




Toxicology Case


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June 2011



Background



- 08:22 Cat 4
 - 26/F
 - Good PH
 - BP/P 128/76 mmHg
 - Temp 36.7
 - Triage notes: chest discomfort since morning, headache, SOB
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- N/A 10:10, 10:14, 10:36, 10:52, 11:00
 - A/V at 11:15
 - Seen at 11:45 at walking clinic



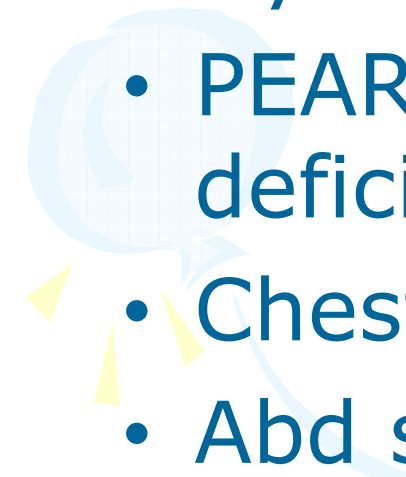
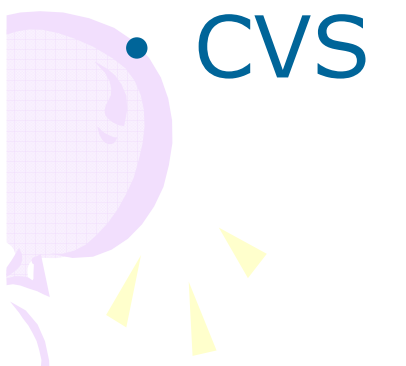
History

Come with 5yo daughter

- c/o dizziness x 1/7, vertigo-like
 - Vomiting x 3 times since 9am
 - Diarrhoea x 2 , loose stool
 - Chills feeling, no documented fever
 - Headache not improve with medication
 - Deny chest pain
 - LMP 1 April 11
 - Request medication for relief dizziness & headache
 - *** name was double checked as totally different complaint from the nursing triage note*
- 
- 

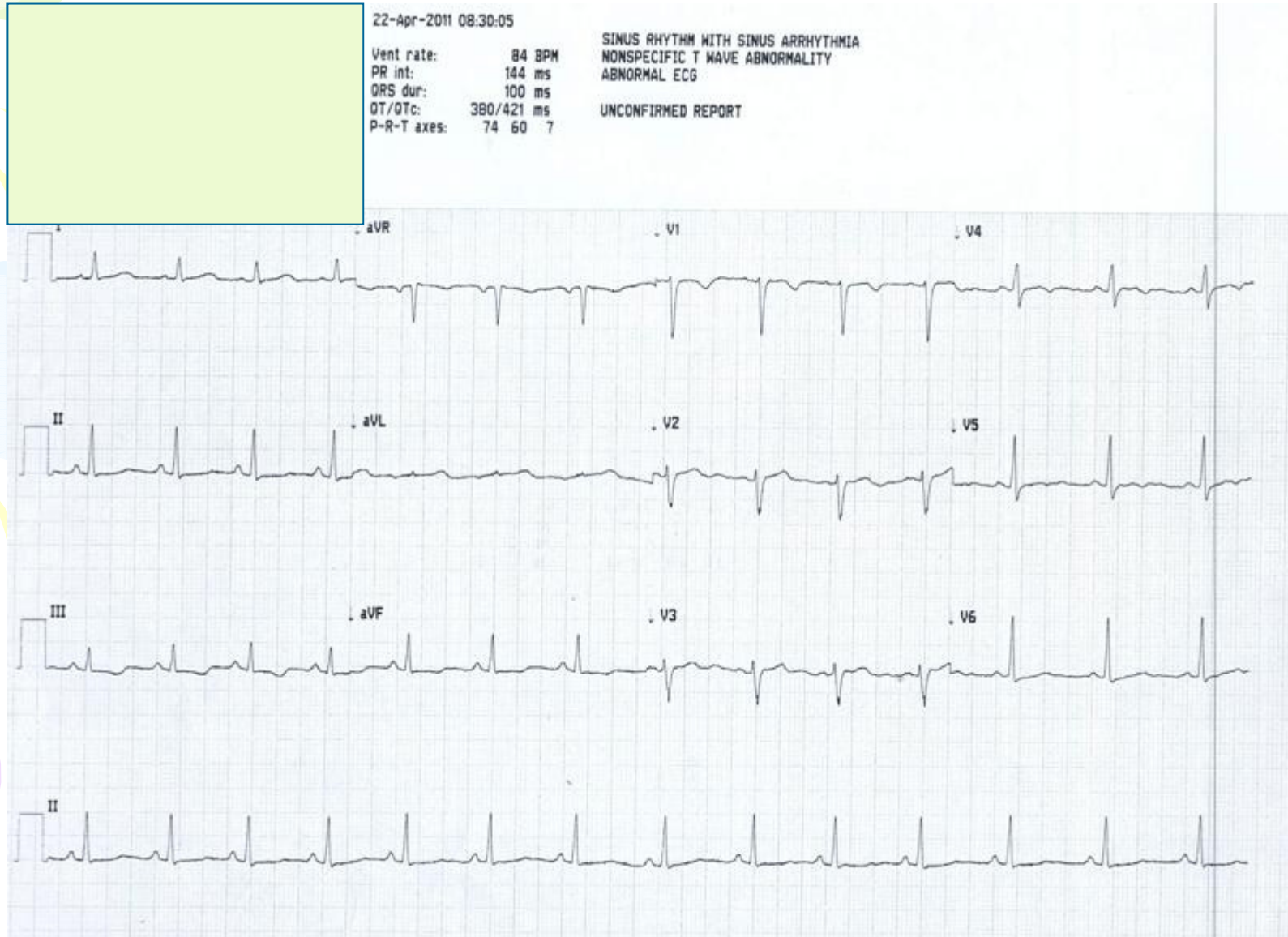


Physical Examination

- Alert, GCS 15/15
 - Hydration satisfactory
 - PEARL 3+/3+ , no neurological deficit
 - Chest clear
 - Abd soft, non-tender, BS +ve
 - CVS HS dual, no murmur
- 
- 

ECG

ECG at 08:30 (shortly after triage) was Normal





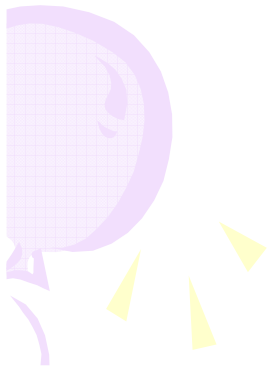
What is on your mind

- DDX:

- 1 GE

- 2 Vertigo

- 3 ? Chest pain





Then....

- IM Stemetil 12.5mg + PO panadol 1 g was prescribed



12:15pm

Patient refused medication and
voluntary history of taken 40-50 tabs
of Panadol this morning

.....



Patient was sent to “Acute Care Room”
@12:30



BP/P 131/81 P90 RR 16



Further history ...

Claim taken 46 tabs of Panadol at ~
07:30am



Deny co-ingestion/ alcohol intake

Voluntary suicidal attempt after conflicts
with husband (a drug addict)

Now regret due to her love towards her
daughter




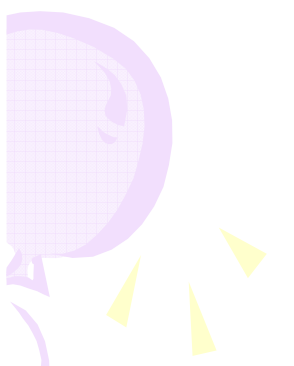
Crying



Panadol Overdose



Management

- Invariably fatal?
 - Potentially fatal?
 - Definitely toxic?
 - Potentially toxic?
 - Non-toxic ingestion?
 - Possible exposure?
- 
- 



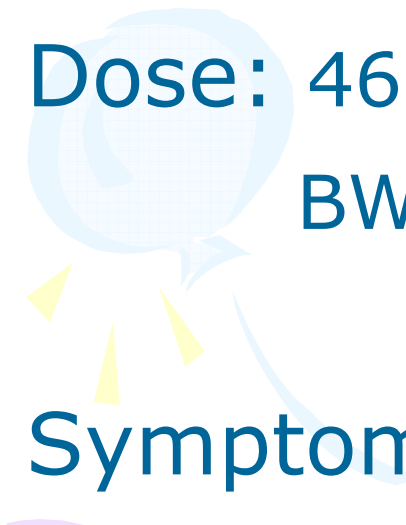
Management

- Life support
- GI decontamination
- Antidote
- Specific treatment



Panadol Overdose

Time: 5 hr post ingestion



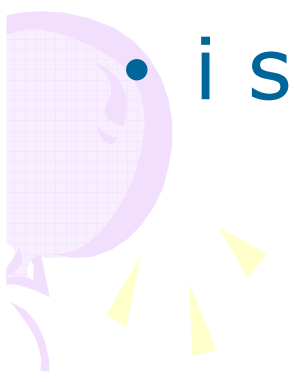
Dose: $46 \times 500\text{mg} = 23000\text{mg}$ acetaminophen
BW $\sim 55\text{kg}$, $\sim 418\text{mg/ Kg}$



Symptoms: repeated vomiting
dizziness



Life support

- ABC
 - BP 128/74 P 90
 - RR 16
 - IVF NS 500mg Q6H
 - Blood x CBC, L/RFT, RG, Clotting, lactate, toxicology screen, Paracetamol level
 - i stat: pH 7.309 BE -8 HCO₃ 18.5
Na 141 K 4.3 (venous)
- 



GI decontamination

- Gastric lavage ?
- Activated Charcoal ?
- MDAC?
- Whole bowel irrigation?



Antidote -- NAC

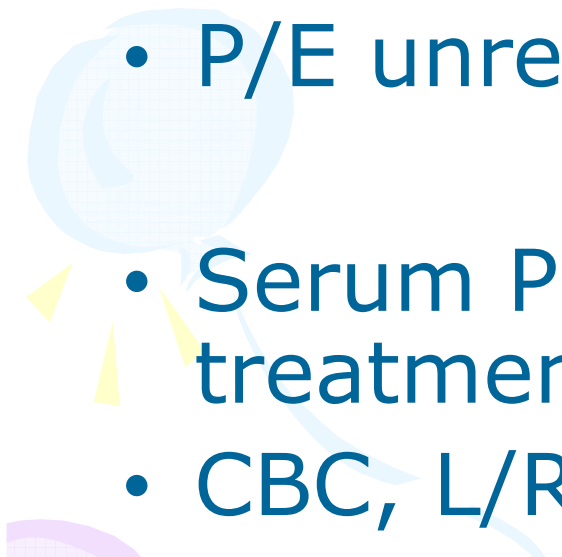

When to start ?

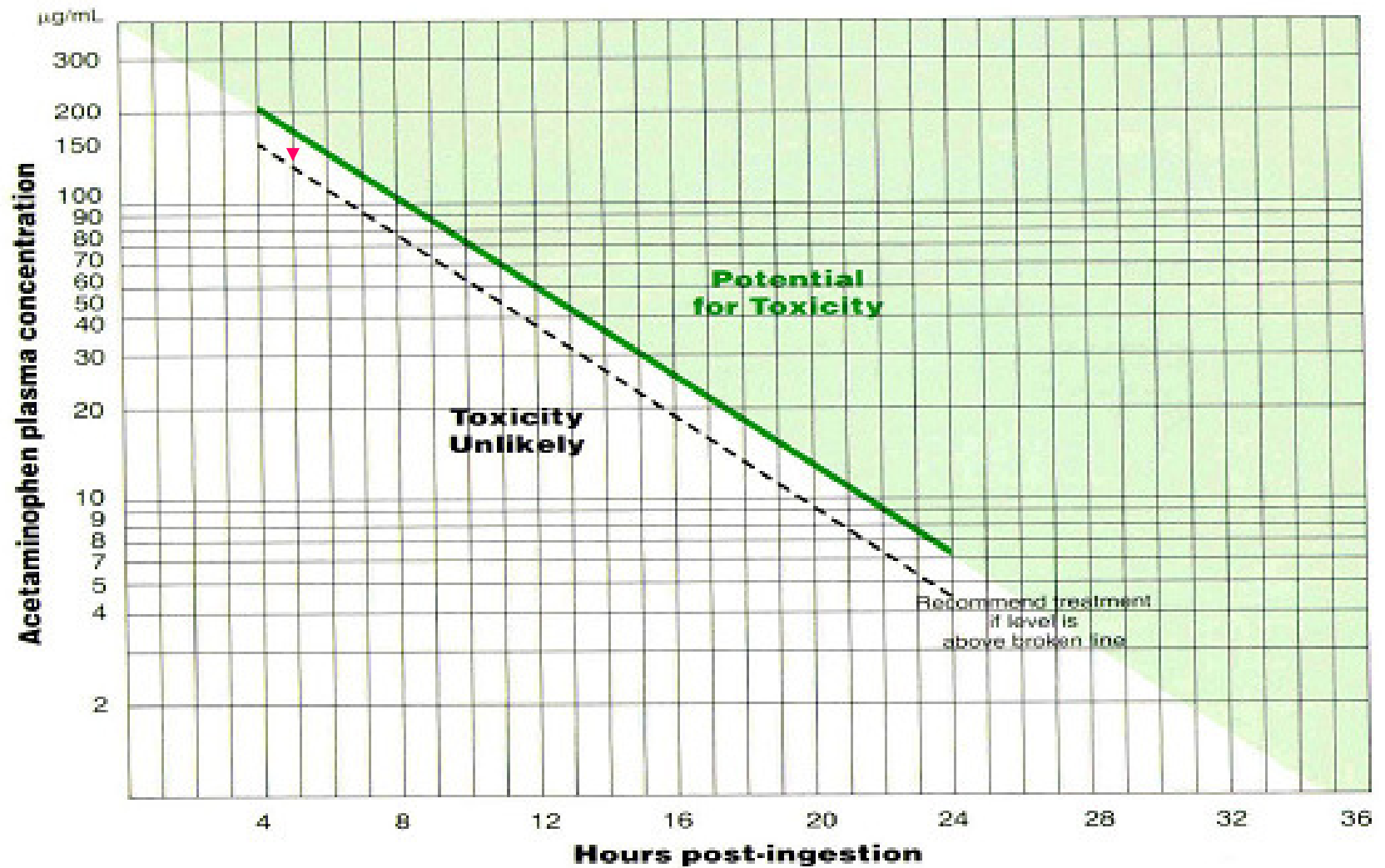
NAC

- Started immediately
- NAC (150mg/kg in 200ml D5, Q1H) at 12:53 (~ 5 hr post-ingestion)



14:00

- Still repeated vomiting, dizziness
 - No abdominal pain
 - P/E unremarkable
 - Serum Paracetamol: $1005\mu\text{mol/L}$ > treatment line
 - CBC, L/RFT, INR unremarkable
 - CI 107
- 
- 



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



**Full Course of
NAC**

- 
- i stat: compensated metabolic acidosis

pH 7.359 pO₂ 15.1 pCO₂ 3.58

BE -10 HCO₃ 15.2

Na 141 K 4.0



Gross anion gap: $141 - 15.2 - 107 = 18.8$ (8-12)

High Anion gap metabolic acidosis





Problem Lists

1. Life threatening panadol overdose



2. Early onset of symptoms (vomiting
& dizziness, post-exposure 2 hr)



3. Early onset of metabolic acidosis
(High anion gap Metabolic acidosis)



Ix on HAGMA

- Blood x lactate, 5-oxoproline
- Urine x ketone, lactate, 5-oxoproline

Progress

- Symptoms improving during NAC infusion
- Lactate 2.7 (0.7-2.1)

I stat/ ABG	12:41	14:31	15:04	22:30
pH	7.31	7.36	7.39	7.38
BE	-8	-10	-9	-5
HCO ₃	18.5	15.2	15	19.7
Na	141	141	137	140
K	4.3	4.0	3.4	3.3
Cl	107	107	107	108
Anion Gap	15.5	18.5	15	12.5



Progress

Clinically improving & emotional stable

No more symptoms

Metabolic acidosis & HAGMA gradually subside

Paracetamol level 17:00 next day: $<20\mu\text{mol/L}$

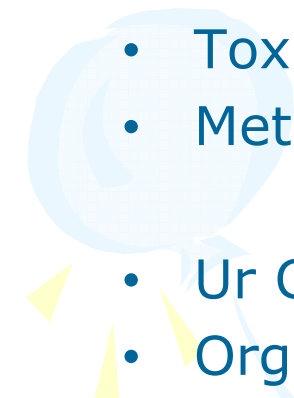
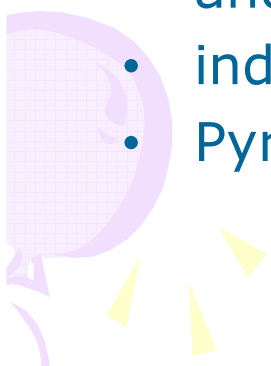
L/RFT unremarkable

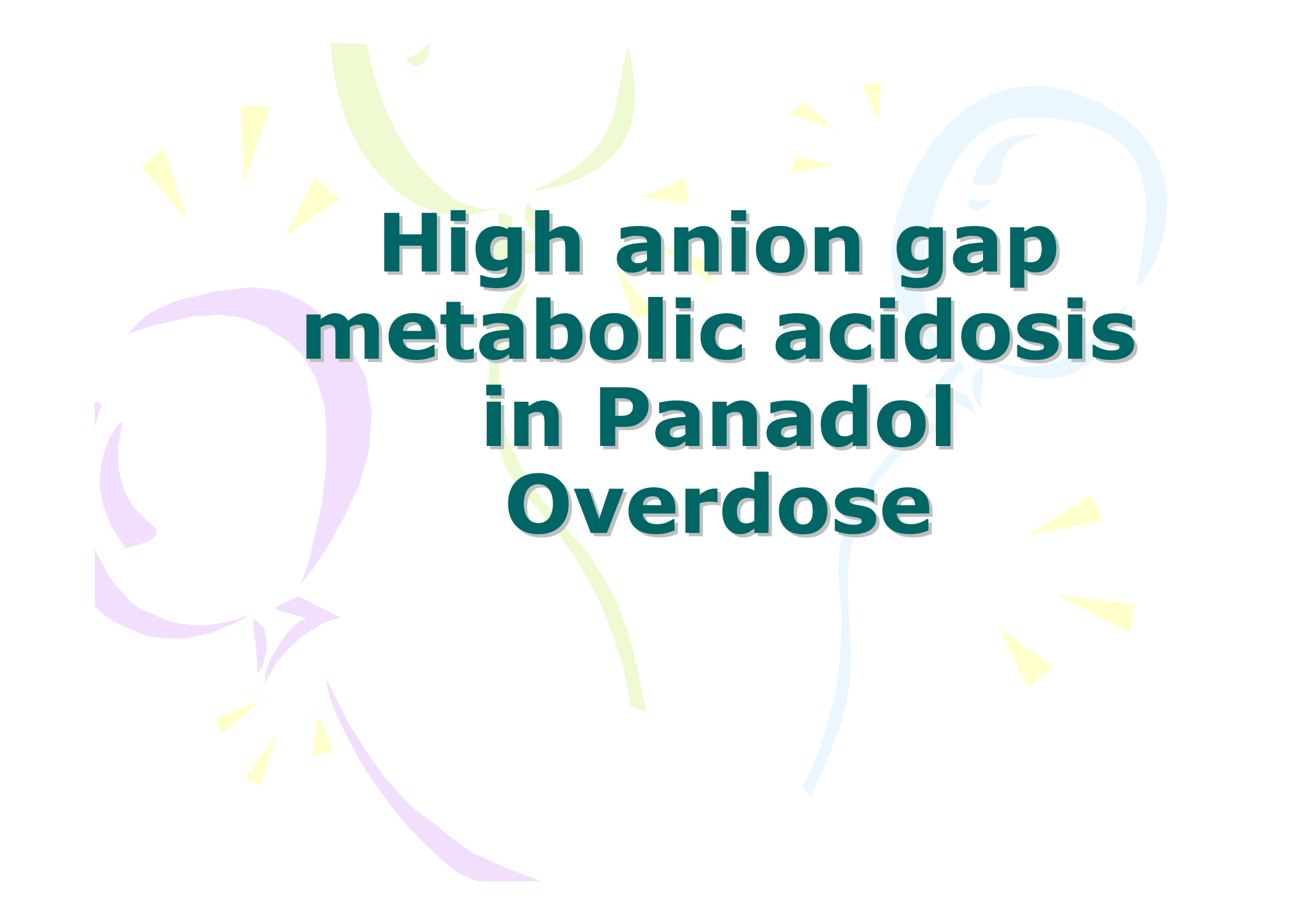
Consulted Psychi: F123





Urine test

- pH 5
 - Ketones Strongly Positive
 - Glucose Trace
 - Toxicology screening (Urine):
 - Metoclopramide, Phenothiazine metabolites, Paracetamol
 - Ur Creatinine 9692 $\mu\text{mol/L}$
 - Organic acids (Urine)
 - Marked excretion of Lactate, Pyruvate, 2-Hydroxybutyrate and 3-Hydroxybutyrate;
 - indicating lactic acidosis and ketosis.
 - Pyroglutamate (5-Oxoproline) excretion was not increased
- 
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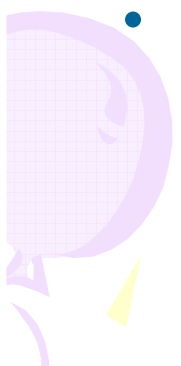
The background features several large, overlapping, curved shapes in shades of green, purple, and blue. Interspersed among these are numerous small, yellow, triangular shapes that resemble sun rays or confetti, scattered across the white background.

**High anion gap
metabolic acidosis
in Panadol
Overdose**



Metabolic acidosis

- Metabolic acidosis are usually due to
 - Lactic acidosis, ketoacidosis, result from toxic substances such as methanol or renal failure
- 5-oxoproline is another under-diagnosed cause for HAGMA
- Reported 4 patients with this syndrome
- Reviewed 18 patients in previously reported
- 21/22 major exposure to acetaminophen
- 82% were women
- Most of them are malnourished with comorbidities



Increased anion gap metabolic acidosis as result of
5-oxoproline (Pyroglutamic acid): a role of acetaminophen Andrew Z Fenves, Clin
J Am Soc Nephrol 1 2006

5-oxoproline

Glutathione- antioxidant sub

Chronic acetaminophen intake

→ depletion of intracellular glutathione stores

→ Generate 5 oxoprolinuria

Urine 5-oxoproline excretion in acetaminophen gp was > 100 times higher than that in control gp.

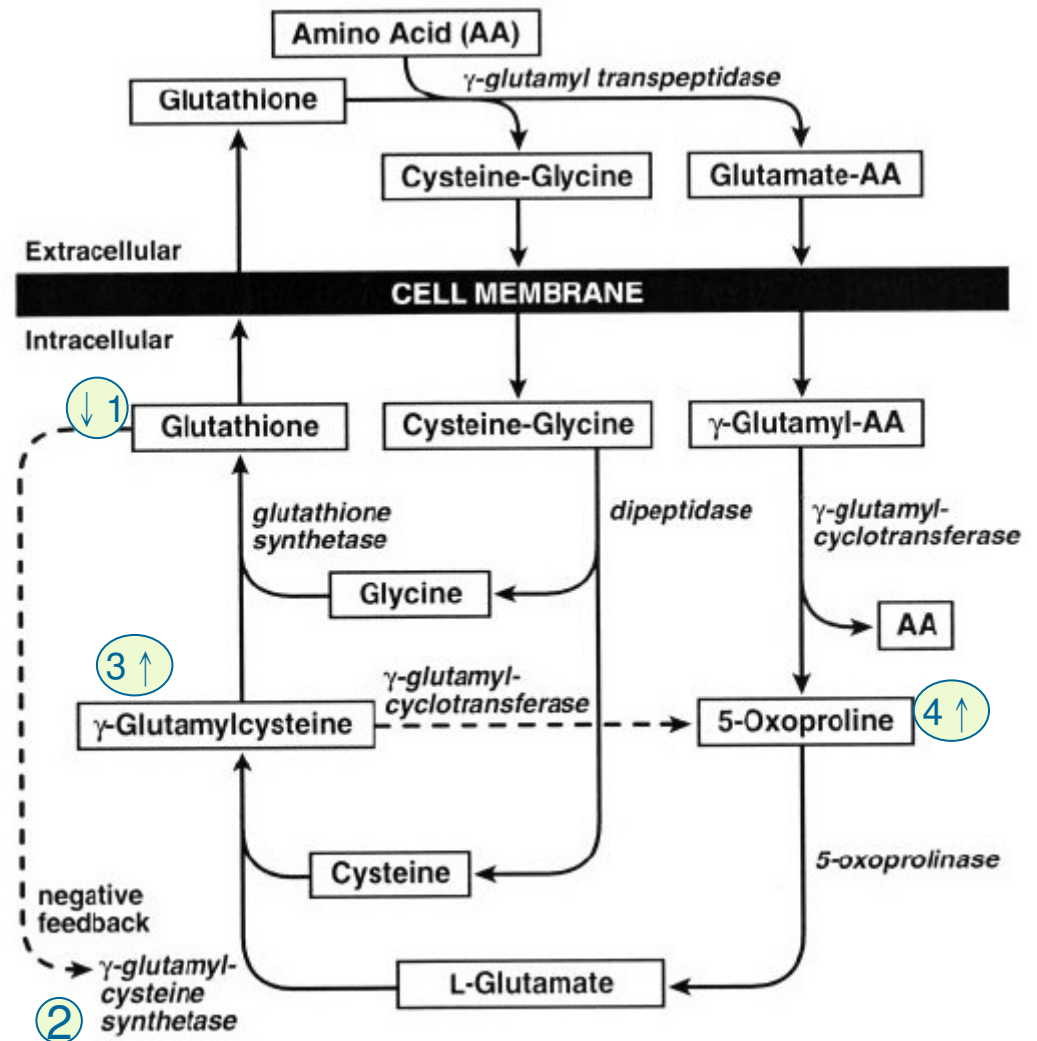


Figure 1. The γ -glutamyl cycle.

Transient 5-oxoprolinuria and HAGMA

- 11 subjects with 5-oxoprolinuria
- Age 1.2-84 (9 F, 2 M)
- All had taken paracetamol, alth in therapeutic amt
- HAGMA in 9/11 + abnormal LFT
- 1 die during an acidotic episode
- 10 recovery with no long-term ill effects after stop paracetamol
- HAGMA and Urinary 5-oxoproline become normalize after the paracetamol discontinued

Transient 5-oxoprolinuria and HAGMA: clinical and biochemical findings in eleven subjects James J Clinical chemistry 1998



High AGMA

- New mnemonics
- **GOLD MARK**

G = Glycols (ethylene & propylene)

O = **Oxoproline** (5-oxoproline/ pyroglutamic acid)

L = Lactate (hypoxia, ischaemia, trauma)

D = D-lactate (short gut syndrome)

M = Methanol

A = Aspirin

R = Renal Failure

K = Ketoacidosis

5-Oxoproline (pyroglutamic) acidosis associated with chronic acetaminophen use
Jennifer L Proc Baylor University Medical Center 2010

Old mnemonics **KULT**

Ketone

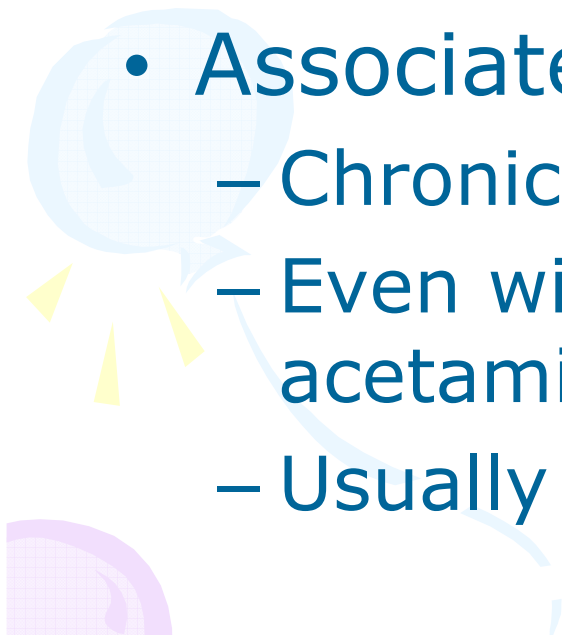
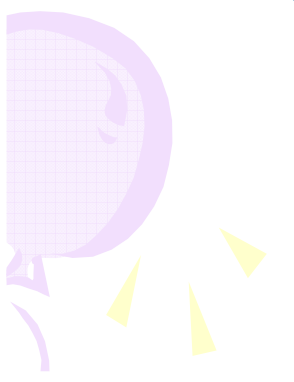
Urea

Lactate

Toxic



5-oxoprolinuria

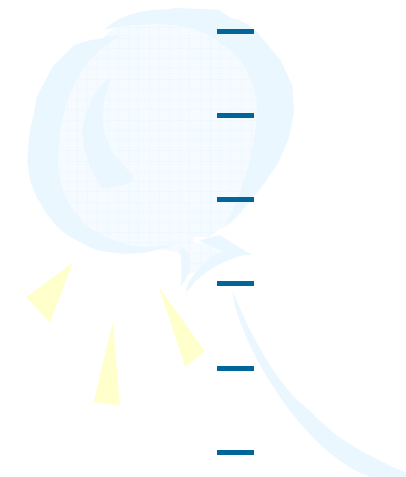
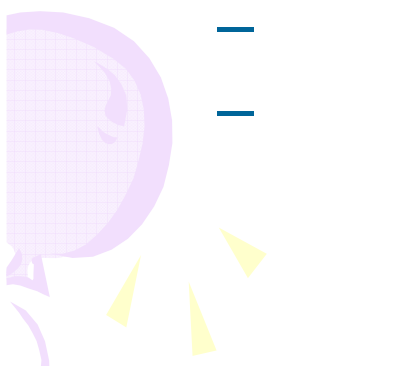
- A condition under-recognized and under-reported
 - Associated with
 - Chronic acetaminophen use
 - Even with therapeutic or low acetaminophen level
 - Usually with other risk factors
- 
- 



5-oxoproline MA

- Common in chronic acetaminophen use +

- Risk Factors

- 
- women
 - malnutrition
 - Pregnancy
 - strict vegetarian
 - sepsis
 - chronic alcohol use
 - underlying liver disease
 - renal insufficiency
- 

A decorative graphic on the left side of the slide features three balloons in light green, light blue, and light purple, each with a grid pattern and a string of yellow streamers. The balloons are arranged vertically, with the green one at the top, the blue one in the middle, and the purple one at the bottom.

Chronic Paracetamol + unexplained HAGMA

- 5-oxoproline acidosis can be a cause
- Check urine and blood x 5-oxoproline
- discontinue paracetamol



Thank you