

Acute Chlorophenoxy Herbicide Poisoning

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America's Forgotten Chemical Warfare <https://www.leftvoice.org/america-s-forgotten-chemical-warfare>



Dicamba

2,4-D

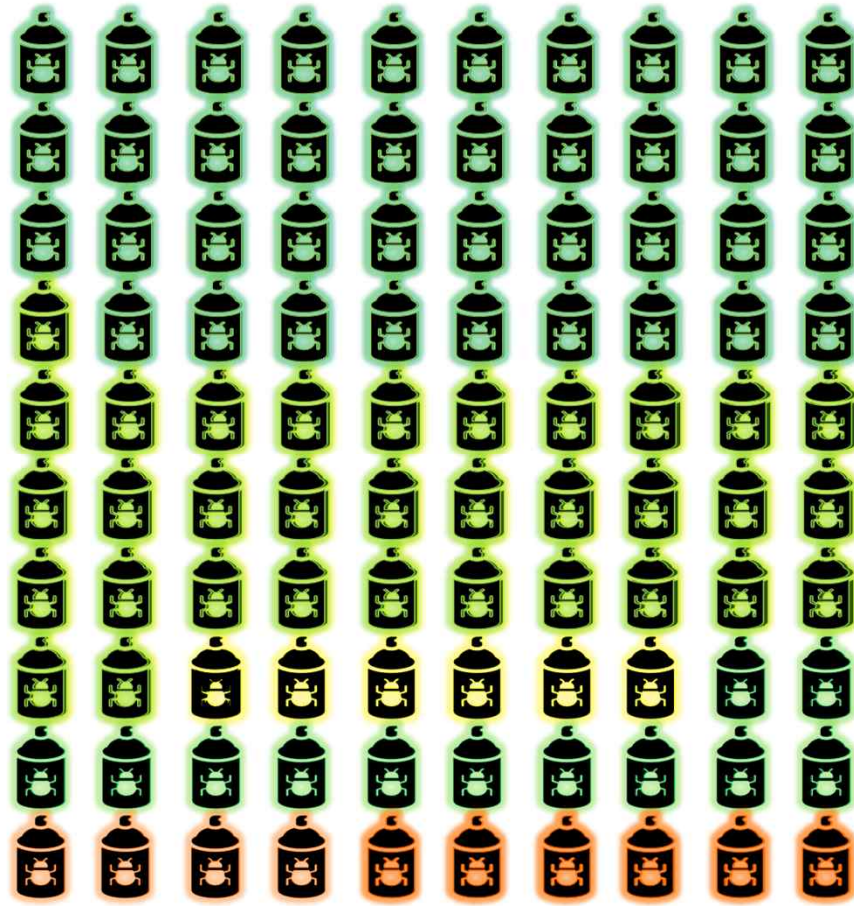
MCPP, Mecoprop (+ Glyphosate)

MCPA

Low Frequency

Low Fatality

-  Glyphosate
-  Paraquat & ect.
-  Glufosinate
-  Chlorophenoxy



49.6% 3%

	Chlorophenoxy	Glyphosate	Glufosinate	Others	Total
	(n=13)	(n=52)	(n =53)	(n=17)	(n=135)
Initial GCS score	10.6±3.3	10.5±3.8	11.9±3.5	12.7±3.0	11.3 ±3.6
Intubation (%)	5 (38.5)	21 (40.4)	20 (37.7)	3 (17.6)	49 (36.3)
Admission (%)	12 (92.3)	43 (82.7)	44 (83.0)	14 (82.4)	113 (83.7)
Mortality (%)	0	6 (11.5)	5 (9.4)	0	12 (8.9)
Urine alkalization (%)	7 (53.8)	1 (1.9)	0	0	8 (5.9)
Hemodialysis (%)	3 (23.1)	8 (15.4)	6 (11.3)	2 (11.8)	19 (14.1)

Chlorophenoxy

- Ingestion >> Inhalation, transdermal
- Renal Excretion
- Half life in flux

2,4-D 13-39 hrs

Mecoprop 17 hrs

Mechanism ?

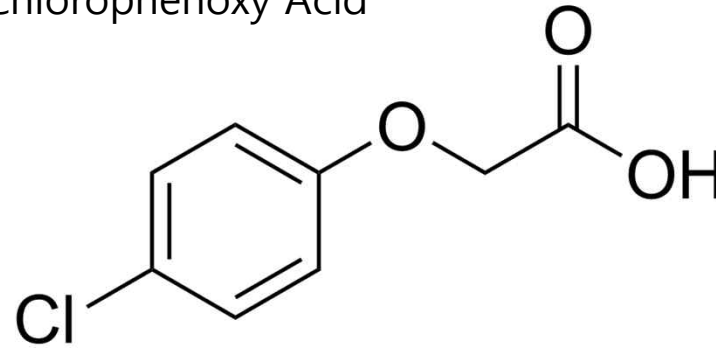
- Dysfunction of Plasma Membrane
- Metabolism – Acetyl-CoA
- Uncoupling of Oxidative Phosphorylation

Dysfunction of Plasma Membrane

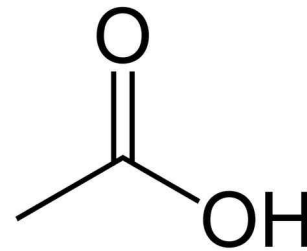


Metabolism – Acetyl-CoA

Chlorophenoxy Acid

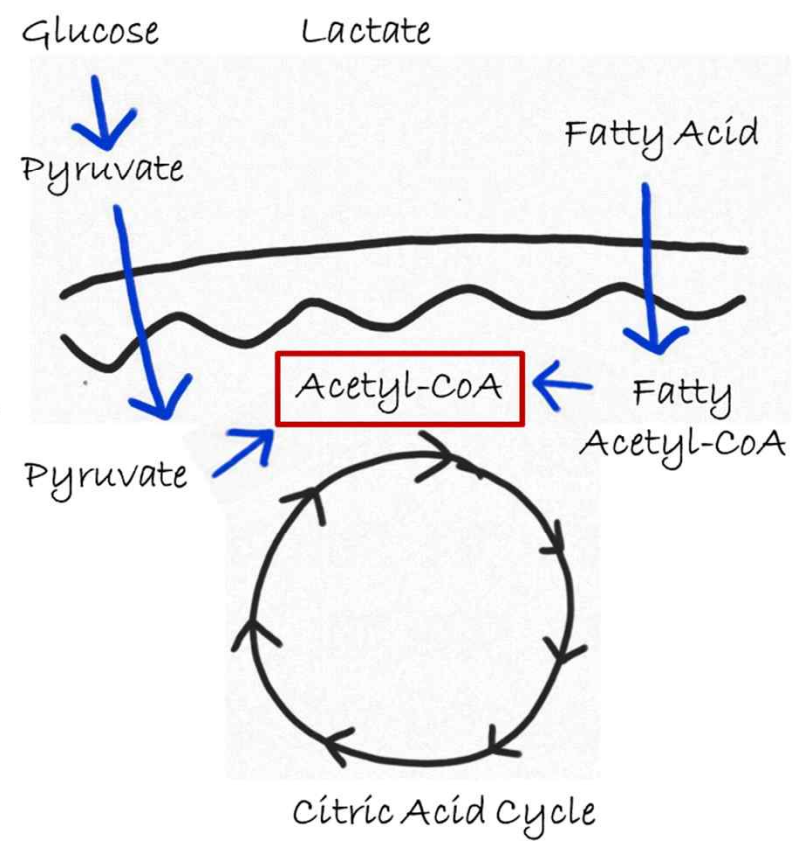
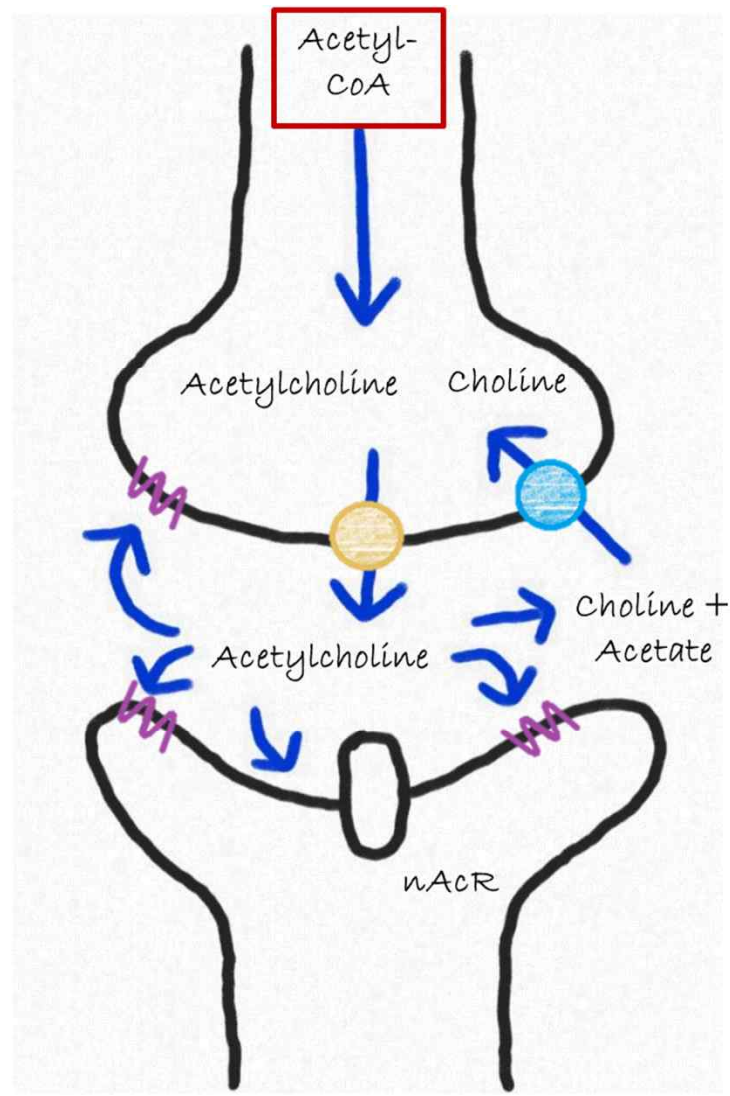


Acetic Acid



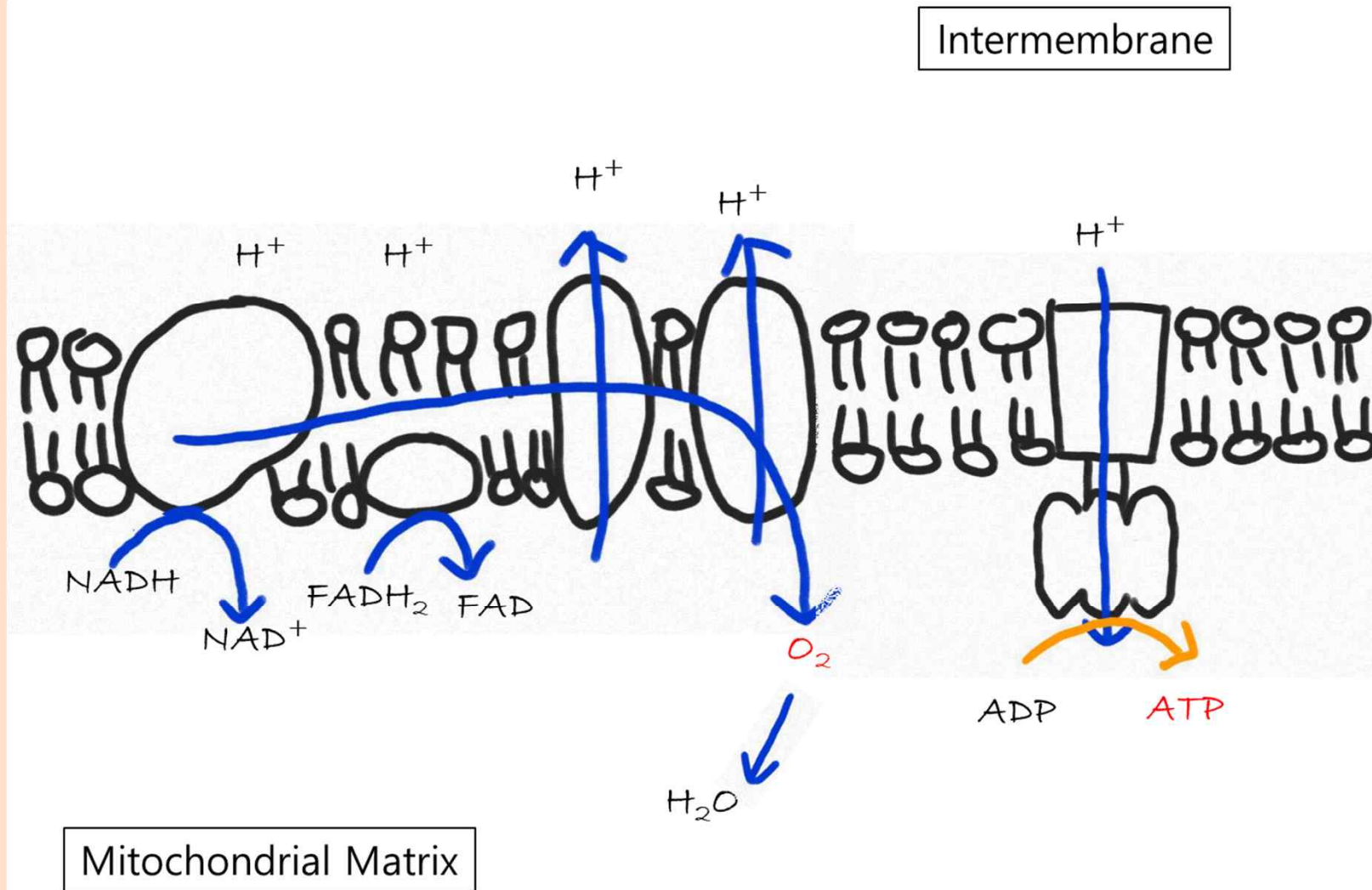
Metabolism – Acetyl-CoA

NM Junction
Lipid Metabolism



Uncoupling of Oxidative Phosphorylation

Impaired Respiration
Cell Death
Lactate
Metabolic Acidosis



Symptoms

From
Cell Death

Mild



1-2 Days

Severe

GI Symptoms

- Nausea
- Vomiting
- Diarrhea
- Abdominal Pain

Corrosive injury

- Hemorrhage
- Hypovolemia

CNS Symptoms

Membrane injury
Penetrating BBB

- Coma
- Hypertonia
- Hyperreflexia

Neuromuscular Symptoms

Synapse
Metabolism Abnormality

- Fasciculation
- Myoclonus
- Rhabdomyolysis
- Peripheral Neuropathy

Cardiac Symptoms

Direct Myocardial injury

- T wave inversion
- QT prolongation
- Cardiogenic shock

Respiratory Symptoms

CNS Depression

Impaired Phosphorylation

- Respiratory Failure
- Hyperventilation

Metabolic Symptoms

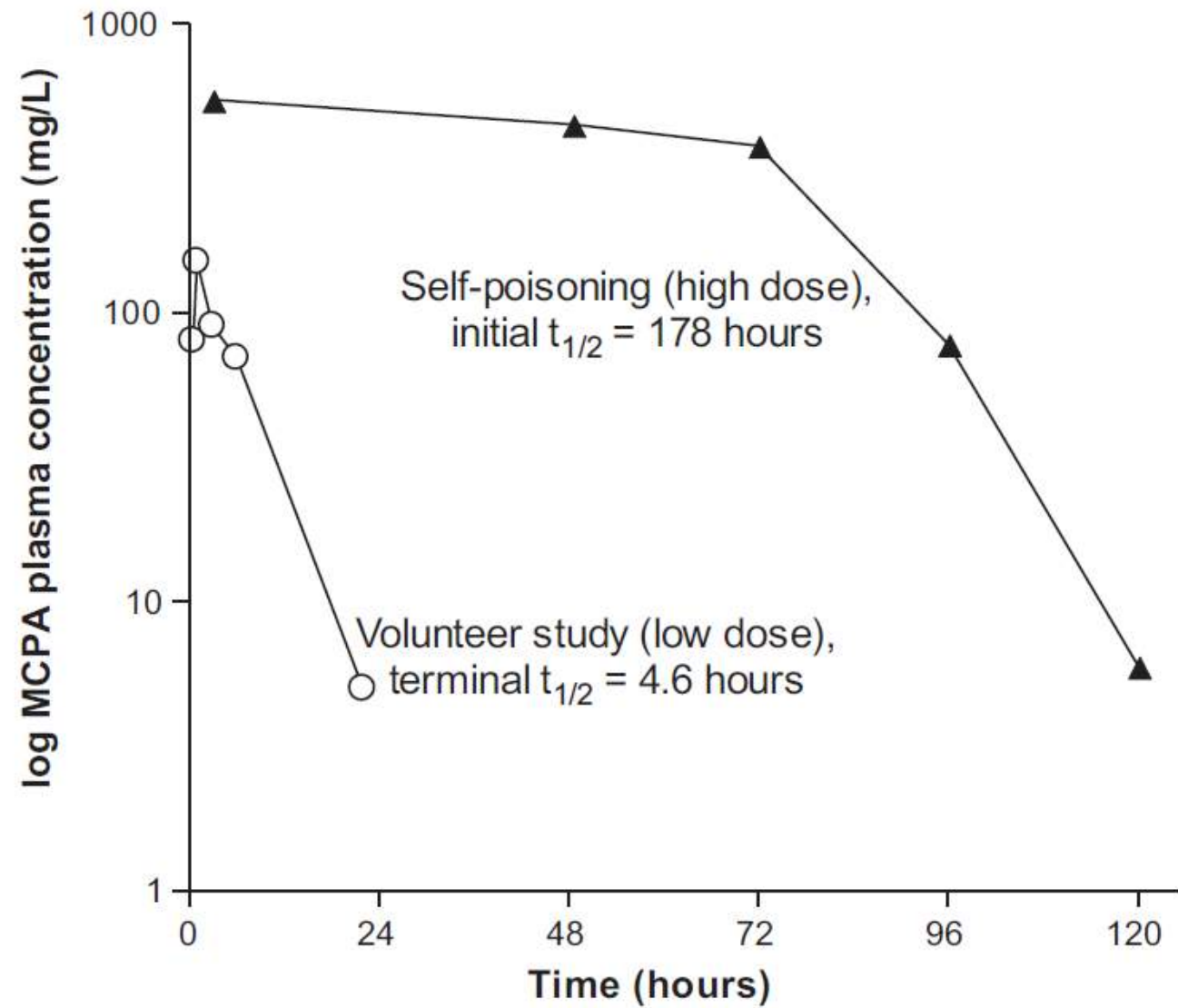
Impaired Phosphorylation

- Metabolic Acidosis
- Hyperthermia
- Shock

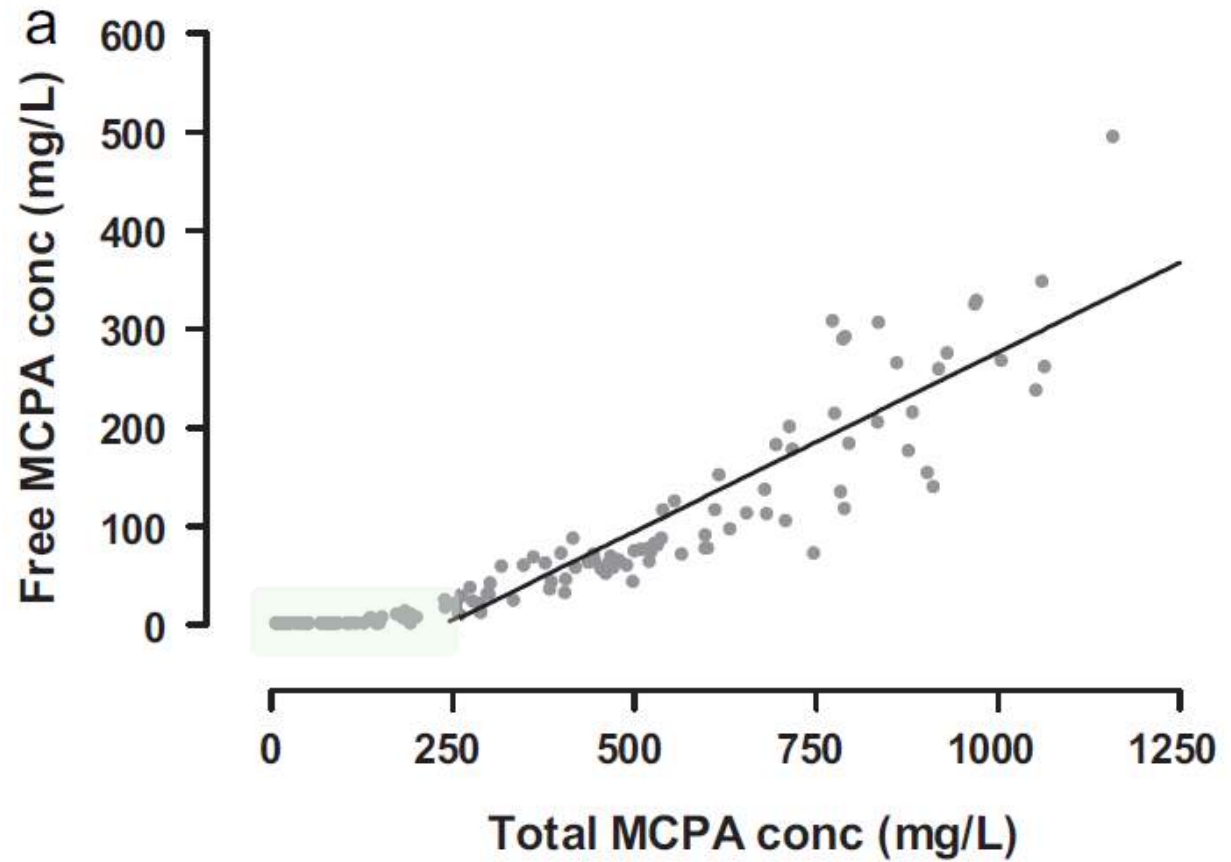
Laboratory Test

- Plasma Concentration
- Creatine Kinase
- Albumin
- Creatinine , LFT
- ABGA

Plasma Concentration

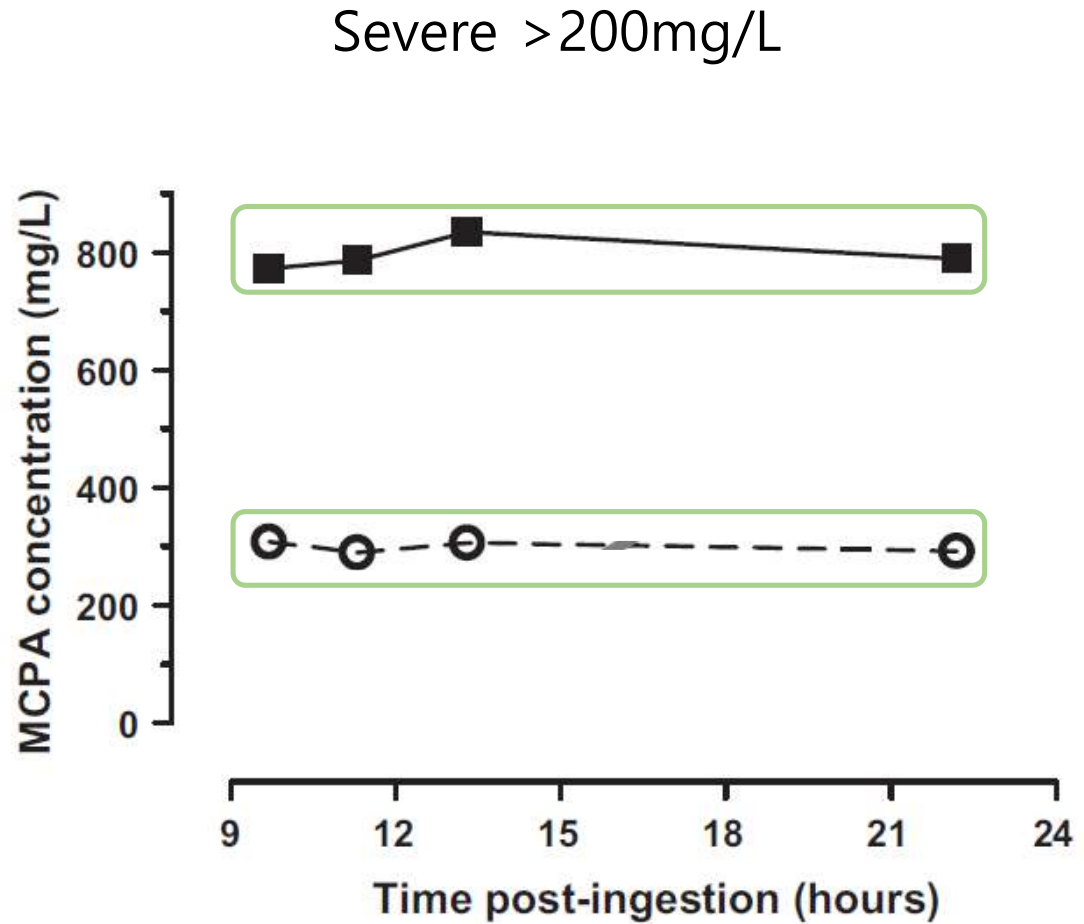


Plasma Concentration & Albumin

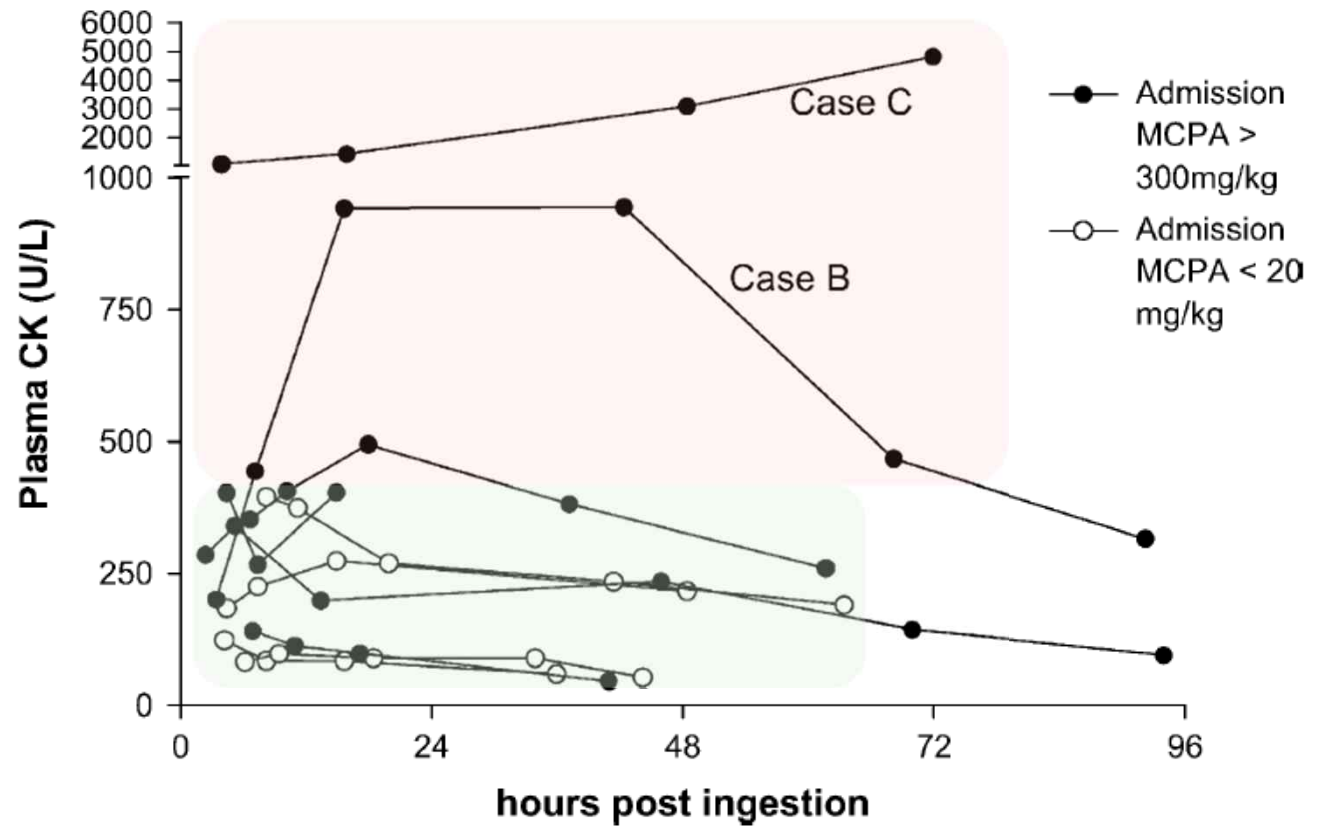


Toxicokinetics, including saturable protein binding, of 4-chloro-2-methyl phenoxyacetic acid (MCPA) in patients with acute poisoning. Toxicol Lett 2011;201:270-6

Plasma
Concentration
≠
Severity ?



Creatine Kinase



Toxicokinetics, including saturable protein binding, of 4-chloro-2-methyl phenoxyacetic acid (MCPA) in patients with acute poisoning. Toxicol Lett 2011;201:270-6

Treatment

- Conservative Care
- Common Treatment of Poisoning
- Urine Alkalization
- Renal Replacement Therapy

Conservative Care

- Fluid Resuscitation
- Vasopressor
- Mechanical Ventilation
- Activated Charcoal

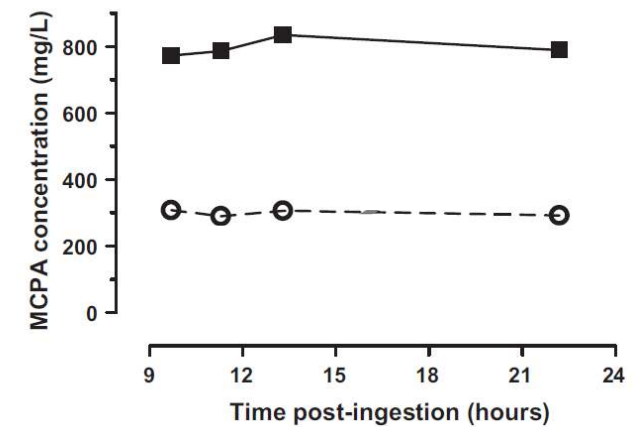
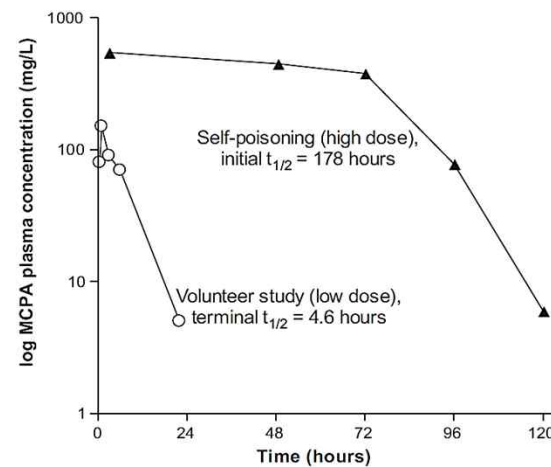
Urine Alkalinization & Renal Clearance

Urine pH Range	2,4-D Clearance (mL/min)	t_{1/2} (h)	Mecoprop Clearance (mL/min)	t_{1/2} (h)
5.10–6.5	0.28	219	0.38	39
6.55–7.5	1.14	42	0.65	22
7.55–8.8	9.60	4.7	2.08	14

Pharmacokinetic studies in severe intoxication with 2,4-D and mecoprop. Proc Eur Soc Toxicol 1977;18:154–155.

Urine Alkalinization & Outcome?

- No Evidence
- May have a Role (Urine pH > 7.5)



HD ?

CRRT ?

- No Evidence
- Other Purpose

Amount of 2,4-D ingested by anamnestic data	Time from ingestion to HD (and HP)	Serum 2,4-D concn before HD (and HP) mg/100 ml	Serum 2,4-D concn after treatment mg/100 ml	Duration of HD-HP	The clearance of 2,4-D ml/min in apparatus
160 g	6,5 h	–	–	4 h	–
40 g	few hours?	177	77,3	3 h	56.3
200 g	10 h	122.5	18.2	4 h	72.9
40–80 g	3 h	37.0	15.8	5 h	68.7

Poisoning with 2,4-dichlorophenoxyacetic acid treated by hemodialysis. Arch Toxicol 1992;66:518-21.

Chlorophenoxy Herbicide

- Less Common but may be Fatal
- Dysfunction of Plasma membrane,
Oxidative Phosphorylation, Acetyl-CoA
- GI, CNS ~ Metabolic acidosis, Shock
- Conservative care with activated Charcoal
- Consider Urine Alkalization / RRT

Thank You