CCM Interhospital Meeting
A Sleepy Man

Intensive Care Unit

North District Hospital

Sept 2009

Case Presentation

Case

- M/48
- Smoker, Lives with family, ADL independent
- Past Medical History:
  - Depression FU PSY
- Drug History:
  - Lorazepam 2 mg nocte
  - Valproate CR 400 mg nocte
  - Venlafaxine extended release 150 mg om

History

- Admitted to medical ward at 23:00
- Because of unconscious on the bed
- Last seen by his wife at 08:00 while having the breakfast
- Found sleepiness since 12:00 afternoon
- Did not wake up for the lunch and dinner
- Wife sent him to AED

History

- No history of head injury / fall
- No limbs twitching / convulsion
- No empty pills bottle / drug bags
- No fever
- Tool the anti-depressants as usual according to his wife

Examination

- BP 130 / 84
- P 110 sinus
- SpO2 100% on 100% NRM
- Temp 37 C
- Hstix 6 mmol/L

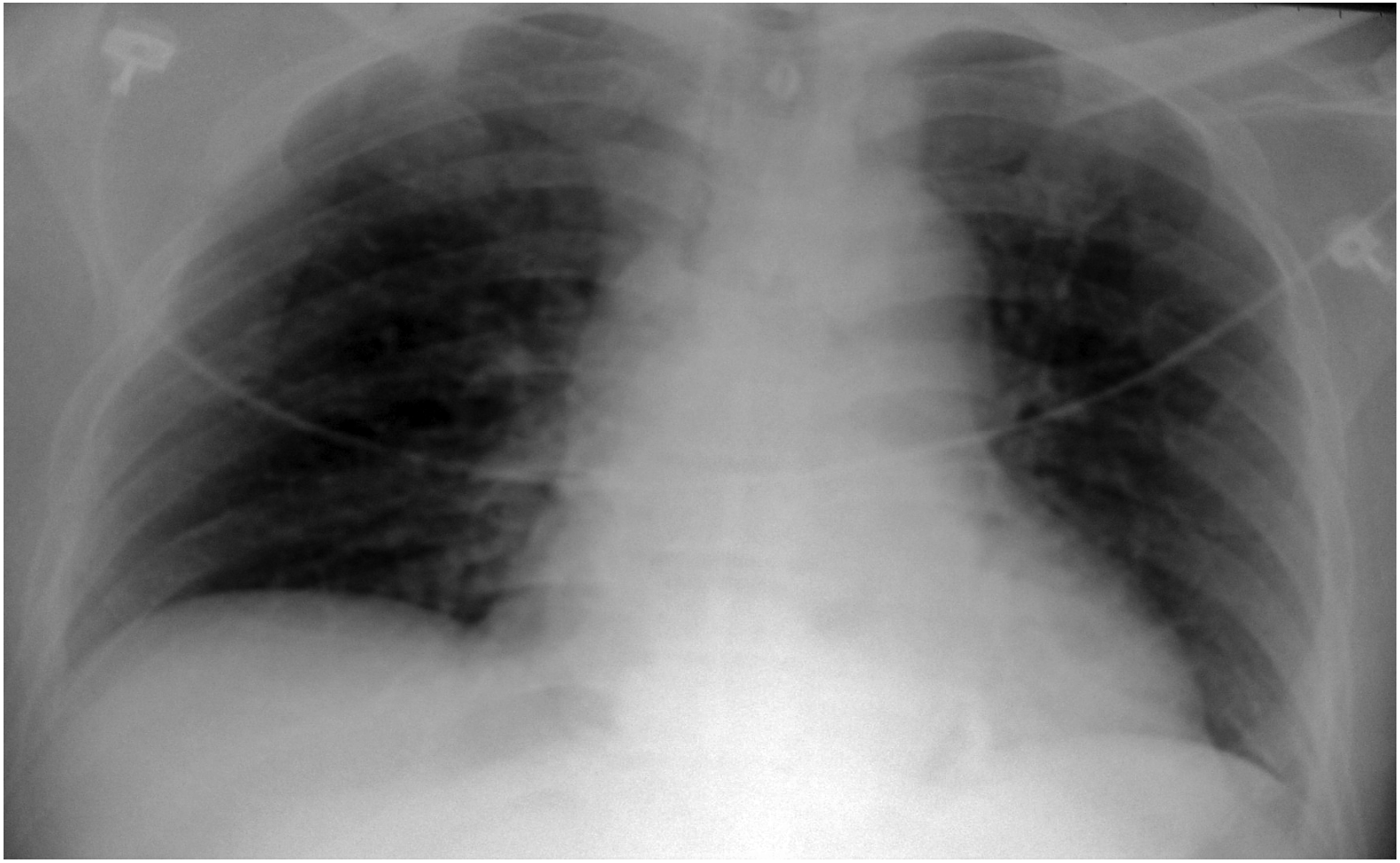
Examination

- GCS 3/15
- PERL 3 mm
- No neck rigidity
- No external wound
- No eyes deviation
- No rash
- No alcoholic smell

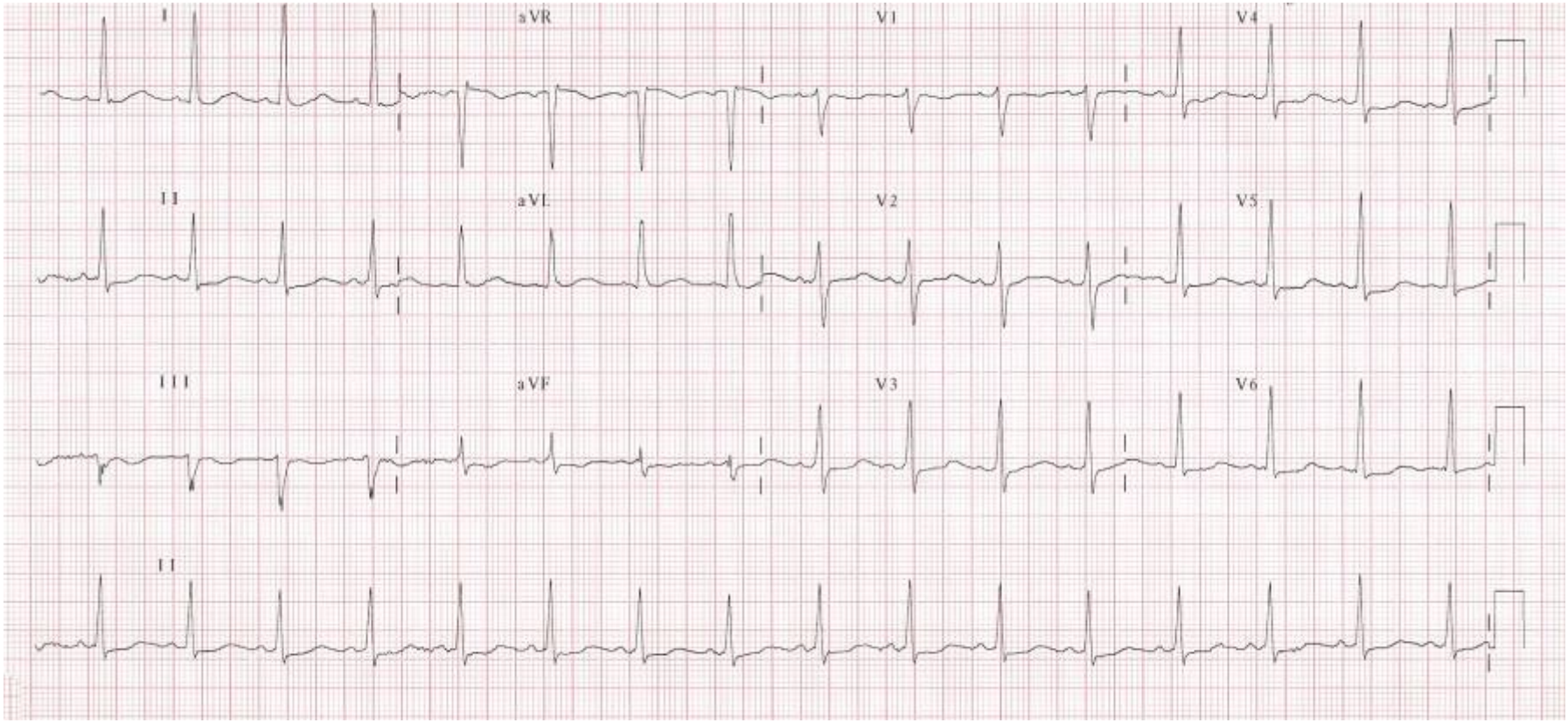
Examination

- Abdomen: soft, non tender, no malena
- Chest: clear
- HS I + II, no murmur

CXR



ECG



Progress

- Intubated for airway protection with mechanical ventilation
- Transferred to ICU
- Remained unarousable and unconscious after ICU admission

Common Causes of Altered Mental Status

- Infection
- Toxic
- Metabolic
- Hypoxemia
- Hypercarbia
- Cerebrovascular
- CNS
- Psychiatric

Approach to the Patient with Altered Mental Status

Approach to the Patient with Altered Mental Status

- Immediate interventions
- Primary survey
- Diagnostic studies
- Supportive care
- Secondary survey

Immediate Intervention

- Ensuring adequacy of airway, breathing, and circulatory function
- Correct systemic derangements
  - Hypertension / Hypotension
  - Hypoxemia
  - Anaemia
  - Hypothermia / Hyperthermia
  - Hyperglycemia
  - Acidosis

Immediate Intervention

- Hypertension
  - A nonspecific hyperadrenergic response to an acutely evolving intracranial or systemic process
  - In the comatose patient suggests elevated ICP, DO (amphetamines / cocaine), HT encelopathy
- Hypotension and shock
  - In comatose patient reflect noneurogenic mechanism of circulatory failure but also be a consequence of severe brain damage
- Acute respiratory failure
  - May occur secondary to airway obstruction, pulmonary aspiration, acute lung injury, or lesions affecting the pontine and medullary respiratory centers

Neurologic Examination

- To recognize the type of consciousness disorder and make inferences about its etiology
- A relatively rapid survey
  - The level of consciousness
  - Cranial nerve examination
  - Motor examination
  - Respiratory pattern

Neurologic Examination

- Important considerations of assessing the level of consciousness:
  - Assessment before sedative agents
  - Also be defined with regard to vital signs
  - Define the responses in descriptive terms rather than emphasising the numerical score

Neurologic Examination

- Presence of normal pupils confirms the integrity of the pupillary pathway (retina / optic n. / optic chiasma / midbrain / 3rd CN nuclei and nerves)
- Respiratory pattern
  - Bradypnoea (drug induced coma / hypothyroid coma)
  - Tachypnoea (central neurogenic hyperventilation / midbrain lesion / metabolic encephalopathy)
  - Cheyne Stokes respiration i.e hyperpnoea alternating regularly with apnoea (deep cerebral lesions / metabolic encephalopathy)
  - Apneustic breathing i.e an inspiratory pause (pontine lesions)
  - Ataxic breathing i.e ataxic breathing normally progresses to agonal gasps and terminal apnoea (medullary lesion)

How about our patient after ICU admission ?

Progress

- GCS remained 3/15 on ICU admission, nearly 12 hrs of unconscious
- Bilateral pupils
  - Were equal in size 3 mm
  - Demonstrated both direct and consensual light reflexes
- No abnormal eye movement / blinking
- No abnormal posture

Progress

- CBP normal
- LFT normal
- Na / K: 149 / 3.0 mmol/L
- Ur / Cr: 3.3 / 239 (Baseline Cr 78)
- Urine multistix: ketone +

Progress

- Random glucose: 8.4 mmol/L
- CK 1097 / LDH 344
- Serial TnI: normal
- Amylase: normal
- Ethanol / Paracetamol / Salicylate levels: not raised
- ABG (100% NRM)
  - pH 7.34, pCO_2 5.55, pO_2 35.99, BE -3.4, HCO_3 22.2, SaO_2 100%

Can he suffer from ……

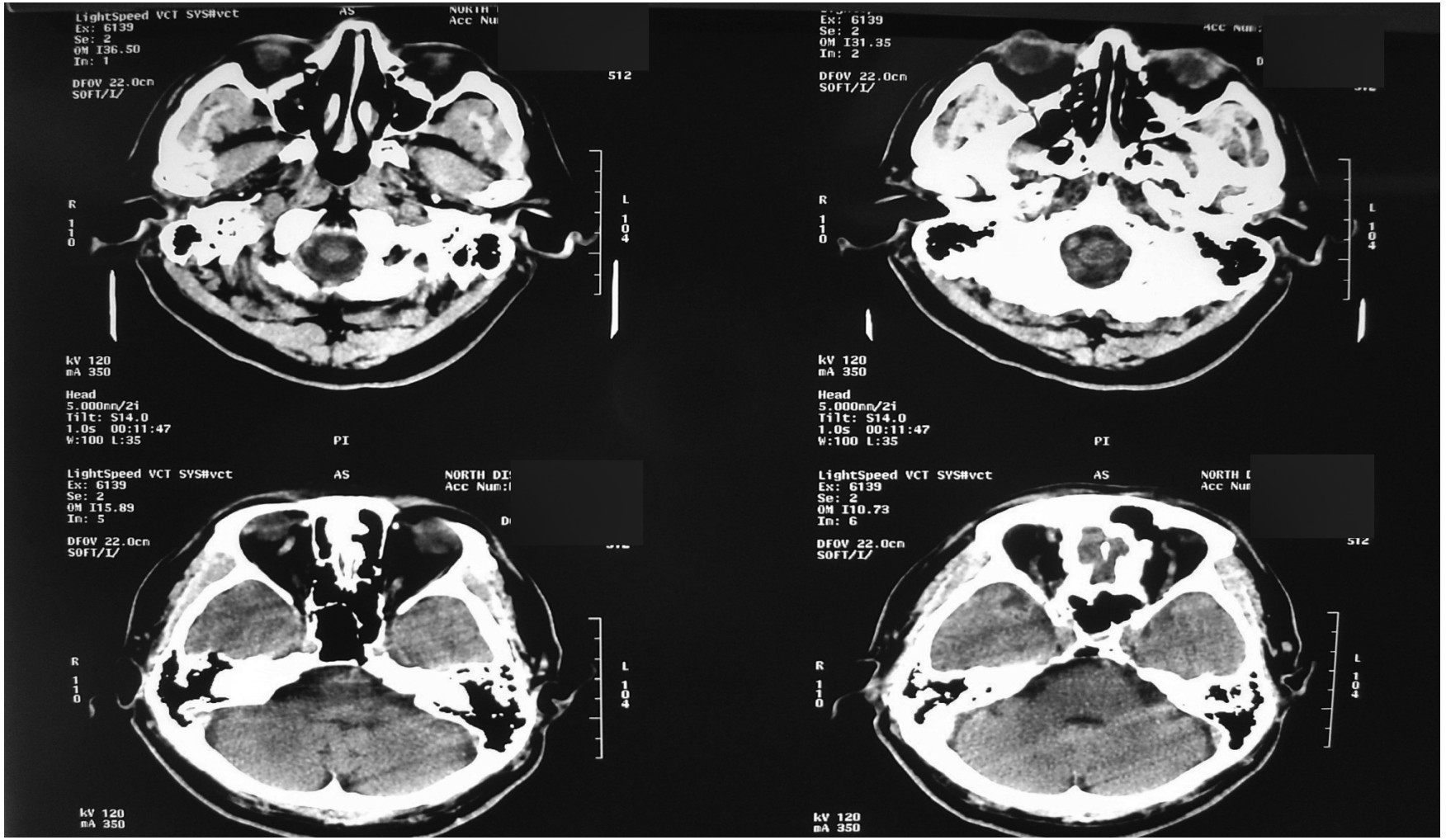
- Cerebrovascular events
  - Brainstem infarct
  - Intracranial haemorrhage
- Seizure
  - Non convulsive status epilepticus
- CNS infection

Can he suffer from ……

- Metabolic
  - Diabetic ketoacidosis
  - Hyperosmolar nonketotic coma
  - Electrolyte disturbance
- Drug overdose
  - Antidepressants
  - Ethanol
  - Methanol / Other toxic alcohol

What further tests can we do ?

CT Brain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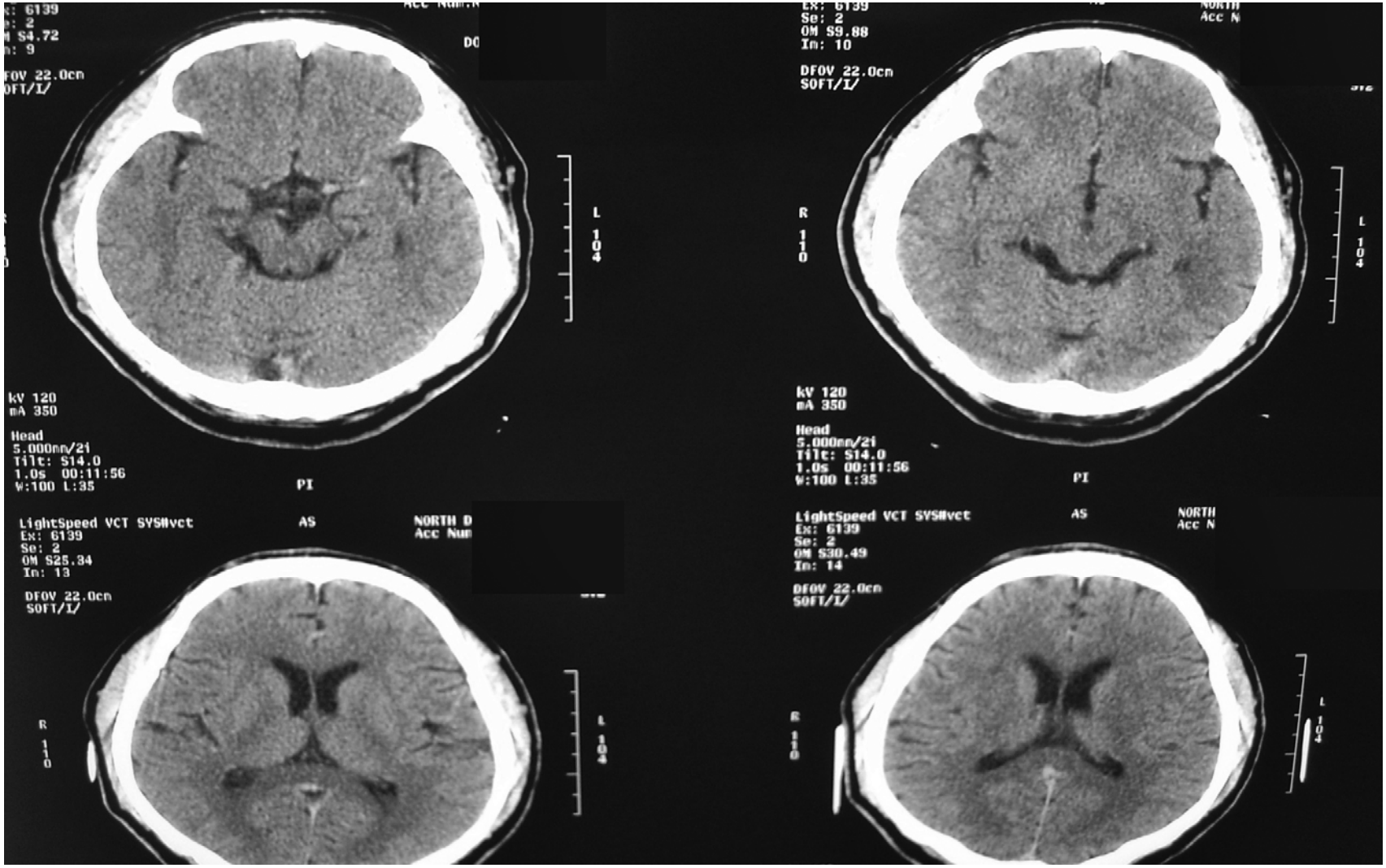
CT Brain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Progress

- Lumbar puncture
  - Not done
  - Because afebrile, no neck rigidity, and normal WCC
- Bedside continuous EEG
  - No epileptiform discharge

Progress

- No inotrope was needed
- No sedation was required
- CPAP ventilation using FiO2 0.4 with respiratory rate 15 breaths / min
- Urine output was maintained at about 60 ml / hr

Why was he so sleepy ?

What we learnt from CCM interhospital meeting before ?

The forgotten are ICU……Fertility? Hyperammonemia in the ICU

Courtesy slide from Dr. P Tsang (TMH A&IC)

Progress

- Serum valporate level: < 87 umol/L
- Ammonia: 24 umol/L

Valproate-related hyperammonemic encephalopathy

- Symptomatic hyperammonemia with valproate therapy is often referred to as VHE, and can sometimes occur without abnormalities of liver function tests
- VHE has the following characteristics:
  - Confusion, lethargy, vomiting, and increased seizure frequency
  - Progression to stupor, coma, and death may rarely occur

Valproate-related hyperammonemic encephalopathy

- Increases in plasma ammonia occur in nearly 50 percent of patients treated with VPA, and are asymptomatic in almost one half of cases
- Hyperammonemia is believed due to propionic acid, a metabolite of VPA, which inhibits mitochondrial carbamyl phosphate synthetase, an enzyme necessary for ammonia elimination via the urea cycle
- If the action of this enzyme is sufficiently impaired, ammonia levels will accumulate, producing encephalopathy

Valproate-related hyperammonemic encephalopathy

- Onset may be immediate with loading of VPA, or insidious with chronic VPA therapy
- The degree of encephalopathy is not clearly related to VPA serum levels, which may be in the normal range

Valproate-related hyperammonemic encephalopathy

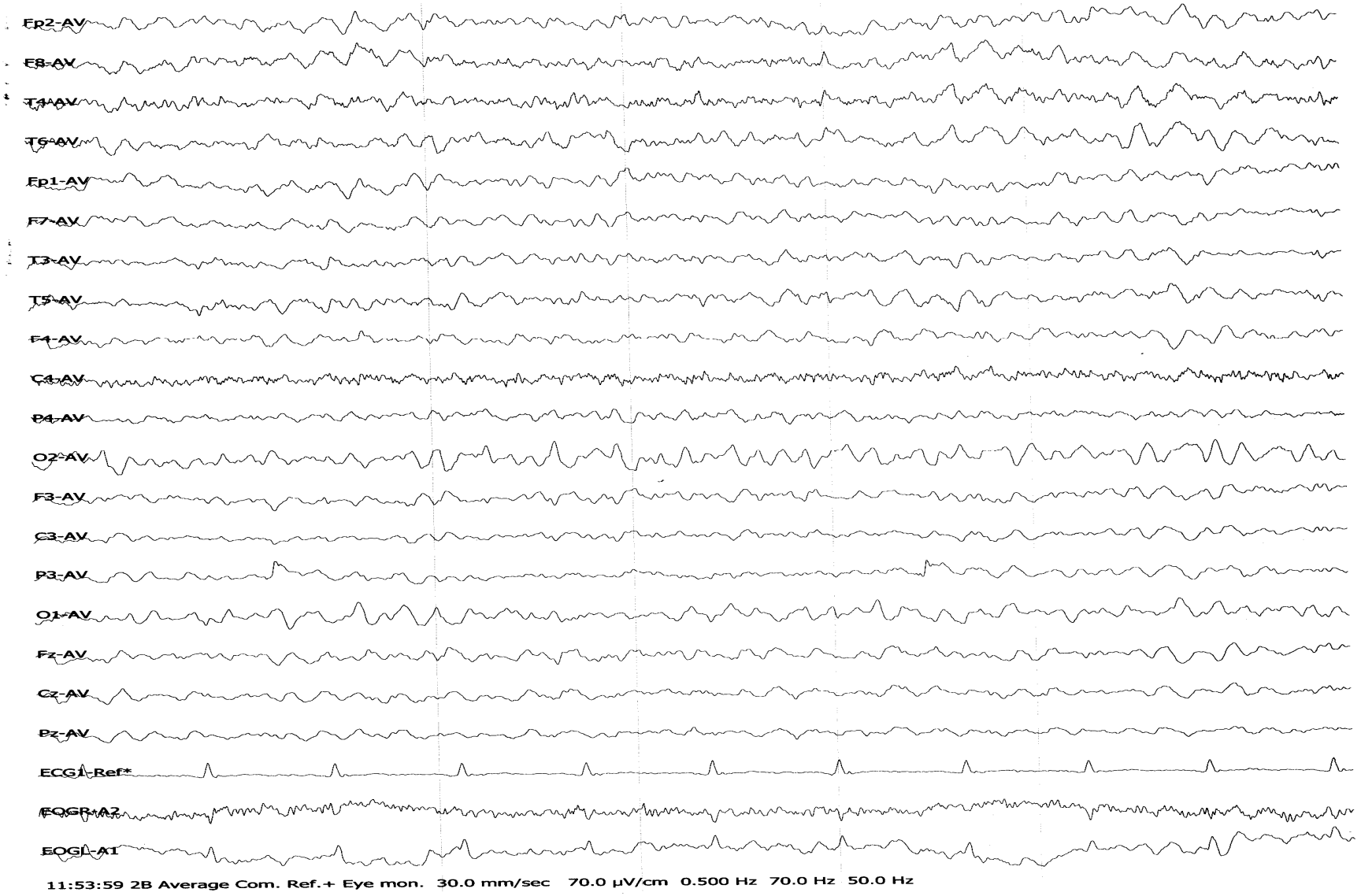
- Serum ammonia levels should be monitored if VHE is suspected clinically
- VPA should be discontinued immediately if serum ammonia is elevated
- VHE is more likely when VPA is used in combination with phenobarbitone, dilantin, carbamazepine

More Investigation ……

Urine

- Urine drug screen
  - Zopiclone, venlafaxine, chlorpheniramine and their metabolites were detected
- Urine myoglobin: negative

EEG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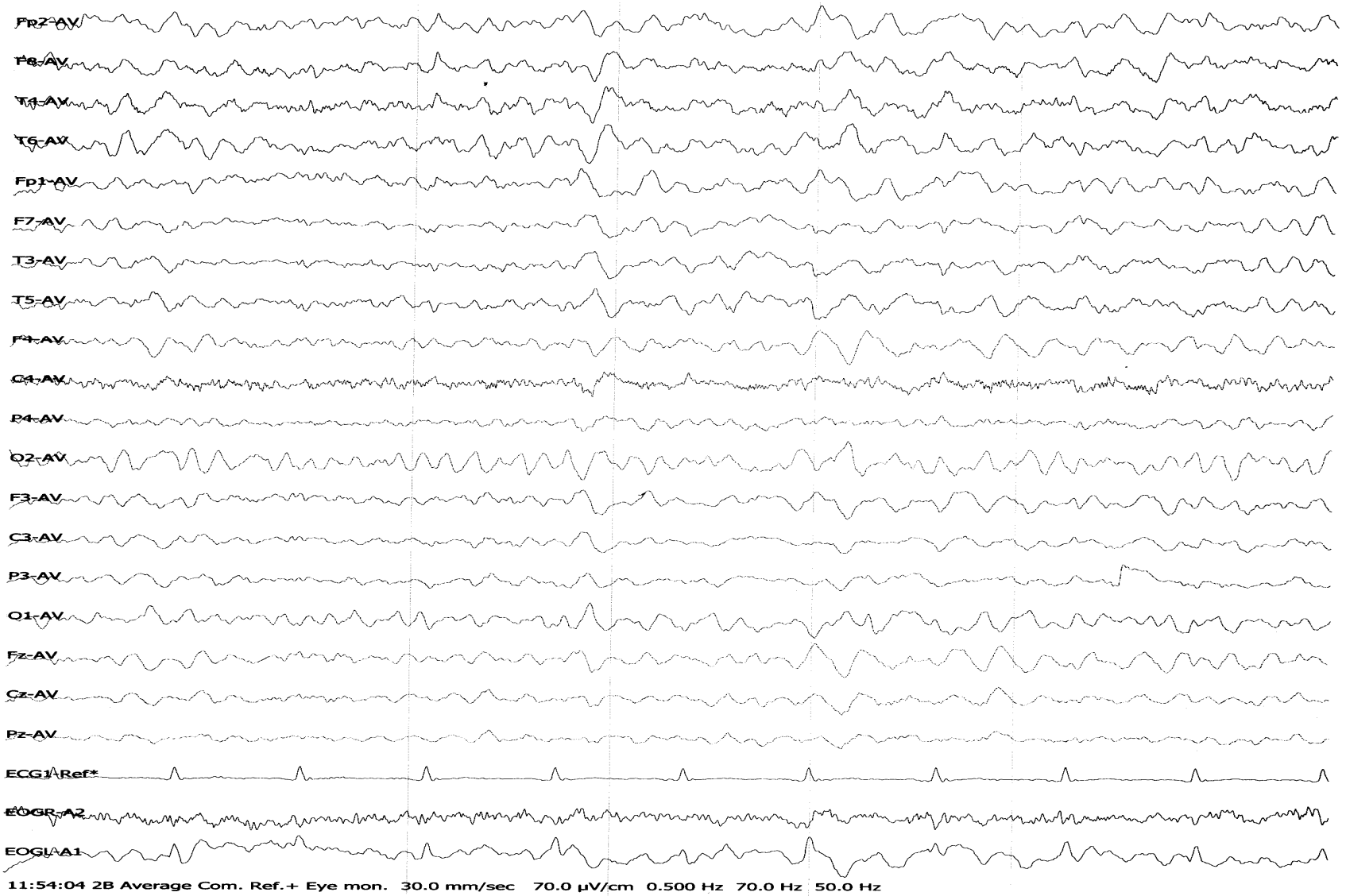
EEG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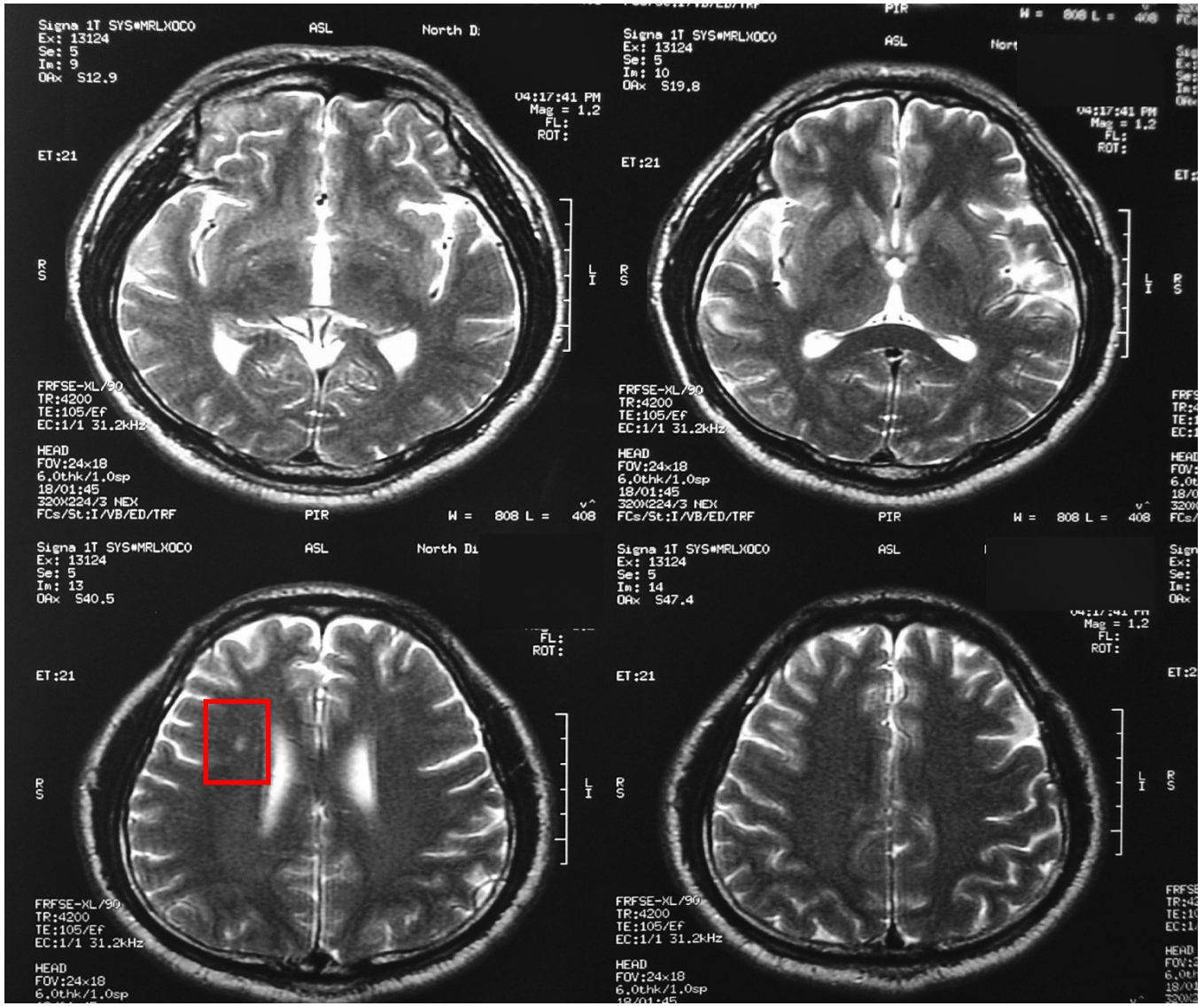
EEG

- EEG by neurology team:
  - Intermittent generalized slowing waves suggesting brain dysfunction
  - No definite epileptiform discharge
  - Imp: Brainstem dysfunction secondary to cerebrovascular accident / metabolic / ischemic / degenerative / infective causes

MRI Brain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Progress

- Our patient
  - Comatose (unarousable and unconscious for nearly 30 hrs)
  - Ketonuria
  - Acute kidney failure (Baseline Cr 78, on admission Cr 239)

What can we do?

Let’s go back to history taking

Progress

- Further history from patient's wife
  - Patient has habit of using disinfectant to soak his feet for the relief of severe itchy skin

Progress

- Osmolality
  - Measured: 364 mOsm / kg
  - Calculated: 328 mOsm / kg
- Osmolal gap
  - Elevated 364 – 328 = 36 mOsm / kg
- Anion gap 8 mmol / L

Progress

- Methanol level: < 3 mmol/L

Progress

- Our patient
  - Comatose
  - Ketouria
  - Acute kidney failure (Baseline Cr 78, on admission Cr 239)
  - High osmolar gap (36 mOsm / kg)
  - Normal anion gap

What was that disinfectant ?

Serum Toxic Alcohols Analysis

- Serum taken on admission:
  - Isopropanol 20 mmol / L
  - Acetone 30.8 mmol / L
- Serum taken 17 hrs after admission:
  - Isopropanol 1.8 mmol / L
  - Acetone 42.1 mmol / L

Isopropranol Intoxication

異丙醇中毒

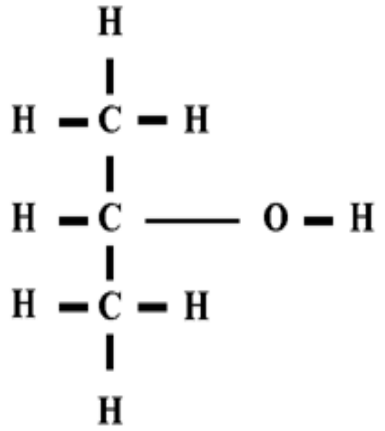
Progress

- Haemodynamically stable
- Patient regained consciousness gradually after nearly 40 hrs of coma
- Mechanical ventilator was weaned off
- Discharged to general ward
- But, he DAMA finally

Discussion

What is Isopropyl Alcohol ?

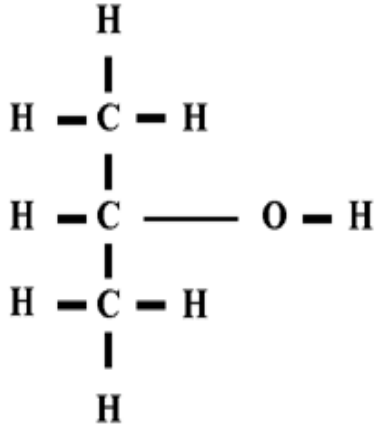
- An alcohol hydrocarbon derivative
- Also known as isopropanol異丙醇
- $(CH_3)_2CHOH$
- Water-soluble
- Volume of distribution
  that is equal to that of
  total body water (0.6 l/kg)
- Molecular weight of 60 g/mol



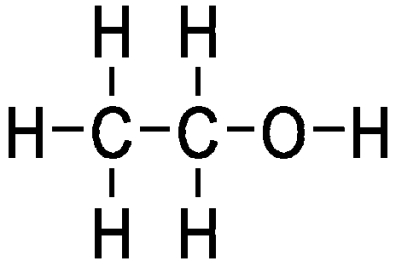
Isopropyl alcohol
C_3H_7OH

What is Isopropyl Alcohol ?

- A sedative-hypnotic agent whose toxicity closely resembles that of ethanol
- Similar structural formula with ethanol



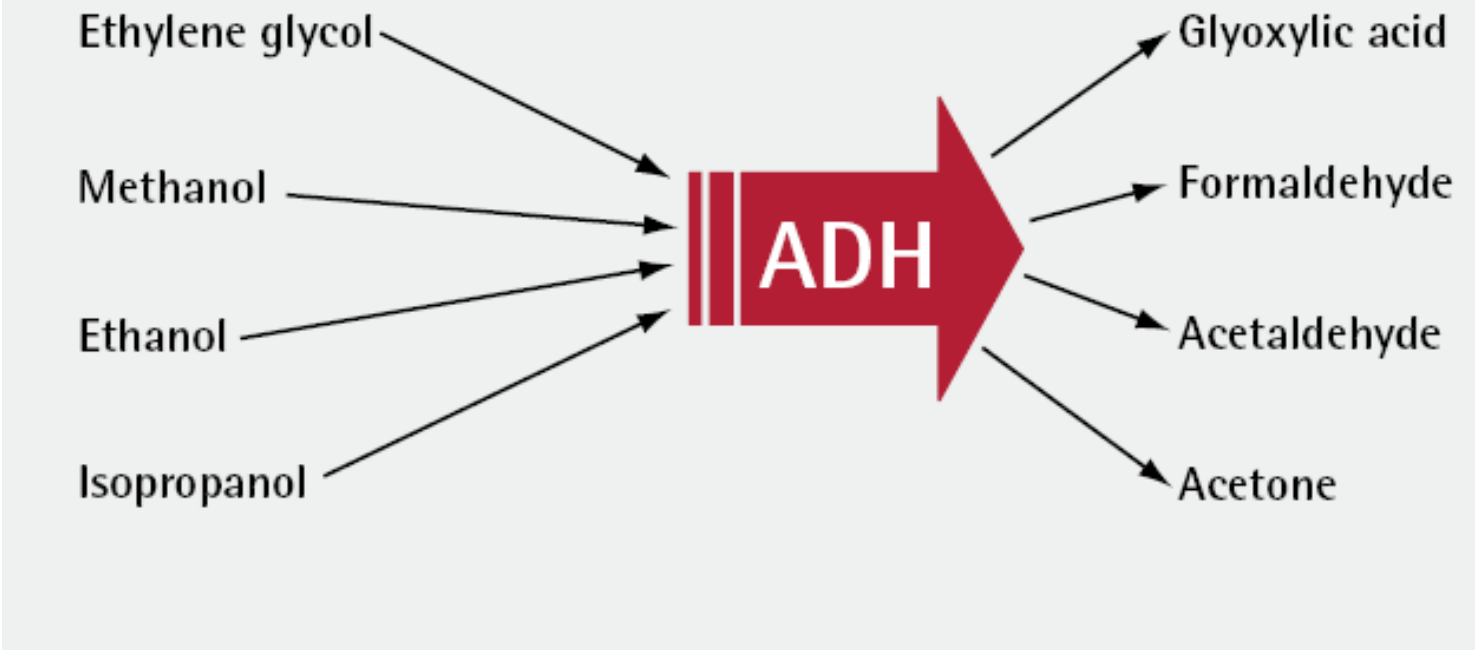
Isopropyl alcohol
C_3H_7OH



Ethanol
C_2H_5OH

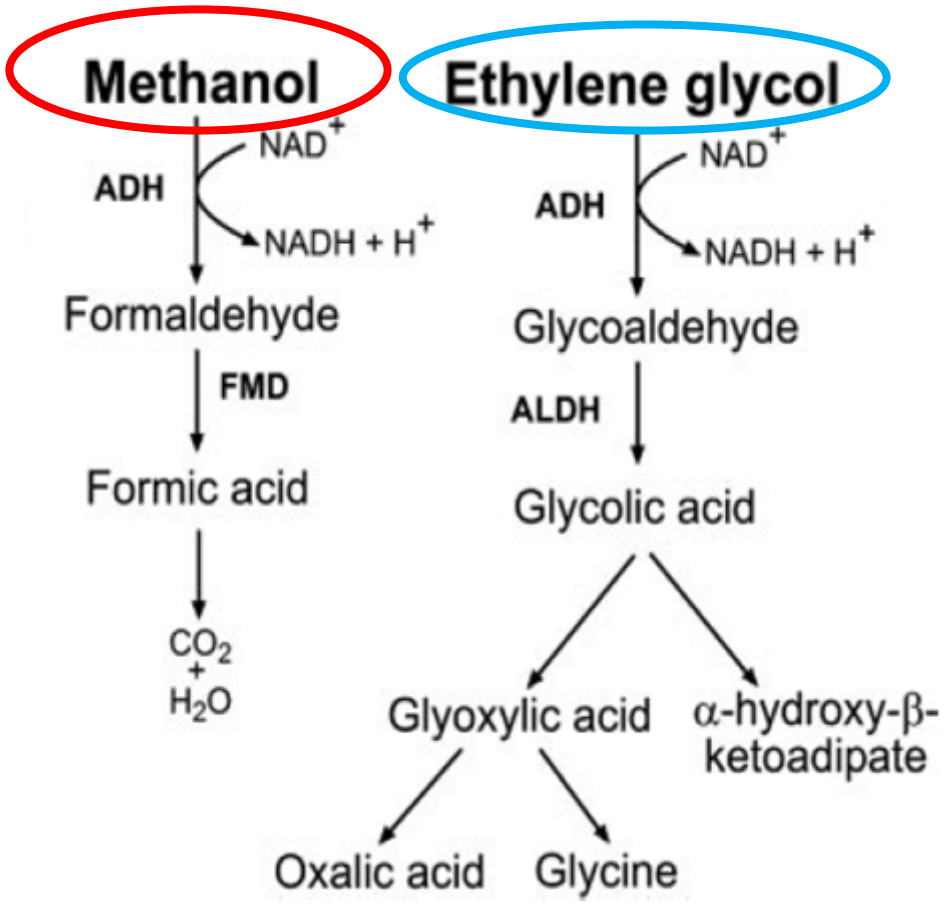
Pharmacokinetics of Alcohol

Figure 1. Metabolic pathway for alcohols via the enzyme ADH



ADH—alcohol dehydrogenase.
* Folic acid dependent.

Pharmacokinetics of Methanol & Ethylene Glycol



- Methanol and ethylene glycol are metabolized to aldehydes primarily via alcohol dehydrogenase
- These aldehydes are then oxidized via aldehyde dehydrogenase to the formic acid (methanol) and glycolic, glyoxylic, and oxalic acids (ethylene glycol)

Pharmacokinetics of Isopropyl Alcohol

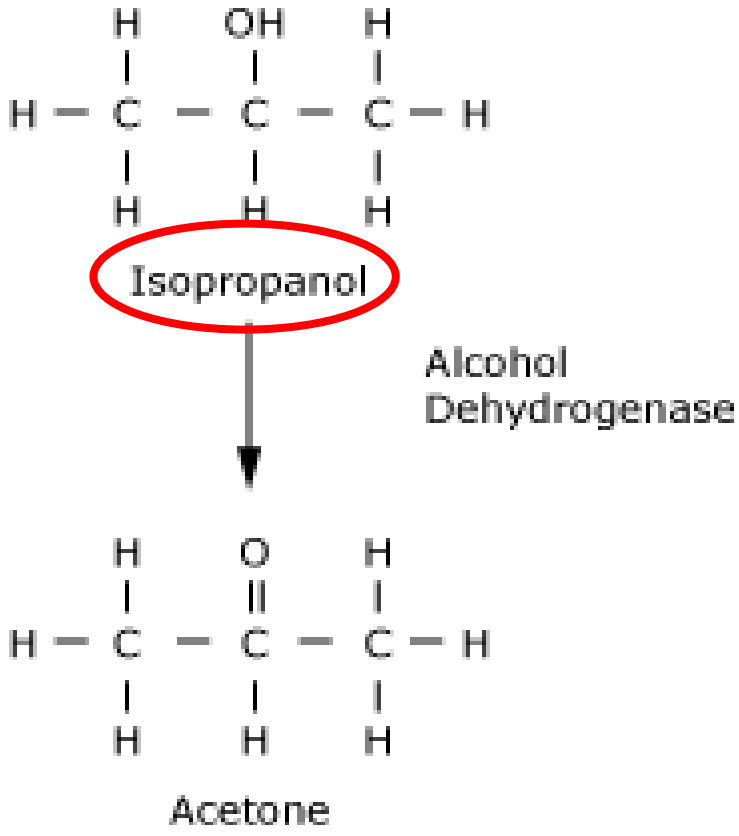
- Rapidly and completely absorbed following oral ingestion
- Peak serum concentration and clinical effects occur approximately 1 to 2 hours after ingestion

Specific symptom	No. of patients	Time of onset
Emesis	9	0.5–1 h
Ataxia	3	0.5–1 h
Lethargy	3	0.5–1 h
Obtunded	1	2 h
Apnea	1	2 h

Pediatr Emerg Care. 2000 Aug;16(4):238-40

Pharmacokinetics of Isopropyl Alcohol

- Isopropranol is metabolized by the alcohol dehydrogenase to acetone
- Acetones cannot be oxidized to carboxylic acids
- Therefore, only very limited acidemia



Pharmacokinetics of Isopropyl Alcohol

Table 3. Volume of distribution, route of elimination, and elimination kinetics of major alcohols

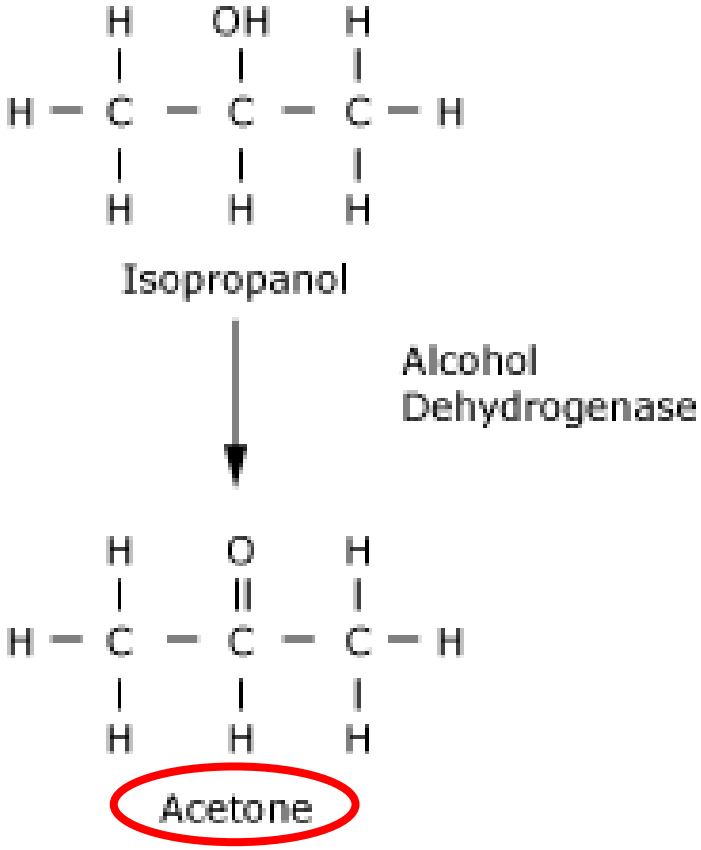
Alcohol	Volume of Distribution (L/kg)	Half-Life (h)[a]		Route of Elimination (%)		
		Alone	With Ethanol	Liver	Lung	Renal
Ethanol	0.5	2 to 6		95	2	3
Methanol	0.6 to 0.7	14 to 30	43 to 96	97	2.5	1
Ethylene glycol	0.5 to 0.8	3 to 8	17 to 18	80	–	20
Diethylene glycol[b]	0.5	4 to 6	?	30 to 50	–	50 to 70
Propylene glycol	0.5	1.4 to 3.3	17	55 to 75	–	25 to 45
Isopropanol	0.5	2.5 to 6.4	?	80 - 90	–	10 to 20

[a]Half-life is longer at the higher blood concentration found with intoxications as a result of saturation of alcohol dehydrogenase.
[b]Elimination kinetics not elucidated in humans; data on route of elimination and byproducts from studies in rats and dogs.

Jeffrey A. Kraut: Toxic Alcohol Ingestions: Clinical Features, Diagnosis, and Management. Clin J Am Soc Nephrol 3: 208–225, 2008

Pharmacokinetics of Isopropyl Alcohol

- The elimination of acetone
  - Is much slower, with a variable half-life of over 10 up to 30 hours
  - Due to excretion in the breath and urine



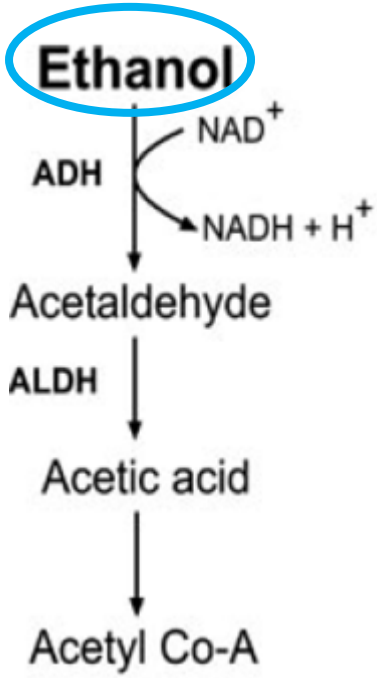
AU Jones AW SO: Elimination half-life of acetone in humans: case reports and review of the literature. J Anal Toxicol. 2000 Jan-Feb;24(1):8-10

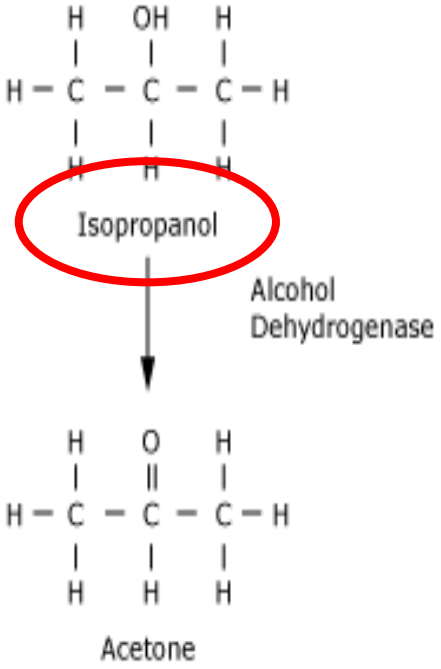
Pharmacokinetics of Isopropyl Alcohol

- Acetone
  - A mild CNS depressant, which exacerbates the CNS depression caused by isopropyl alcohol
  - It is also responsible for the marked ketosis that is present in most isopropyl alcohol ingestions

Pharmacokinetics of Isopropyl Alcohol

- The affinity of ADH for isopropyl alcohol is less than for ethanol
- When ADH inhibitors such as ethanol are present, the isopropyl alcohol clearance is reduced





Uses of isopropyl alcohol

- Can be used as
  - Disinfectant
  - Antifreeze
  - Solvent
  - Frost remover
  - Liquid detergent
  - Jewelry cleaner
  - Stain spot remover

Uses of isopropyl alcohol

- Rubbing alcohol swab: 70% IPA

- Glass window cleaner: 5-25% IPA

Routes of Exposure

- Oral
  - Oral ingestion of rubbing alcohols constitute the most common route of exposure
  - Accidental ingestion of rubbing alcohols / toiletries by children
  - Intentional ingestion for alcoholic effect, or in suicide attempts
  - Doses of above 20 mL may produce toxic effects

Routes of Exposure

- Inhalation
  - Inhalation of vapour from preparations
  - Inhalation may occur in children being sponged with isopropyl alcohol to control fever
  - Occupational or accidental exposure to liquid or its vapour

Routes of exposure

- Dermal
  - Dermal exposure to the liquid and vapour
  - Note risk of inhalation after prolonged skin exposure (sponging, etc.)

Routes of exposure

- Eye
  - Eye exposure to liquid and vapour
  - Both the liquid and solvent are severely irritant

Epidemiology

- In 1997, 1999, and 2004, a total of almost 27,000 exposures (most of them minor) were reported to poison control centersin United States; one third were in children who were younger than 6 y

2004 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 23: 589–666, 2004

Table 22A Demographic profile of exposure cases by generic category of substances and products: nonpharmaceuticals

	No. of Exposures	Age			Reason				Treated in Health Care Facility	Outcome				
		<6	6-19	>19	Unint	Int	Other	Adv Rxn		None	Minor	Moderate	Major	Death
Alcohols														
Ethanol: beverage	45370	1382	6412	37034	5662	37895	399	743	34191	4411	14117	9772	1810	97
Ethanol: other	8264	6340	721	1170	7927	274	36	19	522	2266	866	76	7	5
Higher alcohol	219	91	30	96	202	5	3	9	49	48	52	8	3	0
Isopropanol	7803	4558	676	2525	6623	1069	57	18	1698	2086	1409	387	56	5
Methanol	979	265	126	578	828	121	8	4	495	248	225	63	44	4
Rubbing alcohol														
Ethanol with methyl salicylate	12	11	1	0	12	0	0	0	1	3	1	0	0	0
Ethanol without methyl salicylate	280	194	18	68	257	18	1	4	40	82	25	7	1	0
Isopropanol with methyl salicylate	355	251	24	79	330	24	1	0	65	137	54	13	2	0
Isopropanol without methyl salicylate	3371	2272	224	868	3140	214	12	2	457	684	447	76	7	0
Unknown rubbing alcohol	6601	4029	534	2015	5676	828	55	17	1236	1596	1159	230	27	2
Other	548	413	48	84	532	10	0	4	44	160	54	7	1	0
Unknown	466	105	65	292	217	212	4	14	245	64	127	84	22	1
Category total	74268	19911	8879	44809	31406	40670	576	834	39043	11785	18536	10723	1980	114

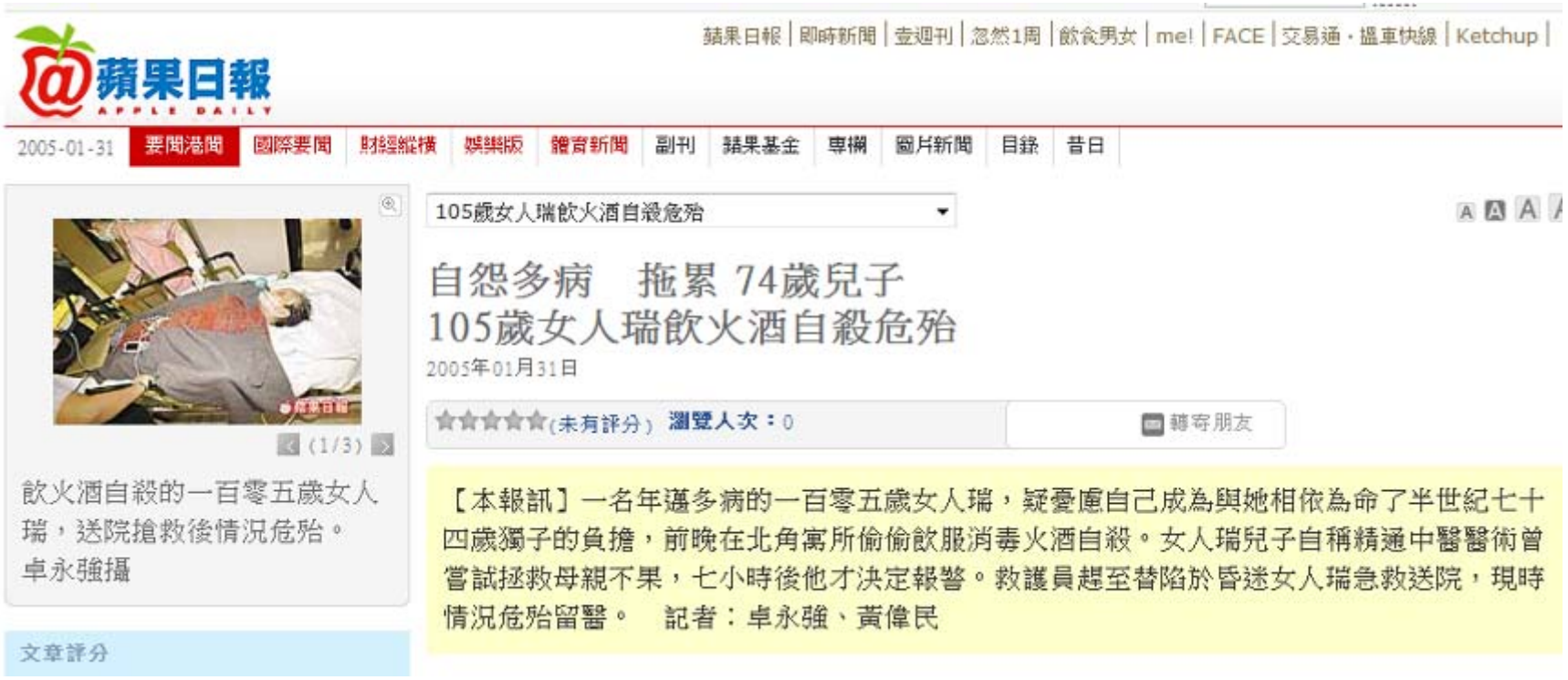
2004 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 23: 589–666, 2004

- More common than methanol intoxication
- Mortality is often less than methanol or ethylene glycol intoxication

- No effect:
  - The patient developed no signs or symptoms as a result of the exposure
- Minor effect:
  - The patient developed some signs or symptoms as a result of the exposure, but they were minimally bothersome and generally resolved rapidly with no residual disability or disfigurement
  - Often limited to the skin or mucus membranes (eg, self-limited gastrointestinal symptoms, drowsiness, skin irritation, first-degree dermal burn, sinus tachycardia without hypotension, and transient cough)

- Moderate effect:
  - The patient exhibited signs or symptoms as a result of the exposure that were more pronounced, more prolonged, or more systemic in nature than minor symptoms
  - Usually, some form of treatment is indicated
  - Symptoms were not life-threatening, and the patient had no residual disability or disfigurement (eg, corneal abrasion, acid-base disturbance, high fever, disorientation, hypotension that is rapidly responsive to treatment, and isolated brief seizures that respond readily to treatment)
- Major effect:
  - The patient exhibited signs or symptoms as a result of the exposure that were life-threatening or resulted in significant residual disability or disfigurement (eg, repeated seizures or status epilepticus, respiratory compromise requiring intubation, ventricular tachycardia with hypotension, cardiac or respiratory arrest, esophageal stricture, and disseminated intravascular coagulation)

How about in Hong Kong ?



蘋果日報 | 即時新聞 | 壹週刊 | 忽然1周 | 飲食男女 | me! | FACE | 交易通・搵車快線 | Ketchup |

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105歲女人瑞飲火酒自殺危殆

A A A A

自怨多病　拖累 74歲兒子
105歲女人瑞飲火酒自殺危殆

2005年01月31日

(1/3)

飲火酒自殺的一百零五歲女人瑞，送院搶救後情況危殆。
卓永強攝

(未有評分) 瀏覽人次：0

轉寄朋友

【本報訊】一名年邁多病的一百零五歲女人瑞，疑憂慮自己成為與她相依為命了半世紀七十四歲獨子的負擔，前晚在北角寓所偷偷飲服消毒火酒自殺。女人瑞兒子自稱精通中醫醫術曾嘗試拯救母親不果，七小時後他才決定報警。救護員趕至替陷於昏迷女人瑞急救送院，現時情況危殆留醫。　記者：卓永強、黃偉民

文章評分

How about in Hong Kong ?

明報 港聞 2006・09・11 星期一

編輯：梁敬欽

11/9/06 明報

酒精濃度50% 衞署已報警

火酒咳水醫生或遭控

【明報專訊】東涌西醫幸凌宇「火酒咳藥水」事件，涉錯的藥水火酒酒精濃度原來高達逾50%，基本上病童吃藥有如喝火酒。由於衞生署調查發現，幸凌宇配予病人的咳藥水本身亦未有註冊，署方已就事件向警方報案，並正研究控告他違反《藥劑業及毒藥條例》。

據幸凌宇向衞生署提供的資料，他曾將懷疑摻錯的「火酒咳藥水」處方予31名病人，衞生署目前仍未能與其中5人聯絡，而已聯絡病人中，6人曾不適，但現已無大礙。

咳藥水亦未經註冊

至於問題咳藥水火酒酒精成分，原來高得很驚人，消息人士透露，專家到醫院毒理參考化驗室化驗顯示，咳藥水含有逾50%火酒酒精成分，而一般的消毒火酒酒精成分約70%。衞生署長梁智鴻上周公布此事故時，亦形容事件問題咳藥水，單是用品嘗，也嘗到一陣火酒味。

雖然衞生署在幸凌宇診所搜出的3樽半原裝咳藥水，未發現含消毒火酒，但藥水含抗敏感藥物成分「氯苯那敏」（chlorpheniramine），濃度約爲每5毫升含9.2至9.9毫克而未經註冊，消息指衞生署已報警，正研究控告幸凌宇違反《藥劑業及毒藥條例》。

消息亦稱，正因原裝的咳藥水藥物成分濃度高，服用一格5毫升，相等於一次過吃2.5粒抗敏感藥piriton，故必須稀釋藥水才適合兒童服用，相信是次火酒消毒咳藥水事故，亦是因稀釋過程出錯引致。

醫學會草擬良好配藥守則

至於幸凌宇向衞生署指出，未經註冊咳藥水來自本地藥廠「煜寶製藥」，衞生署並未在廠內發現有關未註冊藥物，但仍調查是否有其他醫生同樣向其購入過有關未經註冊咳藥水。

醫學會會長蔡堅相信，是次事故可能是診所醫護人員與藥劑師用消毒藥物與藥水放在一起所致。

蔡堅又稱，該會正擬定一份有關《良好配藥守則》的執行情況問卷，以研究出有效的改善方法，預料1至2個月後有結果。

- A six-year-old boy complained burning sensation in the mouth after taking a transparent syrup medicine labeled “piriton” prescribed by a private medical practitioner on 5 September 2006
- Analysis of the syrup medicine revealed isopropyl alcohol in addition to piriton

Clinical presentation

- Isopropyl alcohol toxicity manifests with varying degrees of central nervous system (CNS) depression like drunkenness from ethanol
  - Inebriation
  - Disinhibition
  - Sedation
  - Stupor
  - Coma

Clinical presentation

- The gastrointestinal effects
  - include nausea, vomiting, abdominal pain, and haemorrhagic gastritis
- Patients with severe intoxication can present with hypotension
  - due to cardiac depression and vasodilatation

Clinical presentation

- Hypoglycemia
  - can result from the interference of gluconeogenesis by isopropyl alcohol
- Patients may have `fruity‘ breath
  - from the acetone elimination via respiration

Can we detect the toxin using commercial kit ?

曾蔭權與曾濫藥的學生座談後說，驗毒計劃不能再拖延，顯示出堅決的態度。

Diagnostic Clues

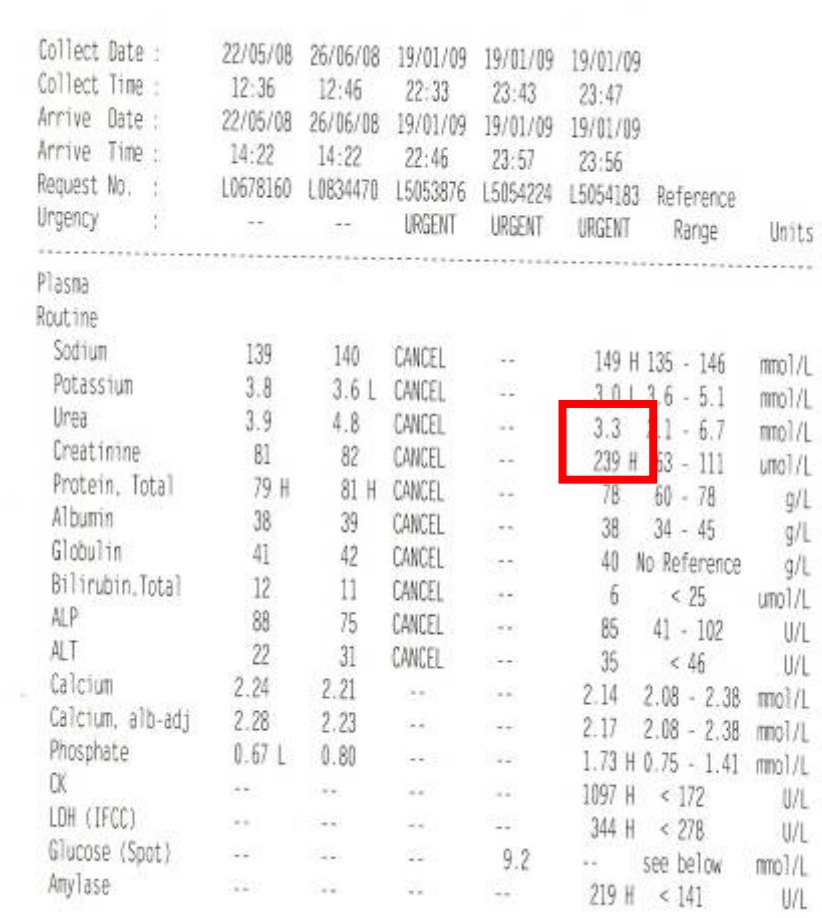
- The triad suggested the diagnosis
  - Normal acid-base parameters
  - Hyperosmolality
  - A positive nitroprusside reaction of urine and/or blood

Diagnosis

- Urine ketones will be positive in the presence of acetone
- Low concentrations of serum ketones exclude any significant isopropyl alcohol exposure
  - Unless < 2 hr of ingestion or co-ingestion of ethanol

Diagnosis

- Acetone concentration of 17.2 mmol/L or greater can falsely increase the serum creatinine
  - Thus, a high serum creatinine with a normal urea and pH suggests the possibility of acetonemia due to isopropyl alcohol ingestion



Collect Date :	22/05/08	26/06/08	19/01/09	19/01/09	19/01/09		
Collect Time :	12:36	12:46	22:33	23:43	23:47		
Arrive Date :	22/05/08	26/06/08	19/01/09	19/01/09	19/01/09		
Arrive Time :	14:22	14:22	22:46	23:57	23:56		
Request No. :	L0678160	L0834470	L5053876	L5054224	L5054183	Reference	
Urgency :	--	--	URGENT	URGENT	URGENT	Range	Units
Plasma							
Routine							
Sodium	139	140	CANCEL	--	149 H	135 - 146	mmol/L
Potassium	3.8	3.6 L	CANCEL	--	3.0 L	3.6 - 5.1	mmol/L
Urea	3.9	4.8	CANCEL	--	3.3	2.1 - 6.7	mmol/L
Creatinine	81	82	CANCEL	--	239 H	53 - 111	umol/L
Protein, Total	79 H	81 H	CANCEL	--	78	60 - 78	g/L
Albumin	38	39	CANCEL	--	38	34 - 45	g/L
Globulin	41	42	CANCEL	--	40	No Reference	g/L
Bilirubin,Total	12	11	CANCEL	--	6	< 25	umol/L
ALP	88	75	CANCEL	--	85	41 - 102	U/L
ALT	22	31	CANCEL	--	35	< 46	U/L
Calcium	2.24	2.21	--	--	2.14	2.08 - 2.38	mmol/L
Calcium, alb-adj	2.28	2.23	--	--	2.17	2.08 - 2.38	mmol/L
Phosphate	0.67 L	0.80	--	--	1.73 H	0.75 - 1.41	mmol/L
CK	--	--	--	--	1097 H	< 172	U/L
LDH (IFCC)	--	--	--	--	344 H	< 278	U/L
Glucose (Spot)	--	--	--	9.2	--	see below	mmol/L
Amylase	--	--	--	--	219 H	< 141	U/L

Diagnosis

- Metabolic acidosis is usually absent
  - Because neither the parent compound nor its metabolites are organic acids
  - Unless hypotension is sufficient to produce lactic acidosis

Causes of Elevated Osmolal Gap

TABLE I–22. CAUSES OF ELEVATED OSMOLAR GAP[a]

Acetone	Mannitol
Dimethyl sulfoxide (DMSO)	Metaldehyde
Ethanol	Methanol
Ethyl Ether	Osmotic contrast dyes
Ethylene glycol and other low-molecular-weight glycols	Propylene glycol
Isopropyl alcohol	Renal failure without dialysis
Magnesium	Severe alcoholic ketoacidosis, diabetic ketoacidosis, or lactic acidosis

[a]Osmolar gap = measured – calculated osmolality. Normal = 0 ± 5.

$$\text{Calculated osmolality} = 2[\text{Na}] = \frac{[\text{glucose}]}{18} + \frac{[\text{BUN}]}{2.8} = 290\ \text{mOsm/l}$$

Na (serum sodium) in meq/L; glucose and BUN (urea nitrogen) in mg/dL.

Osmolal Gap

- The osmolal gap
  - A serum level of isopropyl alcohol equal to 60 mg/dl (~10 mmol/L) will increase the serum osmolarity by 10 mOsm/L
  - Cannot distinguish among isopropyl alcohol, methanol, and ethylene glycol
  - Cannot be used to exclude the ingestion of these more toxic alcohols

Diagnosis

- Serum concentrations of isopropyl alcohol and acetone
  - To confirm the diagnosis
  - Can be quantified directly using gas chromatography
  - However, may not have rapid access to such testing

Toxic Concentration Levels

- Higher the blood levels of isopropyl alcohol will result poor outcome
  - > 25 mmol/L may produce coma and hypotension
  - > 33 mmol/L are incompartible with life

    Jeffrey A. Kraut: Toxic Alcohol Ingestions: Clinical Features, Diagnosis, and Management. Clin J Am Soc Nephrol 3:208-225
  - Some studies have suggested blood levels of 25 to 34 mmol/L can be associated with increased mortality

    Chan KM: Severe isopropanolemia without acetonemia or clinical manifestations of isopropanol intoxication. *Clin Chem 39: 1922–1925, 2993*
  - Some studies showed only blood concentrations of approximately 66 mmol/L were associated with a poor outcome

    Lacouture PG: Acute isopropyl alcohol intoxication: diagnosis and management. *Am J Med 75: 680–686, 1983*

Isopropyl Alcohol Intoxication

- High serum or urine isopropanol level
- High serum or urine acetone level
- Raised serum osmolality gap
- Marked ketonemia and ketonuria
- Absence of metabolic acidosis

Management

- Supportive management in general
- Assessment and stabilization of the airway, breathing, and circulation
- Endotracheal intubation for airway protection and avoiding aspiration
- Fluid resuscitation to correct any hypotension due to vasodilatation

Decontamination

- Gastric emptying procedures are not likely to be useful
  - If the ingestion is small or if more than 30 minutes has passed
  - Because isopropyl alcohol is absorbed rapidly after ingestion
  - Always examine history of chemical exposure before inducing emesis

Decontamination

- Activated charcoal (AC) can adsorb isopropyl alcohol and acetone
  - However, large doses may be required
  - No clinical evidence that charcoal therapy can shorten the half-life of isopropanol and acetone or decrease the duration of supportive care

Alcohol dehydrogenase (ADH) inhibition

- There is no indication for ADH inhibition with fomepizole or ethanol following isopropyl alcohol exposure
  - Because acetone (the primary metabolite) is less toxic than isopropyl alcohol (the parent alcohol)

Massive ingestion

- Rare patients with massive intentional ingestions may be haemodynamically unstable despite intravenous fluid and vasopressors
- Life-threatening isopropyl alcohol intoxication: is hemodialysis really necessary?

Massive ingestion

- Could be considered in exterme cases
  - An isopropanol level greater than 33 mmol/L
  - Renal failure
  - Refractory hypotension
- Hemodialysis will remove both isopropanol and acetone effectively
- No clinical evidence that haemodialysis improves outcome

Take Home Message

- Isopropyl alcohol containing solution is ubiquitous
- Triad suggesting the diagnosis
  - Raised serum osmolality gap / Marked ketonemia and ketonuria / Absence of metabolic acidosis
- Supportive treatment

Haemodialysis

- During HD, up to 400 mL of blood per minute passes through an extracorporeal circuit in which toxic compounds in blood diffuse through a semipermeable membrane down a concentration gradient into a dialysate
- Useful in removing toxins with the following characteristics:
  - Low molecular weight (<500 daltons)
  - Small volume of distribution (<1 L/kg)
  - Low degree of protein-binding
  - High water solubility
  - Low endogenous clearance (<4 mL/min per kg)
  - High dialysis clearance relative to total body clearance

Hemoperfusion

- Refers to the circulation of blood through an extracorporeal circuit containing an adsorbent such as activated charcoal or polystyrene resin
- Devices contain thin, highly porous membranes and adsorbents that provide a large surface area to directly bind toxins
- Clearance rates are higher with hemoperfusion than HD if the adsorbent binds the ingested toxin and drug clearance rates approach the rate of blood flow through the hemoperfusion circuit

End

Thank you