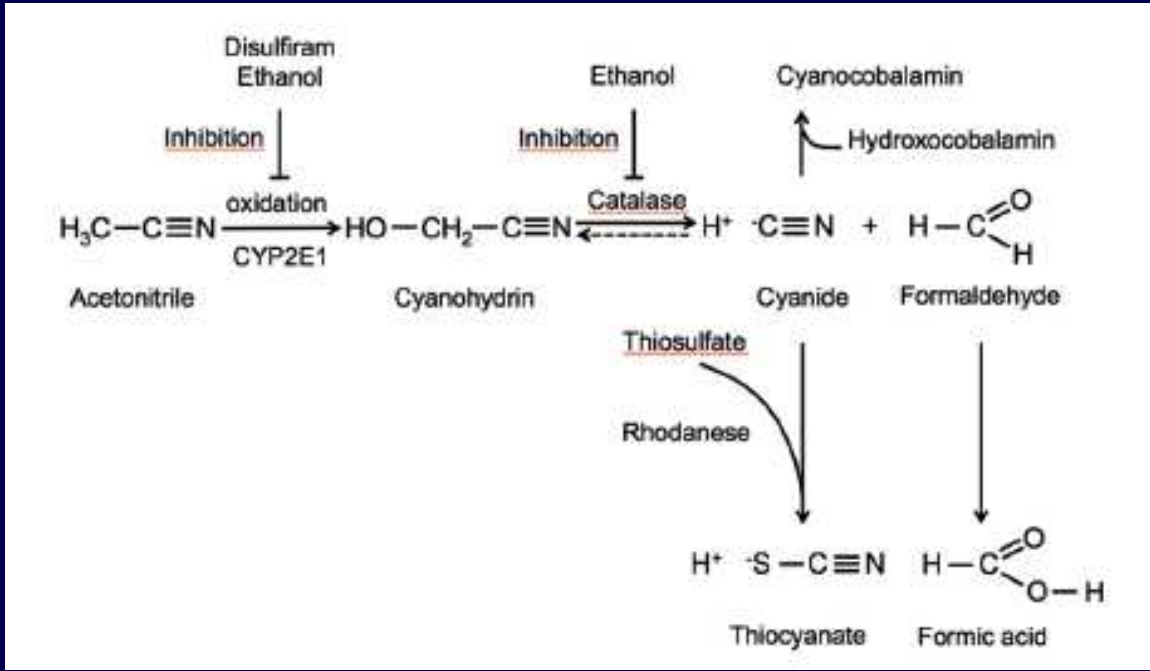
Safety of antidotes to cyanide

Regarding the main clinical condition of cyanide poisoning, i.e. smoke inhalation, we should take into account not only for the efficiency but also for the safety of the antidotal treatment

- Methemoglobin forming agents impair the transport and delivery of oxygen to tissues.
- Cobalt EDTA : numerous side-effects.
- Sodium thiosulfate is safe.
- Hydroxocobalamin is safe. However, the risk of oxalate nephropathy cannot be excluded in the subset of critically burnt smoke-poisoned patients.

Nitroprusside and nitriles poisonings

- Adequate thiosulfate store = limiting step
- Treatment of life-threatening events : hydroxocobalamin
- Prevention of recurrent toxicity: sodium thiosulfate
- If persistent lactic acidosis: disulfiram to inhibit CN production



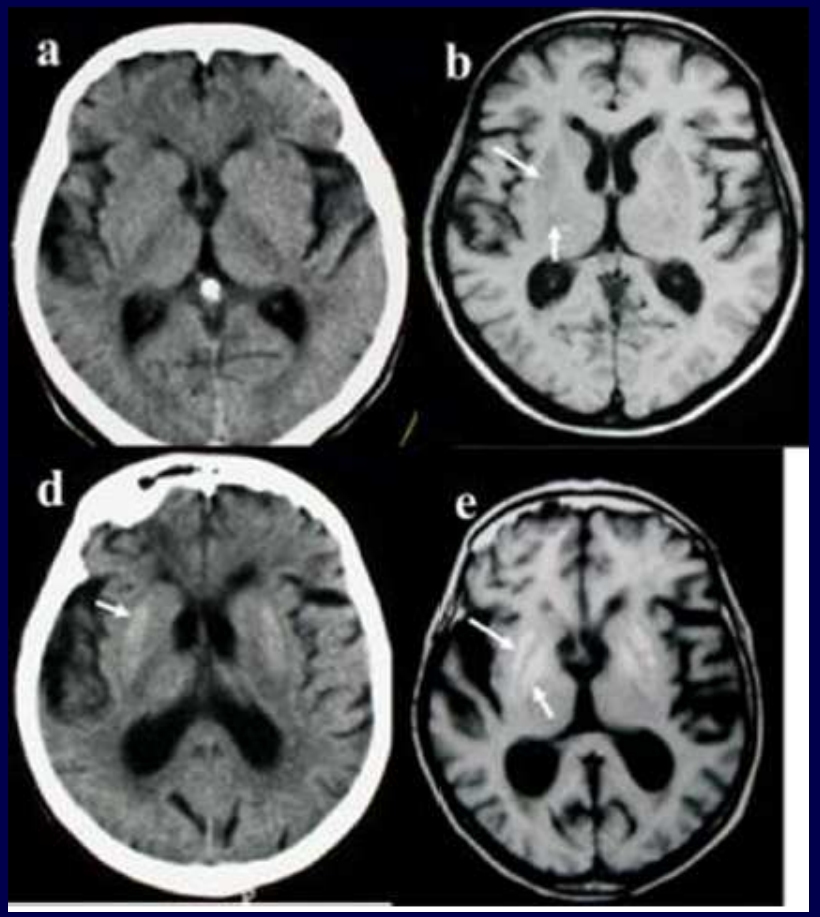
De Paepe P. Clin Tox 2016

Complications and sequellae

- Post-anoxic encephalopathy
- CO-related post-interval syndrome
- CN-related brain injuries

F 50 years, comatose, pulseless and apneic, CPR + 2.5 g HCob +HBO
Blood cyanide (68 µM) HBCO (10.9%)

- Extrapyramidal hypertonia, choreo-athetotic movements
- MRI: increased cerebral atrophy, in the white matter, hemorrhagic putamini and globi pallidi; but respect of hippocampi



Baud FJ. *BMJ Case Reports* 2011

Experimental tested antidotes:

Nucleophiles (alphaketoglutarate, dihydroxyacetone):

- Bind to CN, reducing its availability to cytochrome oxidase
- Decreased toxicity in animal models
- Increased efficiency by the addition of thiosulfate

Other modalities under investigation:

- Isosorbide dinitrate
- Dinitrocobinamide (Vit B12 analogue, IM)
- Sulfanegen (3-mercaptopyruvate sulfurtransferase)
- NMDA inhibitors
- Nitrous oxide
- Antioxydants

Niknahad H. *Toxicol Appl Pharmacol* 1996

Take home message (1)

Both experimental and clinical data support the assumption that antidotal treatment is beneficial in cyanide poisoning.

- Sodium thiosulfate:
  - efficient - safe
  - delayed action
- MetHb forming agents:
  - potent
  - risk of impairment of oxygen delivery to the tissue
- Cobalt EDTA:
  - very potent - immediate action - effective if late
  - numerous side effects
- Hydroxycobalamin:
  - less potent - immediate action - safe

Take home message (2)

In patients suspected of CN poisoning:

- We recommend the use of hydroxocobalamin as first-line antidote according to its safety
- in association with supportive treatment
- administered as rapidly as possible.

In massive CN poisoning (ingestion) or nitriles poisoning, the potency of hydroxocobalamin even at high dose is limited

➡ The continuous infusion of sodium thiosulfate +/- disulfiram should be recommended