ASM 2009

The Changing Face of an Old Trades: Challenges of ICU

Toxicology Problems in ICU

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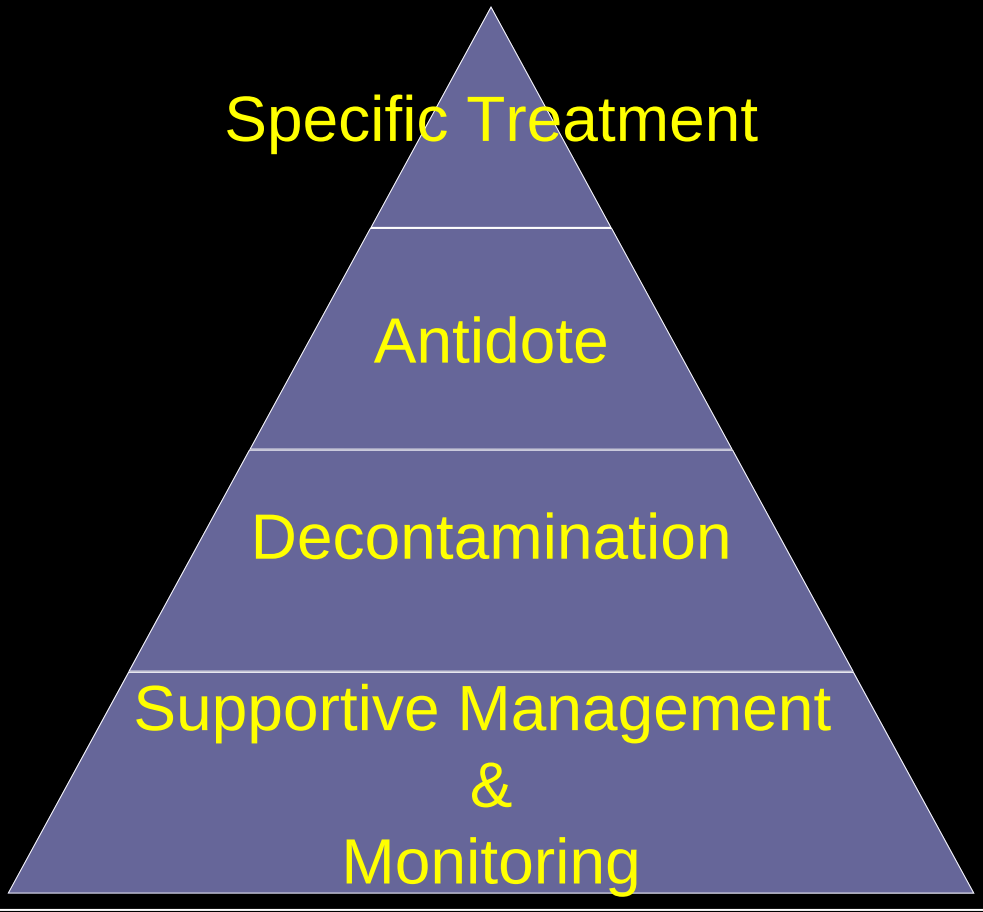
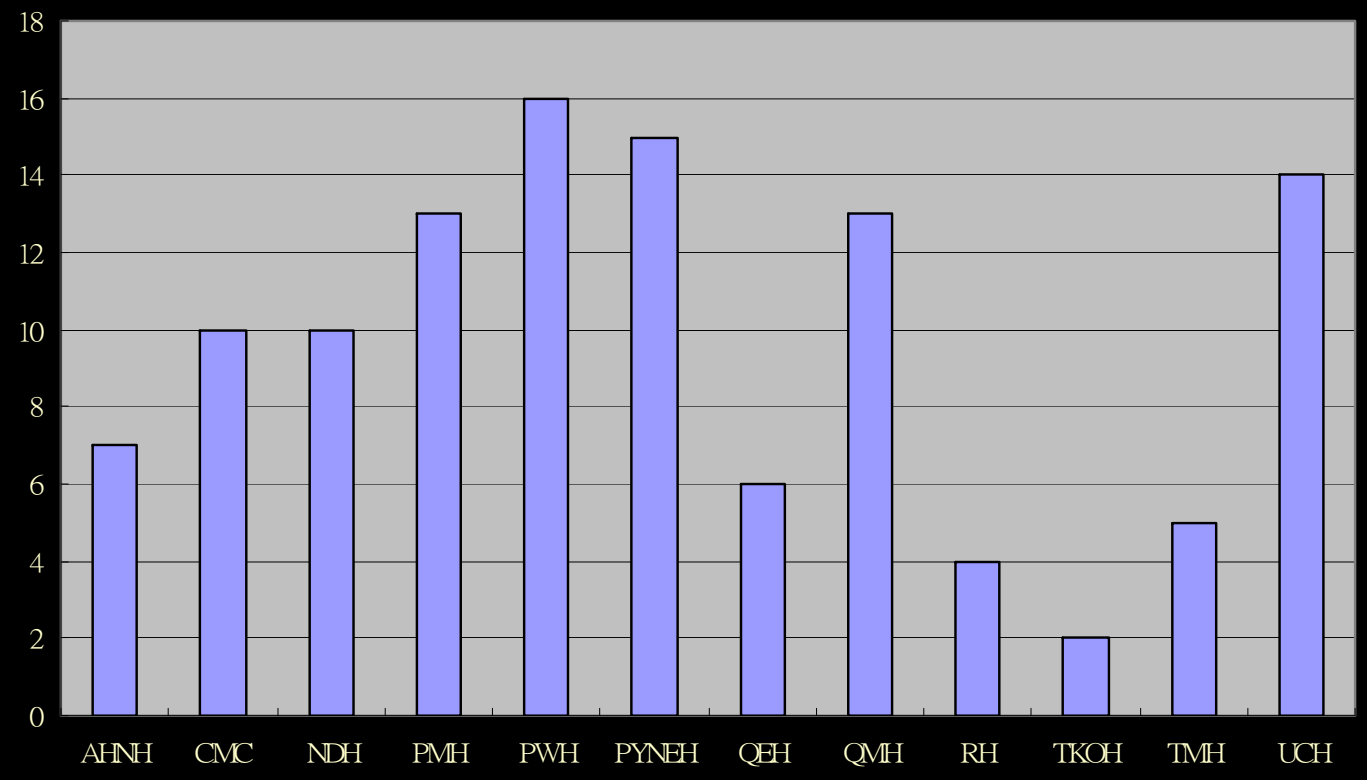
Acute Poisoning - Management

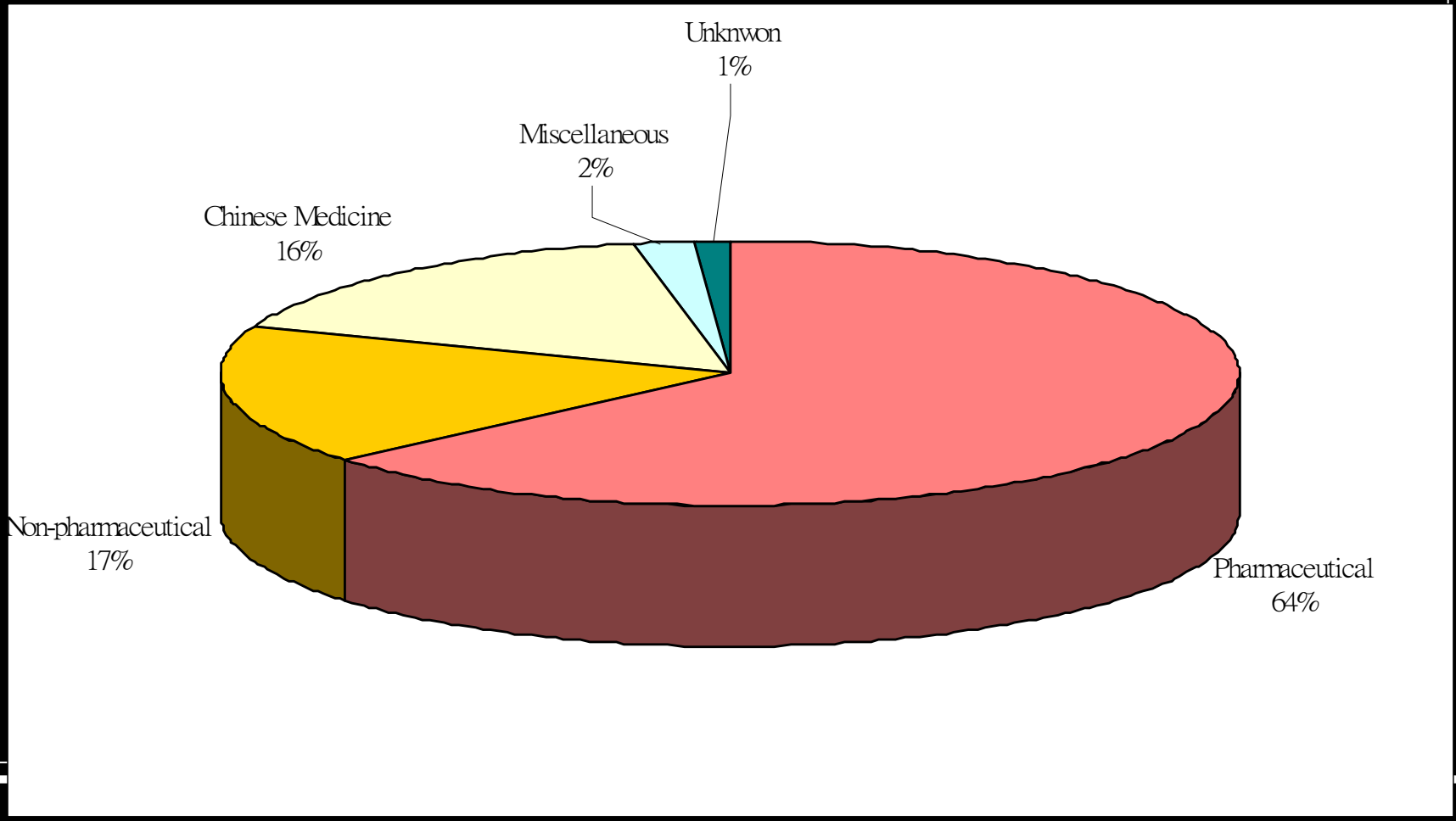


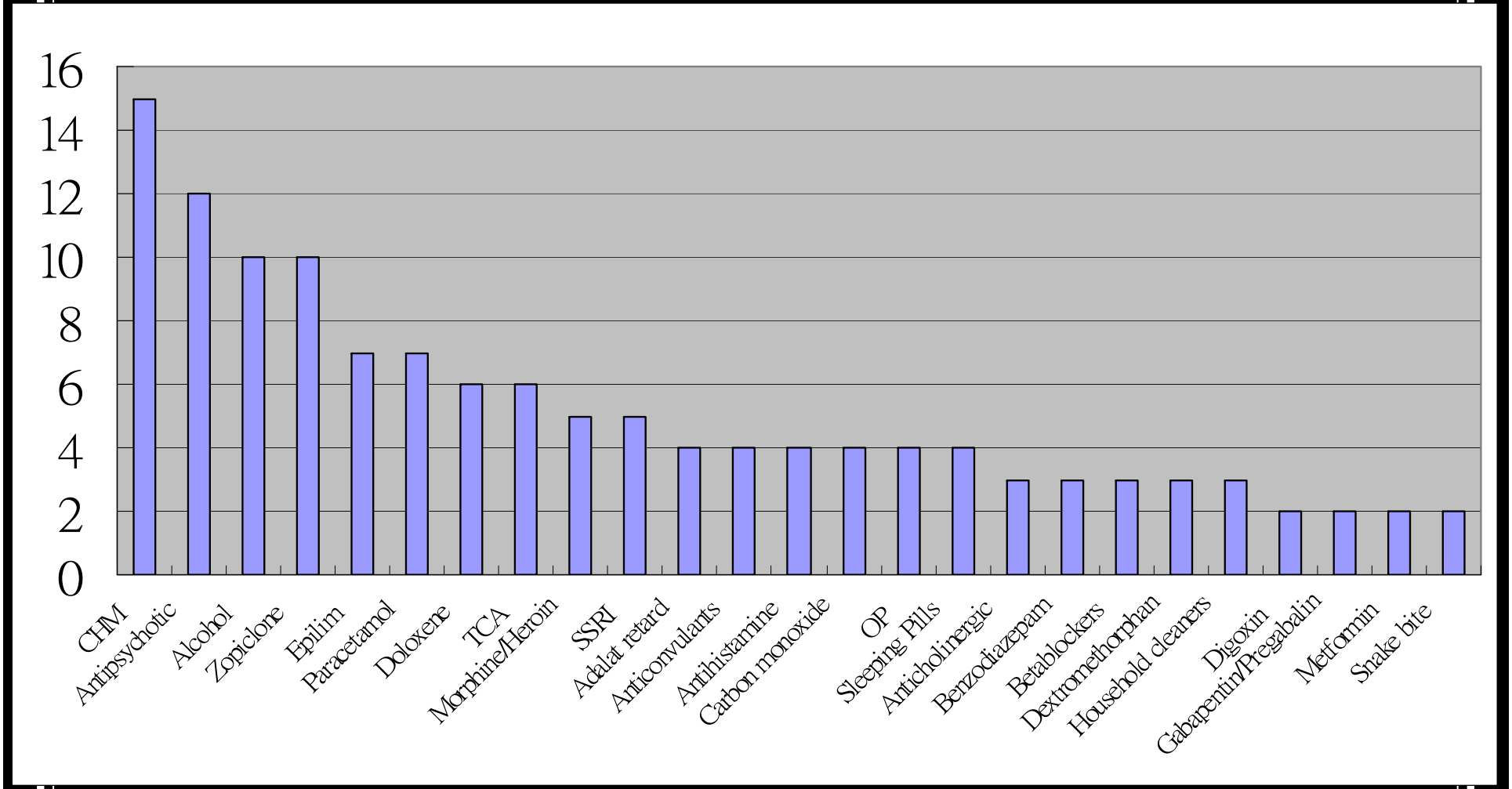
HKPIC Data (Adult ICU Consultation) Jul 08 – Jul 09



115 Cases (~ 5% of our consultation)

Poison Type


Unknwon
1%
Miscellaneous
2%
Chinese Medicine
16%
Non-pharmaceutical
17%
Pharmaceutical
64%


16
14
12
10
8
6
4
2
0
CHM
Antipsychotic
Alcohol
Zopiclone
Epilim
Paracetamol
Doloxene
TCA
Morphine/Heroin
SSRI
Adalat retard
Anticonvulants
Antihistamine
Carbon monoxide
OP
Sleeping Pills
Anticholinergic
Benzodiazepam
Betablockers
Dextromethorphan
Household cleaners
Digoxin
Gabapentin/Pregabalin
Metformin
Snake bite

Toxicology Problem in ICU

- GI Decontamination
- Poison induced Refractory Shock
- Chinese Medicine Poisoning
- OP poisoning – Update in Oxime Use
- Venomous Snake Bites
- Secondary Contamination Prevention

GI Decontamination

MDAC / WBI

Methods of GI decontamination

- Single Dose Activated Charcoal (AC)
- Gastric Lavage (GL)
- Multiple Dose Activated Charcoal (MDAC)
- Whole Bowel Irrigation (WBI)
- Surgical Intervention

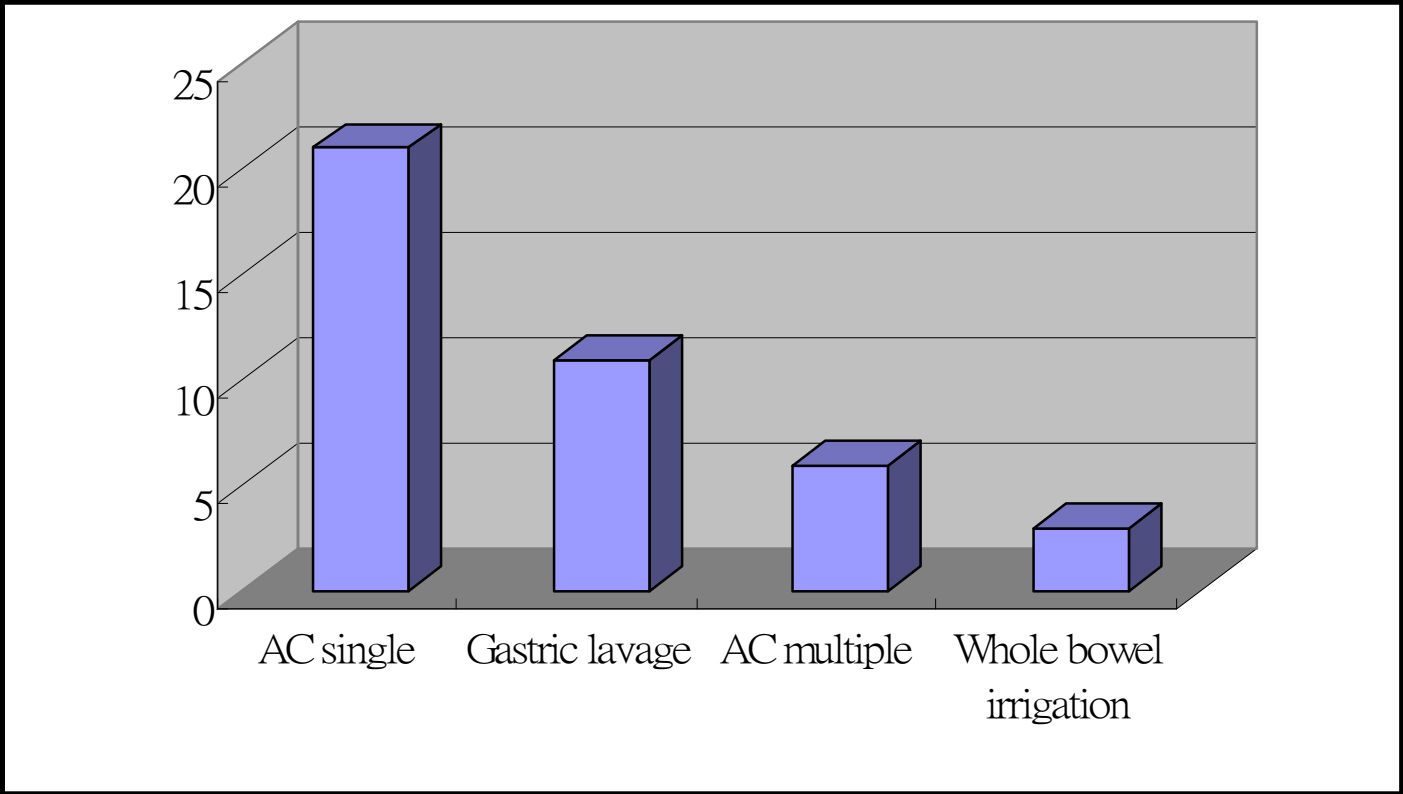
- *Ipecac Induced Vomiting (Outdated)*

GI Decontamination – Local Data

	GL	*AC*	*MDAC*	*WBI*
Multi-AED Study 2001 [~ 1500]	7%	35%		0%
UCH AED 2000-2004 [~ 1800]	2.6%	28%		0.2%
HKPIC Data 2006 [~ 2700]	2.3%	17%	0.7%	0.1%
HKPIC Data 2007 [~ 2842]	0.6%	7.8%	0.4%	0.04%
HKPIC Data 2008 *	1.6%	8.4%	1.1%	0.1%

* To be clear

The 115 Cases



Indication of MDAC

- GI decontamination
  - Delayed GI absorption
    - Sustained release preparations
    - Bezoars
- Enhanced Elimination
  - Enterohepatic re-circulation
  - Gut dialysis

When to consider MDAC

- Recommended by Position Statement (ABCDQ)
  - Aminophylline
  - Barbiturates
  - Carbamazepine
  - Dapsone
  - Quinine
- Possible Beneficial (ABCDEQ)
  - Aspirin, Aminophylline
  - Barbiturates
  - Carbamazepine
  - Dapsone, Digoxin, Dilantin
  - Extended release, Epilim
  - Quinine

Multiple-dose activated charcoal for treatment of yellow oleander poisoning: a single-blind, randomised, placebo-controlled trial

H A de Silva, M M D Fonseka, A Pathmeswaran, D G S Alahakone, G A Ratnatilake, S B Gunatilake, C D Ranasinha, D G Lalloo, J K Aronson, H J de Silva

Lancet 2003; **361**: 1935–38

	Placebo (n=200)	Activated charcoal (n=201)	Difference (95% CI)	p
Primary endpoint				
Death	16 (8%)	5 (3%)	5·5 (0·6–10·3)	0·025
Secondary endpoints				
ICU admission	16 (8%)	5 (3%)	5·5 (0·6–10·3)	0·025
Patients given anti-digoxin antibody Fab fragments	7 (4%)	0	3·5 (0·6–6·6)	0·022
Cardiac pacing	11 (6%)	1 (<1%)	5·0 (1·2–8·8)	0·008
Life-threatening arrhythmias at 24 h	14/190 (7%)	3/195 (2%)	5·9 (1·7–10·6)	0·010
Mean dose of atropine in mg (SD)	5·2 (3·8)	3·6 (2·7)	1·6 (0·9–2·2)	<0·0001
Boluses of atropine (median [range])	2 (1–12)	1 (1–6)	0 (0·0–1·0)	<0·0001*
Time in hospital (days) (median [range])	3 (0·5–10)	3 (0·25–24)	0 (0·0–0·0)	0·902*

Clinical Trials Recently

- Multiple-dose activated charcoal in acute self-poisoning: a randomized controlled trial

  M Eddleston. *Lancet 2008; 371; 579-581*

- A randomized clinical trial of activated charcoal for the routine management of oral drug overdose

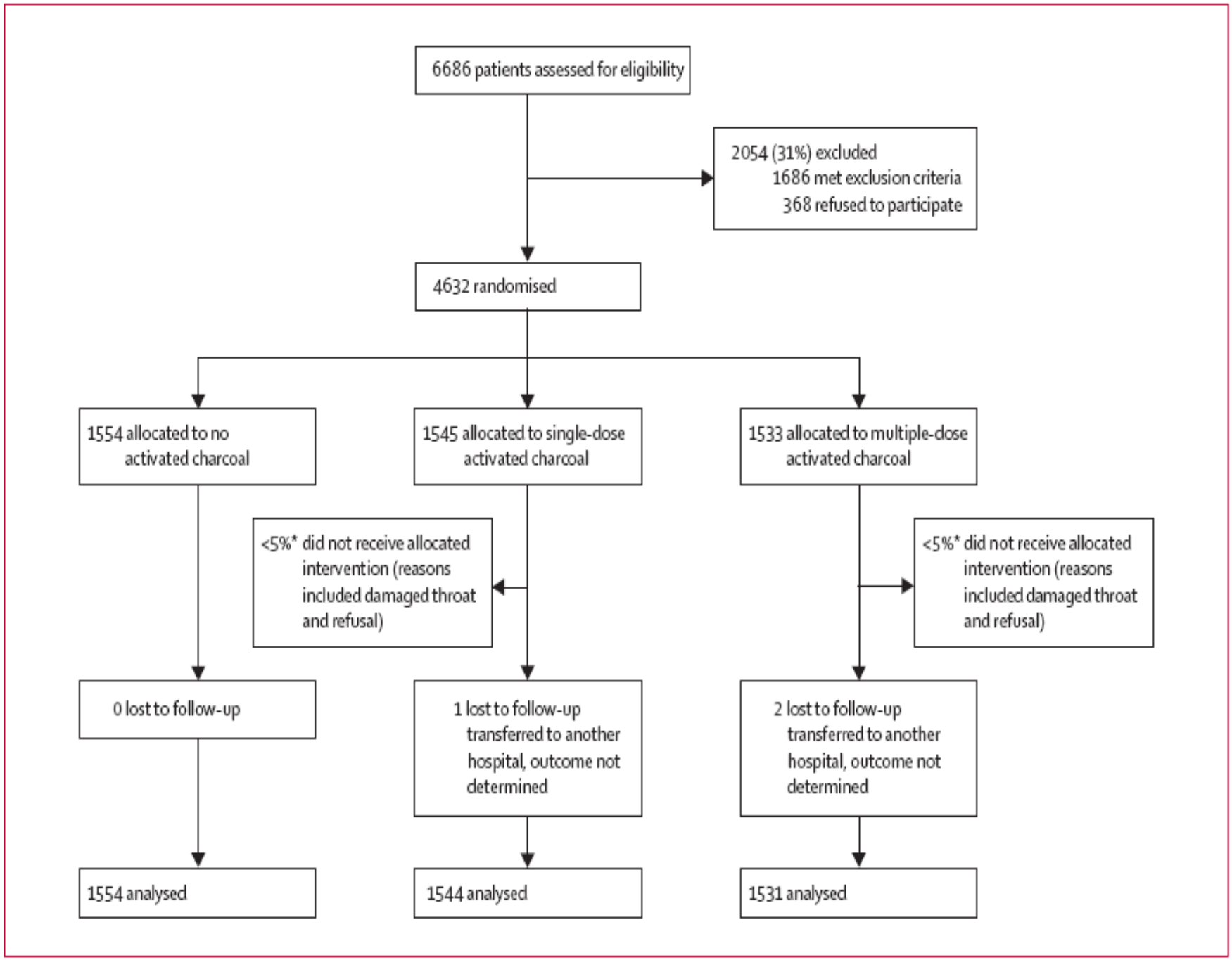
  GM Cooper. *QJ Med 2005; 98; 655-660*

- Activated charcoal decreases the risk of QT prolongation after citalopram overdose

  GK Isbister. Annals of EM 2007; 50(5); 593-600

Eddleston et al

- RCT, Sri Lanka
- Poisoning patients
- 3 Arms
  - No AC
  - SDAC - 50g AC once
  - MDAC - 50g AC Q4H X6
- Outcome – 1^{o} death, multiple 2^{o} outcomes


6686 patients assessed for eligibility
2054 (31%) excluded
1686 met exclusion criteria
368 refused to participate
4632 randomised
1554 allocated to no activated charcoal
1545 allocated to single-dose activated charcoal
1533 allocated to multiple-dose activated charcoal
<5%* did not receive allocated intervention (reasons included damaged throat and refusal)
<5%* did not receive allocated intervention (reasons included damaged throat and refusal)
0 lost to follow-up
1 lost to follow-up transferred to another hospital, outcome not determined
2 lost to follow-up transferred to another hospital, outcome not determined
1554 analysed
1544 analysed
1531 analysed

Results

	No AC (n=1554)	SDAC (n=1544)	MDAC (n=1531)	Odds ratio (95% CI)		
				MDAC vs no AC	SDAC vs no AC	MDAC vs SDAC
Died	105 (6·8%)	109 (7·1%)	97 (6·3%)	0·93 (0·69–1·25)* 0·96 (0·70–1·33)†	1·05 (0·79–1·40)* 1·11 (0·82–1·52)†	0·89 (0·66–1·19)* 0·87 (0·64–1·18)†
Needing intubation for ventilation						
Baseline	75	71	66			
Follow-up	76 (4·9%)	73 (4·7%)	73 (4·8%)	0·97 (0·69–1·37)* 0·96 (0·67–1·37)†	0·97 (0·68–1·36)* 0·96 (0·67–1·37)†	1·01 (0·71–1·43)* 1·02 (0·71–1·45)†
Seizures						
Baseline	9	8	7			
Follow-up	7 (0·5%)	13 (0·8%)	14 (0·9%)	2·04 (0·77–5·99)* 1·92 (0·75–4·94)‡	1·88 (0·69–5·57)* 1·98 (0·78–5·06)‡	1·09 (0·47–2·52)* 0·97 (0·44–2·14)‡

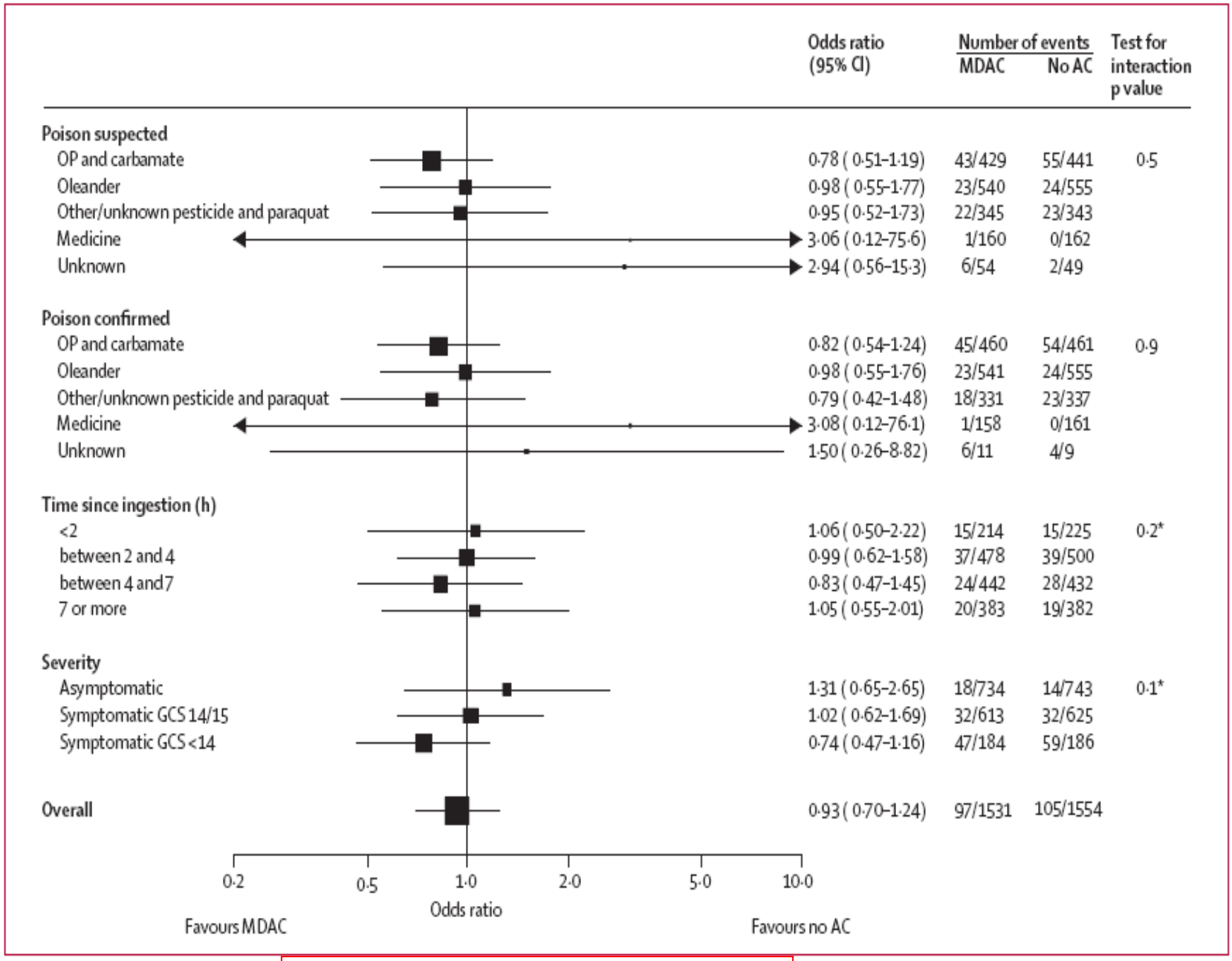


Figure 2: **Forest plot of mortality for multiple-dose activated charcoal versus no activated charcoal**

MDAC=multiple-dose activated charcoal. AC=activated charcoal. OP=organophosphorus. GCS=Glasgow comma score. *Test for trend.

Hong

Presentation most > 2 hrs

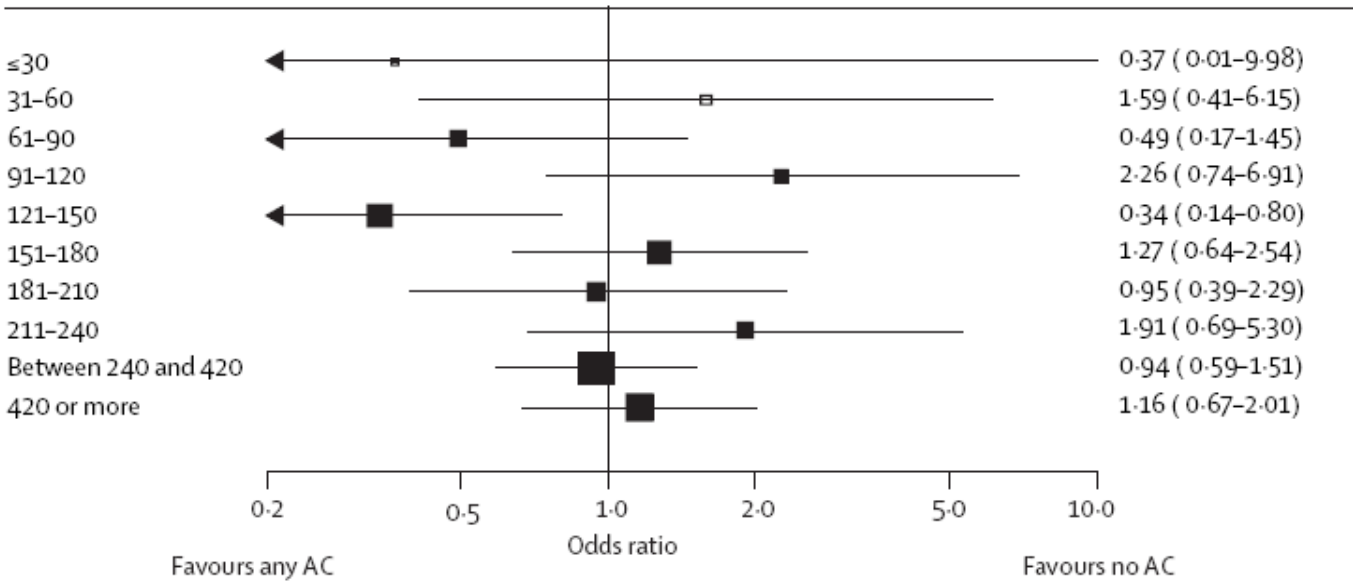


Figure 5: **Forest plot of effect of time to recruitment on mortality for multiple-dose or single-dose activated charcoal versus no activated charcoal, with detailed breakdown of less than 4 h**

AC=activated charcoal.

Conclusion

- Author's conclusion
  - Routine use of MDAC is not recommended
- My view
  - Presentation < 2 hours basically not studied
  - Poison nature different from HK
    - More Toxic in Sri Lanka

Interpreted as routine use of AC in late presentation (>2 hours) showed no benefit

Activated Charcoal in 2009

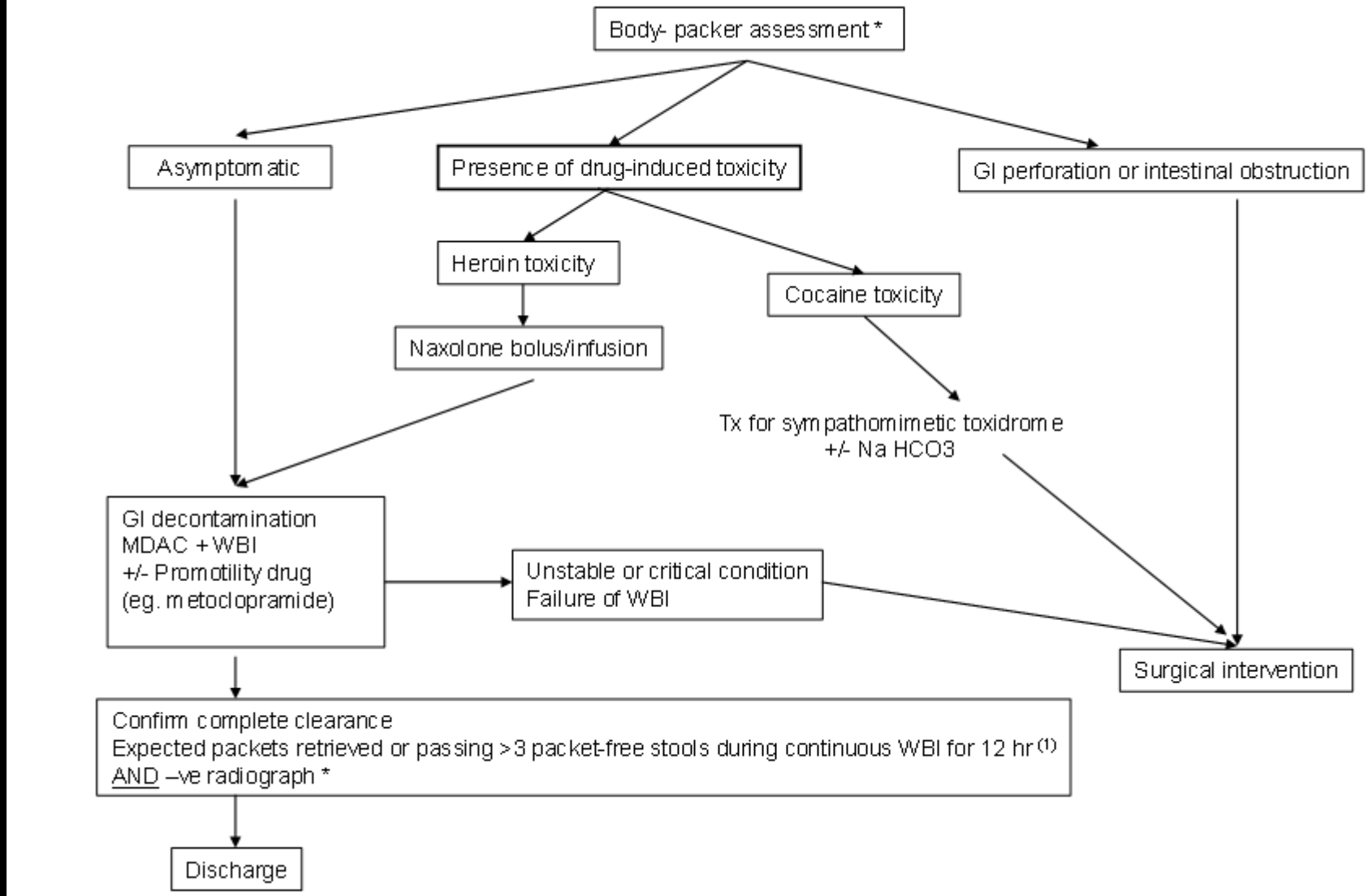
- High level of evidence still scanty
- Should not be a “routine” anymore
- Compose the majority of GI decontamination, but its use is decreasing
- Aim to identify indicated patient for its use

Whole Bowel Irrigation

- PEG to wash the entire GI tract

Possible WBI Uses

- Body packers and stuffers
- Ingestion of significant toxic substances
  - Not well absorbed by charcoal
    - Iron, lithium and other metals
  - Sustained release products or delayed absorption


Body- packer assessment *
Asymptomatic
Presence of drug-induced toxicity
GI perforation or intestinal obstruction
Heroin toxicity
Cocaine toxicity
Naxolone bolus/infusion
Tx for sympathomimetic toxidrome
+/- Na HCO3
GI decontamination
MDAC + WBI
+/- Promotility drug
(eg. metoclopramide)
Unstable or critical condition
Failure of WBI
Surgical intervention
Confirm complete clearance
Expected packets retrieved or passing >3 packet-free stools during continuous WBI for 12 hr (1)
AND –ve radiograph *
Discharge

MDAC Vs WBI

- ABCDQ
  - Preferably MDAC
- Others
  - Risk benefit consideration
  - Practical concerns
- Certainly can give both in severe cases

Poison induced refractory shock

TCA / Na channel blocking agent

CCB

“Last Bullet” Therapy

Mechanisms

- ↓ Cardiac Output [Pump]
  - ↓ Contractility and/or arrhythmia
- Vasodilatation [Pipe]
  - Central sympathetic effect
  - α-1 antagonist / blocker
  - β-2 stimulation
- ↓ Preload [Volume]
  - GI volume loss
  - Third space sequestration

Toxicology Concern

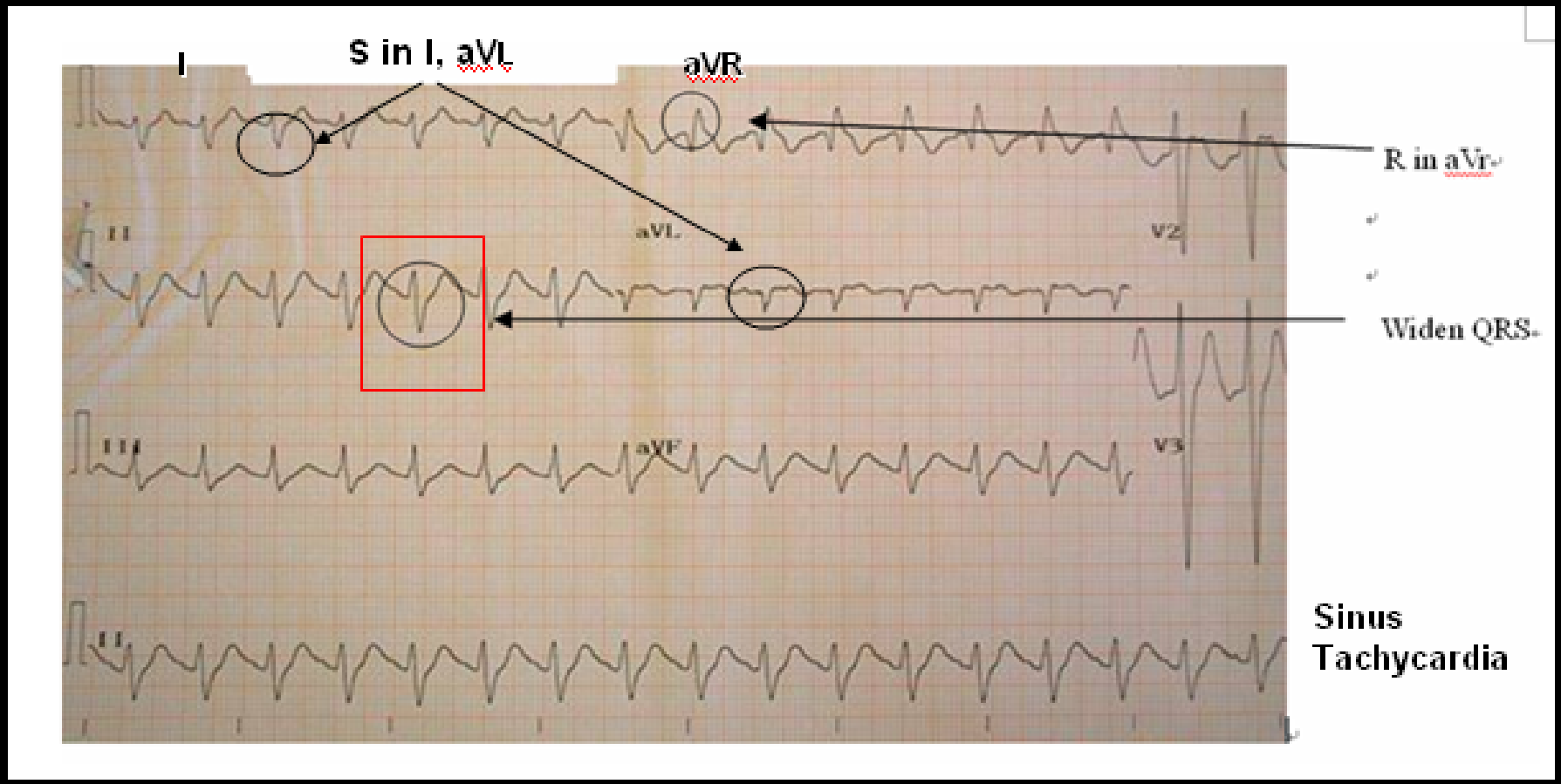
- General Supportive Therapy
  - Adrenaline is the preferred 1st line inotropes/vasopresser
- Antidotes
  - Sodium bicarbonate / hypertonic saline
  - Calcium
  - Glucagon
  - Dextrose Insulin
- Cautious
  - Anti-arrhythmia agent less preferred
  - Electro-therapy usually fails
- Investigational Therapy

Na Channel Blocking Drugs

- T – TCA
- C – Cocaine, Citalopram, Carbamazepine
- A – Antiarrhythmics (1a, 1c), Amantidine

- P – Propranolol
- P – Phenothiazine

- D – Doloxene (Dextropropoxyphene)
- V – Venlafaxine
- D – Diphenhydramine


I
S in I, aVL
aVR
R in aVr
II
aVL
V2
Widen QRS
III
aVF
V3
II
Sinus
Tachycardia

Antidotes - $NaHCO_3$

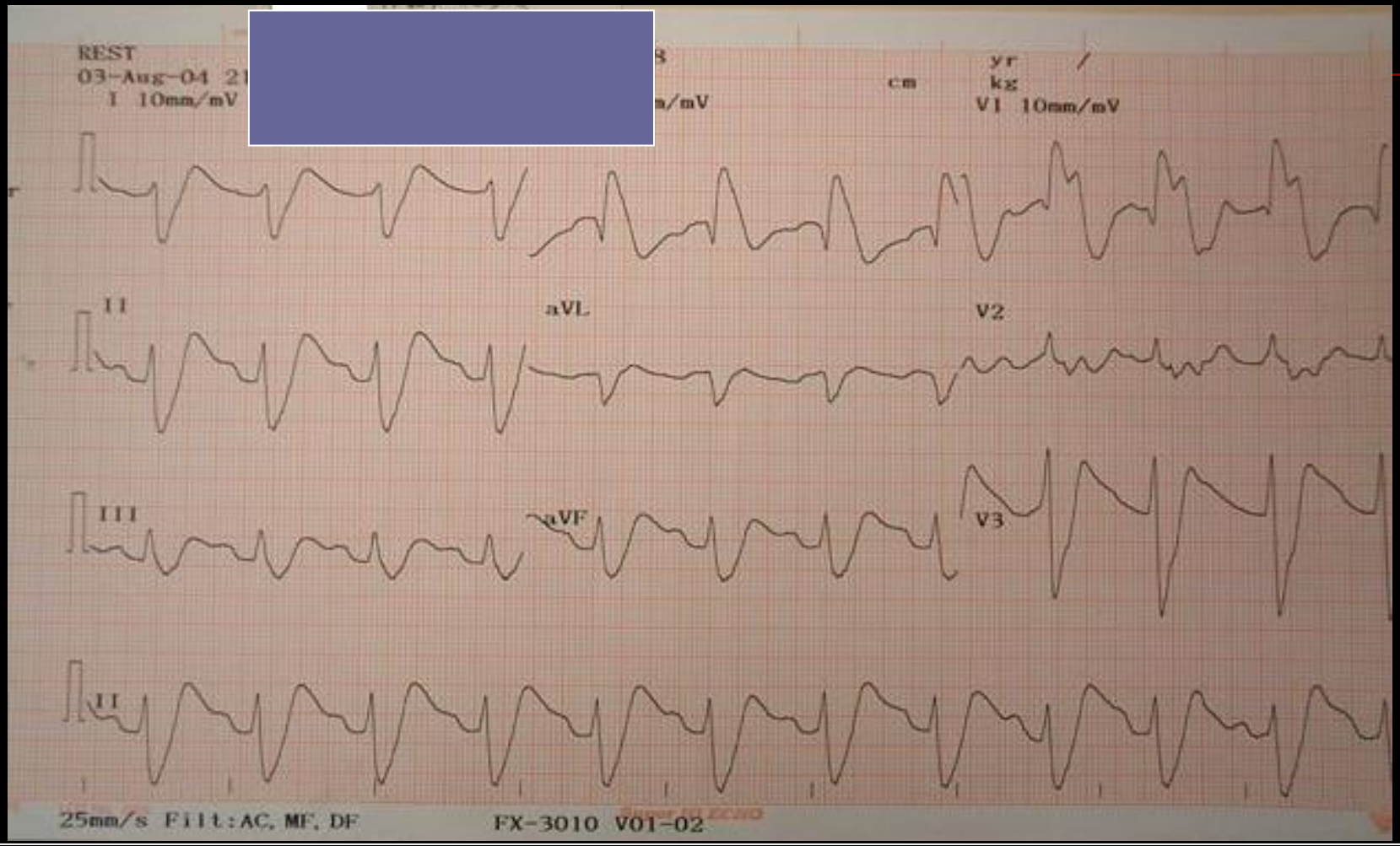
- Na effect
- Alkalization effect
  - Serum, Urinary

Serum alkalization by $NaHCO_3$

Indications	**QRS > 100ms**	**Ventricular arrhythmia**	**Hypotension**
Dose	1-2 mEq per kg IV bolus May need repeated bolus or infusion to meet endpoints		
End points	QRS <100ms* or pH 7.5-7.55	Reversal of arrhythmia or pH 7.5-7.55	Correction of BP or pH 7.5-7.55
Contraindications	pH > 7.55 (Consider hypertonic saline (2)) Intolerable to Na/fluid load (Consider hyperventilation (3))		

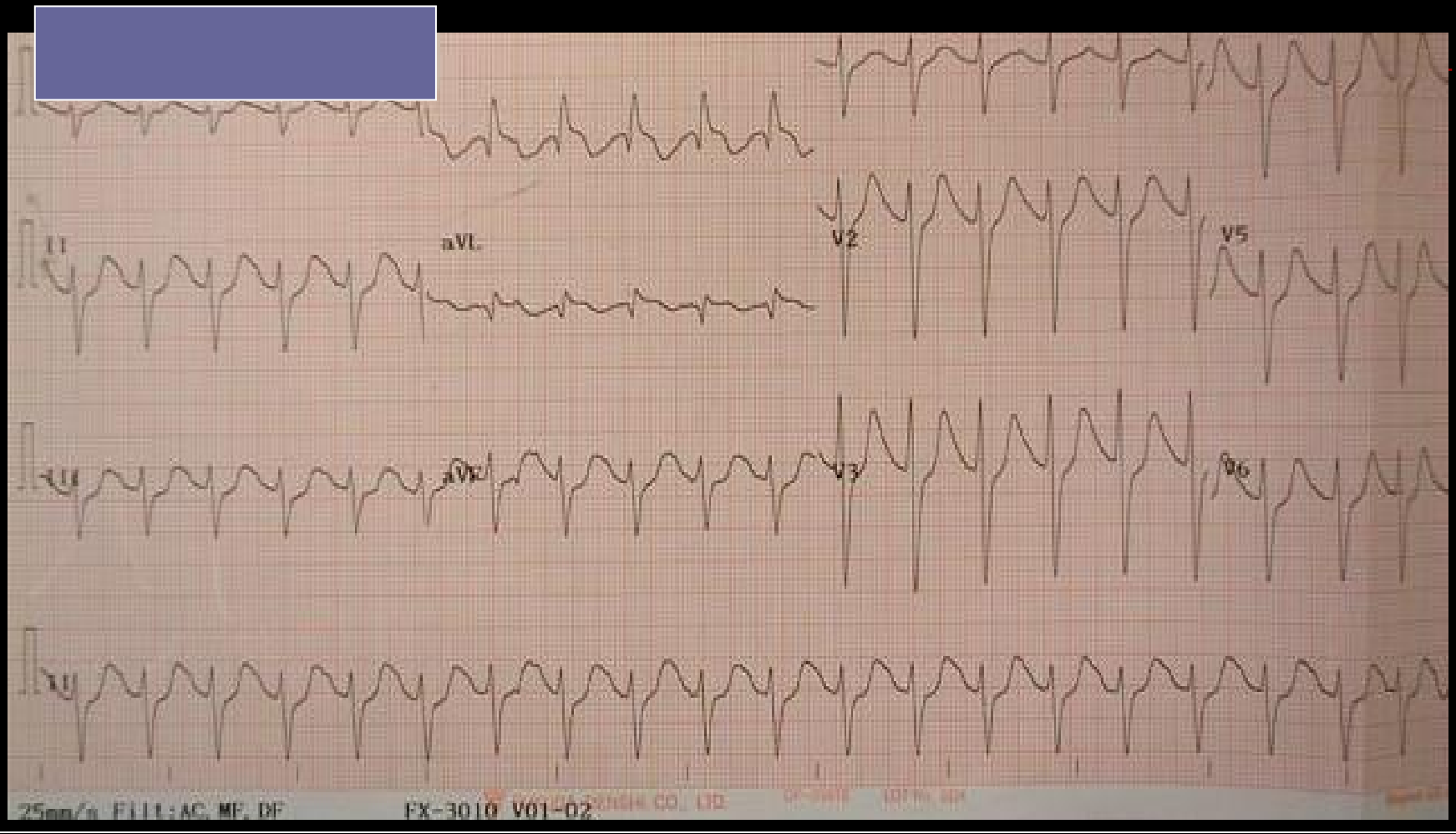
** QRS endpoint may be interpreted with reference to patient baseline ECG if available*

Response to $NaHCO_3$



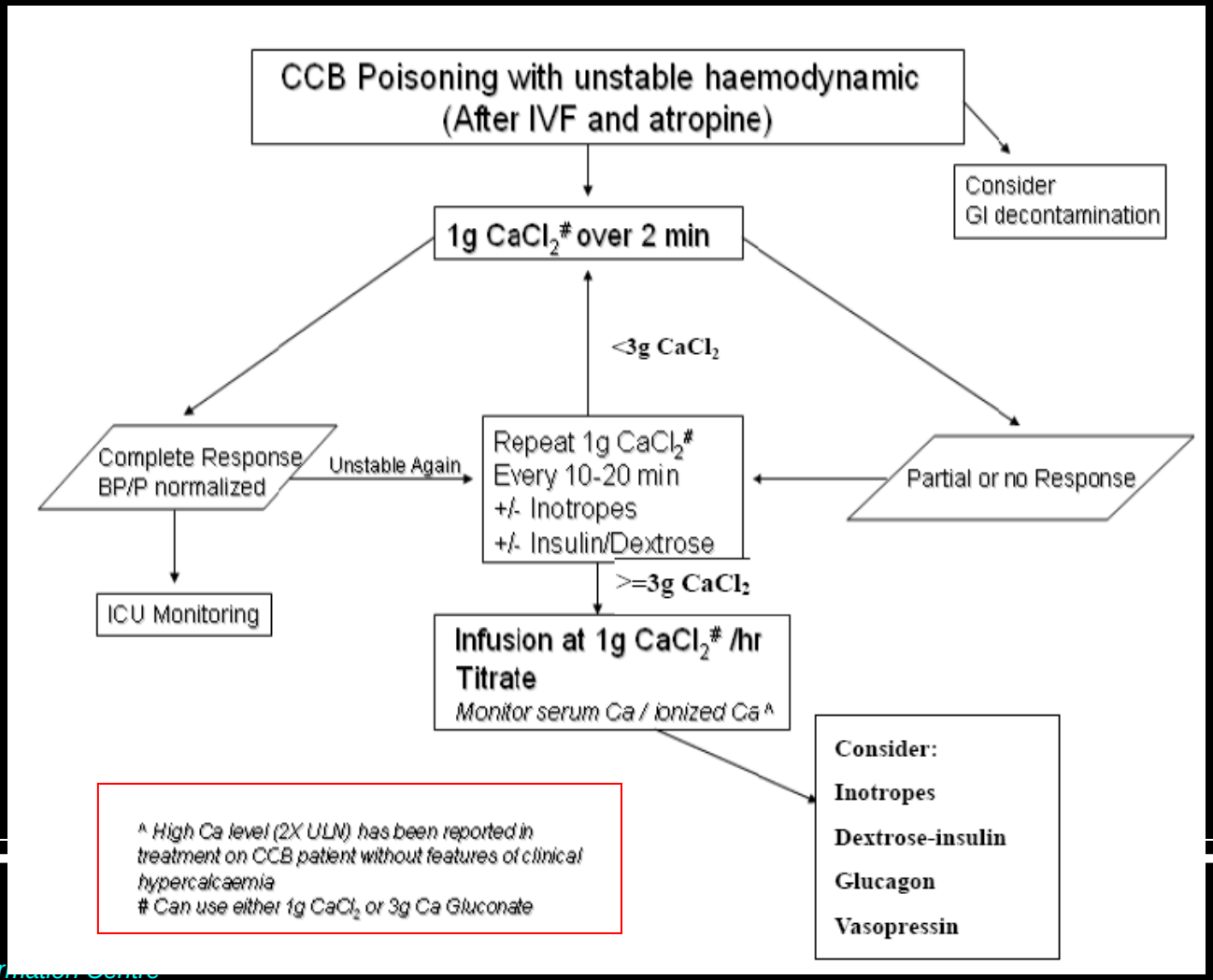
QRS 190ms

Response to NaHCO3



QRS 126 ms

Calcium in CCB Poisoning



Calcium in CCB

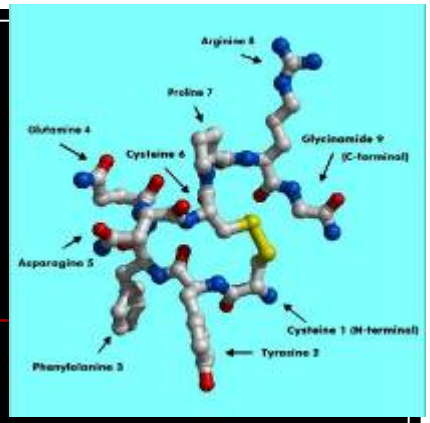
	Bolus	Infusion	Check Ca level
POISINDEX®	1-2g CaCl2 Repeat as needed	2g CaCl2 /hr	Not mentioned
TOXBASE®	1g CaCl2 Repeat Q10-20min Max 4 doses	1g CaCl2 /hr	Monitor Ca In repeated doses and infusion
Dewitt CR 04 Toxicology Review	1-2g CaCl2 Repeat Q10-20min Max 4 doses	2g CaCl2 /hr	Monitor Ca In repeated dose and infusion Continue Ca even in elevated level if responsive to Ca
Shannon MW 03 Drug Safety	1g CaCl2 Repeat Q15-20min Max 4 doses	1-2g CaCl2 /hr	Measure Ca at least twice a day level in infusion Keep at therapeutic level
7th Goldfrank 02	1g-2g CaCl2 Q15-20mins for 4 dose	1-2g CaCl2 /hr	Not mentioned

“Last Bullet” Therapy

- Vasopressin
- Intralipid
- Levosimendan

- May be considered in severe case where standard therapy fails

Vasopressin in Poisoning



- Counteract Vasodilatory Shock
- Animal Study
  - CCB / BB in dogs
- Case Reports
  - TCA , CCB, Caffeine , ARB II, PDI
- Vasopressin may be considered in poisoned patients with catecholamine resistant shock

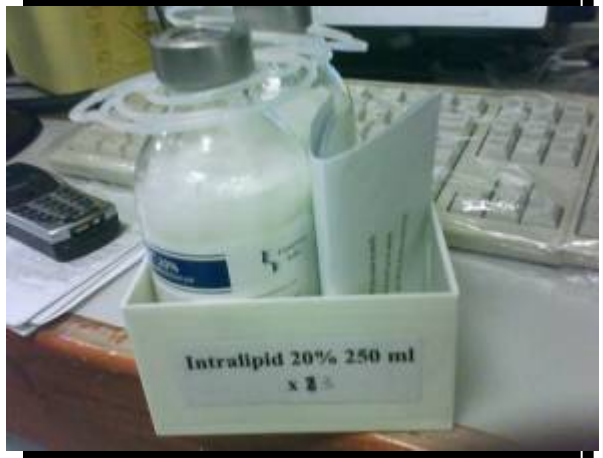
Intralipid rescue therapy

Updated by CK Chan, 21st September, 2009

Indications

Intralipid rescue therapy should be considered when maximal standard therapy failed in treating patient from cardiac arrest or life-threatening toxicity caused by the following drugs:

Drugs	Supporting evidence
Local anesthetics	Multiple human case reports and animal studies
Bupropion, lamotrigine, atenolol, calcium channel blocker (verapamil), sertraline, quatiapine, haloperidol	Human case report(s)
Tricyclic antidepressants, propranolol	Animal studies only.



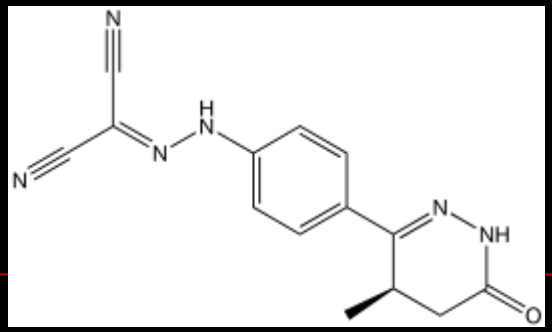
Dosage (Each bottle contains Intralipid 20% 250ml)

Intralipid 20% 100ml bolus IV injection through large bore IV catheter (preferably 18G or larger)

Follow by an infusion at 0.25ml/kg/min for 30 minutes

Repeat bolus 1-2 times if no improvement

Levosimendan



- Myocardial calcium sensitizer
- Inotropes supports
  - Acute severe CHF
- Poisoning
  - Animal Study – Verapamil, Propanolol
  - Human case reports – Verapamil, Amlodipine

CM Poisoning

Aconitine

Gelsemium Elegans

Cardiac Active Steroids

Aconitine Toxidrome

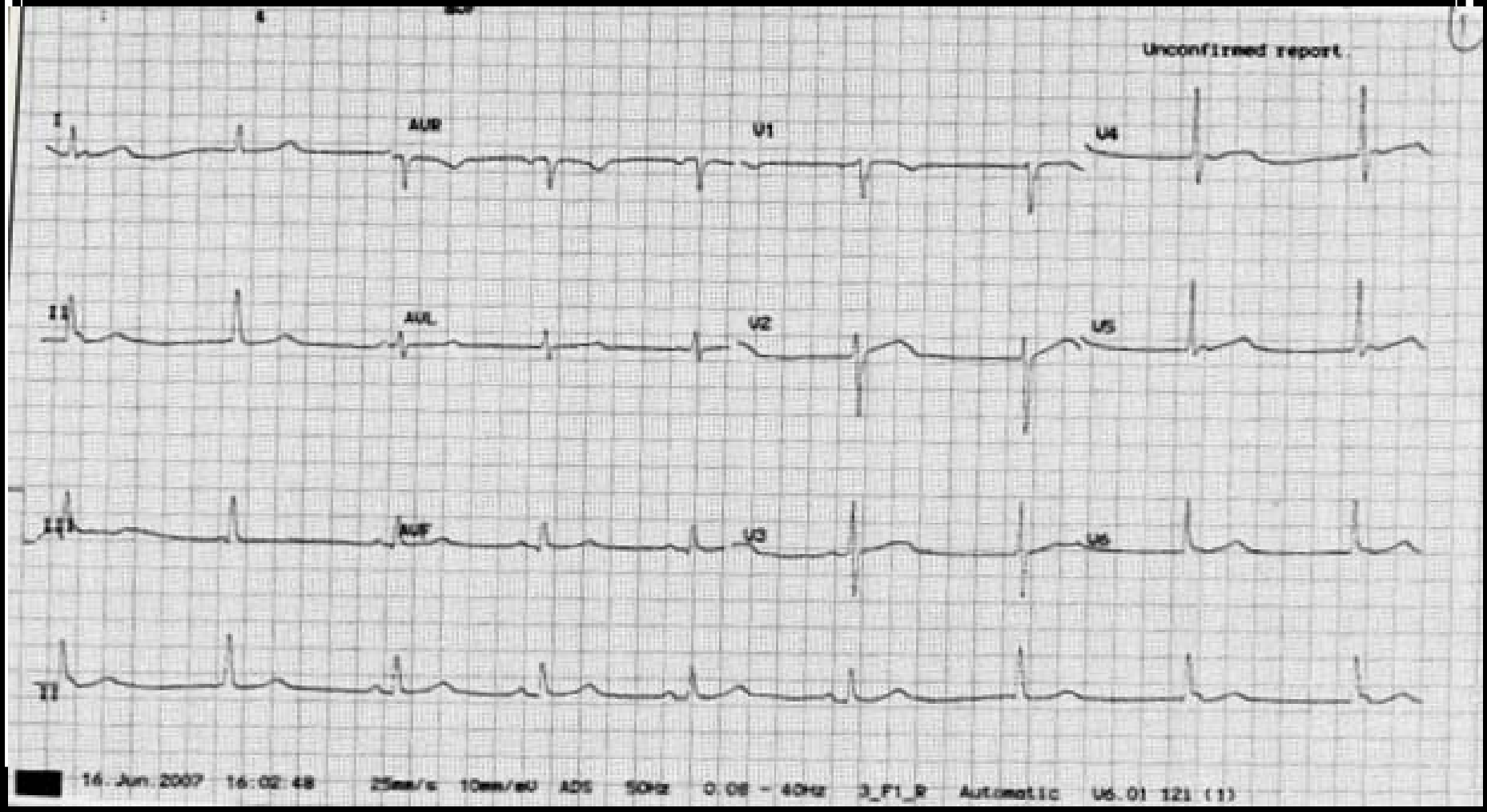
- Rapid onset
- Neurological features
  - Numbness / Weakness
- CVS features
  - Brady or tachyarrhythmia
  - Hypotension
  - ECG Pattern
- GI features

- *No matter what the CM prescription look like !*
  - *Presence of 川烏, 草烏, 附子 - Better*

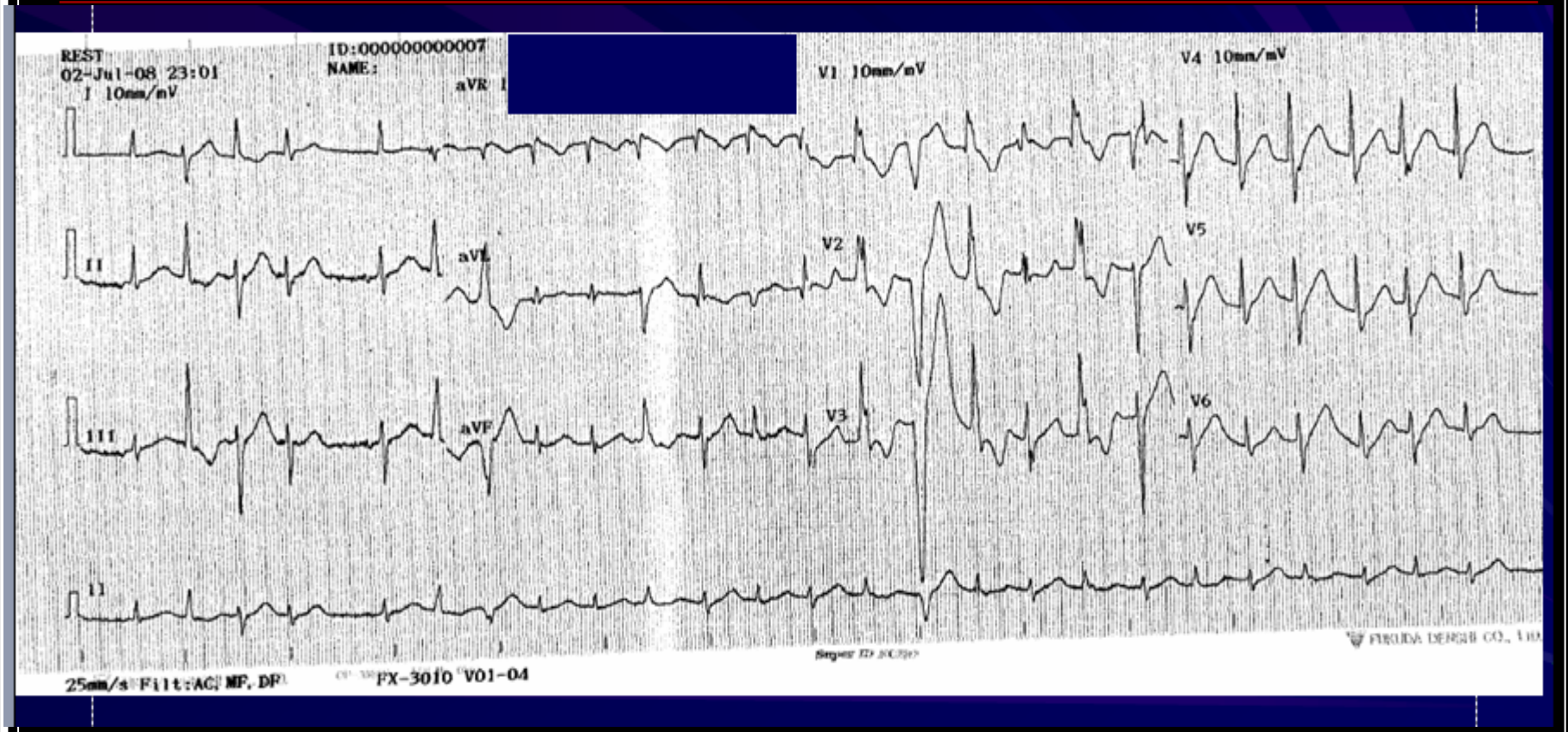
Aconitine ECG Pattern

- A spectrum
  - Mild
    - Bradycardia (sinus, junctional)
  - Moderate
    - Tachycardia (sinus, AF, frequent VEB)
  - Severe
    - Tachycardia (VT, non-sustained and sustained)

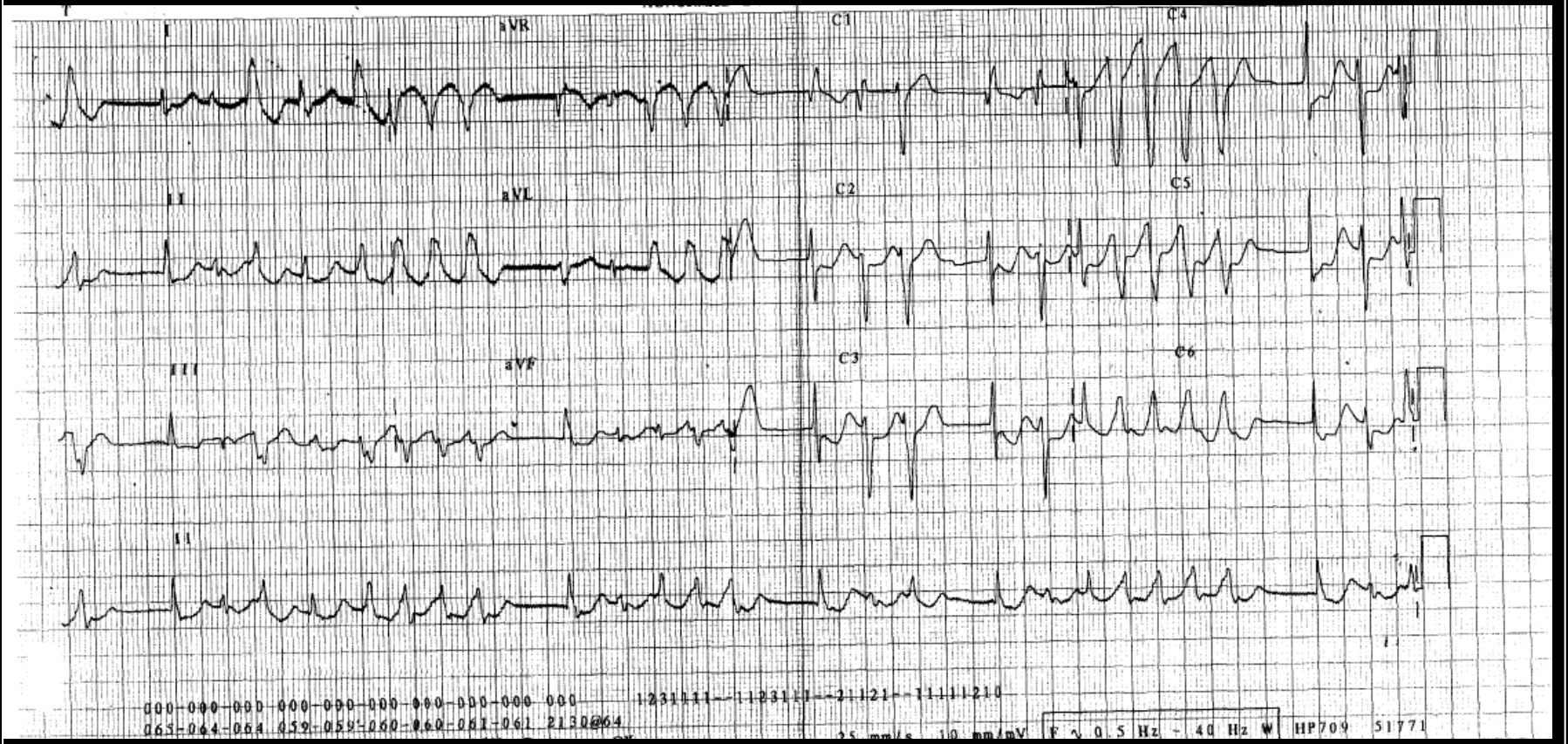
Mild


Unconfirmed report.
I
AUR
V1
V4
II
AUL
V2
V5
III
AUF
V3
V6
II
16 Jun 2007 16:02:48
25mm/s 10mm/mV ADS 50Hz 0.05 - 40Hz 3_F1_R Automatic V6.01 121 (1)

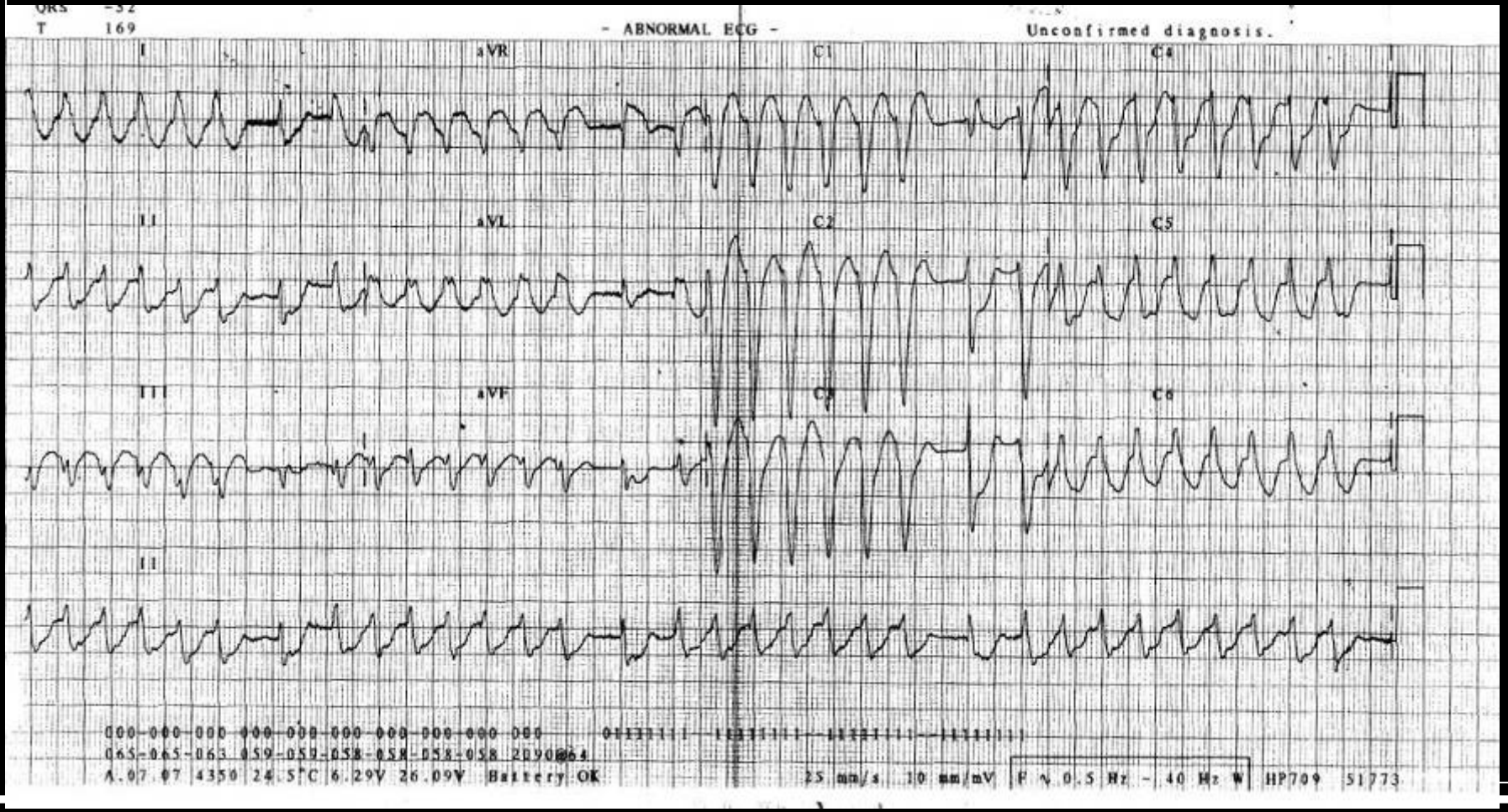
Moderate


REST
02-Jul-08 23:01
I 10mm/mV
ID:000000000007
NAME:
aVR
V1 10mm/mV
V4 10mm/mV
II
aVL
V2
V5
III
aVF
V3
V6
II
25mm/s Filt:AC MF, DF
FX-3010 V01-04

Severe



Life Threatening



Aconitine Poisoning

- GI decontamination / Supportive / Inotropes
- Bradycardia
  - Atropine
- Tachyarrhythmia
  - Consider amiodarone
  - Next choice probably flecanide
  - Lignocaine not recommended
  - Withhold electrotherapy as much as possible
- Usually improve within a few hours

Gelsemium Elegans 斷腸草

- Typical
  - Rapid onset of CNS depression, +/- nausea, vomiting
- Other features
  - CNS: Dizziness, numbness, weakness, ptosis, diplopia, seizures, coma
  - Respiratory: depression
  - GI: nausea, vomiting, abdominal pain
  - CVS: Hypotension
- Mixing up with 五指毛桃，玉葉金花, 巴, 金銀花

Hong Kong Experience

	No. (n=11)	%
Dizziness	9	82%
Nausea	3	27%
Vomiting	1	9%
Diplopia	2	18%
Nystagmus	1	9%
Tremor	2	18%
Ataxia	1	9%
Coma	1	9%
Resp depression	1	9%
Palpitations	1	9%
Death	1	9%

Management

- High index of suspicion
  - Rapid onset CNS depression with N/V after ingestion of herbs / 涼茶
  - Report to HA/CENO
- Supportive
  - Airway
  - Circulatory
  - Closed monitoring of CNS / Respiratory function

Cardiac Active Steroids Poisoning

- CHM
  - Venenum Bufonis (蟾酥)
  - Rhizoma Tupistrae (川三七)
- PCM
  - 六神丸,救心
- Plants
  - Nerium oleander (夾竹桃)
  - Strophanthus divaricatus (羊角拗)
  - Rohdea japonica (萬年青)

Special Concerns

- Digoxin immunoassays
  - Different cross sensitivity
    - Instruments
    - Particular cardiac active steroids from the source
  - Cannot be used to calculate Dig –Fab dose
- 2 types of Dig-Fab available in HA

Digoxin Fab in HA

		AHNH	CMC	KWH	NDH	PMH	POH	PWH	PYN	QEH	QMH	RHTSK	TKO	TMH	UCH	YCH
CPO Data		0	B	10B	A	A	6B	10B (CCU)	6A B	A B	A 10B	0	0	B	0	10B
PIC Survey (2009)	CCU	0	0	NR	0	NR	0	10B	NR	4A	0	0	0	0	12B	10B
	ICU	0	NR	0	0	0	0	0	0	0	0	0	0	0	0	0
	AED	0	0	0	0	10B	6B	0	0	0	0	0	6A	0	0	0

A - Digitalis antidote injections 80mg / Vial

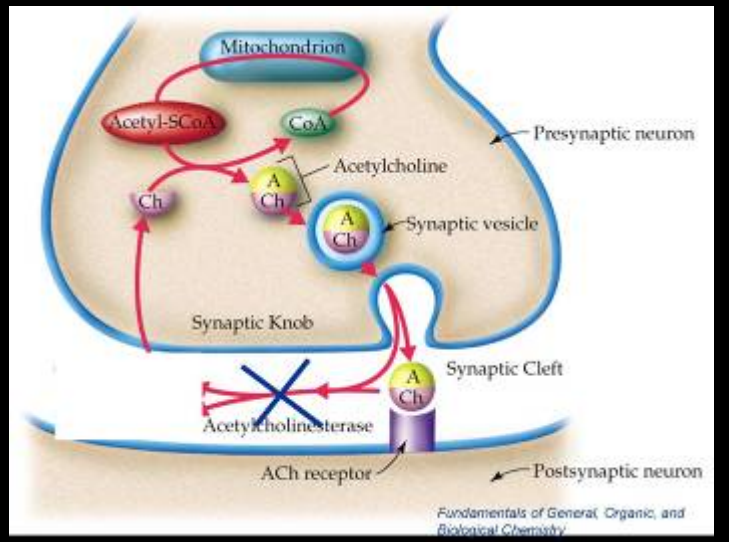
B - Digoxin immune fab 40mg / Vial

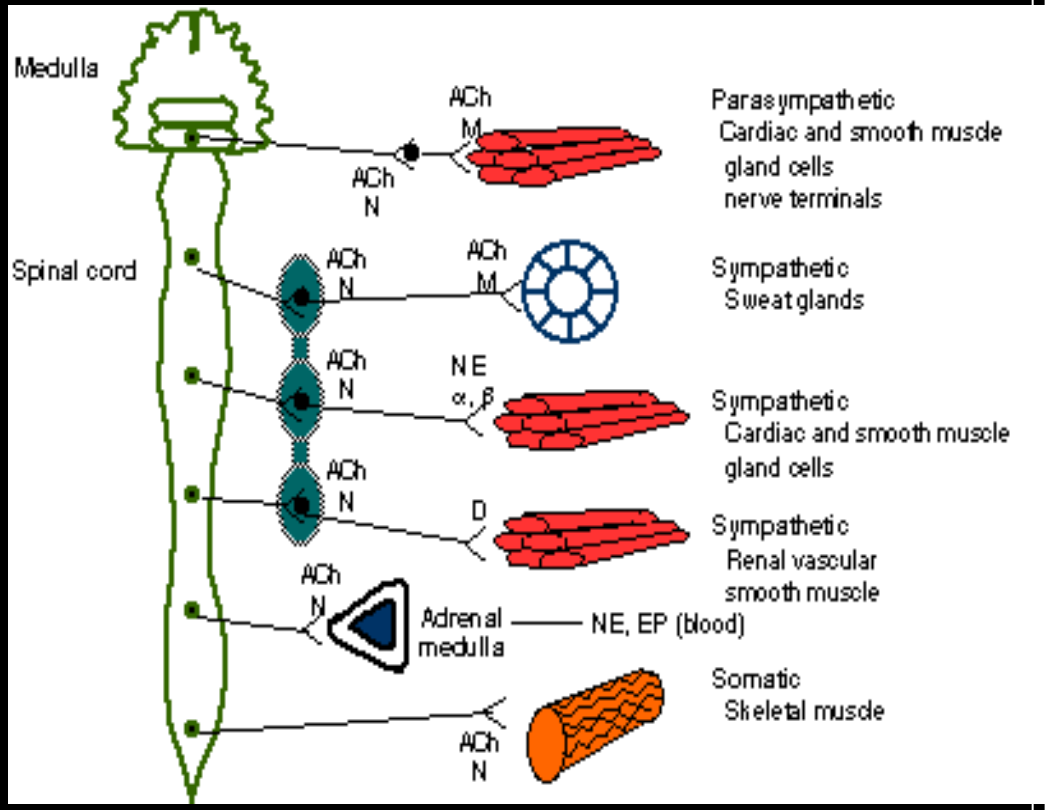
NR = Not replied

Organophosphate Poisoning

An update on the use of oxime

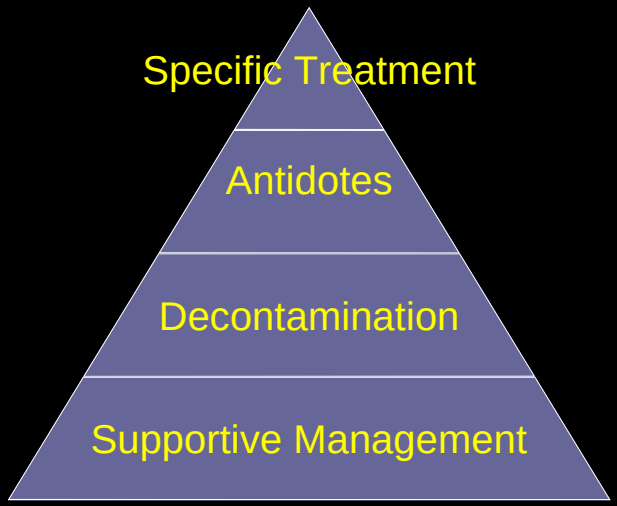
OP Poisoning – Simplified View



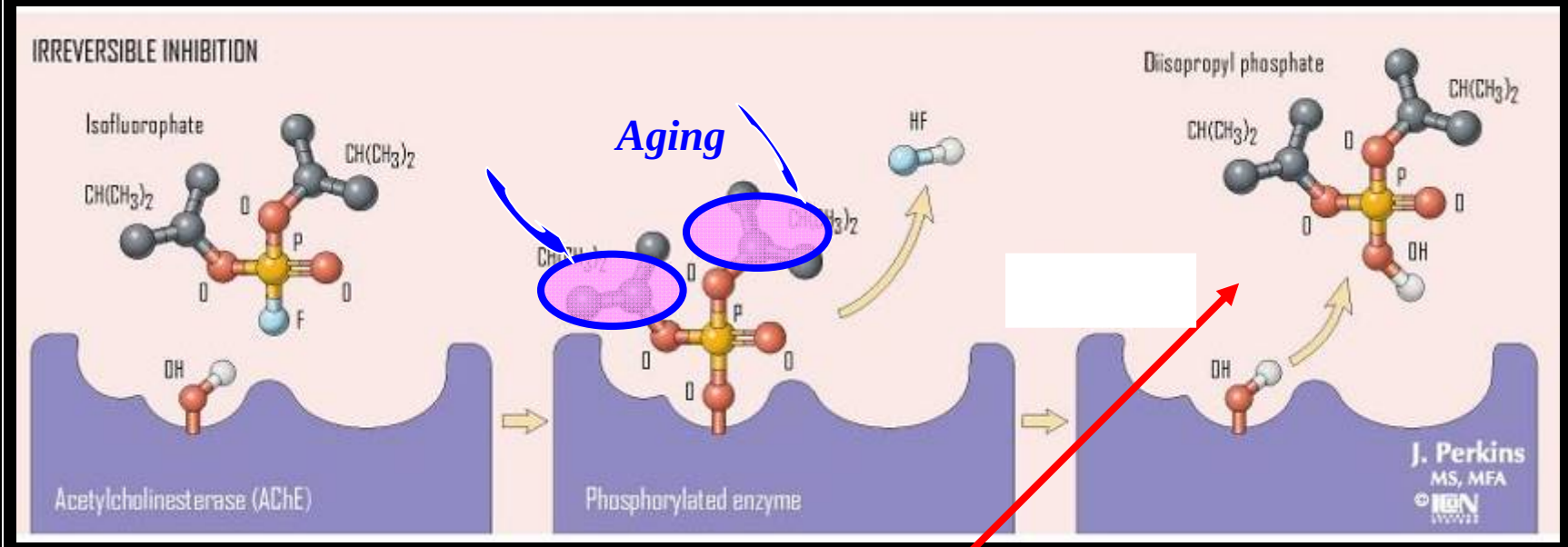


General Management

- Supportive measures
  - ABC
- Decontamination
- Antidotes
  - Atropine
  - Benzodiazepine
  - Oxime
  - Others investigational



How oxime works



↑ with oxime before aging

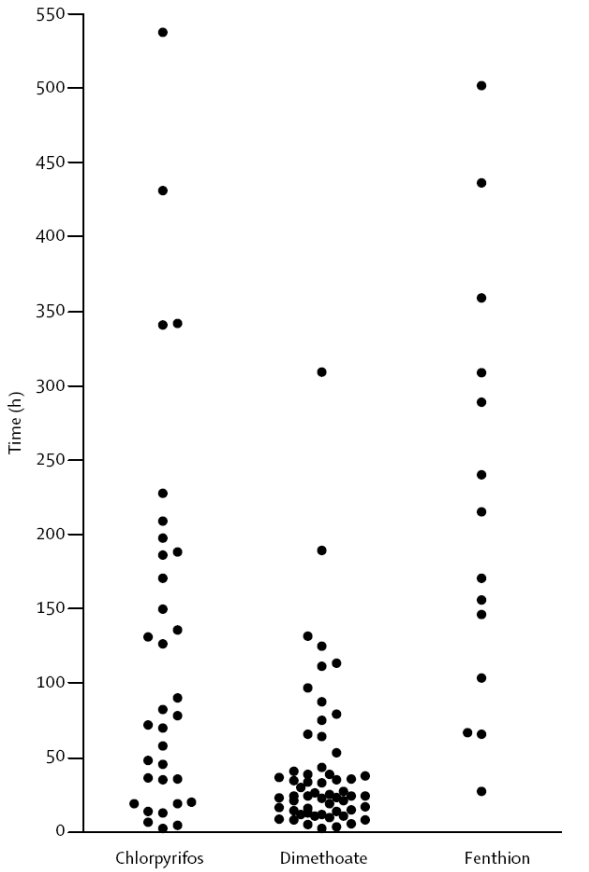
Life is not that simple !

- Different OP are different
  - Aging
  - Clinical features
  - Toxicity apart from Ach
- Pralidoxime
  - ? Optimal dose
  - ? Duration
- Other ingredients apart from OP in the pesticide and its contribution to the clinical toxicity

Differences between organophosphorus insecticides in human self-poisoning: a prospective cohort study

Michael Eddleston, Peter Eyer, Franz Worek, Fahim Mohamed, Lalith Senarathna, Ludwig von Meyer, Edmund Juszczak, Ariyasena Hittarage, Shifa Azhar, Wasantha Dissanayake, M H Rezvi Sheriff, Ladislaus Szinicz, Andrew H Dawson, Nick A Buckley

Lancet 2005; 366: 1452–59



	Chlorpyrifos (n=439)	Dimethoate (n=264)	Fenthion (n=99)
Outcomes			
Number of deaths	35	61	16
Case fatality ratio (95% CI)	8·0% (5·8–10·9)	23·1% (18·4–28·6)	16·2% (10·2–24·7)
Number requiring intubation	66	93	31
Proportion (95% CI)	15·0% (12·0–18·7)	35·2% (29·7–41·2)	31·3% (23·0–41·0)
Number with seizures	8	0	5
Proportion (95% CI)	1·8% (0·9–3·6)	0·0% (0·0–1·4)	5·1% (2·2–11·3)
Admission characteristics for fatal cases			
Glasgow Coma Score	6 (3–14)	3 (3–7)	12 (8–15)
Butyrylcholinesterase activity* (mU/mL)	6 (0–94)	735 (269–1240)	0 (0–941)
Organophosphorus insecticide plasma concentration (μmol/L)	4·7 (3·6–5·9)	846 (657–1183)	12·3 (0·94–30·3)
Acetylcholinesterase activity over time			
Number	18	10	4
On admission (mU/μmol Hb)	63·5 (27·0–124·6)	69·0 (22·1–145·7)	64·2 (32·5–75·4)
After 1 h (mU/μmol Hb)	391·8 (294·8–507·8)	110·2 (59·4–166·9)	68·1 (53·8–122·0)
After 12 h (mU/μmol Hb)	312·5 (205·9–480·2)	42·5 (13·7–67·9)	41·9 (14·6–100·6)
Aged acetylcholinesterase on admission	19·4% (6·4–26·1)	71·9% (57·2–86·8)	70·3% (65·6–82·2)
Aged acetylcholinesterase after 12 h	19·8% (3·5–26·2)	84·5% (80·5–96·0)	85·7% (75·4–91·1)

Literature on Oxime Clinical Use

- Cochrane Review 2005
  - Unchanged status in 2009, Search up to Nov 2003
  - 2 RCT included only (Samuel 95', Cherian 97')
  - No clear benefit or harm
- Landmarks
    - 2 systemic reviews in 2006
    - Pawar in 2006
    - A recent one in 2009

Review 1

Review Articles

Oxime therapy and outcomes in human organophosphate poisoning: An evaluation using meta-analytic techniques

John V. Peter, MBBS, MD, DNB (Med), FRACP; John L. Moran, MBBS, FRACP, FJFICM;
Petra Graham, MS, BSc, PhD

(Crit Care Med 2006; 34:502–510)

From the Department of Intensive Care Medicine, the Queen Elizabeth Hospital, Woodville SA, Australia

- 7 studies included
  - 4 retrospective studies
  - 3 prospective studies
    - 2 RCT (Cherian 97', Cherian 05')
    - 1 non-randomized (Balali Mood 98')

Conclusions: Based on the current available data on human organophosphate poisoning, oxime was associated with either a null effect or possible harm. The lack of current prospective randomized controlled trials, with appropriate patient stratification, mandates ongoing assessment of the role of oximes in organophosphate poisoning. (Crit Care Med 2006; 34:502–510)

Review 2

Increased morbidity and mortality in acute human organophosphate-poisoned patients treated by oximes: a meta-analysis of clinical trials

Human & Experimental Toxicology (2006) **25:** 157–162

Roja Rahimi, Shekoufeh Nikfar and Mohammad Abdollahi

Department of Toxicology and Pharmacology, Faculty of Pharmacy, and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran

- 6 studies included
  - 5 overlapped with review 1

It can be concluded that oximes are not effective in the management of organophosphate-poisoned patients and, surprisingly, they can be dangerous and worsen the patient's clinical situation.

In conclusion, this meta-analysis strongly demonstrates that oximes are not the appropriate choice for OP poisoning.

Continuous pralidoxime infusion versus repeated bolus injection to treat organophosphorus pesticide poisoning: a randomised controlled trial

Kirti S Pawar, Ramesh R Bhoite, Chandrakant P Pillay, Sujata C Chavan, Dhananjay S Malshikare, Saraswati G Garad

Lancet 2006; 368: 2136–41

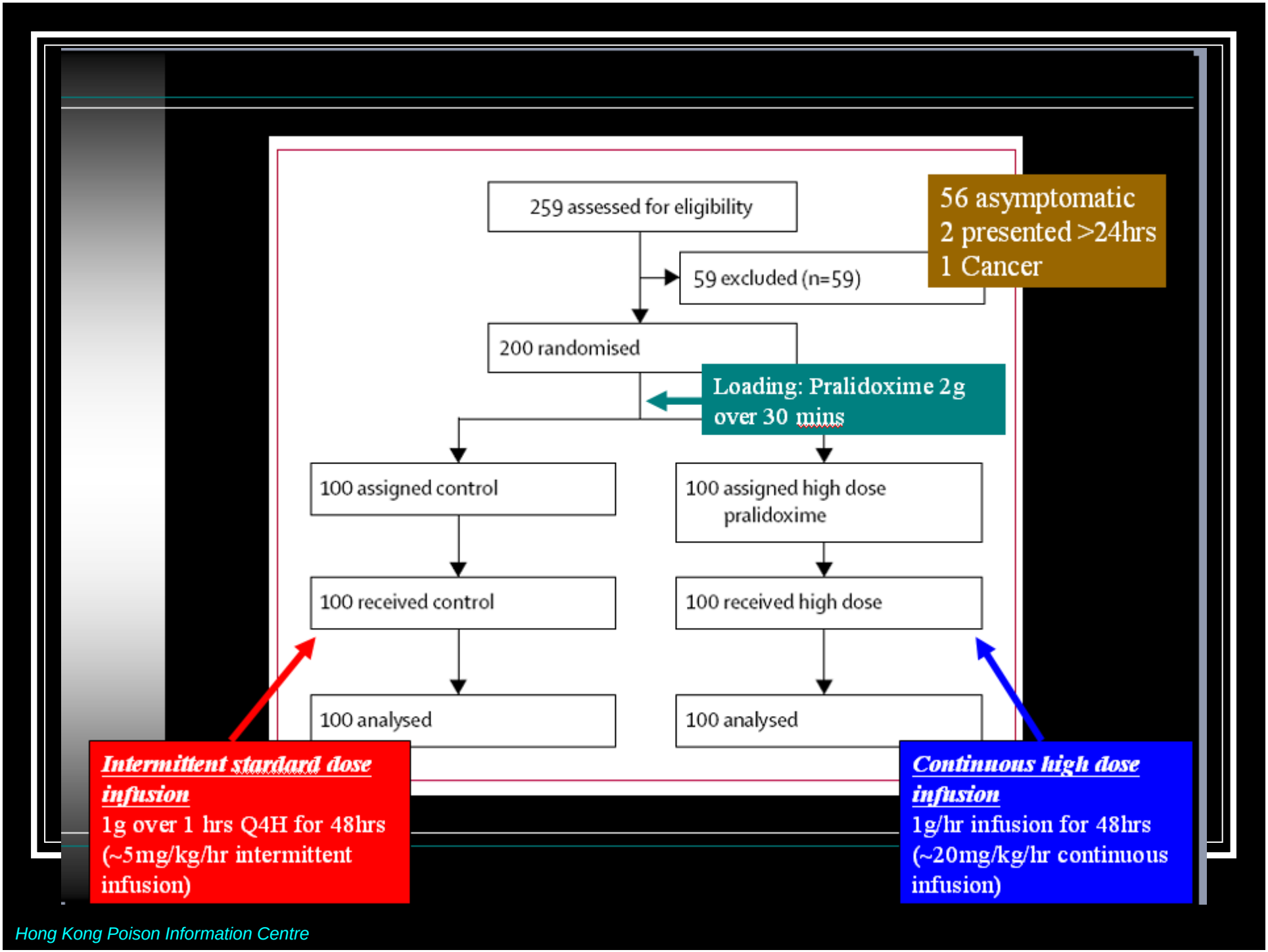
See Comment page 2110

Giriraj Hospital and Intensive Care Unit, Baramati, Pune, Maharashtra, India (K S Pawar MBBS, R R Bhoite MD, C P Pillay BHMS, S C Chavan BHMS, D S Malshikare BHMS); and Department of Preventive & Social Medicine, B J Medical College, Pune, Maharashtra, India (S G Garad MSc)

Hypothesis:

Currently used Pralidoxime dose may not be adequate in antagonizing the effect of OP

Infusion is better than regular bolus injection


259 assessed for eligibility
56 asymptomatic
2 presented >24hrs
1 Cancer
59 excluded (n=59)
200 randomised
Loading: Pralidoxime 2g over 30 mins
100 assigned control
100 assigned high dose pralidoxime
100 received control
100 received high dose
100 analysed
100 analysed
Intermittent stardard dose infusion
1g over 1 hrs Q4H for 48hrs (~5mg/kg/hr intermittent infusion)
Continuous high dose infusion
1g/hr infusion for 48hrs (~20mg/kg/hr continuous infusion)

	Control group (n=100)	Study group (n=100)	Difference or relative risk(95%CI)	p
Primary outcomes				
Median days ventilated	10 (8–12)*	5 (4 to 5)†	5 (5–6)	<0·0001
Median atropine dose in first 24 h (mg)	30 (25 to 45)	6 (4 to 6)	24 (24–26)	<0·0001
Neck muscle weakness	94 (94%)	80 (80%)	0·85 (0·76–0·95)‡	0·0054‡
			0·86 (0·65–0·98)§	0·0054§
Intubated during admission	88 (88%)	64 (64%)	0·72 (0·62–0·86)	0·0001
Intubated after randomisation	19/31 (61·3%)	1/37 (2·7%)	0·044 (0·063–0·31)‡	<0·0001‡
			0·045 (0·005–0·31)§	0·0001§
Secondary outcomes				
Deaths	8 (8%)	1 (1%)	0·13 (0·016–0·98)‡	0·0349‡
			0·11 (0·01– 0·84)§	0·00350§
Pneumonia	35 (35%)	8 (8%)	0·23 (0·11–0·47)‡	<0·0001‡
			0·23 (0·10–0·47)§	<0·0001§
Mean systolic blood pressure in first 24 h (mm Hg)	115·4 (6·10)¶	136·2 (4·97)‖	20·6 (19·0–22·2)	<0·0001
Mean diastolic blood pressure in first 24 h (mm Hg)	75·6 (4·96)¶	84·1 (2·56)‖	8·3 (7·2–9·5)	<0·0001

*n=80. †n=63. ‡Unadjusted values. §Adjusted values. ¶n=97. ‖n=99.

Table 2: **Summary of primary and secondary outcomes with comparative statistics**

OPEN ACCESS Freely available online

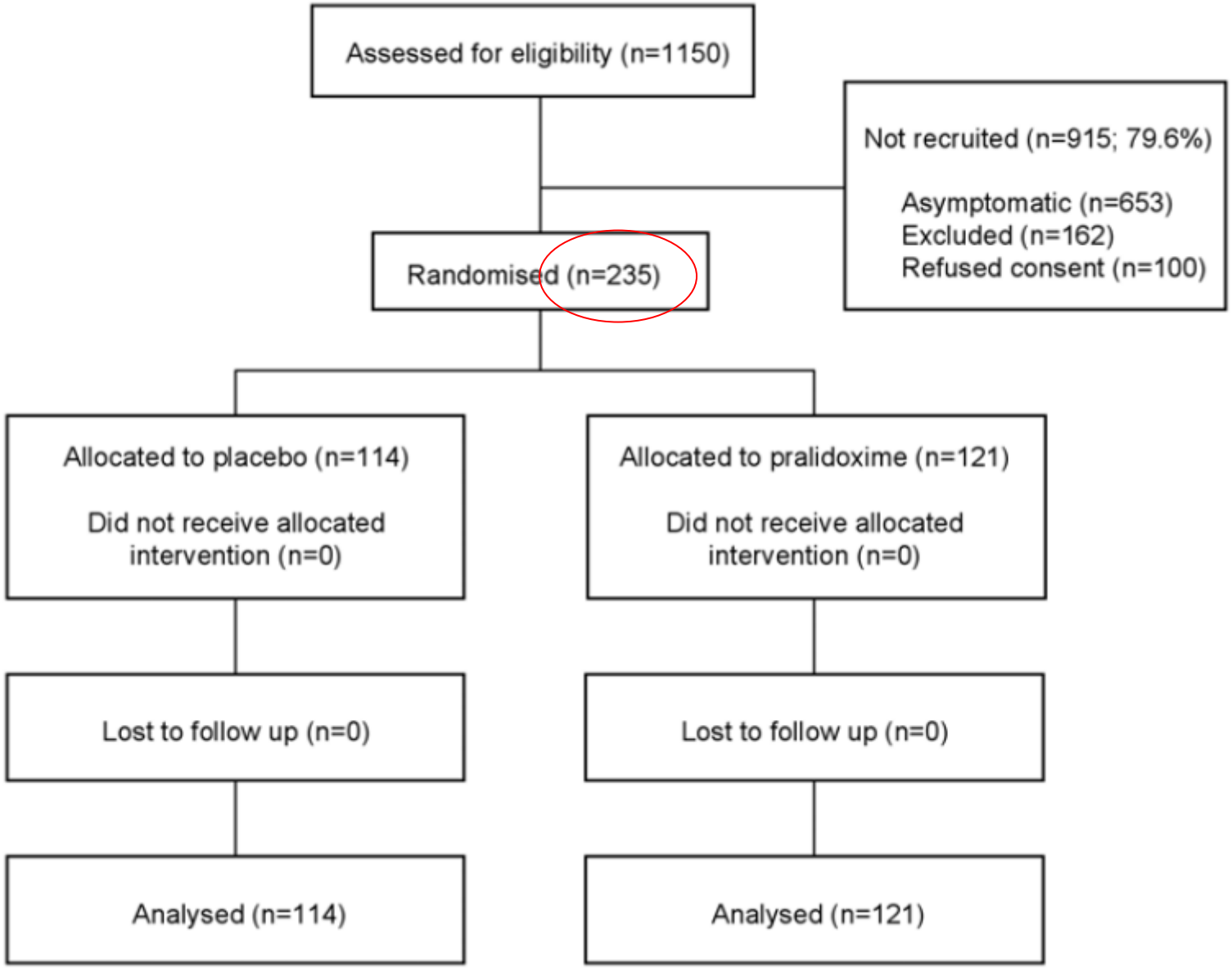
PLoS MEDICINE

Pralidoxime in Acute Organophosphorus Insecticide Poisoning—A Randomised Controlled Trial

Michael Eddleston[1,2,3]*, Peter Eyer[4], Franz Worek[5], Edmund Juszczak[6], Nicola Alder[6], Fahim Mohamed[2,3], Lalith Senarathna[2,3], Ariyasena Hittarage[7], Shifa Azher[8], K. Jeganathan[7], Shaluka Jayamanne[8], Ludwig von Meyer[9], Andrew H. Dawson[3,10], Mohamed Hussain Rezvi Sheriff[2,3], Nick A. Buckley[3,11]

1 Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, United Kingdom, **2** Ox-Col Collaboration, Department of Clinical Medicine, Faculty of Medicine, University of Colombo, Sri Lanka, **3** South Asian Clinical Toxicology Research Collaboration, Sri Lanka, **4** Walther Straub Institute of Pharmacology and Toxicology, Ludwig Maximilians University, Munich, Germany, **5** Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany, **6** Centre for Statistics in Medicine, Wolfson College, University of Oxford, England, **7** Anuradhapura General Hospital, North Central Province, Sri Lanka, **8** Polonnaruwa General Hospital, North Central Province, Sri Lanka, **9** Institute of Legal Medicine, Ludwig Maximilians University, Munich, Germany, **10** School of Public Health, University of Newcastle, Australia, **11** Professorial Unit, Department of Medicine, University of New South Wales, Sydney, Australia

PLoS Medicine | June 2009 | Volume 6 | Issue 6 | e1000104


Assessed for eligibility (n=1150)
Not recruited (n=915; 79.6%)
Asymptomatic (n=653)
Excluded (n=162)
Refused consent (n=100)
Randomised (n=235)
Allocated to placebo (n=114)
Did not receive allocated intervention (n=0)
Allocated to pralidoxime (n=121)
Did not receive allocated intervention (n=0)
Lost to follow up (n=0)
Lost to follow up (n=0)
Analysed (n=114)
Analysed (n=121)

Primary Outcome

- Overall fatality 48/235 (20.4%)
- Pralidoxime 30/121 (24.8%) Vs Placebo 18/144 (15.8)
- Hazard Ratio
  - Crude 1.82 [p = 0.05]
  - Adjusted 1.69 [p=0.12]

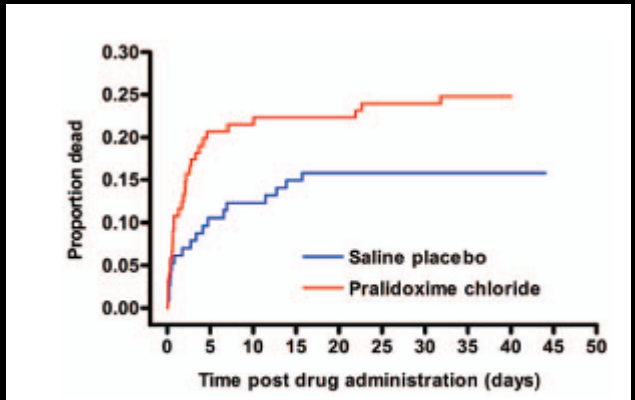


Figure 4. Timing of deaths in the two study arms. Cumulative percentage of patients who died. For the purposes of survival analysis, the clock has been started at randomisation and stops either at death or discharge (assumed to be 40 d if discharged alive sooner than 40 d).

Author Conclusion

- Found no evidence of the WHO regimen improves survival or intubation
- Provide evidence that routinely following the WHO recommended high dose pralidoxime regimen in all OP self poisoned patients does not improve survival
- Further study is needed to assess the benefit/risk of oximes and to explore using lower or shorter dosing regimens or different oximes

Current Suggested Pralidoxime Dose

	Loading	Maintenance	Duration
WHO	30 mg/kg	>8mg/kg/hr	
TOXBASE	30 mg/kg	30mg/kg Q4-6H OR 8-10 mg/kg/hr	Not mentioned
TOXNIZ	1-2 g over 15-30min	1-2g Q6-12H OR 0.5g/hr (8-10mg/kg/hr)	- Need to be continued for some time after apparent clinical recovery -Symptom free for 8 hours -Static or improving cholinesterase trend
Poisindex	30 mg/kg OR 1-2 g over 15-30min	>8mg/kg/hr 0.5g – 1g/hr	-Minimal 24 hours after symptom resolved
GF 8th	1-2 g over 15-30min	0.5g/hr	-Minimal 24 hours after symptom resolved -Normalization of RBC cholinesterase activity
HKPIC	1-2g over 30min	0.5-1g/hr	-24-48 hours, titrate with clinical response

Our Experience on Pralidoxime DATOX (Jul 05 – Jun 08)

		OP	2-PAM	Duration	Outcome
05-40003	F/22	Omethoate	1g + 1g + 1g Infusion 2-4mg/kg	24 hours	ICU/Major
06-11247	M/66	Malathion	1g + infusion	Not mentioned	ICU/Major
06-11715	M/31	Amitraz (Not an OP)	Given	Shortly	Med/Moderate
06-11844	F/37	Malathion	1g + infusion	>10 days	ICU/Major
06-11845	F/78	Malathion	1.5g + infusion (10mg/kg/hr)	3-4 days	ICU/Major
08-11044	F/29	Propoxur (Carbamate)	1g + infusion	<1 day	ICU/Major
08-11822	M/20	OP or carbamate	Infusion	48 hours	ICU/Major

Our Experience on Pralidoxime PIC-MS (Jul 08 – Jun 09)

		OP	2-PAM	Duration	Outcome
08-12207	M/41	Diazinon	Initial infusion X 10 hours Restart for IMS	< 5 days	ICU/Major
08-12975	F/33	Propoxur (Carbamate)	1-2 g loading 0.5-1g/hr	< 1 days	Death
09-12107	M/52	Malathion	0.75g/hr	5 days	ICU/Major
09-12463	M/52	Chlorpyrifos	Given for about 25 hours on day 2	< 1 days	Death

8 cases of OP and 5 cases of carbamate exposure – 4 given 2-PAM

My Bottom Line

- Routine use of 2-PAM in unselected OP exposure cannot be recommended based on current evidence
- Individual case consideration
  - Type of OP
  - Clinical status
- If decide to use, a bolus followed by continue infusion is preferred

Venomous Snake Bites

Antivenom Use

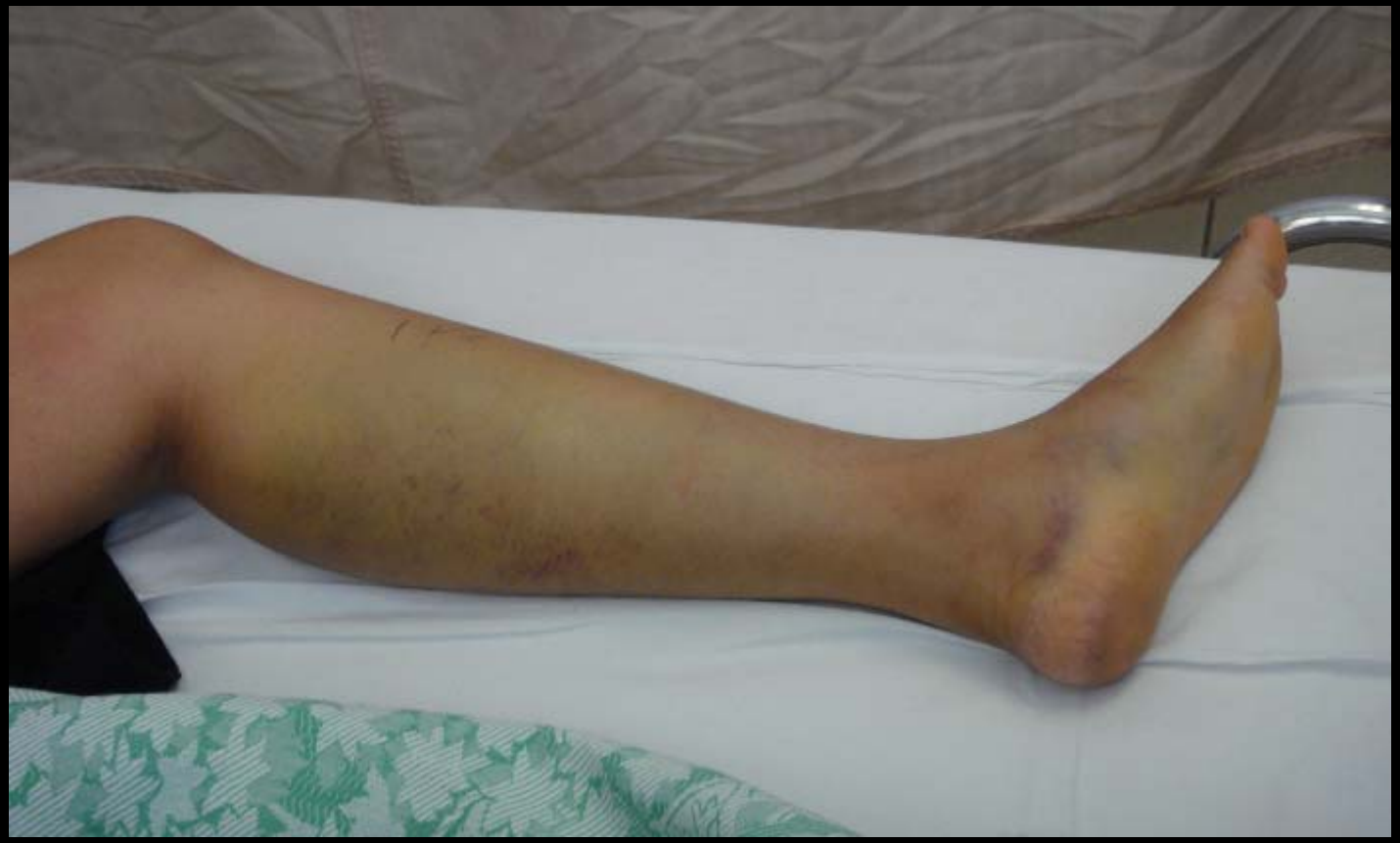
Important Venomous Snakes in HK

		Local	Systemic
Vipers	青竹蛇 山烙鐵 烙鐵頭 	Severe Swelling	Coagulopathy
Kraits	金腳帶 銀腳帶 	Minimal	Paralysis
Cobras	飯鏟頭 過山烏 	Pain++ Necrosis	Paralysis CVS

Antivenom Indications

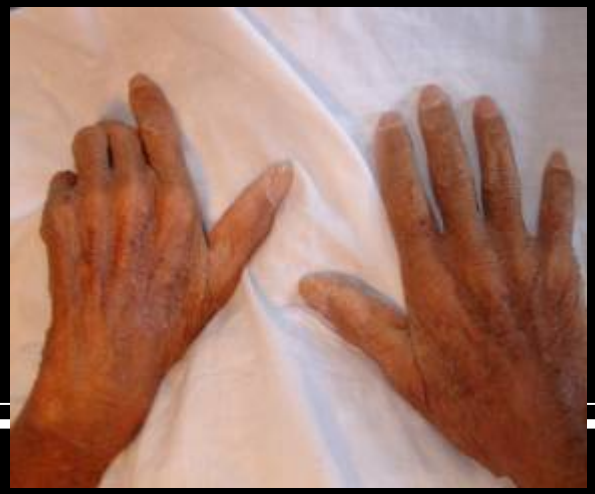
- Progressive / Severe Local
  - Progressing local symptoms, ongoing necrosis
  - Risk of compartment syndrome
- Systemic Toxicity
  - Coagulopathies, weakness, rhabdomyolysis, hypotension
- Consider “prophylactic” antivenom for all confirmed krait envenomation
  - Established paralysis is not reversible by antivenom

Bamboo Snake

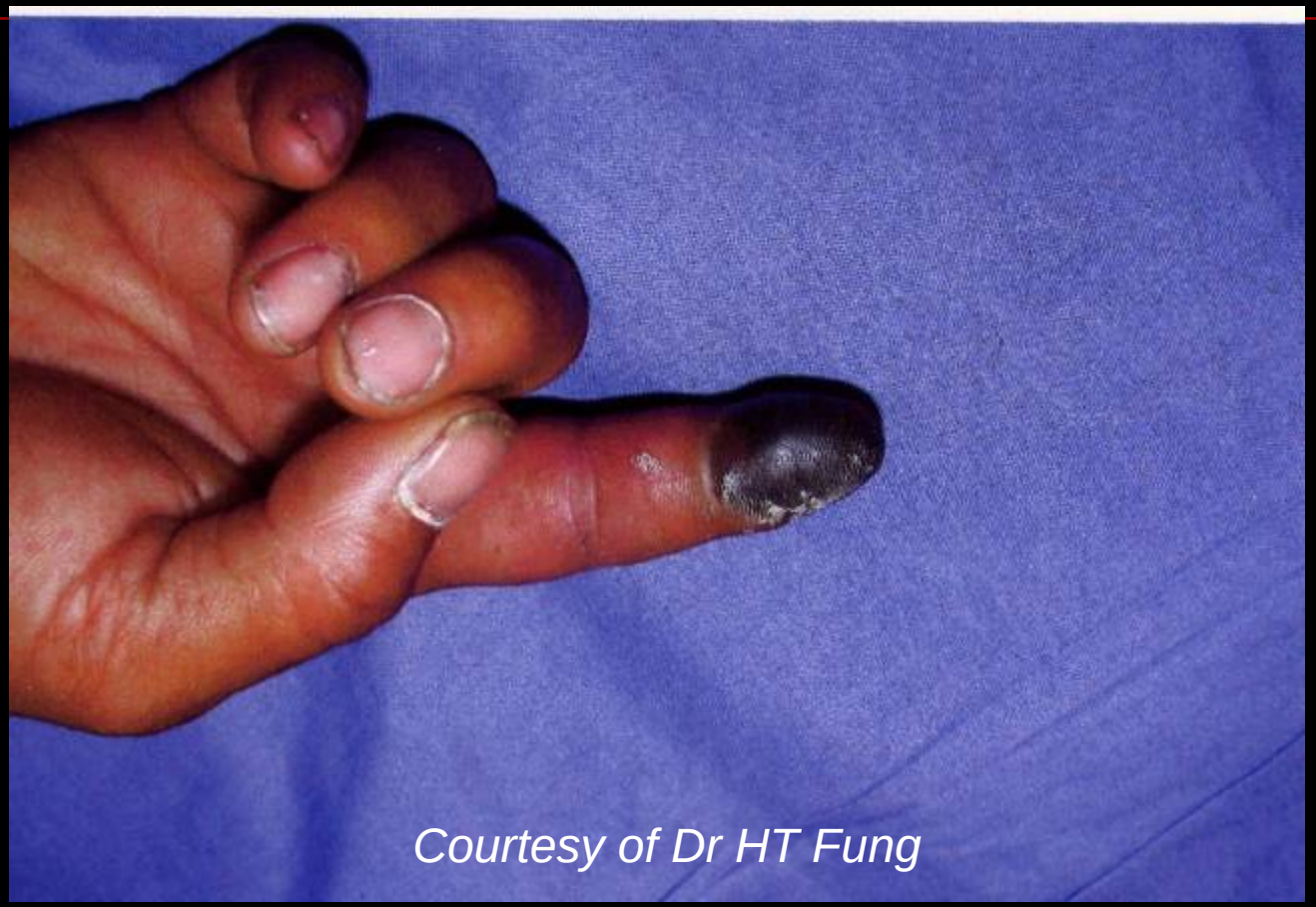


Many Banded Kraits

Pt at 3rd week



Chinese Cobra



Snake Antivenom in HA

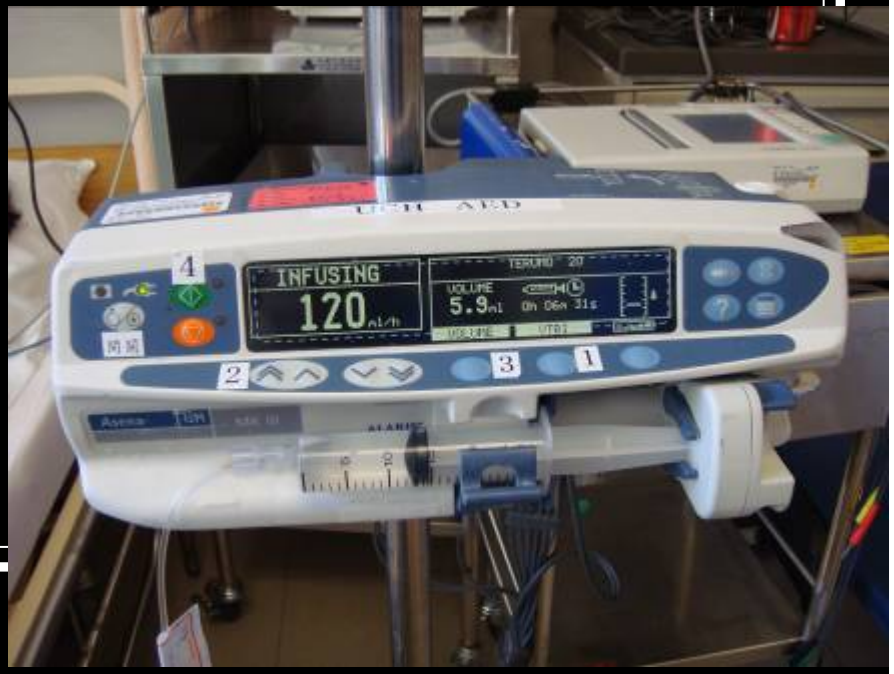
Level II

Agkistrodon halys[=] 抗蝮蛇毒血清	蝮蛇、山區蝮蛇/山烙鐵頭、 烙鐵頭/龜殼花、竹葉青/赤尾青竹絲
Bungarus fasciatus[=] **(Banded Krait)** **抗金環蛇毒血清**	金腳帶/金環蛇
Bungarus mulitcinctus[=] 抗銀環蛇毒血清	銀腳帶/雨傘節/銀環蛇、過山烏/眼鏡王蛇
Green pit viper [=+]	青竹蛇/白唇竹葉青
Naja naja[=] **抗眼鏡蛇毒血清**	飯鏟頭/眼鏡蛇

Level III

Agkistrodon acutus[=] 抗五步蛇毒血清	五步蛇/百步蛇/尖咀蝮
Russell's viper[=]	鎖鏈蛇/金錢豹/蛙蛇
Tiger snake[= ^]	海蛇


Green Pit Viper


INFUSING
120
5.9
0h 06m 31s

To Give

- Skin test is not recommended
- Resuscitation equipment stand-by
- Anti-histamine and hydrocortisone pre-treatment
- Consider SC adrenaline if high risk of severe allergy
- 1st vial
  - First vial made up to 500 ml NS, give at 100ml/hr
  - If no allergy after 5-10 min, ↑ rate to finish the vial in 30 min
  - Subsequent vials can be given faster and less diluted then

HKPIC Data Jul 08 – Sep 09

- 38 consultation cases
- 24 given antivenom (9 in ICU)
  - Most given 1-2 vials
  - No significant adverse reactions

Snake	Antivenom
Bamboo Snake	9 AH 10 GPV
Cobra	3 NN 1 NK
Krait	1 BF + BM

2º Contamination Prevention

OP / Pesticide Poisoned Patient

Q J Med 2004; **97**:75–80
doi:10.1093/qjmed/hch020

Original papers

QJM

Secondary contamination in organophosphate poisoning: analysis of an incident

- OP ingestion
- Clothing contaminated by vomitus
- Foul smell in “R” room
- Resuscitation before decontamination
- 10 staffs got sick

Table 2 *Staff complaining of symptoms*

Patient	Occupation	Exposure	Symptoms	Signs	Investigations	Management
1	Anaesthetic Registrar	Airway management, 4 h	Chest tightness	HR 53–60/min, BP 139/86. No wheeze, salivation or miosis	ECG sinus bradycardia, PEFR 490 l/min	Observed 4 h, discharged home
2	Anaesthetic SHO	Airway management, 6.5 h	Hot, lightheaded	HR 69, BP 150/96. Clear chest	None	Observed 1 h, then discharged
3	Medical Registrar	Coordinating medical care, 3–4 h with patient	Hypersalivation	HR 97/min, BP 135/94. No miosis or wheeze	None	Discharged
4	ED Sister	Coordinating nursing care, 6 h with patient	Transient chest tightness	HR 83/min, BP 142/67. No miosis or wheeze	None	Discharged
5	ED Registrar	Initial medical care, hand ventilated patient	Transient chest tightness	HR 67/min, BP 122/77. No miosis or wheeze	None	Discharged
6	Medical SHO	Assisting medical care, 3 h with patient	Transient chest tightness	HR 80/min, BP 131/69. No miosis or wheeze	None	Discharged
7	ED Sister	Nursing care	Transient chest tightness	HR 77/min, BP 163/78	None	Discharged
8	ED Staff Nurse	Nursing care	Chest tightness	HR 104/min, BP 110/63	None	Discharged
9	ED Staff Nurse	Nursing care. 1 h same room, different patient	Chest discomfort	HR 93/min, BP 163/78. No miosis or wheeze	None	Discharged
10	ED Porter	Portering, 30 min in room with patient	Giddiness	HR 60/min, BP 132/79. No miosis or wheeze	None	Discharged

HR, heart rate; BP, blood pressure; ECG, electrocardiograph; PEFR, peak expiratory flow rate.

Sri Lanka experience

Q J Med 2004; **97**:697–699

- "The risk of secondary OP poisoning is low, perhaps negligible, when universal precautions are used"
- >700 cases of OP poisoning treated in a single hospital in Sri Lanka in 2 years without PPE
- Discomfort including nausea & dynpnoea have been reported, which quickly settled with improved ventilation / breathing fresh air
- Resuscitation & atropinization under universal precautions before dermal & GI decontamination

Source of 2^{o} Contamination

- High risk
  - Vomitus
  - Lavage fluid
  - Contaminated skin and clothing
- Low risk
  - Faeces, urine, body tissue
  - Post-mortum specimen

Others than OP

- Organic solvents e.g. xylene
- Cause the pungent smell
- Low acute toxicity, can cause symptoms

3M R95 Particulate Respirator With Nuisance-Level Organic Vapor Relief

HKPIC Recommendation

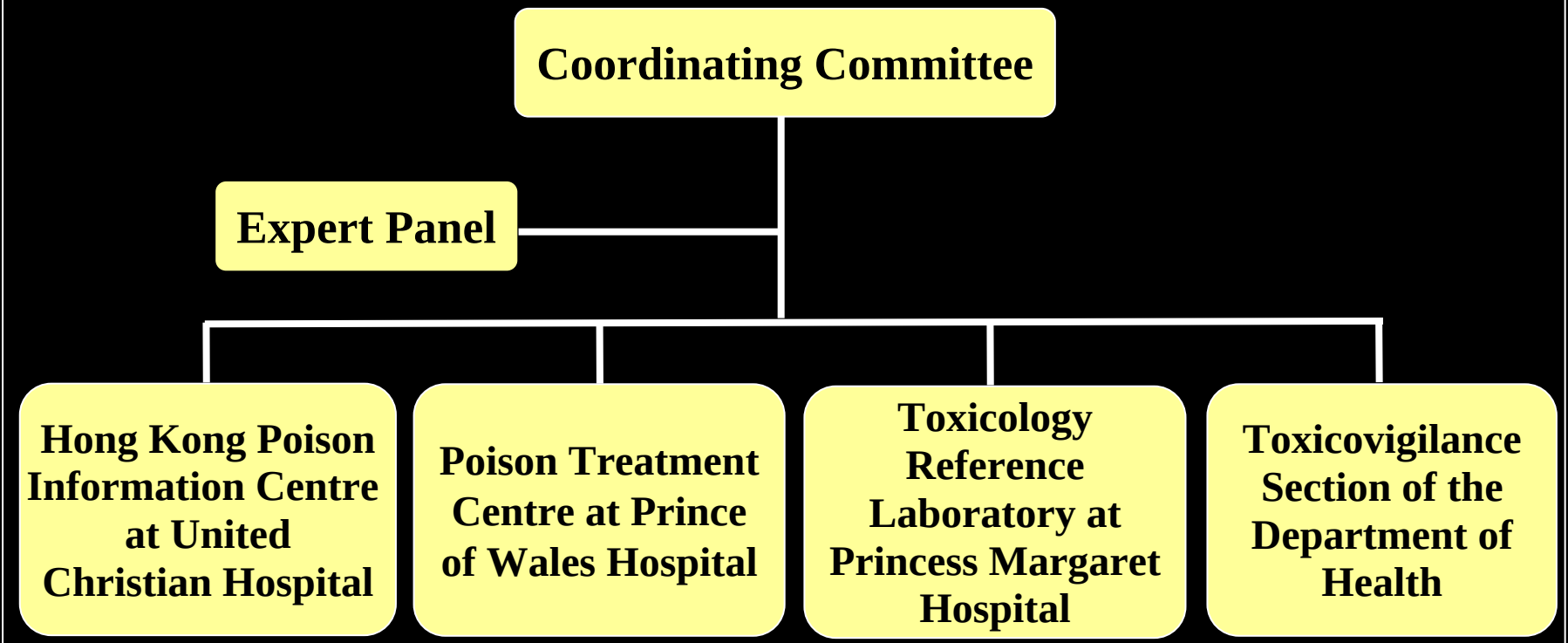
- Universal Precautions
- Preferably negative pressure ventilation
- Level C PPE if high risk of 2^{o} contamination
- Remove & discard contaminated clothings
- Nitrile or butyl rubber gloves are preferred in handling the high risk materials.
- Surface decontamination by copious soap & water as needed

Acknowledgement

THANK YOU

Q & A

香港中毒防控網絡
Hong Kong Poison Control Network



Hong Kong Poison Information Centre (HKPIC)

- Set up in Jul 2005
- Poison information & management advice to HCW
  - 24 hours daily
- Clinical Toxicology Training
- Toxicovigilance
- Central stocking of Level III Antidote