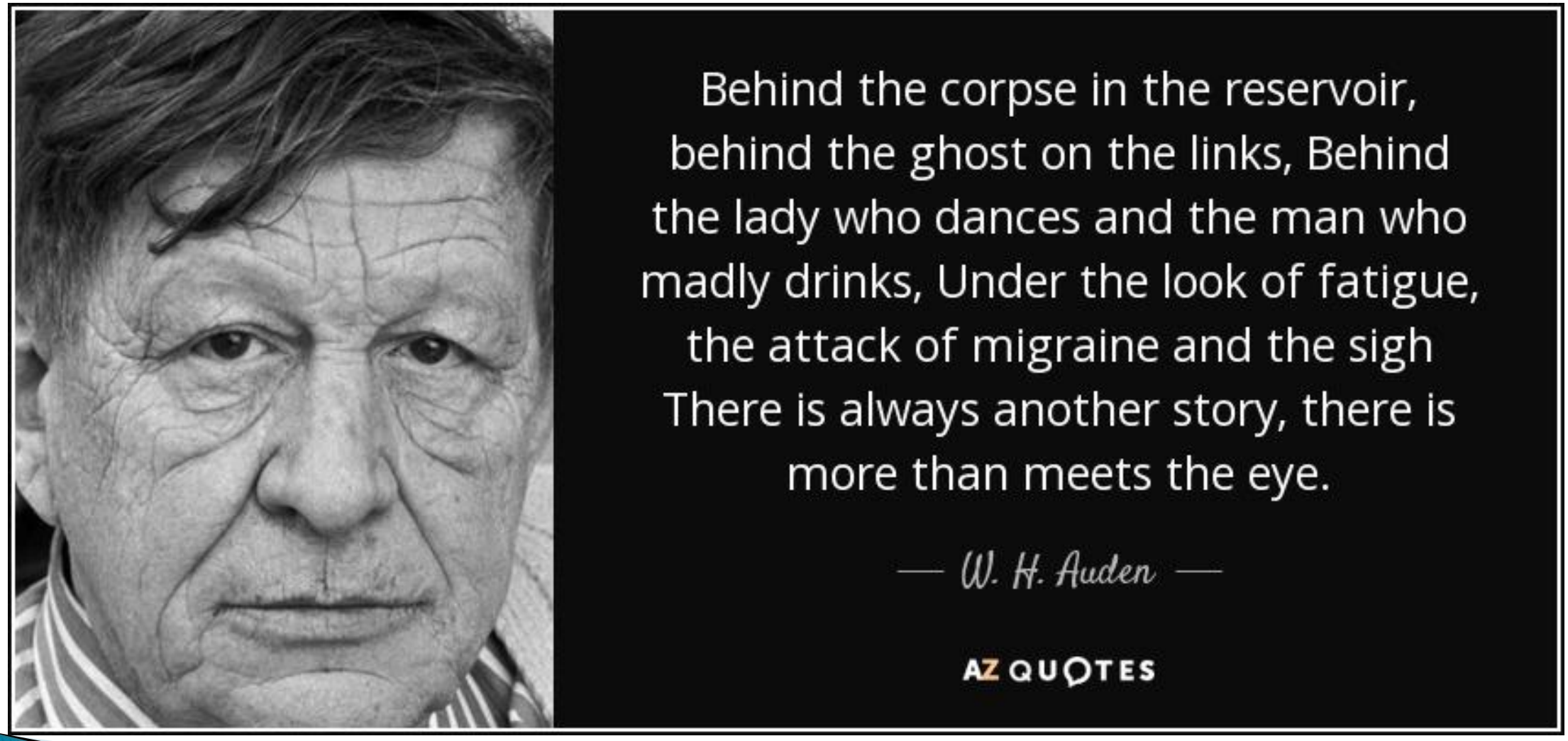
ISRAELI CLINICAL CASE

UTI & Metabolic Acidosis–More than meets the eye

Internal Medicine E
Sheba Medical Center


www.arab-album.com


Behind the corpse in the reservoir, behind the ghost on the links, Behind the lady who dances and the man who madly drinks, Under the look of fatigue, the attack of migraine and the sigh There is always another story, there is more than meets the eye.
— W. H. Auden —
AZ QUOTES

Case presentation

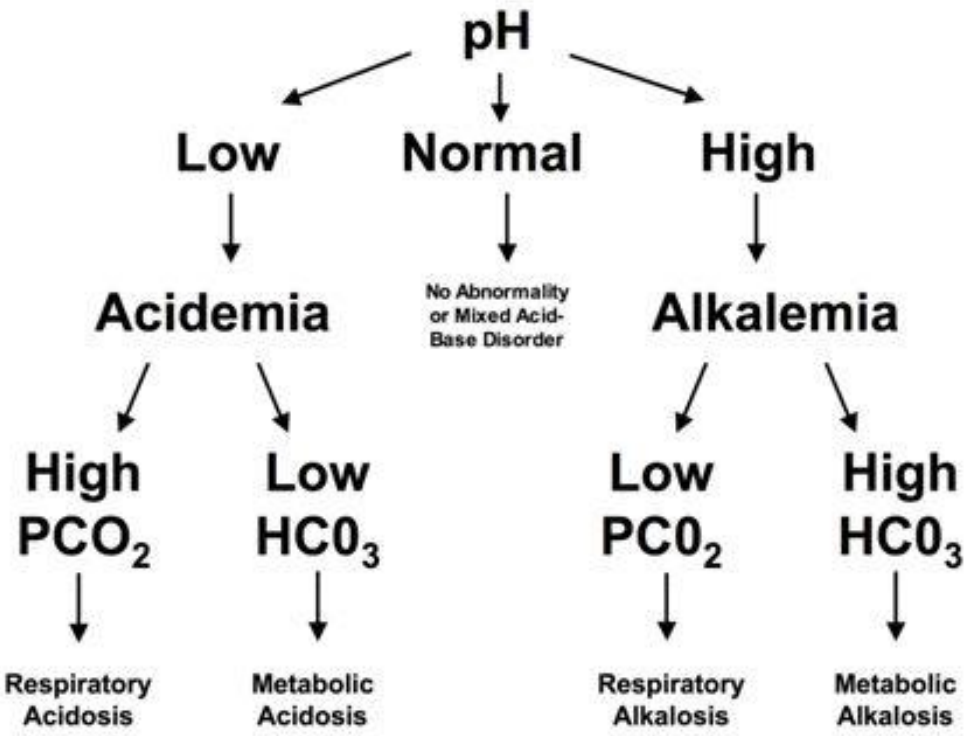
- 77 y/o female
- Background-
  - Cognitive decline
  - IHD(pci+stent in 1995)
  - Paroxysmal A.FIB
  - Ischemic CVA
  - Epilepsy
  - APLA (known PE&DVT)
  - OP & S/P hip replacement

Case presentation

- Presenting complaint:
  - mildly reduced level of consciousness.
  - polyuria + dysuria
  - fever – 38.8
- Urine dipstick- Leucocyte +3, Nitrite +.
- Laboratory- dehydration
- Diagnosis – Urinary Tract Infection.
- Started on antibiotic treatment – Clindamycin+Ofloxacin→Meropenem
- Venous Blood Gas – PH 7.29, HCO3- 15.9 mmol/L , PCO2- 33 mmHg.

Acid base disturbances

Figure 1: Identifying the Primary Process



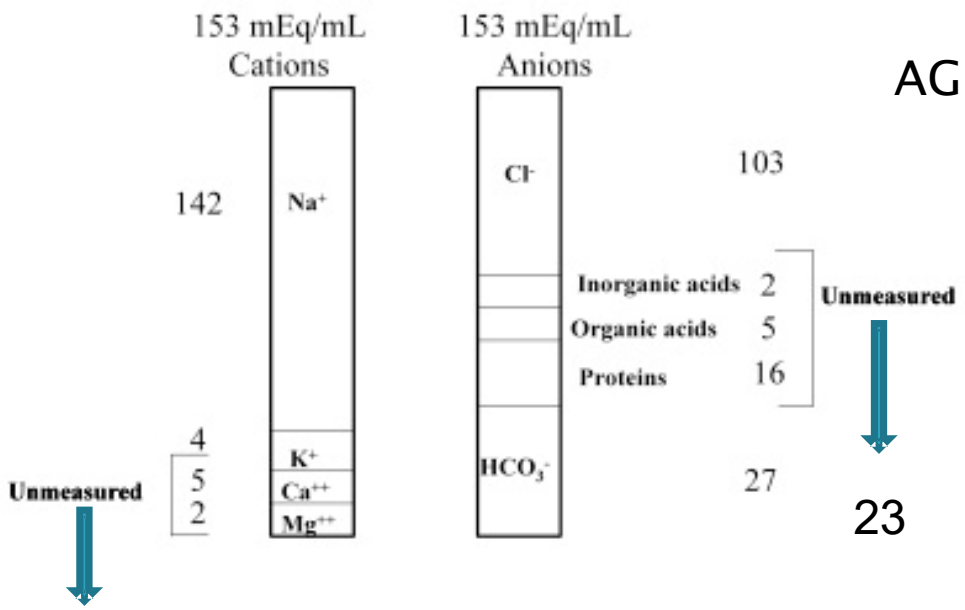
Metabolic Acidosis

- Metabolic acidosis can be produced by three major mechanisms:
  - Increased acid generation due, for example, to lactic acidosis or ketoacidosis
  - Loss of bicarbonate due, for example, to diarrhea
  - Diminished renal acid excretion due, for example, to RTA

Respiratory compensation- Prediction of compensation

Metabolic acidosis		$Pa_{CO2} = (1.5 \times HCO_3^-) + 8 \pm 2$
Metabolic alkalosis		Pa_{CO2} will↑ 0.75 mmHg per mmol/L ↑ in $[HCO_3^-]$ or $Pa_{CO2} = 40 + \{0.7(HCO_3^- - 24)\}$
Respiratory acidosis	Acute	$[HCO_3^-]$ will ↑ 1 mmol/L per 10 mmHg in Pa_{CO2}
	Chronic	$[HCO_3^-]$ will ↑ 4 mmol/L per 10 mmHg in Pa_{CO2}
Respiratory alkalosis	Acute	$[HCO_3^-]$ will ↓ 2 mmol/L per 10 mmHg ↓ in Pa_{CO2}
	Chronic	$[HCO_3^-]$ will ↓ 4 mmol/L per 10 mmHg ↓in Pa_{CO2}

$$Anion\ Gap = Na^+ - (Cl^- + HCO_3^-)$$



AG= 142- (103+27)= 23-11= 12

NORMAL AG= 10 OR NORMAL AG=10+2

Don't forget the albumin-

- For every 1g/dL (normal albumin), add 2.5 to the gap.
- Adj gap= calc gap + 2.5(4-measerued albumin)

Delta delta

$$\textbf{DELTA RATIO} = \frac{\Delta \text{ anion gap}}{\Delta\ HCO_3^-} = \frac{[\,AG - 12\,]}{[\,24 - HCO_3^-\,]}$$

Diarrhea ⇐	< 0.4	Hyperchloraemic non-anion gap metabolic acidosis
DKA + diarrhea ⇐	0.4 - 0.8	HAGMA + NAGMA [may be isolated renal failure]
DKA ⇐	1 -2	uncomplicated HAGMA
	> 2	Metabolic acidosis w/ pre-existing elevated HCO3- [metabolic alkalosis or respiratory acidosis]

Osmolar gap

$$\text{Calculated osmolality (osm)} = 2[Na^{+}(meq/L)] + \frac{\text{Glucose (mg/dL)}}{18} + \frac{\text{BUN (mg/dL)}}{2.8}$$

$$\Delta osm = \text{Measured osmolality} - \text{Calculated osmolality}$$

Table 9. Agents That Increase The Osmolar Gap.

ME DIE

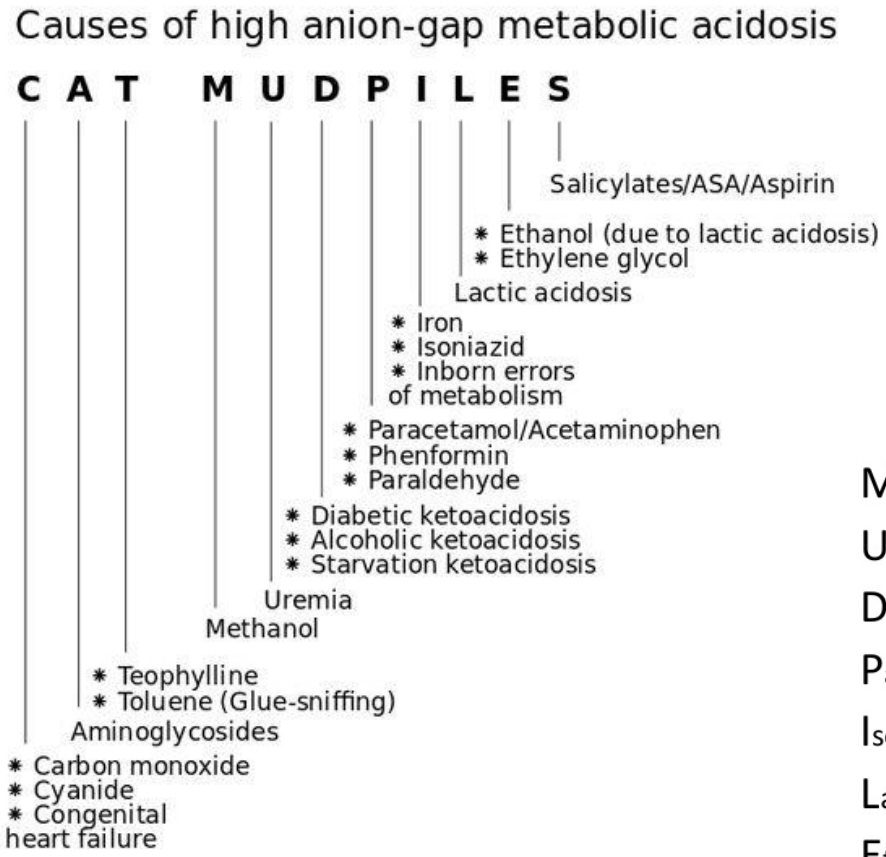
- **M**ethanol
- **E**thylene glycol
- **D**iuretics (osmotic diuretics like mannitol)
- **I**sopropyl alcohol
- **E**thanol

Case presentation

- Interpretation of LAB results-
  - Acid base disturbance- PH 7.29, HCO3- 15.9, PCO2- 33 : metabolic acidosis
  - Compensation status- PCO2-33.3 (1.5X15.9)+8=31.8 ± 2=33: full respiratory compensation.
  - Anion gap- Na- 152, Cl- 116, HCO3- 15.9: High AG= 20. Adj gap= 24.5
  - Delta delta- (20-12)/(24-16)=8/8=1: Pure high AG metabolic acidosis.
  - Osmolar gap- measured-321, calculated- 321.83: no gap.

	03/01/17	05/01/17	06/01/17	08/01/17	09/01/17	10/01/17
PH	7.298	7.244	7.273	7.255	7.204	7.268
PCO2	33.3	34	26.5	25.9	30.9	22.5
HCO3	15.9	14.4	12	11.2	11.9	10.1

High AG metabolic acidosis



Methanol

Uremia

Diabetic Ketoacidosis

Paraldehyde

Isoniazid or Iron tablets

Lactic Acidosis

Ethylene Glycol

Salicylate Toxicity

MUDPILES

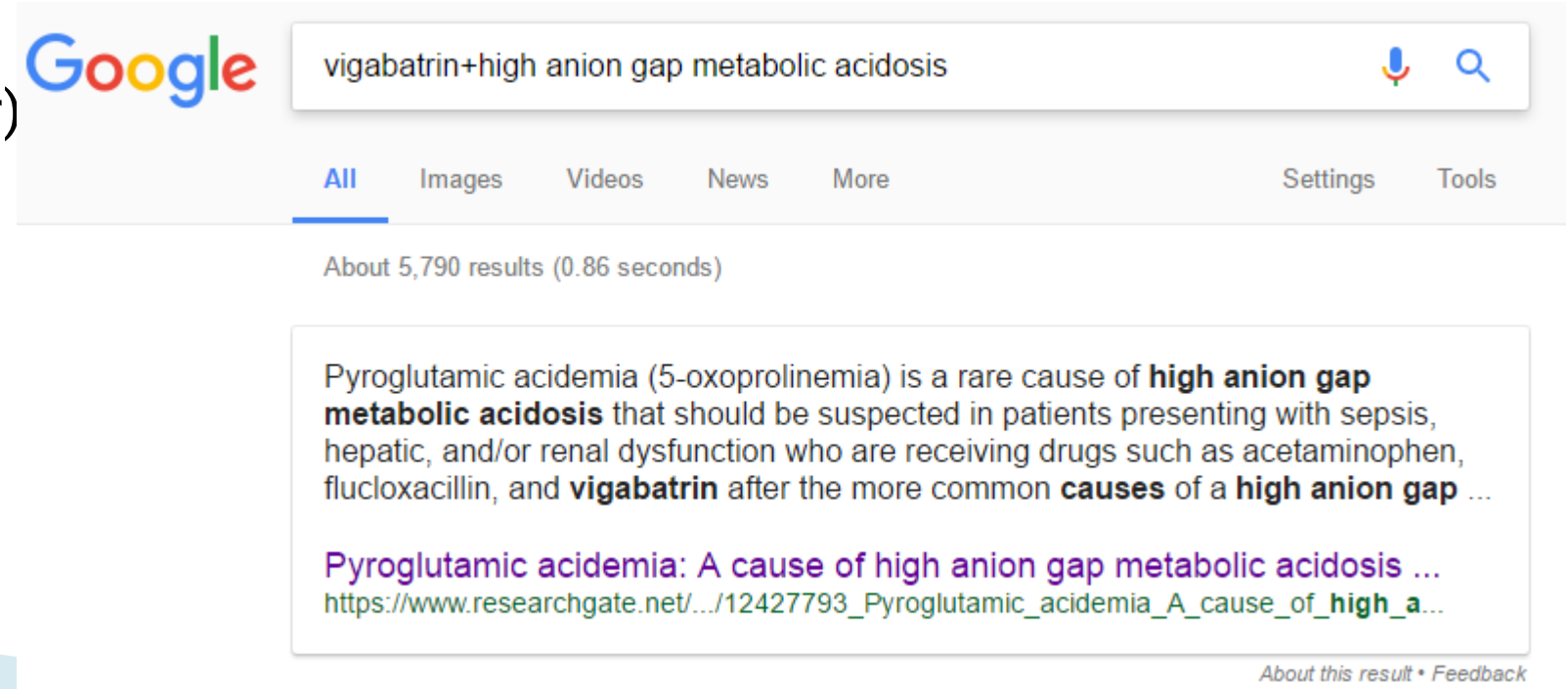
D- lactate

What Do I Do Now

High AG metabolic acidosis

Google for Education

- List of patients drugs:
  - Clexane (Enoxaparin)
  - Phenytoin(Epanutin)
  - Tegretol (Carbamezabine)
  - Vigabatrin(Sabrilan)
  - Risperdal
  - Cipramil
  - Fusid(Furosemide)
  - Atorvastatin(Lipitor)
  - Omepradex(PPI)
  - Aerovent
  - Slow-K SR
  - Osmolite HN



Pyroglutamic Acidemia

CASE REPORT • RAPPORT DE CAS

Profound metabolic acidosis from pyroglutamic acidemia: an underappreciated cause of high anion gap metabolic acidosis

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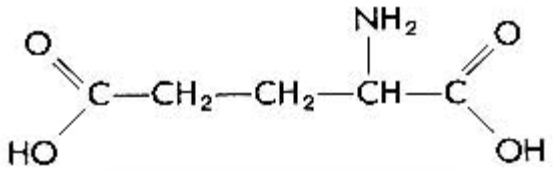
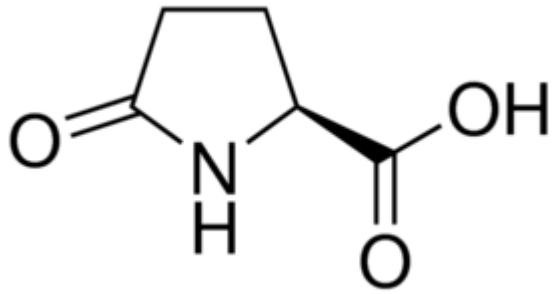
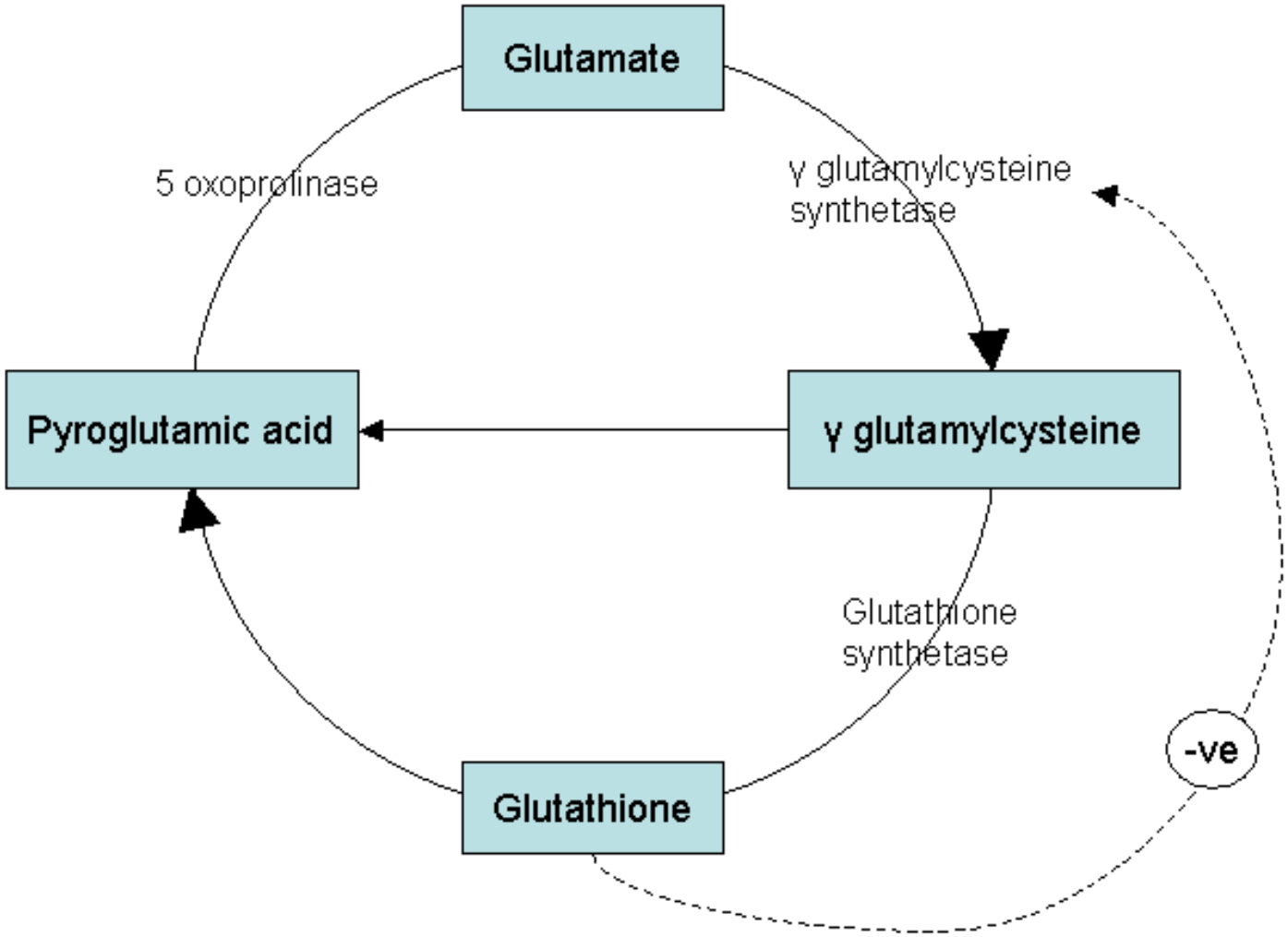
CJEM • JCMU

Pyroglutamic Acidemia



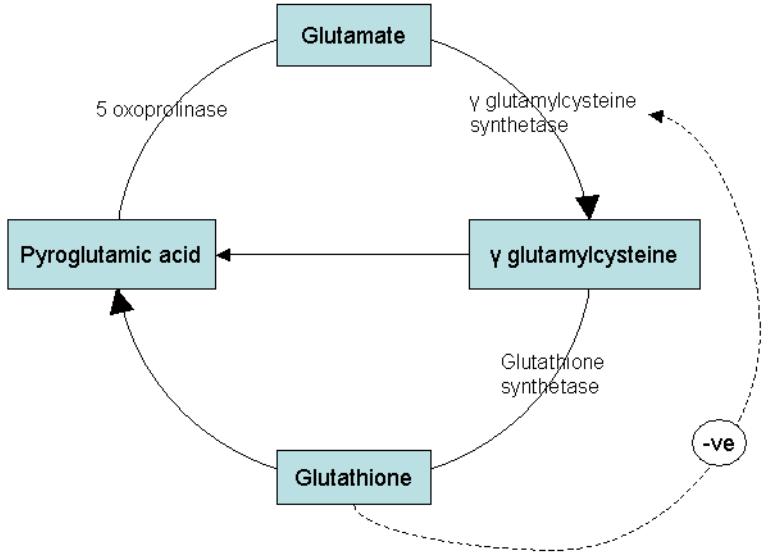
Glutamate
(glutamic acid)





Factors which predispose patients to Pyroglutamic Acidemia

- **Depletion of glutathione**
  - Paracetamol
  - **Severe sepsis**
  - Chronic alcoholism
  - Chronic liver failure of any cause
  - **Malnutrition**



- **Dysfunction of 5-oxoprolinase**
  - Flucloxacillin
  - **Vigabatrin**
  - Netlimicin
  - Inherited enzyme deficiency (Known only from case reports)
  - **Gender-specific- women**

- **Diminished 5-oxoproline clearance**
  - Renal failure

- **Old age is also associated**

Literature

- Only case studies

Crit Care Med 2000 Vol. 28, No. 6

THE LANCET, JUNE 24, 1989

Pyroglutamic acidemia: A cause of high anion gap

PYROGLUTAMICACIDURIA FROM VIGABATRIN

SIR,—Your March 11 editorial on the anticonvulsant agent vigabatrin (γ-vinyl-γ-aminobutyric acid) cites efficacy in refractory epilepsy and the absence of toxicity in 300 patients treated for over a year in support of restricted use of this drug in specialist centres. Others[1] have also proposed its use in conditions not associated with convulsions but in which γ-aminobutyric acid metabolism may be affected.

During routine metabolic screening of organic acid excretion by gas chromatography we detected excessive excretion of pyroglutamic acid in urine (5·1 and 0·23 mmol/mmol creatinine) from two unrelated children receiving vigabatrin. The children aged 14 months and 15 months, respectively, had poorly controlled seizures and were receiving clonazepam, phenytoin, and vigabatrin (50 mg/kg daily) at the time. Urine taken before treatment with vigabatrin showed no trace of pyroglutamate excretion.

"mention" analyses are not done routinely by the Office of Population Censuses and Surveys.

While far from conclusive, these data do suggest that patients who can be presumed to have ingested large amounts of antacids containing Al are not at a greatly increased risk of Alzheimer's disease. We await with interest further information from workers who have kept large numbers of ulcer patients under observation.

ive management should be instituted. (Crit Care Med 2000; 28: 1803–1807)

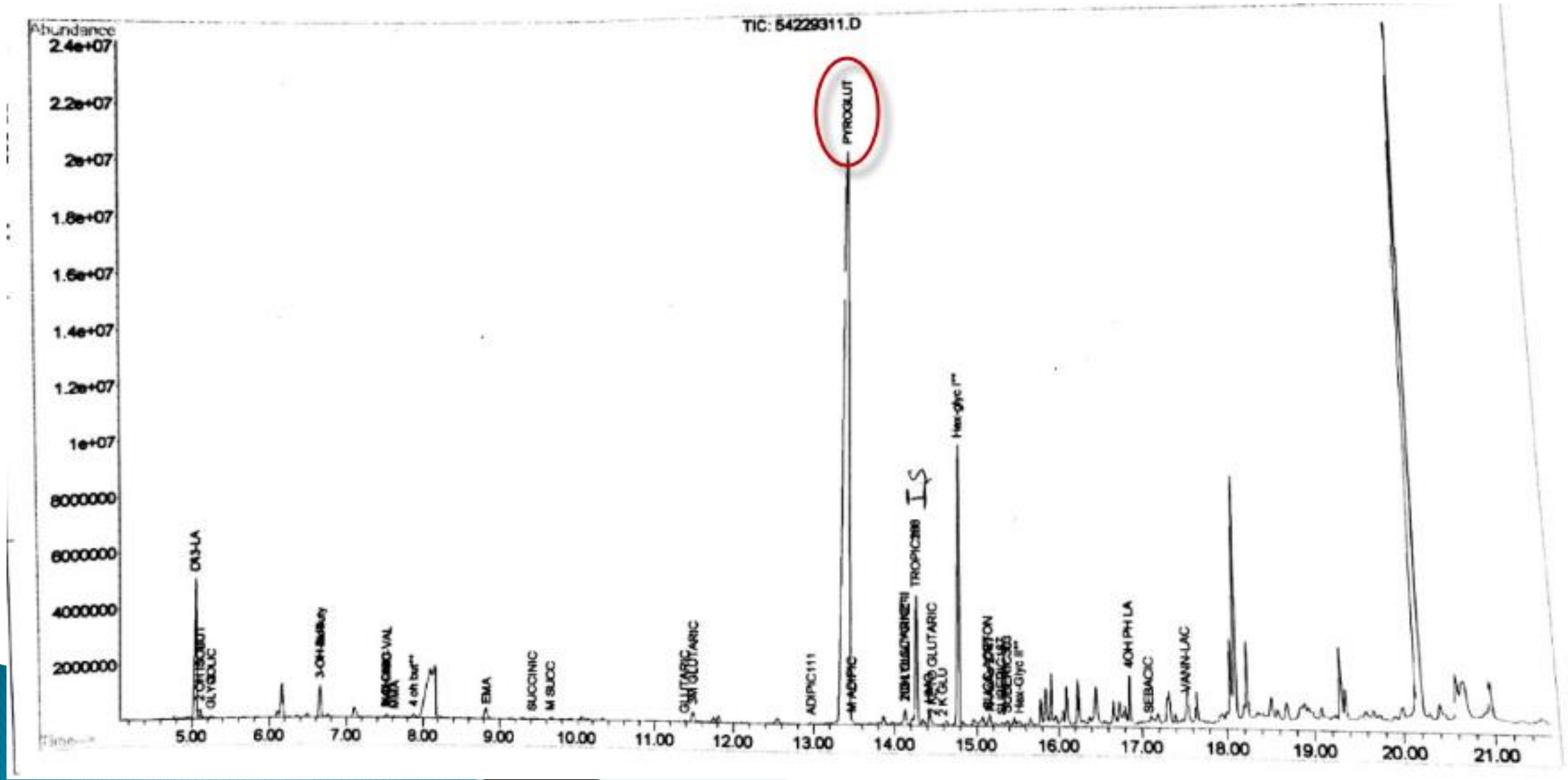
KEY WORDS: pyroglutamic acidemia; 5-oxoprolinemia; high anion gap acidosis

acidemia (5-oxoprolinemia) is a netabolic acidosis that should be ing with sepsis, hepatic, and/or

Diagnosis

- High anion gap metabolic acidosis without a good explanation.
- Plasma assay by gas chromatograph mass spectrometry.
- Urine assay (by same method).
- Normal value of pyroglutamic acid in urine is up to 63 µmol/mmol creatinine.

Case presentation

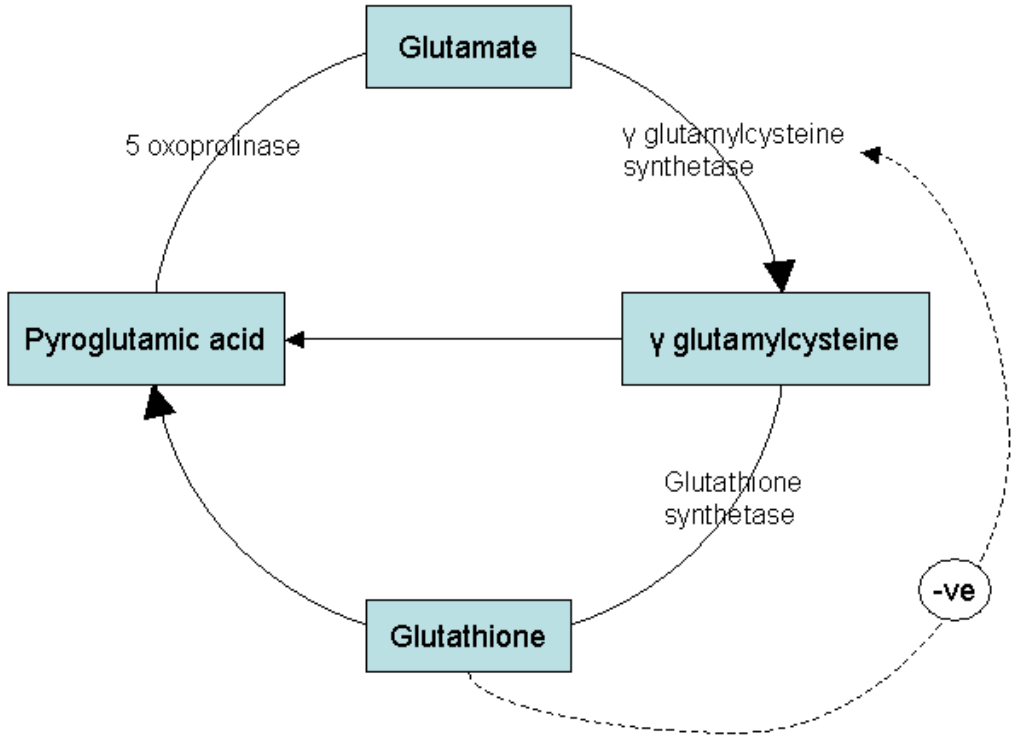


Treatment

- Cessation of the causative agents.
- Remove source of sepsis.
- Supportive care and monitoring.
- Glutathione repletion with N-acetylcysteine.
- Dialysis- 5-oxoproline is cleared renally.
- Bicarbonate- when the bicarbonate is very low and the pH is below 7.1.

N-acetylcysteine

- restoring hepatic glutathione
- serving as a glutathione substitute
- *IV* 21-hour regimen consists of 3 doses; total dose delivered- 300 mg/kg

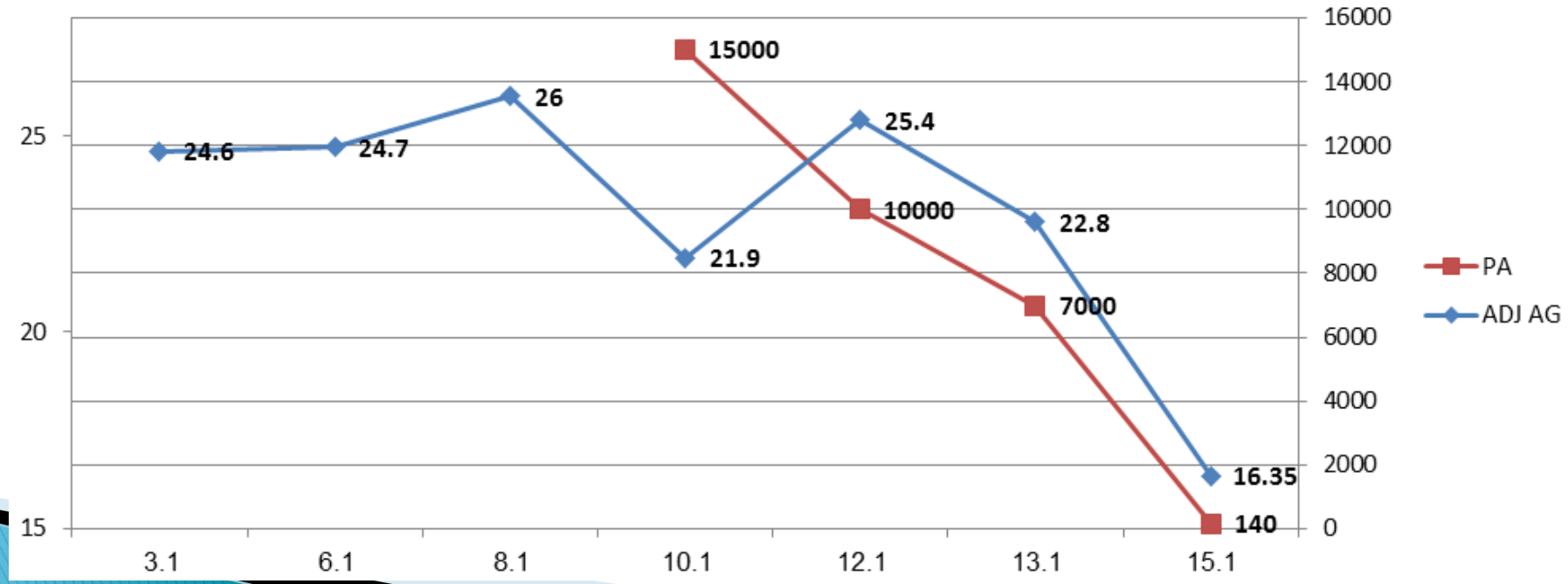


Case presentation

- Cessation of Vigabatrin.
- N-acetylcysteine- (as protocol for Acetaminophen overdose).
- Meropenem for UTI.
- Dialysis.

Case presentation- outcome

- Patient regained consciousness
- Urine assay shows decreased levels of pyroglutamic acid
- AG decreased



Take home messages

- Aim to find out the cause to metabolic acidosis.
- Pyroglutamic Acidemia- a rare/underdiagnosed entity.
- Majority of cases linked to acetaminophen use.

THANK YOU

for

LISTENING TO MY PRESENTATION