



Rational use and interpretation of Toxicology tests

**Dr SH Tsui, Toxicology Subcommittee
JCM May 2012**



Contents

- Ten principles (**commandments**) on use of ancillary tests in Toxicology
- To Illustrate by real cases
- ECG not included in this talk



Commandment 1

- **Rely on your clinical judgment; perform a test only when it is indicated**
- Emergency Physicians: The last fortress to practice '**Clinical**' Medicine?



Case

- F 3y.o.
- Witnessed by grandma to have overdosed ~ 30ml of Chlorpheniramine (piriton)
- Patient was sleepy on arrival
- Attempted to take blood for paracetamol, salicylates and ethanol levels; but with great difficulty.....

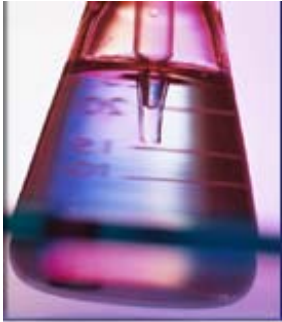


Is blood test indicated in this case?

- Screening for paracetamol, salicylates and ethanol levels only advocated for suicidal patients who may hide or unable to give a reliable history
- Or unexplained liver toxicity, renal toxicity or acidosis
- May pick up potentially treatable poisoning

Acetaminophen and Salicylate Serum Levels in Patients With Suicidal Ingestion or Altered Mental Status

KARL A. SPORER, MD,* HASSAN KHAYAM-BASHI, PhD†



Case

- M51, good past health
- Hit by a private van at unknown speed while pushing a cart (working)
- BP 175/91, P 98 bpm, T 35.9C
- RR 16/min, SpO₂ 100%
- GCS: E3 V2 M5
- 'Confused'
- Pupils 4mm E&R



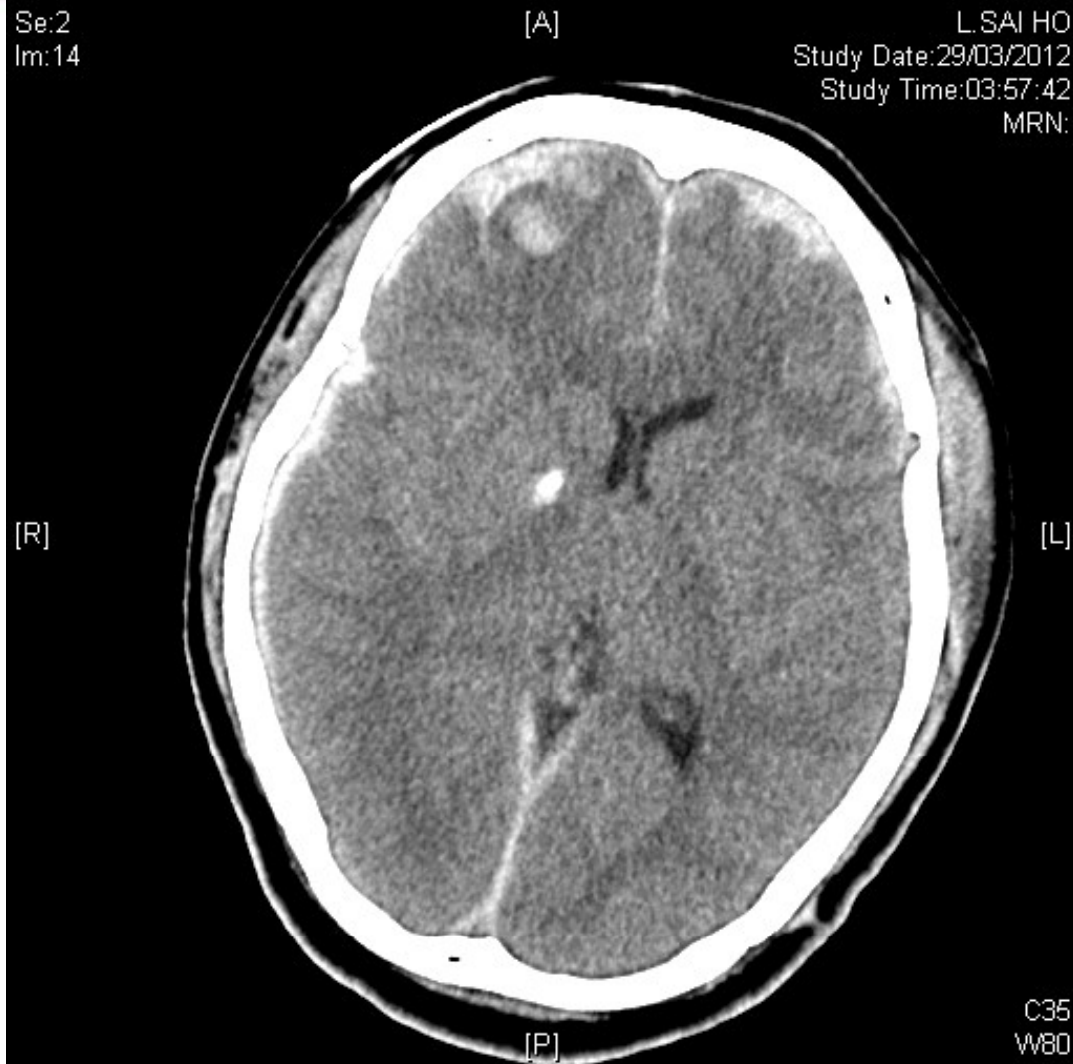
Case

- Left frontal wound
- Glucose 8.4, Hb 14
- Trauma series: No #
- FAST: -ve
- ECG: SR

- Urine ACON.... Faint line next to ketamine
- Any comment?



Cause of confusion





Commandment 2

- Know the implications and limitations of the tests concerned
- Point-of-care urine test for substance of abuse (ACON[®])
- Laboratory Toxicology screening test



Case

- M/ 24, good PH
- Quarreled with girlfriend recent 1 week
- Had dinner with GF and returned home
- Found confused the next morning by relatives
- 2 empty bottles found alongside: ~ 200 tabs of sleeping pills containing valerian and cyproheptadine



Case on arrival

- GCS E4M5V2 (11/15),
- BP 150/97, P 104
- SpO₂ 100% (High flow O₂), RR 22
- Temp 36.1 °C, dry skin
- Pupil 3mm, reactive
- Power 3/5
- Bladder distended



Case

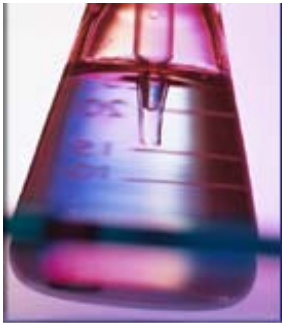
- Glucose 5.6, i-stat normal
- ECG: SR 100/min, QRS 100ms, QTc 412ms
- Foley inserted
- Urine ACON test
 - To do or not to do?
- Urine ACON test: +ve
 - Are you concerned?
 - Will you give physostigmine?





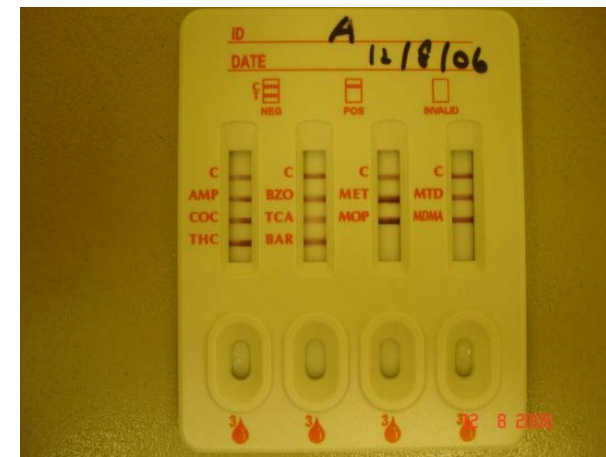
ACON® DOA Kits

- Lateral flow chromatographic immunoassay
- For **qualitative** detection of multiple drugs and its metabolites
- Fast and easy to use
- Presence of drug above cut-off conc:
 - Saturate all the binding sites of Ab
 - No labeled Ab retained in captured zone
 - **No colored line → +ve**



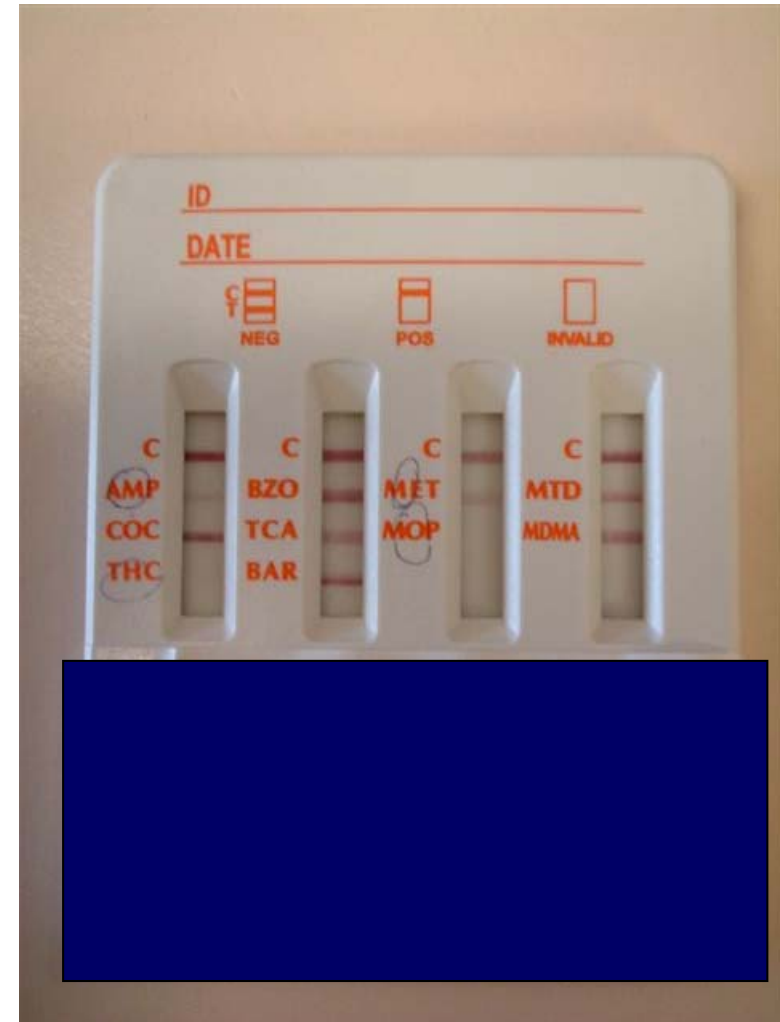
ACON[®] Kit

- Control (C):
 - A colored line will always appear at the control line region
 - Indicating sufficient specimen volume, adequate membrane wicking and correct procedure technique
- Make sure the Control line appear before you accept the result





- How to interpret this result?
- Only positive or negative
- **Weakly positive NOT exist!!**
- Faint line means negative





ACON[®] Kit

| Test | Calibrator | Cut-off (ng/ml) |
|--|---|-----------------|
| Amphetamine (AMP) | D-Amphetamine (P) | 1000 |
| Barbiturates (BAR) | Secobarbital (M) | 300 |
| Benzodiazepines (BZO) | Oxazepam (M) | 300 |
| Cannabinoid (THC) | 11-nor-THC-9 COOH (P) | 50 |
| Cocaine (COC) | Benzoylcegonine (M) | 300 |
| Ketamine (KET) | Ketamine (P) | 1000 |
| Methadone (MTD) | Methadone (P) | 300 |
| Methylenedioxy-methamphetamine (MDMA) | D,l Methylenedioxy-Methamphetamine (P) | 500 |
| Methamphetamine (MET) | D-Methamphetamine (P) | 1000 |
| Opioids/Morphine (MOP) | Morphine (P,M) | 300 |
| Tricyclic Antidepressants (TCA) | Nortriptyline (P,M) | 1000 |

P: parent compound, M: metabolites



Bedside drug screening

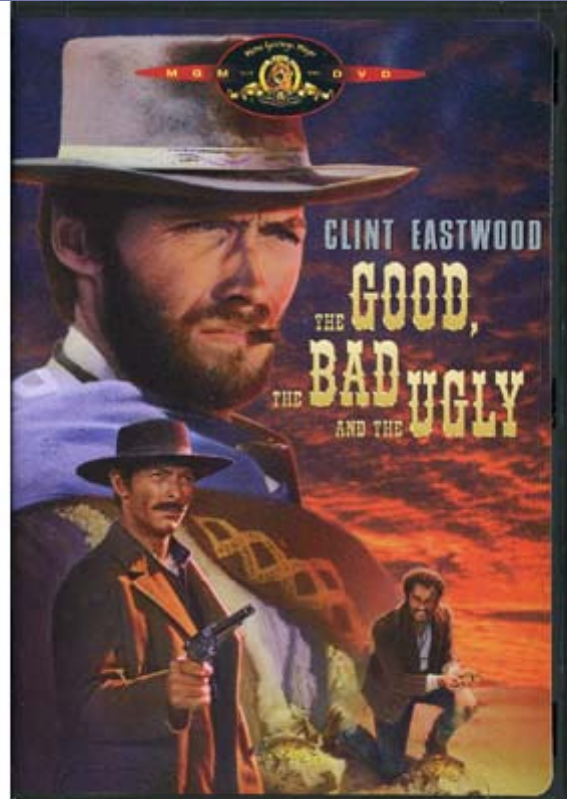
Specific Limitations:

- False positive (cross reactivity)
- False negative



The Good, the Bad and the Ugly (by YC Chan)

The Good:
Cocaine
Cannabinoid
Barbituates
Methadone



The Bad:
Amphetamine
MDMA
Opioids
Benzo
PCP

The Ugly: TCA



General Limitations

- Negative ACON test does not rule out poisoning, it only covers a number of abusive drugs
- True positive only indicates exposure, not necessarily poisoning; and may not be even recent exposure
- Technical error: adulteration of urine by dilution, addition of acids, bases, oxidizing agents (bleach, nitrite, peroxide, peroxidase) etc. may produce erroneous results



Laboratory Toxicology Screening Test

- Usually works on urine, blood and gastric aspirates
- By employing multiple analytic methods: Immunoassay, HPLC, GC, GC/MS, LC/MS/MS
- More comprehensive but still **not exclusive**
- Panels established by **individual laboratory varies** and **performance** also **varies**

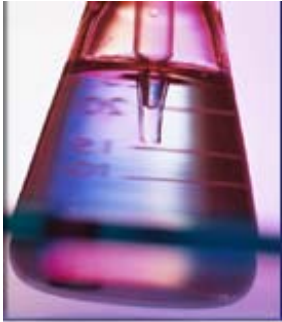


TABLE 6-6. Positive and Negative Predictive Values of Toxicology Screens

| Sensitivity/ Specificity (%/%) | Prior Probability | | |
|-----------------------------------|-------------------|---------|-----------|
| | 10% | 50% | 95% |
| 98/98 (excellent) | 84%/99.8% | 98%/98% | 99.9%/72% |
| 80/95 (mediocre) | 64%/98% | 94%/83% | 99.7%/20% |

+ve and -ve predictive values of two hypothetical toxicology screens

Goldfrank's 9th



Laboratory Toxicology Screening Test

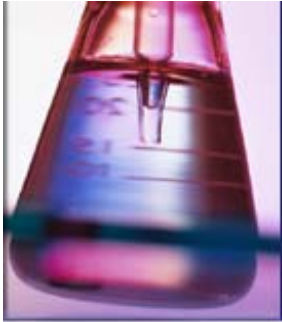
Applications

- May provide additional information to confirm an episode of poisoning
- Sometimes may give unexpected results and **shine light on difficult cases**
- But most of the time NO ONE is paying attention to the result when it comes back few days later
- Role of A&E Toxicology Team



Case

- M/51
- Caucasian living with friend in Central
- Occupation: pilot
- Good past health
- Found vomiting with altered consciousness at home by his friend
- ? Limb twitching
- his friend claimed that patient had gone out to a pub in Wan Chai tonight; unsure if he had taken alcohol or not



Vital sign and P/E on arrival to AED

- BP 167/87mmHg, P 46 bpm
- Temp 35.7C (rectal)
- RR 16
- GCS E1V1M6 (total 8/15)
- SpO2 97% on RA
- Pupil size 3mm bilaterally, reactive
- Resp and CVS: unremarkable
- Abd: soft
- neck soft
- Neurological exam: unremarkable
- small area of abrasion at right forehead



A typical clinical course follows

- You suspect **GHB poisoning**
- Urine sent to laboratory for Toxicology screening

| F. OBSERVATION/VITAL SIGNS | | Handwritten notes: 0101 0106 2137 0109 0107 0108 0109 | | | | | |
|----------------------------|----------|---|-----|-----|-----|----------|----------|
| BP | Pulse | | | | | | |
| 260 | 260 | | | | | | |
| 240 | 240 | | | | | | |
| 220 | 220 | | | | | | |
| 200 | 200 | | | | | | |
| 180 | 180 | | | | | | |
| 160 | 160 | 160 | 160 | 160 | 160 | 160 | 160 |
| 140 | 140 | | | | | | |
| 120 | 120 | | | | | | |
| 100 | 100 | | | | | | |
| 80 | 80 | 80 | 80 | 80 | 80 | 80 | 80 |
| 60 | 60 | | | | | | |
| 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| R pupil | Size(mm) | 3 | | | | 3 | 3 |
| | Reaction | Sluggish | | | | Sluggish | Sluggish |
| L pupil | Size(mm) | 3 | | | | 3 | 3 |
| | Reaction | Sluggish | | | | Sluggish | Sluggish |
| T°(O/R/T) (°C) | | 37 | | | | | |
| RR | | 16 | 16 | 16 | 16 | 18 | 18 |
| SpO ₂ (%) | | 97 | 98 | 98 | 98 | 98 | 98 |
| O ₂ Used (%) | | PA | PA | PA | PA | PA | PA |
| ETCO ₂ (kPa) | | | | | | | |
| CVP (cmH ₂ O) | | | | | | | |

Refer to Memo obs chart



Here is the result

Date Collected: 09/11/08 01:45

Clinical Details: AGITATED

pH 6

Ketones Negative

Glucose Negative

Toxicology screening (Urine):

None of the compounds on the following list are detected.

The following drugs (if present) can be identified by this laboratory:

| | | | |
|----------------|-----------------|--------------------------|-------------------|
| ANALGESICS | ANTIDEPRESSANTS | ANTI-HISTAMINES | Carbamazepine |
| Mefenamic acid | Amitriptyline | Diphenhydramine | Cimetidine |
| Meperidine | Amoxapine | Pheniramine | Cyproheptadine |
| Naproxen | Desipramine | | Dextromethorphan |
| Paracetamol | Doxepin | SYMPATHOMIMETIC AMINES | Haloperidol |
| Propoxyphene | Imipramine | Amphetamine | Ketamine |
| Salicylate | Loxapine | MDMA (ecstasy) | Lidocaine |
| | Maprotiline | Methamphetamine | Metoprolol |
| | Nortriptyline | Ephedrine/Pseudo- | Phenytoin |
| BARBITURATES | Trazadone | Phentermine | Triamterene |
| Amobarbital | Trimipramine | Phenylpropanolamine | Trimethoprim |
| Aprobarbital | | | Procainamide |
| Barbital | HYPNOTICS | NARCOTICS | Propranolol |
| Butobarbital | Glutethimide | Benzoyllecgonine/cocaine | Quinine/Quinidine |
| Pentobarbital | Methaqualone | Codeine | |
| Phenobarbital | | Methadone | PHENOTHIAZINES |
| Secobarbital | BENZODIAZEPINES | Morphine | |



Commandments 3 & 4

3. Has a fair idea what tests are provided by your hospital laboratory, cluster laboratory and Toxicology Reference Laboratory
4. Maintain good communication with your laboratory counterparts



- Every laboratory is different
- Some tests are routinely done
- Some tests cannot be done
- Some tests can be done on special request

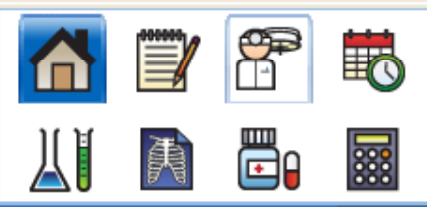
TABLE 6-5. Xenobiotics of Concern that are Often not Detected by Toxicology Screens

| | |
|---------------------------------------|--------------------------------|
| Antidysrhythmics | γ-Hydroxybutyrate ← |
| Anticholinergics | Herbal preparations |
| Anticoagulants | Hypoglycemics |
| Anticonvulsants | Iron |
| Antipsychotics | Isopropanol |
| β-Adrenergic agonists and antagonists | Ketamine ← |
| Calcium channel blockers | Lithium |
| Carbon monoxide | Lysergic acid diethylamide |
| Clonidine | Methylene dioxyamphetamine |
| Cyanide | Methylene dioxymethamphetamine |
| "Designer drugs" | Metals |
| Digoxin | Methanol |
| Diphenhydramine | Methemoglobin |
| Ethylene glycol | Solvents |
| Fentanyl | Serotonin reuptake inhibitors |
| | Strychnine |



What is meant by good communication?

- Input important **clinical information** into the laboratory request form; esp Toxidrome, suspected culprit drug or class of drugs
- **Electronic poisoning form** in CMS
- **Direct discussion** with laboratory counterparts concerning your worry and see what helps they can offer



Print Patient Summary

Clinical Notes and Summary

Clinical Notes

A&E

IP

IP + OP

Operation / Endoscopy

Nil.

Laboratory

QMH 19/04/12 UTOX

QMH 19/04/12 APTT, INR, PT

QMH 19/04/12 MEHB

QMH 19/04/12 CBC

QMH 19/04/12 APTT, INR, PT

Radiology All images Local images

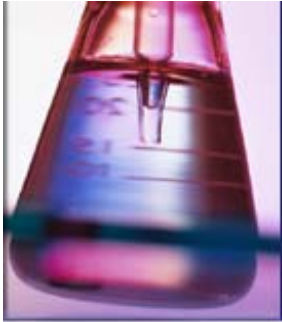
CMC 06/05/96 US Urinary system

CMC 13/01/96 XRAY KUB

AED Poisoning Case Management Form

| | |
|--|---|
| Hospital Authority Queen Mary Hospital | [Redacted] |
| AED Poisoning Case Management Form | |
| Chief complaints: DO Stilnox of 30 tabs from MN to 4 am Presented with decrease in responsiveness | |
| Medical history: Bipolar disorder FU private | |
| Poison details: | |
| Poison name: Zolpidem | Sex: F Age: 32y |
| Category: Pharmaceutical | Ward: AE01 Spec: A&E |
| Dose: 30 tablet | Route: Oral |
| Start from: 19/04/2012 to 19/04/2012 04:00 | |
| Poison type: Self-harm | Reason of exposure: Intentional |
| Place of exposure: -- | Category of exposure place: Home |
| Exposure address: -- | |
| Exposure district: -- | |





What is meant by good communication?

- Input important **clinical information** into the laboratory request form; esp Toxidrome, suspected culprit drug or class of drugs
- **Electronic poisoning form** in CMS
- **Direct communication** with laboratory counterparts concerning your worry and see if what helps they can offer



GHB

- rapidly absorbed and metabolized
- Mean elimination half-life is 30 to 50 minutes
- Detection period:
 - <6-8 hrs in plasma
 - <10-12 hrs in urine
- Preferred specimen: first catch urine



- In QMH: Targeted analysis with GC-MS is necessary for detection of GHB and **must be specifically requested.**
- In our case: **Marked excretion of GHB was detected in the urine and diagnosis was confirmed**



Commandment 5

- **Toxicology tests should be performed and interpreted timely**
- Have you got some examples in your mind?

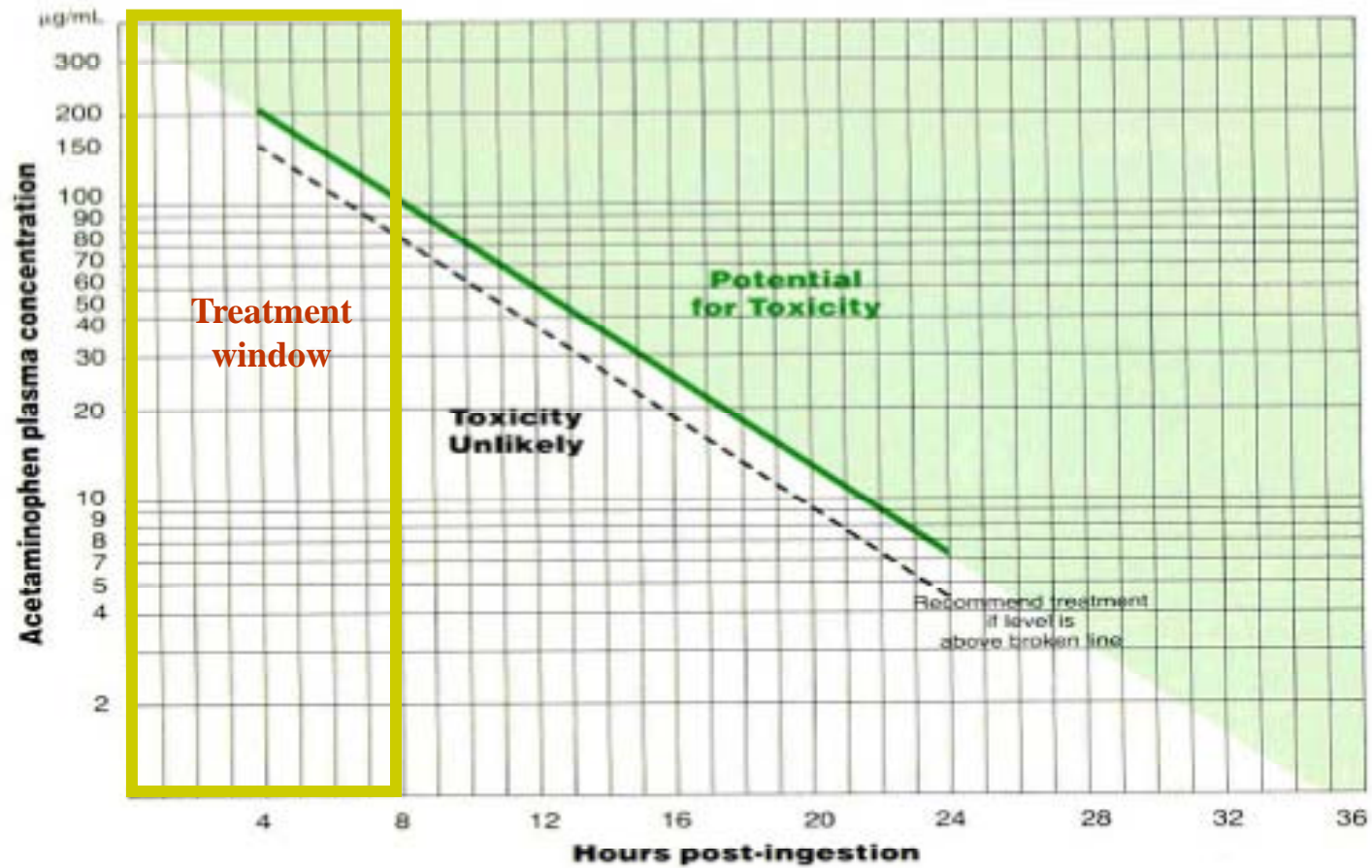


Paracetamol poisoning

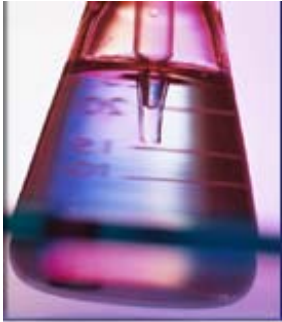
- F25, DO of paracetamol 20 tabs 5 hours ago before presentation to A&E
- Together with beer, vomited twice
- Paracetamol level checked in A&E (6 hours post ingestion)
- Patient admitted EMW but
- **No one remember to trace the result...**



Paracetamol normogram



Unit conversion : $1\text{mg/L (or } \mu\text{g/ml)} = 6.6 \mu\text{mol/L}$



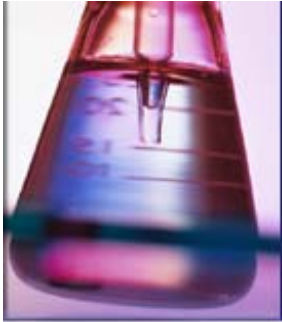
Rat poison ingestion

- Warfarin or superwarfarin: expected delay for prolongation of INR:
 1. Time needed to deplete the existing store of Vit K
 2. Time needed to deplete the existing coagulating factors (VII)
- $\sim 3 \times T_{1/2}$ of Factor VII = 15 hours



Rat poison ingestion

- For acute accidental ingestion and symptomatic: repeat INR at 48 hours to clear patient
- For intentional overdose: check baseline, then every 12 hours to identify coagulopathy. Increase frequency of monitoring if INR prolongation occurs

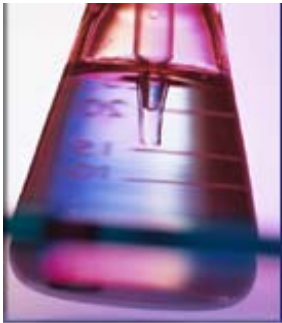


Case

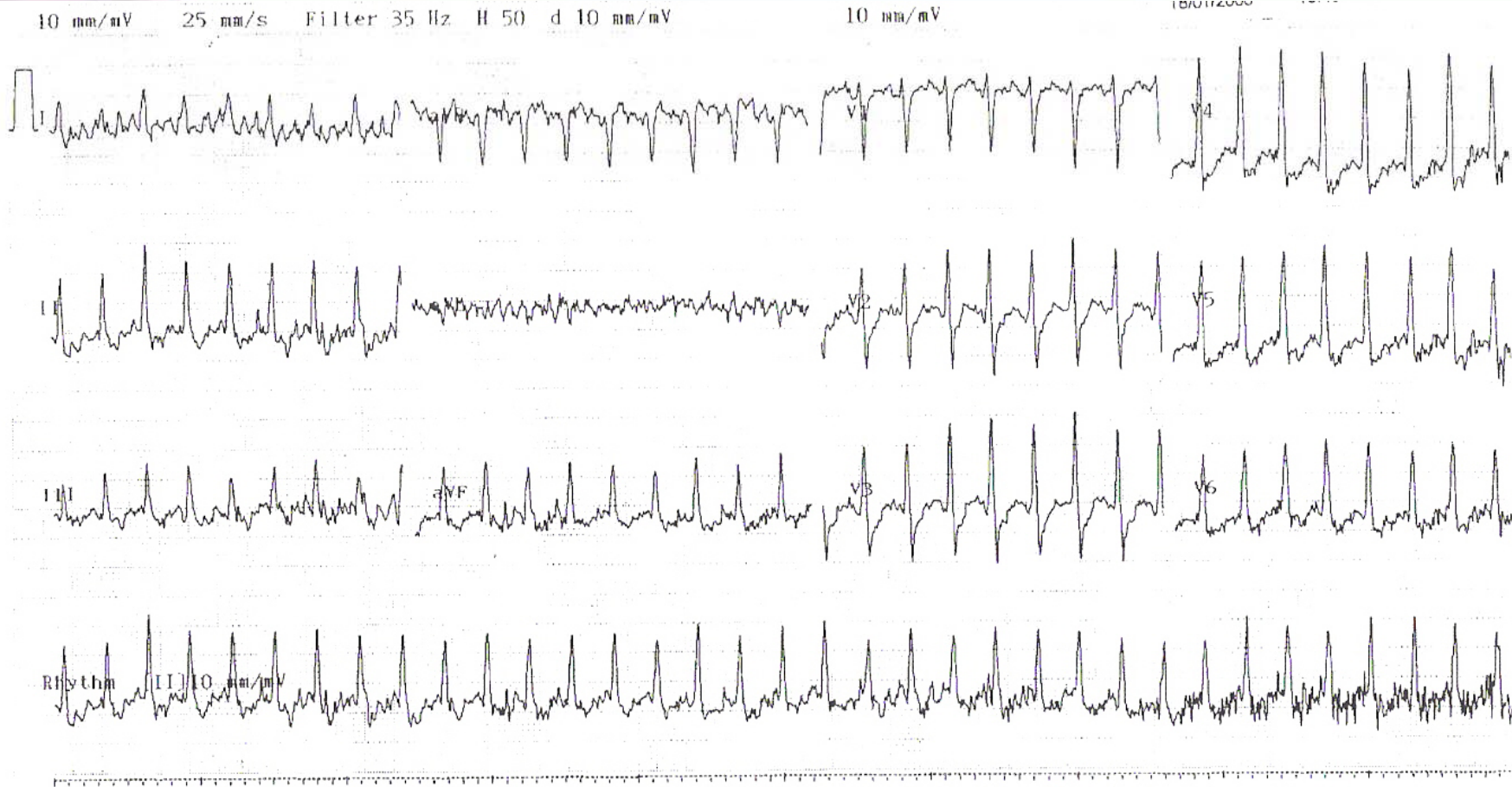
- F/45, asthma FU QMH
- Depression FU Western Psychiatric Centre
 - Venlafaxine
 - Zolpidem
- C/O: **Dizziness, vomiting** and **generalised weakness** for 1/7
- BP 111/53 mmHg, **P 117 bpm**
- Temp 36°C
- RR 16/min, SpO₂ 98% R.A.
- Noticed to have intermittent **limb twitching** in cubicle



- GCS 15/15 all along, **restless⁺**, **agitated⁺**
- CVS: **tachycardia**, **irregular pulse⁺**, no murmur
- Resp: unremarkable except **tachypnoea**
- CNS:
 - Tone normal at rest
 - Intermittent **4 limbs twitching and spasm**
 - Power full over 4 limbs
 - No neck rigidity, pupils E/R bilaterally
- Abdomen: NAD



ECG



9130K 01-15 01 02 01-08



- CXR: normal findings
- **H'stix = 15.3mmol/L**
- **Serum ketone = 0.8 (low)**
- Urine tests
 - Acon test all –ve
 - WBC –
 - RBC –
 - **Glucose +++**
 - Albumen –
 - **Ketone +++**

| | |
|--------------|----------------------|
| Na | 141 mmol/L |
| K | 2.9 mmol/L |
| TCO2 | 12 mmol/L |
| iCa | 1.32 mmol/L |
| Hct | 42 %PCV |
| Hb* | 148 g/L |
| | *via Hct |
| At 37C | |
| PH | 7.209 |
| PCO2 | 3.73 kPa |
| PO2 | 6.9 kPa |
| HCO3 | 11.2 mmol/L |
| BEecf | -17 mmol/L |
| sO2* | 79 % |
| | *calculated |
| sample Type: | Urine |
| 18JAN08 | 14:35 |
| Oper: | |
| Physician: | |
| ser# | 32103 |
| ver: | JAMS056D CLEW A14 |



Causes to consider

- Metabolic cause
 - DKA
 - Thyroid storm
- Cardiovascular cause
 - Myocarditis
 - Cardiomyopathy
- Sepsis
- CNS disease
 - ICH

Poisoning to be considered

- Theophylline
- Salicylates

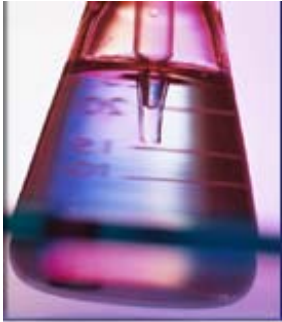
But patient strongly denies DO



Progress

- Urgent theophylline level arranged with Clinical Biochemist
- They can give us the result in **half hour!**

| Collect Date : | 18/01/08 | 18/01/08 | 19/01/08 | 19/01/08 | 20/01/08 | Ref. Range | Units |
|----------------|---|-------------------|--------------|-----------------|----------|------------|--------|
| Collect Time : | 16:00 | 16:00 | 01:25 | 06:00 | 06:00 | | |
| Request No. : | C1183095 | C1183097 | C1196002 | C1190123 | C1206004 | | |
| Remark : | PSY ILLNESS KNOWN ASTHMA | ASTHMA SEIZURE | THEO O.D. | THO OVERDOSE | THO DO | | |
| ----- | | | | | | | |
| Theophylline | -- | NOTE | 229 H | 202 H | 83 | See Below | umol/L |
| Paracetamol | <30 | -- | -- | -- | -- | See Below | umol/L |
| Salicylate | <0.3 L | -- | -- | -- | -- | 1.4 - 1.8 | mmol/L |
| Ethanol | <3.0 | -- | -- | -- | -- | Toxic >33 | mmol/L |
| ----- | | | | | | | |
| Comment: | | | | | | | |
| 08C1206004 | Result Faxed. | | | | | | |
| 08C1190123 | Result Faxed. | | | | | | |
| 08C1196002 | Taken 150mg BC(pm), time & date unknown. | | | | | | |
| 08C1183097 | Result Faxed. | | | | | | |
| | Taken 150mg BD (pm), time & date unknown. Theophylline=900 umol/L | | | | | | |
| 08C1183095 | Result Faxed. | | | | | | |
| Footnotes: | | | | | | | |
| Theophylline | - Reference Range : Therapeutic 28-111 | | | | | | |



Commandment 6

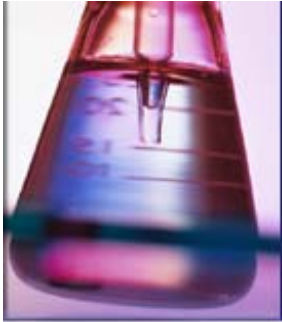
- One should know which drug/toxin levels have to be done; which really affect patient management



Drug/Toxin levels that affects management

| | |
|-------------|--------------|
| COHb, MetHb | Paracetamol |
| Digoxin | Salicylate |
| Ethanol | Theophylline |
| Iron | Valproate |
| Lithium | |

•Recommended by COC (Path) to be available round the clock



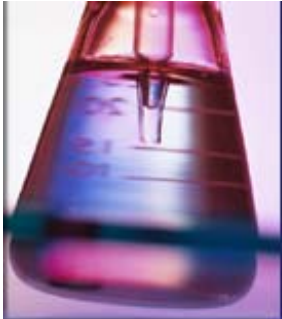
Ethanol level

- Should we routinely check ethanol level in drunk patients?
- From time to time there are drunk patients dead in A&E because of complications or other missed diagnosis
- Some clinicians recommend checking ethanol levels for all drunk patients
- Practical difficulty in situation in HK



My baseline

- Patient in deep coma
- Patient with prolonged depression of conscious level with no improvement upon observation
- Patient with atypical presentation



Many more drug levels are not useful in patient management

Pharmacology

Original Paper

Pharmacology 2011;88:260–265
DOI: 10.1159/000331867

Received: July 29, 2011
Accepted after revision: August 8, 2011
Published online: October 13, 2011

Metformin-Associated Lactic Acidosis in Chinese Patients with Type II Diabetes

Chun Wing Yeung^a Ho Yin Chung^b Bonnie Mei Wah Fong^a Nga Wing Tsai^c
Wai Ming Chan^c Tak Shing Siu^a Sidney Tam^a Sik Hon Tsui^b

^aDivision of Clinical Biochemistry, ^bDepartment of Accident and Emergency, and ^cAdult Intensive Care Unit, Queen Mary Hospital, Hong Kong, SAR, China

Risk factors of mortality were identified as shock and high plasma lactate levels. The majority of patients were found to have significantly raised creatinine versus a normal baseline value before the acute illness. Concomitant illnesses taking place alongside MALA were common. With a high utility rate of renal replacement therapy (82.6%) in the study group, the mortality rate was 30.4%. Copyright © 2011 S. Karger AG, Basel



Case

- F / 91yo
- HT, AF with VVIR, dementia
- Accidentally took **8 times** the normal dose of medications
 - Aspirin (x80mg)
 - Digoxin (x62.5mcg)
 - Lisinopril (x2.5mg)
 - Adalat Retard (x20mg)
- Last dose 30min before admission



Case

- Alert
- BP 79/39 P 89
- Temp. 36.1°C
- GCS 15/15
- Glucose 8.4
- Hb 10.9
- Na/K 140/4.1



GMH DOB: 27/06/1920

(AAE)

13-Nov-2011 09:09:23



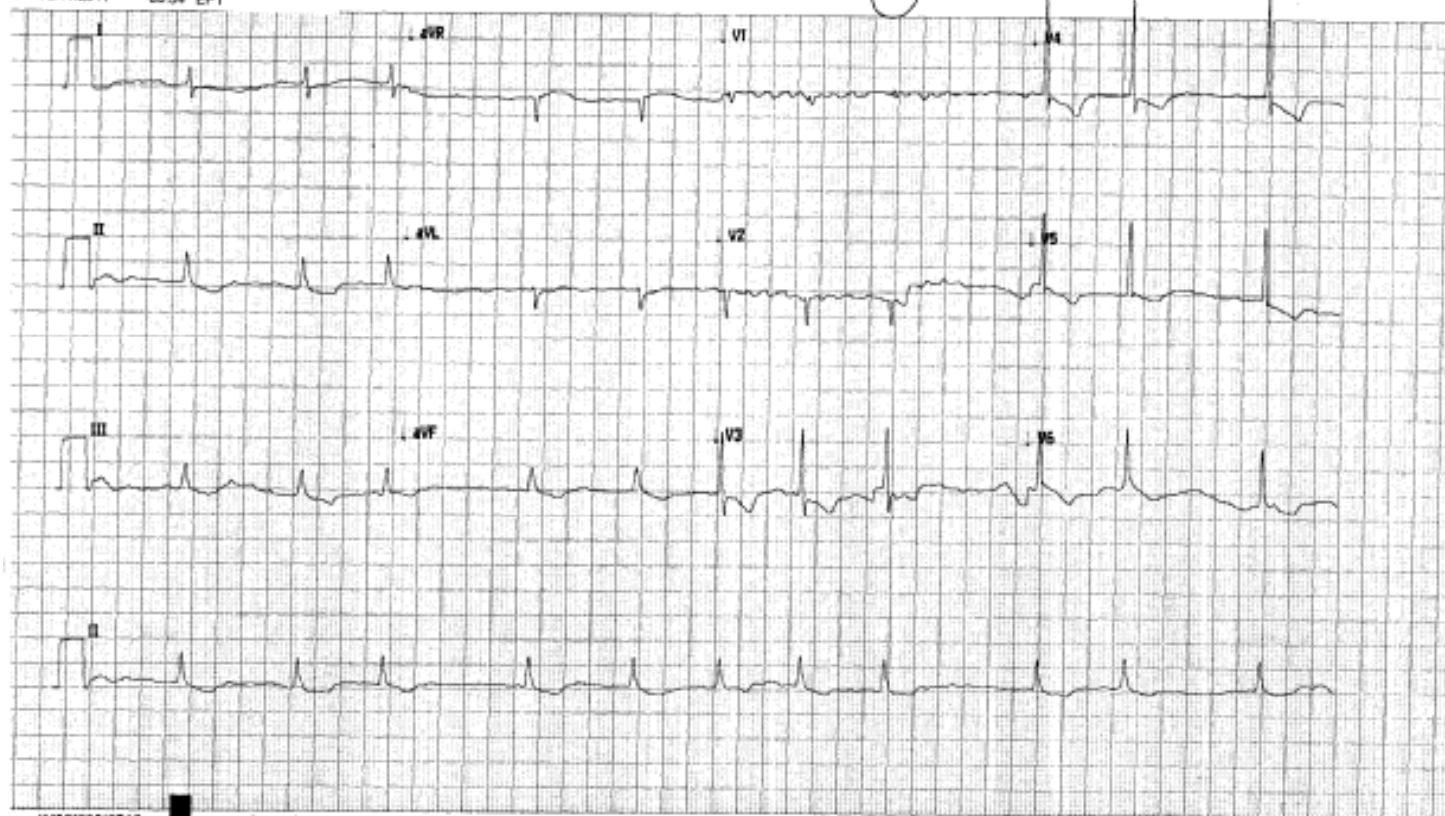
F/ 91 y

Vent rate: 69 BPM
PR int: 0 ms
QRS dur: 76 ms
QT/QTc: 344/363 ms
P-R-T axes: 999 85 -81

ATRIAL FIBRILLATION
SEPTAL INFARCT (40+ MS Q WAVE IN V1/V2), AGE UNDETERMINED
ST & T WAVE ABNORMALITY, POSSIBLE ANTEROLATERAL ISCHEMIA (-0.3+ MV T WAVE IN V2-V6) OR
DIGITALIS EFFECT
ST & T WAVE ABNORMALITY, POSSIBLE INFERIOR ISCHEMIA (-0.1+ MV T WAVE IN II/AVF) OR
DIGITALIS EFFECT
ABNORMAL ECG

UNCONFIRMED REPORT

13/11/2011 09:54 EP1



1109170018545

Queen Mary Hospital

Site: B Part: B Version: 1.0.17 Copyright © 2008 GE Healthcare. All rights reserved.



Calcium and IV fluid given

13/11/2011

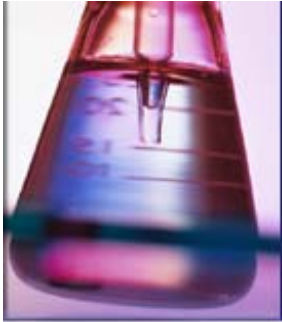
F. OBSERVATION/VITAL SIGNS

| BP | Pulse | 0856 | 0907 | 0919 | 0927 | 0934 | 0937 | 0942 | 0950 | 0958 | 1008 | 1016 | | | | | | | | | | |
|-----|-------|--------------------------------|------|------|------|------|------|------|------|------|------|------|----|----|----|----|-----|-----|-----|-----|-----|-----|
| 260 | 260 | RC BP: 71/59 P: 89. (sitting). | | | | | | | | | | | | | | | | | | | | |
| 240 | 240 | | | | | | | | | | | | | | | | | | | | | |
| 220 | 220 | | | | | | | | | | | | | | | | | | | | | |
| 200 | 200 | | | | | | | | | | | | | | | | | | | | | |
| 180 | 180 | | | | | | | | | | | | | | | | | | | | | |
| 160 | 160 | | | | | | | | | | | | | | | | | | | | | |
| 140 | 140 | | | | | | | | | | | | | | | | | | | | | |
| 120 | 120 | | | | | | | | | | | | | | | | 107 | 102 | 109 | 111 | 105 | 121 |
| 100 | 100 | | | | | | | | | | | | 95 | 91 | 94 | 98 | ^ | ^ | ^ | ^ | ^ | ^ |
| 80 | 80 | | | | | | | | | | | | 79 | 73 | 69 | 77 | 81 | 73 | 76 | 76 | 77 | 77 |
| 60 | 60 | | | | | | | | | | | | | | | | | | | | | |
| 40 | 40 | 46 | 43 | 43 | 38 | 48 | 50 | 49 | 47 | 57 | 60 | 49 | | | | | | | | | | |



- Digoxin level came back soon: **11.2 nmol/L**
- Reference level: 1.3 – 2.6 nmol/L
- Digitalis antibody was given

- Was the treatment indicated?



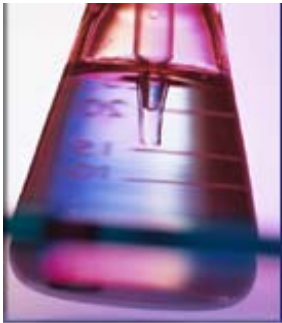
Criticism

- Patient was stable at that juncture; no clinical indication
- Action level quoted by HKPIC was **>12nmol/L** for acute toxicity
- However it refers to post distribution, i.e. >6 hours post ingestion

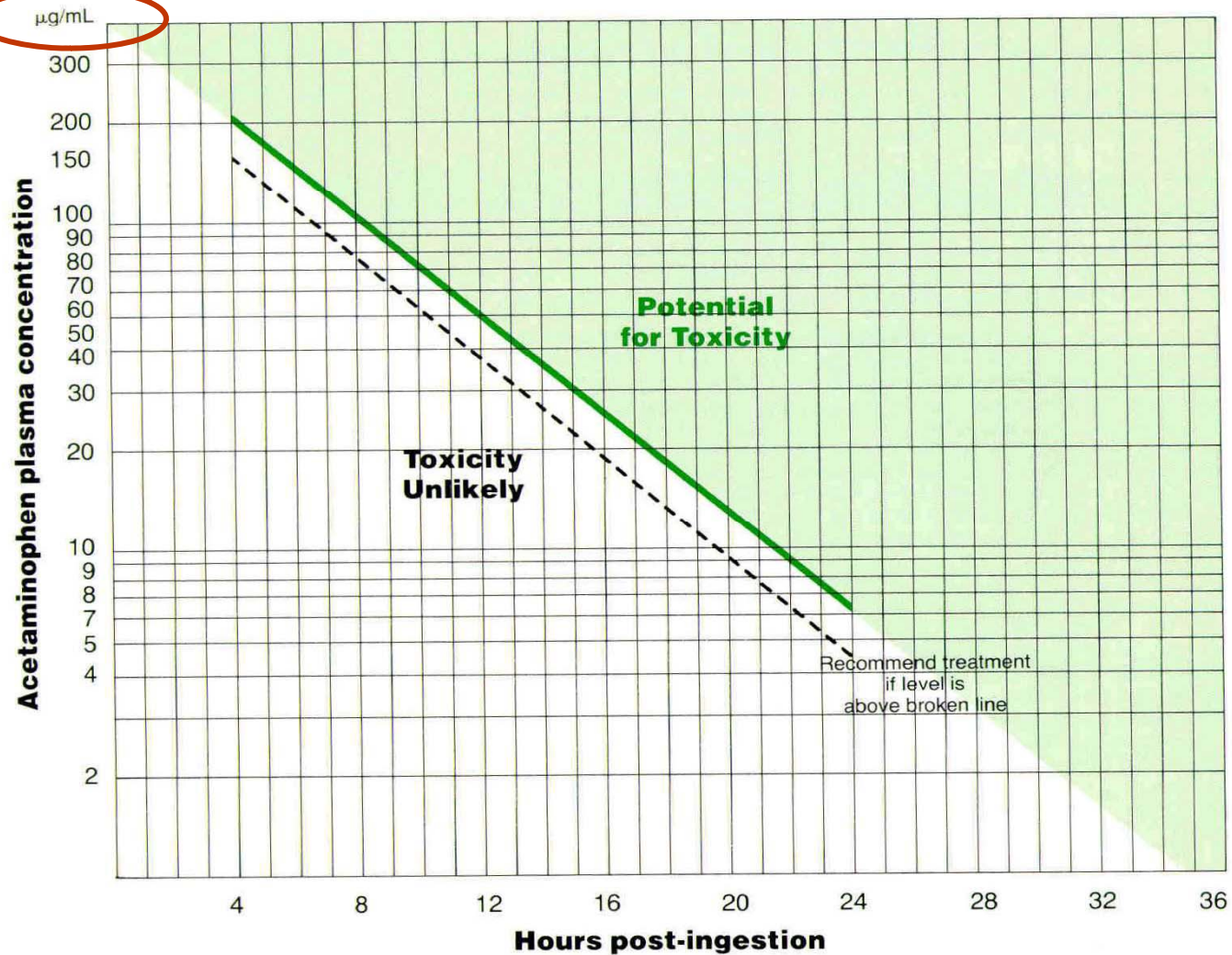


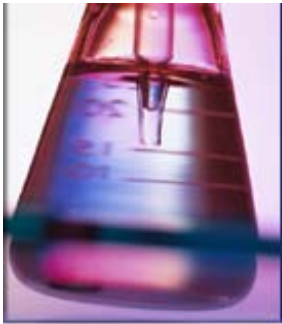
Commandment 7

- Treat the patient, not the laboratory result
- Be careful with the Units (Conventional vs SI) for laboratory results and take reference to individual laboratory reference levels when making clinical decisions

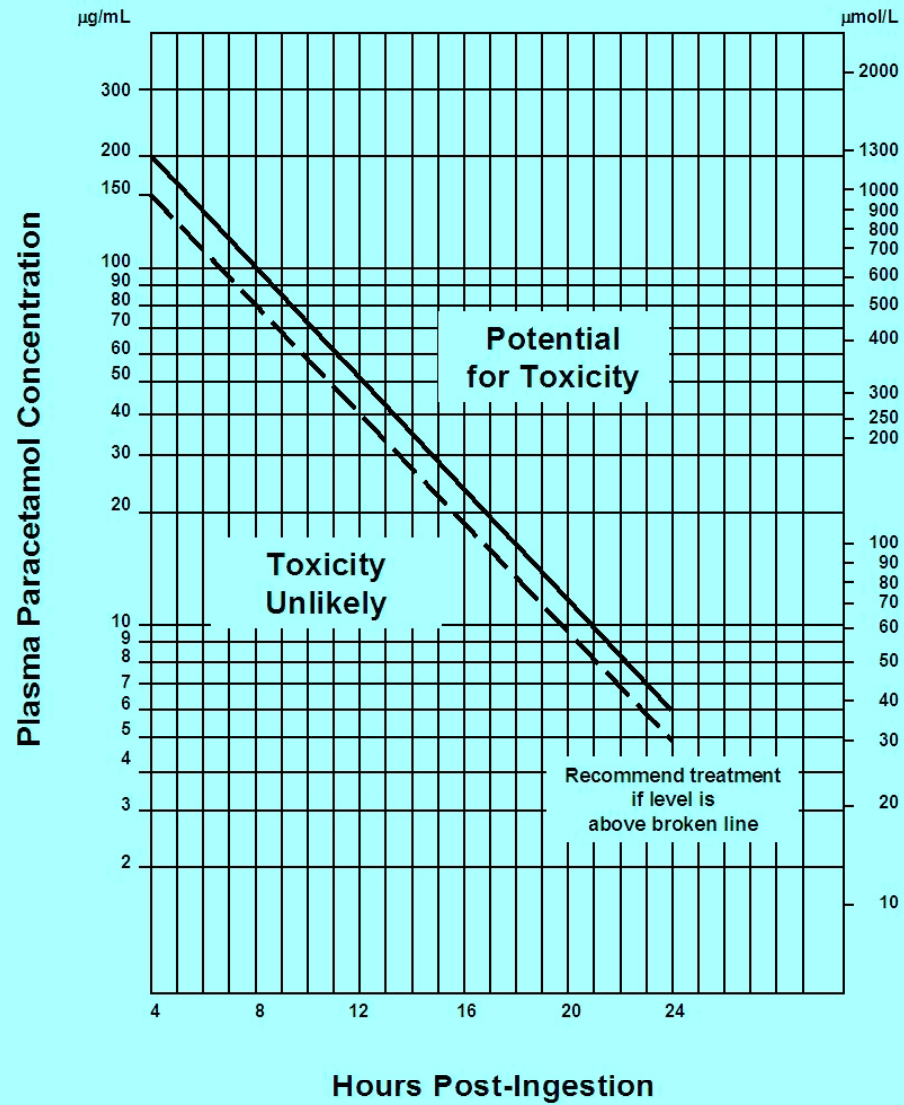


Paracetamol normogram





Nomogram for Paracetamol Poisoning



Unit conversion : 1mg/L (or $\mu\text{g/mL}$) = $6.6\ \mu\text{mol/L}$

(adapted from the HKPIC Nomogram)



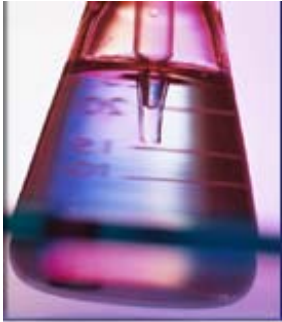
Commandment 8

- Be familiar with the use and interpretation of common tests that are very useful for poisoning diagnosis and management



Examples include

- COHb, MetHb levels
- RFT
- Blood gas analysis
- Lactate
- Anion Gap
- Osmolar Gap (serum osmolarity)



Case

- M/45, chronic alcoholic
- c/o palpitation, chest & epigastric discomfort, SOB for 1/52
- Poor oral intake, vomiting +
- GCS 15, BP 115/73, P 141, RR 28, SpO₂ 100% in RA, Temp 36.7C
- P/E: mild dehydration, chest clear, no abd. sign



Case

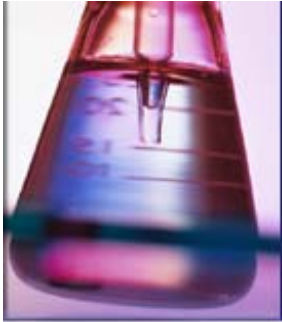
Not
Specified
15/11/06
18:22
CT753564
URGENT

Reference
Range

Units

| | | Reference Range | Units |
|-------------------|---------|--------------------|--------|
| Blood pH | 7.09 L | 7.35 - 7.45 | |
| Blood pCO2 | 1.42 L | 4.70 - 6.00 | kPa |
| Blood pO2 | 18.25 H | 10.60-13.30\$ | kPa |
| Base Excess (vt) | -24.3 L | -3.0 - 3.0 | mmol/L |
| Bicarbonate (act) | 3.1 L | 20.0 - 26.0 | mmol/L |
| O2 Saturation | 98 | >95 | % |

- How to interpret?
- What additional information do you need?



Analysis

- pH 7.09 → **Acidaemia**
- Acidaemia with low HCO_3 level 3.1 (20 – 26) → **metabolic acidosis**
- Metabolic acidosis with low pCO_2 1.42 (4.7 – 6) → **respiratory compensation** occurs
- Is the respiratory compensation appropriate /adequate or in fact hyperventilation occurring?



Winter's equation

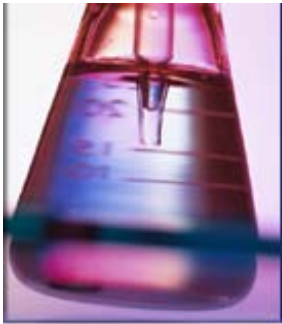
- Predicts the degree of respiratory compensation in the setting of metabolic acidosis
- PCO_2 (mmHg) = $(1.5 \times \text{HCO}_3^-) + 8 \pm 2$
- In our case: calculated $\text{PCO}_2 = 1.5 \times 3.1 + 8 \pm 2 = 12.65 \pm 2$ mmHg
- Measured blood $\text{PCO}_2 = 1.42$ kPal = $1.42 \times 7.5 = 10.65$ mmHg
- **Conclusion: Metabolic acidosis with respiratory compensation**



A case of severe metabolic acidosis

More information that may help your case analysis

- Na 147, Cl 91
- Glucose 3.3
- Urea 3.3, ethanol level 38
- Serum osmolarity 355
- Serum lactate: 6.3mmol/L (0.5-2.2)



- Anion gap
 - **Na – Cl - HCO₃** = 147 – 91 - 3.1 = 52.9 (normal 12+/-4)
- Osmolar gap = Measured osmolality – calculated osmolality
 - Calculated osmolality
 - **Na x 2 + urea + glucose + ethanol (all in mmol/L)**
 - 147 x 2 + 3.3 + 3.3 + 38 = 338.6
 - OG = 16.4 (normal -10 to 14)

Measured
serum osmol 355



High AG metabolic acidosis (52.9)

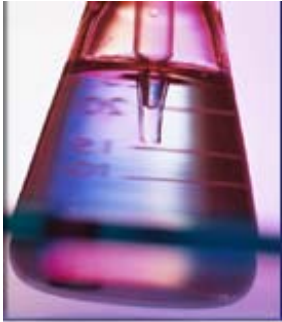
- Lactate: 6.3
- Urine ketostix[®] **negative**
- Urine ketones by laboratory (acetoacetate and β -hydroxybutyrate) : **50mg/dL ++**
- Consider **KULT**

- **Dx: Alcoholic ketoacidosis**



Commandment 9

- **Do no harm!**
- E.g. Multi-panel metal testing on hair or mobilized urine samples
- For children with eczema, autism, hyperactivity, poor academic performance...
- Result bound to be positive for some panels



Case

- F36, good PH
- Paracetamol overdose, claimed 20 tabs
- Delayed presentation at 12 hours
- Epigastric pain and vomiting
- NAC given



Mx in EMW

Collect Date : 13/10/09 13/02/11
 Collect Time : 17:12 14:48
 Request No. : CA130761 C2131662
 Remark : left Panadol
 : neck overdose
 : mass

| | | |
|------------------|------|--------|
| Na | 140 | 140 |
| K | 4.4 | 3.4 L |
| Chloride | 106 | 110 H |
| Urea | 4.3 | 3.7 |
| Creatinine | 57 | 59 |
| R Glucose | -- | 7.3 |
| Calcium | -- | 2.23 |
| Adjusted Calcium | -- | 2.21 |
| Phosphate | -- | 0.87 L |
| Total Protein | 80 | 72 |
| Albumin | 42 | 43 |
| Globulin | 38 | 29 |
| Total Bili | 4 | 14 |
| ALP | 64 | 55 |
| ALT | 28 | 49 H |
| AST | 36 H | 35 H |
| GGT | -- | 38 H |
| LDH | -- | 152 |
| CK | -- | 65 |
| Urate | -- | 252 |

Collect Date : 13/02/11
 Collect Time : 14:48
 Request No. : C2133026
 Remark : Panadol
 : overdose.
 : Therapeut
 : ic

| | |
|-------------|--------|
| Paracetamol | 240 |
| Salicylate | <0.3 L |
| Ethanol | <3.0 |



Serial LFT

| | | | | | | | |
|----------------|------------------|------------------|------------------|------------------|---------------------------------------|------------|-------|
| Collect Date : | 13/02/11 | 14/02/11 | 15/02/11 | 15/02/11 | 15/02/11 | | |
| Collect Time : | 14:48 | 07:14 | 05:40 | 14:54 | 21:52 | | |
| Request No. : | C2131662 | C2141428 | C2151397 | C2152771 | C2161259 | Ref. Range | Units |
| Remark : | Panadol overdose | panadol overdose | panadol overdose | panadol overdose | panadol overdose. panadol overdose | | |

| Comment | | Below | Below | Below | Below | | |
|------------------|--------|-------|-------|--------|---------|--------------|--------|
| Na | 140 | 136 | 137 | -- | 142 | 136 - 148 | mmol/L |
| K | 3.4 L | 3.0 L | 3.7 | -- | 3.6 | 3.6 - 5.0 | mmol/L |
| Chloride | 110 H | 107 | 107 | -- | 107 | 100 - 109 | mmol/L |
| Urea | 3.7 | 2.2 L | 2.4 L | -- | 2.2 L | 2.5 - 6.4 | mmol/L |
| Creatinine | 59 | 50 | 41 L | -- | 46 L | 49 - 82 | umol/L |
| R Glucose | 7.3 | -- | 4.9 | -- | 8.4 H | 2hr pp < 7.8 | mmol/L |
| Calcium | 2.23 | -- | -- | -- | -- | 2.11 - 2.55 | mmol/L |
| Adjusted Calcium | 2.21 | -- | -- | -- | -- | 2.11 - 2.55 | mmol/L |
| Phosphate | 0.87 L | -- | -- | -- | -- | 0.88 - 1.45 | mmol/L |
| Total Protein | 72 | 62 L | 61 L | 59 L | 64 L | 67 - 87 | g/L |
| Albumin | 43 | 36 L | 37 L | 33 L | 37 L | 39 - 50 | g/L |
| Globulin | 29 | 26 | 24 L | 26 | 27 | 26 - 40 | g/L |
| Total Bili | 14 | 13 | 11 | 11 | 12 | 4 - 23 | umol/L |
| ALP | 55 | 50 | 46 | 48 | 51 | 32 - 93 | U/L |
| ALT | 49 H | 279 H | 639 H | 2596 H | >3000 H | 7 - 36 | U/L |
| AST | 35 H | 331 H | 511 H | 2210 H | 2643 H | 14 - 30 | U/L |
| GGT | 38 H | -- | -- | -- | 55 H | up to 35 | U/L |
| LDH | 152 | -- | -- | -- | -- | 107 - 218 | U/L |
| CK | 65 | -- | -- | -- | -- | 40 - 161 | U/L |
| Amylase | -- | -- | -- | -- | 140 H | 25 - 124 | U/L |
| Urate | 252 | -- | -- | -- | -- | 177 - 400 | umol/L |



Commandment 10

- Don't hesitate to consult the experts if needed



Suggested Management

- Frequent clinical evaluation and monitoring
- Check prognostic markers: ABG, RFT, PT, Lactate, PO_4 , α FP
- Continue NAC
- Monitor LFT



When to stop NAC?

Textbook guideline:

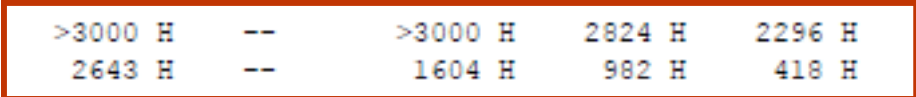
- Asymptomatic
- AST / ALT <1000
- Negligible paracetamol level



When to stop NAC?

| | | | | | | | |
|----------------|-------------------|----------------------|----------------------|------------------|------------------|------------|-------|
| Collect Date : | 15/02/11 | 16/02/11 | 16/02/11 | 16/02/11 | 17/02/11 | | |
| Collect Time : | 21:52 | 07:01 | 07:01 | 15:30 | 05:11 | | |
| Request No. : | C2161259 | C2160120 | C2161370 | C2162817 | C2170735 | Ref. Range | Units |
| Remark : | panadol overdose. | panadol overdose. | panadol overdose. | panadol overdose | panadol overdose | | |
| | panadol overdose | panadol liver damage | panadol liver damage | | | | |

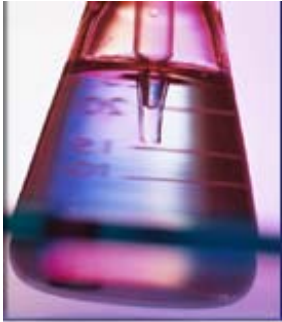
| Comment | Below | | Below | Below | Below | | |
|------------------|---------|-----|---------|--------|--------|--------------|--------|
| Na | 142 | -- | 139 | 143 | 145 | 136 - 148 | mmol/L |
| K | 3.6 | -- | 3.7 | 3.6 | 4.0 | 3.6 - 5.0 | mmol/L |
| Chloride | 107 | -- | 105 | 109 | 112 H | 100 - 109 | mmol/L |
| Urea | 2.2 L | -- | 2.0 L | 1.8 L | 2.0 L | 2.5 - 6.4 | mmol/L |
| Creatinine | 46 L | -- | 40 L | 44 L | 46 L | 49 - 82 | umol/L |
| R Glucose | 8.4 H | -- | 5.3 | 5.4 | 4.3 | 2hr pp < 7.8 | mmol/L |
| Calcium | -- | -- | 2.13 | 1.99 L | 2.15 | 2.11 - 2.55 | mmol/L |
| Adjusted Calcium | -- | -- | 2.27 | 2.15 | 2.25 | 2.11 - 2.55 | mmol/L |
| Phosphate | -- | -- | 0.89 | 0.78 L | 0.91 | 0.88 - 1.45 | mmol/L |
| Total Protein | 64 L | -- | 61 L | 60 L | 63 L | 67 - 87 | g/L |
| Albumin | 37 L | -- | 35 L | 34 L | 37 L | 39 - 50 | g/L |
| Globulin | 27 | -- | 26 | | 26 | 26 - 40 | g/L |
| Total Bili | 12 | -- | 11 | | 10 | 4 - 23 | umol/L |
| ALP | 51 | -- | 45 | 47 | 43 | 32 - 93 | U/L |
| ALT | >3000 H | -- | >3000 H | 2824 H | 2296 H | 7 - 36 | U/L |
| AST | 2643 H | -- | 1604 H | 982 H | 418 H | 14 - 30 | U/L |
| GGT | 55 H | -- | 55 H | 57 H | 61 H | up to 35 | U/L |
| Amylase | 140 H | -- | 105 | -- | -- | 25 - 124 | U/L |
| Lactate | -- | 0.9 | -- | -- | -- | 0.7 - 2.1 | mmol/L |





Expert opinion

- AST (cytosolic and mitochondrial) vs. ALT (cytosolic)
 - AST higher intracellular abundance
 - AST shorter half-life
 - AST initially higher than ALT
 - **AST declines more rapidly due to shorter $T_{1/2}$**
- **AST the better marker to gauge the clinical course**



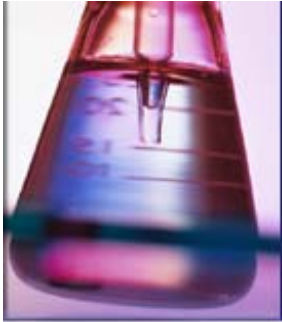
Take home message

- 1. Rely on your clinical judgment; perform a test only when it is indicated**
- 2. Know the implications and limitations of the tests concerned**
- 3. Have a fair idea what tests are provided by your hospital laboratory, cluster laboratory and Toxicology Reference Laboratory**



Take Home Message

- 4. Maintain good communication with your laboratory counterparts**
- 5. Toxicology tests should be performed and interpreted timely**
- 6. Know which drug/toxin levels that will affect your patient management**



Take Home Message

- 7. Treat the patient, not the laboratory result; and beware of the units**
- 8. Be familiar with other common tests that are very useful for poisoning management**
- 9. Do no harm!**
- 10. Consult the experts**



Thank you!