Patient presentation

Date Of Medical Event:

- July 30, 2007

Identification:

- Mr. E.N. A 32 year old Inuit man of Hall Beach (Sanirajak), Nunavut. On the Melville Peninsula, west of Baffin Island.

Chief Complaint:

- Coma with noisy breathing

Patient presentation

History of Present Illness:

- Available information minimal and vague. Hunting Caribou on foot for two or three days. May have drank bad water. Returned feeling ill and later found to be unresponsive and was carried to the nursing station.
- No history on depression or suicidality.
- No active TB.
- Dr. M. Allan was contacted by the Hall Beach outpost nurse by telephone. Dr. S. Lloyd a visiting physician from Hamilton was dispatched along with a flight paramedic by plane form Iqaluit to Hall Beach. Dr. Lloyd astutely noted that E.N. had Kussmaul's breathing, was not able to protect his airway and had tall peaked T waves on cardiac monitor.

What is your diagnosis and what needs to be done?

Initial Stabilization and Transport

- Primary Survey
  - **A = Airway**; Orotracheally intubated without drugs.
  - **B = Breathing**; He was allowed to breathe on his own.
  - **C = Circulation**; I.V. normal saline bolus. Because of clinical indicators of metabolic acidosis and hyperkalemia, sodium bicarbonate infusion and I.V. lasix given empirically.
  - Adjuncts to primary survey – Foley catheter, blood was drawn and transported with patient for subsequent testing including blood culture. Intravenous ceftriaxone 2 grams and flagyl 500mg because of likelihood of earlier aspiration given unprotected airway. EKG – tall peaked T waves, widened QRS.
  - Transport time from Hall Beach at least 3 hours.

Are there any other interventions that you could have or would have carried out before or during transport?

Arrival to BRH, Iqaluit

- I was on duty in the ER when Dr. Lloyd and the transport team arrived with E.N. at 22:45 Hrs. History and transport information reviewed.

Examination:

- Comatose (unsedated). Orotacheally intubated. Breathing on his own with large tidal volume and powerful prolonged expiratory phase (Kussmaul's breathing).
- Vital signs: BP 79/40, HR 129, RR 35, Temp 38.2 C
- No Positive physical findings except for abdominal scar

Old Charts:

- Congenital imperforate anus with rectourethral fistula, repaired as a child.

Laboratory From Sample Drawn in Hall Beach

Chemistry			
Test Name	Results	Ref. Range	Units
Sodium	146	135 - 148	mmol/L
Potassium	7.4	3.5 - 5.3	mmol/L
Chloride	112	98 – 108	mmol/L
Glucose – Rand	5.9	4.1 – 6.4	mmol/L
Urea Nitrogen	3.8	3.0 – 7.0	mmol/L
Creatinine	195	71 - 115	mmol/L
Total Bili	7	< 17	umol/L
Alk Phos	108	38 - 126	U/L
AST	44	15 - 46	U/L
ALT	41	11-66	U/L
CK	511	55 - 117	U/L
Acetaminophen	<66	66 - 119	umol/L

Hematology			
Test Name	Results	Ref. Range	Units
WBC	23.3	4.8 – 10.8	X10^9/L
Neutrophils	18.6	2.4 – 8.1	X10^9/L
Hemoglobin	176	134 - 166	g/L
Platelets	455	156 - 416	X10^9/L

Initial Lab Report in Iqaluit

Street Drug Screen negative	
NA+	152
K+	8.3
CL-	116
Glucose	6.3
Creatinine	309
BUN	5.3
CK	427
WBC	39.1
Neutrophils	30.5
INR	1.5 (.8-1.2)
PTT	39 (23 – 35)
Lactate	4.9 (0.7 – 2.1)
Calcium	2.17 (2.10 – 2.65)

ABG	
PH	6.82
PC02	17
PO2	645
Total C02	3
HC03	3

What is the ABG interpretation?

What is the Anion gap?

What is the Osmol gap?

Toxicology detective work

- Answer ABG:

  Profound metabolic acidosis, severe life threatening, compensatory, brain threatening, respiratory alkalosis

- Anion GAP:

  33 Sodium – (Chloride + Bicarbonate) = 152 – (116 + 3)

  Normal Anion gap less than 10 to 12

- Osmol GAP:

  Unable to measure serum osmolality at BRH

What are the causes of anion gap metabolic acidosis?

Mnemonic for Metabolic acidosis

M Methanol Metformin (lactate) Metabolic disease (inherited)

U Uremia

D Diabetic Ketoacidosis (DKA), alcoholic Ketoacidosis (AKA), Starvation ketoacidosis (SKA)

P Paraldehyde, Phenacetin

I Isoniazid (INH), Iron (lactate)

L Lactic acidosis (Including from carbon monoxide, cyanide and methemoglobinemia

E Ethanol (Mild only), Ethylene glycol

S Salicylates , toluene

If anion gap greater than 33 not due to lactate

What are causes of Osmol gap?

Osmol Gap Substances

- Ethanol
- Methanol
- Ethylene Glycol
- Isopropyl Alcohol
- Mannitol
- Glycerol
- Sorbitol
- Acetone (DKA, AKA)
- IVP Dye

Osmol Gap E.N.

Osmol gap in mosm/L = **Calculated Osmolality - Measured Osmolality**

Normal measured serum Osmolality = **280 to 295 mosm/L** (Not measured in BRH)

Calculated Osmolality = **(2 x Sodium) + Glucose + BUN** (all in SI units)

Calculated Osmolality E.N. = **(2 x 152) + 6.3 + 5.3 = 315.6**

315.6 – 280 to 295 = **35.6 to 20.6** (Estimated)

Normal Osmol gap = **10 to 12**

How should this man be resuscitated in ER?

ER Treatment

- A = Reassess airway. Suction. Portable chest X-ray shows ET tube down right main stem bronchus. Cuff deflated, tube pulled back, cuff re-inflated.
- B = Breathing: Let him breath on his own. He is titrating this physiologically.
- C = Circulation: Second or third I.V. Bolus NS because of BP down HR up.

Sodium Bicarbonate infusion? Good idea? Bad Idea? Increase? Decrease?

What other treatments would possibly be helpful?

Intensive Care

- I spoke with Dr. Rick Hodder adult intensivist at Ottawa Civic Hospital. We designed the following treatment plan, based on a presumptive diagnosis of a toxic alcohol ingestion, metabolic acidosis and severe hyperkalemia:
    - Glucose 50cc of 50%
    - Humulin R insulin 10 units I.V.
    - Calcium Chloride 5ml of 10% solution I.V.
    - Sodium Bicarbonate 2amps I.V then 3 ampoules in 1 liter D5W at 125cc/hour
    - Ethanol infusion with 100ml of ethanol in one Liter of NS, 500cc in 1 hour, the 50 cc's per hour.
    - Medivac ASAP to nearest ICU (Ottawa 5 hours by air) for dialysis.

Treatment critique

What is the rational and the expected results of the intensivists advice?

What other treatments could have been administered?

What simple test could be done to assess for possible ethylene glycol poisoning?

What would the other most likely toxic culprits be?

Treatment to Tertiary Care

- E.N. urgently needed transfer to tertiary care for dialysis. Usual site would be Ottawa. Dr. Rick Hodder, a senior respected intensivist had agreed to take him into Ottawa civic ICU and have dialysis.
- There was no jet air ambulance in Iqaluit.
- There was a fixed wing propeller plane but transport time would have been very long ant the available flight crew would have timed out in flight and this is not legal and despite pressure I decided not to take this route.
- The air ambulance jets and crews in Ottawa were all busy.
- A jet and transport team including an experienced emergency physician and critical care nurse were dispatched from Toronto. It was about seven hours before they arrived and another one to two before they left for Ottawa.
- Time from E N's presentation to the nursing station in HB to his arrival in ICU in Ottawa was over 24 hours.
- Ethanol level monitored in Iqaluit 12 to 18 mosm/L

In Ottawa ICU

PH	7.14
$pC0_2$	23
$P0_2$	193
Hco_3	7
Base Excess	-20.5

CXR – Bibasilar Pneumonia

CT HEAD - Negative

Lactate	4.4
Ketones	Negative
Anion Gap	33
Osmol	10
Ethanol	0?
Methanol	0
Isopropanol	0
Acetone	0
Ethycene Glycol	3 mmol/L
Creatinine	532
BUN	13.9
Ionized Calcium	.66 (1.15 – 1.32)
Potassium	4.5

Treatment

- Ethanol Infusion 75cc/Hr 10% ETOH
- Thiamine
- Pyridoxine
- Sodium Bicarbonate Infusion
- Dialysis
- Piperacillin and Tazobactam

- His highest creatinine was 703 on August 6th. On August 19th he left hospital for Largo house. He required dialysis for two to three months.

- Ultimately he was able to return home to his own community of Hall Beach.

- Later he confirmed that while hunting Caribou he became thirsty and drank form a bottle containing a sweet liquid presumably antifreeze containing ethylene glycol.

Anions, Osmols and Alcohols

Toxic Alcohols

1. Ethyl Alcohol
2. Isopropyl Alcohol
3. Ethylene Glycol
4. Methyl Alcohol

All metabolized in the liver by alcohol dehydrogenase enzyme

Toxic Effects

Ethyl Alcohol

- Decreased Inhibitions
- Visual Impairment
- Muscular Incoordination
- Slowing of reaction time
- Diplopia
- Nystagmus
- Stupor
- Hypoglycemia
- Hypoventilation
- Cardiovascular collapse

Treatment

Supportive

Toxic Effects

Isopropyl Alcohol (Rubbing Alcohol)

- Toxicity twice that for ethanol for the same amount ingested
  - As above
  - Hypothermia
  - Hypotension
  - Respiratory Failure
- Metabolized (By ADH) to acetone, C02 and H2O, leading to ketonemia but no acidosis.
- Treatment is DONT, supportive care and monitoring, rarely dialysis.

D = Dextrose
O = Oxygen
N = Narcan
T = Thiamine

Toxic Effects

Methanol (Wood Alcohol)

- Slowly metabolised by ADH to formic acid and formaldehyde (30% of dose still present after 48 hours). (Show chemical structure)

- Skin exposure, inhalation and oral ingestion all very toxic.

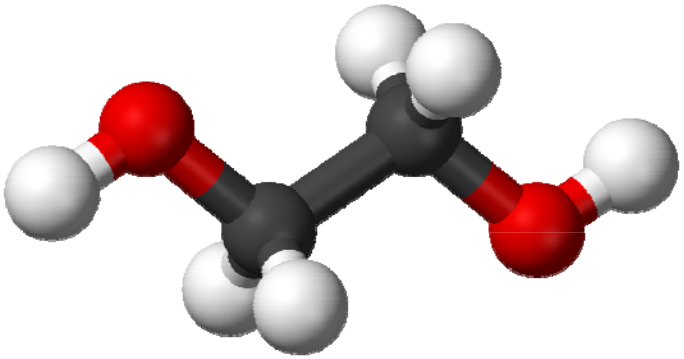
- As little as 15cc PO Has caused:

  - Death in an adult.
  - Visual loss and blindness
  - Dizziness, headache, seizures, pseudomeningitis
  - Anorexia, nausea and vomiting (50%)
  - Abdominal Pain (Sometimes very severe)

Toxic Effects

Ethylene Glycol (Antifreeze)

- Colorless, odorless, sweet taste (Pets like it) Fluorescence or color often added. Parent compound not very toxic. Metabolites can be lethal.



Toxicity

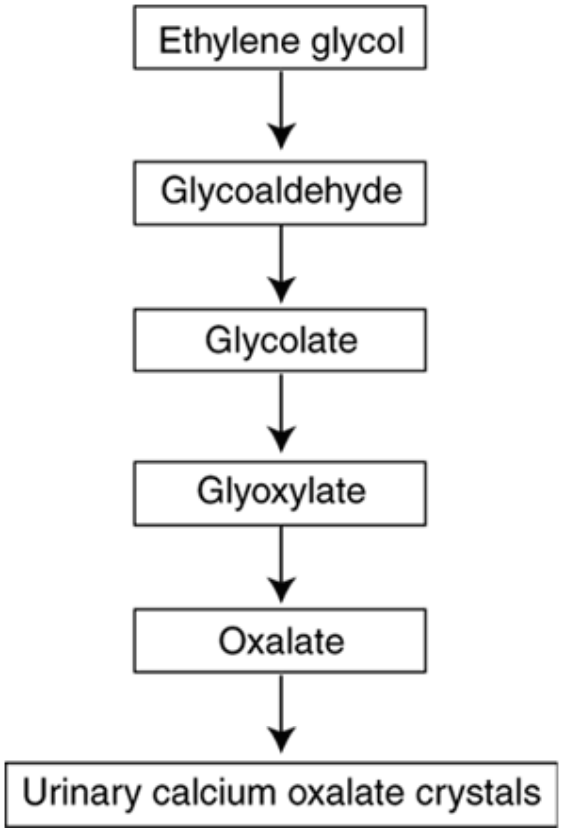
Skin – None

Inhalation – None

Ingestion – Very - lethal dose for adult, about 100cc

Metabolism

Metabolism (ADH)



EG Stages of Clinical Syndrome

- **Clinical Syndrome** – Patient Appears intoxicated without the smell of alcohol.

- **Stage 1 CNS (½ -1 Hours)**

  - Nausea and vomiting
  - Anion gap osmol gap metabolic acidosis
  - Seizures
  - Coma
  - If death; from cerebral edema

- **Stage 2 Cardiopulmonary (12 – 24 Hours)**

  - Tachypnea
  - Tachycardia
  - Hypertension
  - Cyanosis
  - Pulmonary edema
  - Bronchopneumonia

- **Stage 3 - Renal (36 – 48 Hours)**

  - Oxaluria (Can be seen earlier)
  - CVA Tenderness and flank pain
  - Acute renal failure

Rx of Ethylene Glycol

- **MANAGEMENT** — Rapid decision-making is critical in the management of the patient poisoned with methanol or ethylene glycol. The clinician must often make treatment decisions without definitive serum drug levels, based only upon clinical suspicion and readily available laboratory data. A summary table to facilitate emergent management is provided.

- The management of methanol and ethylene glycol poisoning involves the following:

  - Securing the patient's airway, breathing, and circulation, and providing appropriate supportive care

  - Administering sodium bicarbonate to correct systemic acidosis, which limits the penetration of toxic acids into end-organ tissues such as the retina

  - Inhibiting the enzyme alcohol dehydrogenase, with either fomepizole 4- methylpyrazole (preferred) or ethanol (if fomepizole is unavailable)

  - Performing hemodialysis for elevated toxic alcohol levels, severe acid-base derangements, or evidence of end-organ toxicity

  - Treating with cofactors (folic acid, thiamine, and pyridoxine) to optimize nontoxic metabolic pathways for the elimination of the parent alcohol or its metabolites

Rx of Ethylene Glycol

- **Fomepizole** — Fomepizole has been used successfully for years to treat both methanol and ethylene glycol poisoning. There is a virtual consensus among toxicologists that it is a superior antidote to ethanol. Fomepizole is easy to dose, easy to administer, and side effects are rare. Its main disadvantage is its high cost ($1075 per vial). This cost compares favorably, however, with the total cost of managing patients treated with ethanol, including ethanol titration, and possibly hemodialysis and intensive care unit admission.

- Fomepizole is loaded at 15 mg/kg intravenously, followed by 10 mg/kg every 12 hours, with adjustments for hemodialysis or after more than two days of therapy. (See "Extracorporeal elimination" below).

- There is no benefit to adding ethanol therapy to fomepizole therapy in methanol and ethylene glycol-poisioned patients.

Rx of Ethylene Glycol

- Ethyl Alcohol – Methonol and ethylene alcohol all are metabolized be alcohol dhydrogenase
- The enzyme ‘prefers’ ethyl alcohol, and so the rational is to supply ethyl alcohol thereby retarding breakdown of the ethylene glycol and methanol to more toxic compounds
- Object is to obtain an ethyl alcohol blood level of approximately 100mg%
- Loading 1cc/kg of 95% ethanol maintenance 0.1cc/kg/hr
- Therapy should continue for approximately 2-3 days if necessary

Rx of Ethylene Glycol

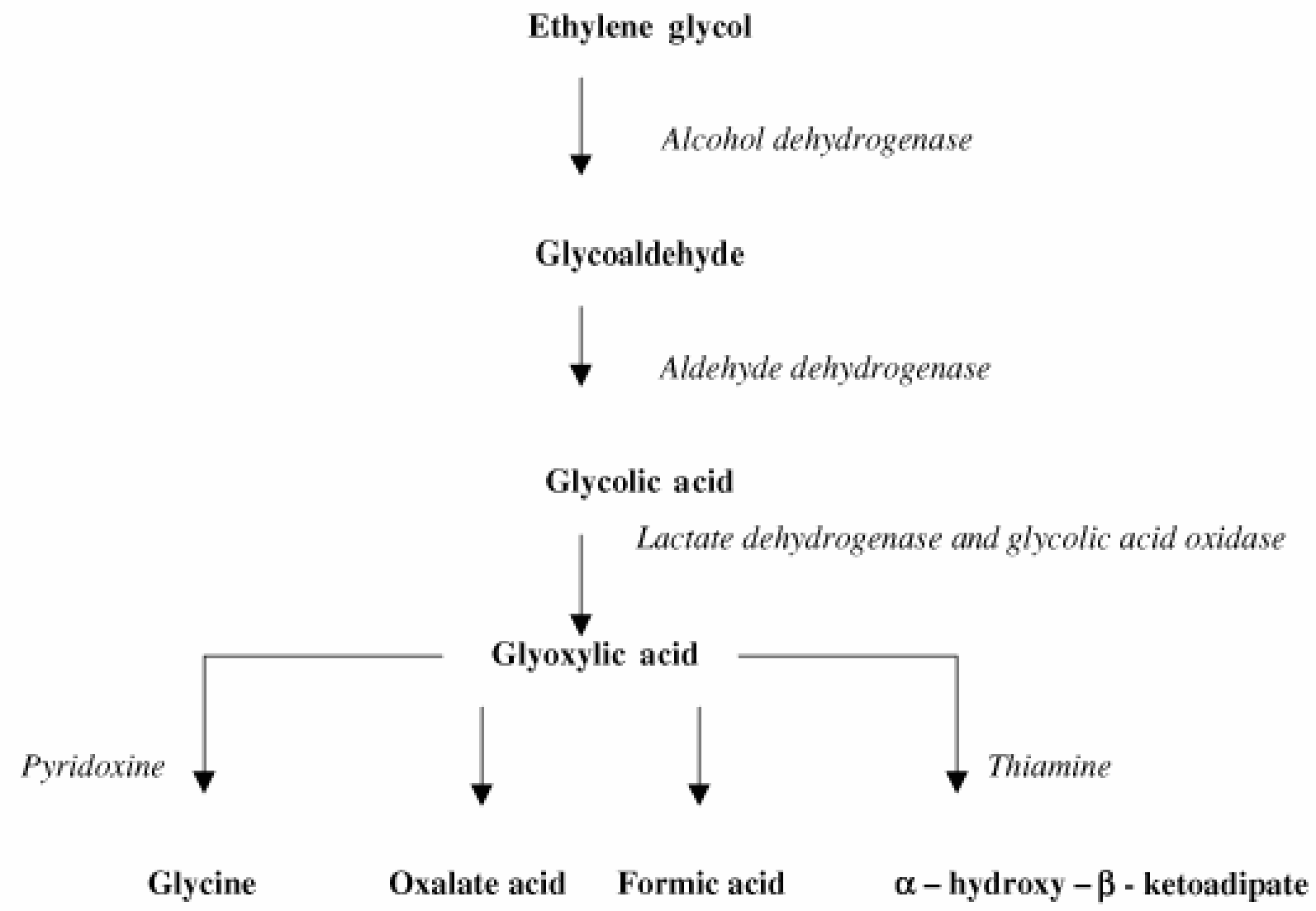
- **Calcium** – for hypocalcaemia from ethylene glycol

- **Cofactor therapy** - All methanol patients treated with ADH inhibition should also receive cofactor therapy: either folinic acid (leucovorin) 50 mg IV or folic acid 50 mg IV every six hours. It is not known whether supplemental thiamine (100 mg IV) or pyridoxine (50 mg IV) benefits patients poisoned with ethylene glycol, but we routinely administer both, particularly if the patient's nutritional status is suspect.

- **Hemodialysis** – Indications

  Metabolic acidosis with positive history or suspicion for methanol or ethylene glycol

Rx of Ethylene Glycol



Rx of Ethylene Glycol

- **PEDIATRIC CONSIDERATIONS** - A common clinical presentation involves the child who may have swallowed one or two mouthfuls of a concentrated methanol or ethylene glycol solution. These children should not be managed at home, but must be formally examined by a clinician. Most victims of unintentional exposure present for evaluation shortly after ingestion and do not manifest significant metabolic acidosis or any evidence of end-organ dysfunction. The ideal approach is to measure the serum concentration of the specific alcohol in order to quantify the absorbed dose and predict the clinical course. Unfortunately, such concentrations are rarely available within a few hours of the ingestion, creating a diagnostic and therapeutic dilemma.

- **Adolescents** - Groups of adolescents trying to become inebriated may consume toxic alcohols knowingly or accidentally in contaminated beverages. When treating an adolescent for a possible toxic alcohol ingestion, clinicians should always consider the possibility of other as-yet unidentified victims.