

The Kingdom of Cambodia
Nation Religion King



METHANOL POISONING

Cambodian National Guidelines
for Diagnosis and Treatment

Developed by

CDC, Ministry of Health Cambodia

In Collaboration with:

World Health Organization (WHO)

Médecins Sans Frontières (MSF)

Oslo University Hospital (OUH)

The Methanol Poisoning Initiative (MPI)

May 2019



World Health
Organization



MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS



Oslo
University Hospital

PREFACE

The present National Guidelines on Methanol Poisoning has been made possible by a collaboration between several institutions: The Cambodian Ministry of Health/The Communicable Disease Control Department (CDC), Calmette Hospital, Kratie Provincial Hospital, Department of Drug and Food (DDF), Khmer Soviet Friendship Hospital, China Cambodia Friendship Preah Kossamak Hospital, Kampong Cham Hospital, Kampong Chhnang Hospital, Médecins Sans Frontières (MSF/Doctors without Borders), the World Health Organization (WHO), Oslo University Hospital (OUH), and The Methanol Poisoning initiative (MPi; A collaboration between OUH and MSF).

Methanol poisoning is a global health threat killing thousands globally, as well as leaving patients blinded and/or with permanent brain damage. While this highly toxic substance also occurs regularly in Cambodia, it affects not only the patients, but also their families and whole societies, as the breadwinner often is the one being killed or disabled.

The diagnosis is typically difficult and the patients may easily be overlooked. Based on these concerns, an expert group were put together in order to make systematic, scientific based guidelines that could be implemented in areas with various – and often limited - available means of diagnosis and treatment.

It is with great enthusiasm I see this novel work developing in the Kingdom of Cambodia, which I also hope can be a model for other countries in the South East Asian region. It is, however, important to recognize that the job is not accomplished with the development of these guidelines: Now is the time for implementing the knowledge into daily practice.

My sincere acknowledgements go to the teams of the Communicable Disease Control department and the national- and regional hospitals of Cambodia that have seen the necessity of developing these guidelines. I also want to thank the Methanol Poisoning initiative (MPi) Oslo University Hospital, WHO, and MSF for their coordinating role, and for bringing in world leading expertise to put this all together.

I hope this guideline along with the implementation of trainings and adapted risk communications will save lives and health, and thereby benefit the patients and their families in the years to come.



Prof. ENG HUOT
SECRETARY OF STATE



Abbreviation

MoH	Ministry of health
CDC	Communicable disease control
DSB	Disease surveillance bureau
EDB	Essential drug bureau
DDF	Department Drug and Food
ICU	Intensive care unit
ED	Emergency department
GD	General medicine
CCFPKH	Cambodia-China Friendship Preah Kossamk hospital
KSFH	Khmer-Soviet Friendship hospital
RRT	Rapid Response Team
WHO	World health organization
MSF	Medecins Sans Frontieres
ADH	Alcohol dehydrogenase
RR	Respiratory rate
RF	Respiratory frequency
HD	Hemodialysis
IHD	Intermittent hemodialysis
CRRT	Continuous renal replacement therapy
CVVHD	Continuous veno-venous hemodialysis
CVVHDF	Continuous veno-venous hemofiltration
WBC	White blood cell
CRP	Creative reaction protein
ABG	Arterial blood gaz
OG	Osmolar gap
hrs	Hours
IV fluid	Intravenous fluid
BD	Base deficit
pH	Potential hydrogen

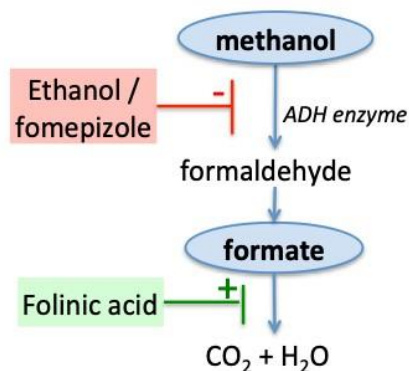
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METHANOL POISONING AT A GLANCE

1. Background/Mechanisms of toxicity:



Methanol is not toxic itself, but it is metabolised to the highly toxic formic acid/formate. Treatment focuses on blocking the enzyme (ADH) with **antidote** (either ethanol or fomepizole), **buffer** the metabolic acidosis with bicarbonate, and - if possible - using **dialysis** to remove methanol and formic acid/formate, as well as correcting the metabolic acidosis: Formic acid becomes more toxic the more acidotic the patient is.

Folic acid may also be given to enhance the endogenous (the body's own) metabolism of formate.

All of the above should be initiated as early as possible, but any of these treatments are important – **use what you have available**.

2. Diagnosis

A detailed history is very important: Can this be methanol? Intake of illegal/bootleg/spurious alcohol or alcohol of unknown origin, others in the environment (family or friends) with confirmed or suspect methanol poisoning (seriously ill, fatalities, blindness etc.).

Symptoms appear after 12-24 hrs or more (if shorter time from drinking to symptoms: Unlikely to be methanol).

Symptoms: *hyperventilation* (respiration frequency (RF) >20-25/min)/dyspnea, visual disturbances (of all kinds), gastrointestinal symptoms (frequently vomiting, but also gastric pain etc.), chest pain, severe/unusual “hangover” (feeling very sick 1-2 days after drinking).

Lab diagnosis: Diagnosis can be supplemented by the use of a blood gas analysis (see Flow-chart 2 below), by the specific analysis of the toxic metabolite formate (see Flow-chart 3 below) or by analysing for methanol itself (rarely available). Use of osmolal gap (OG) requires a special osmometer (freezing-point depression method) and will not be further mentioned in this text.

3. Management

3.1 Management of suspected methanol poisoning (no blood gas analysis (ABG) available – based on clinical signs and symptoms only. See also flow-chart 1):

- A) *Asymptomatic patients:* Observe for up to 24 hours (depending on level of suspicion).
- B) *Hyperventilation, no visual disturbances, conscious:* Give 1-2L of IV fluids (e.g. NaCl 0.9%) + Thiamine (e.g. 100mg or 250mg) + Glucose (e.g. 1000 mL of 50mg/mL (5%)) within 30-60 min. If acidosis is corrected/improved (less or no hyperventilation): likely alcoholic or diabetic ketoacidosis, not methanol poisoning. If not improved after 1 hr: Give ethanol/fomepizole and bicarbonate. Transport to dialysis facilities if possible. Observe min. 24 hours after treatment is terminated (see “Suggested dosing”).
- C) *Hyperventilation, visual disturbances, conscious:* Give ethanol/fomepizole, bicarbonate, folic acid, and transport to dialysis facilities if possible. Observe min. 24 hours after treatment is terminated (see “Suggested dosing”).



- D) *Hyperventilating, unconscious*: Give ethanol/fomepizole, bicarbonate, folic acid, and transport to dialysis facilities. Observe min. 24 hours after treatment is terminated (see “Suggested dosing”).
- E) *Normoventilating/slow breath, unconscious*: Likely poor prognosis if methanol poisoning. Be careful with ethanol in case this is an ethanol intoxication instead: Treat symptomatically, or treat as a methanol poisoning if definite suspicion.

3.2 Management of suspected methanol poisoning (when blood gas analysis (ABG) is available – based on patient blood gases. See also flow-chart 2):

- A) *Asymptomatic patients, normal blood gas*: Observe for up to 24 hours (depending on level of suspicion).
- B) $HCO_3^- > 15$ or $BD < 10$, pH typically > 7.2 : 1-2L IV fluids (e.g. NaCl 0.9%) + Thiamine (e.g. 100mg or 250mg) + Glucose (e.g. 1000 mL of 50mg/mL (5%)) within 60min. If acidosis is corrected/improved: likely alcoholic/diabetic ketoacidosis, not methanol poisoning. If not improved after 1 hr: Give ethanol/fomepizole and bicarbonate*). Transport to dialysis facilities if possible. Observe min. 24 hours after treatment is terminated (see “Suggested dosing”).
- C) $HCO_3^- 10-15$ or $BD 10-15$, pH typically 7.0-7.2: 1-2L IV fluids (e.g. NaCl 0.9%) + Thiamine (e.g. 100mg or 250mg) + Glucose (e.g. 1000 mL of 50mg/mL (5%)) within 60min. If acidosis is corrected/improved: likely alcoholic/diabetic ketoacidosis, not methanol poisoning. If not improved after 1 hour: Give Ethanol /Fomepizole and Bicarbonate*). Transport to dialysis facilities if possible. Observe min. 24 hours after treatment is terminated (see “Suggested dosing”).
- D) $HCO_3^- < 10$ or $BD > 15$, pH typically < 7.0 : Give ethanol/fomepizole and bicarbonate, hemodialysis, folic acid. Observe min. 24 hours after treatment is terminated (see “Suggested dosing”).

* Lower threshold for starting Bicarbonate + Ethanol in group C than B if acidosis worsening.

4. Treatment

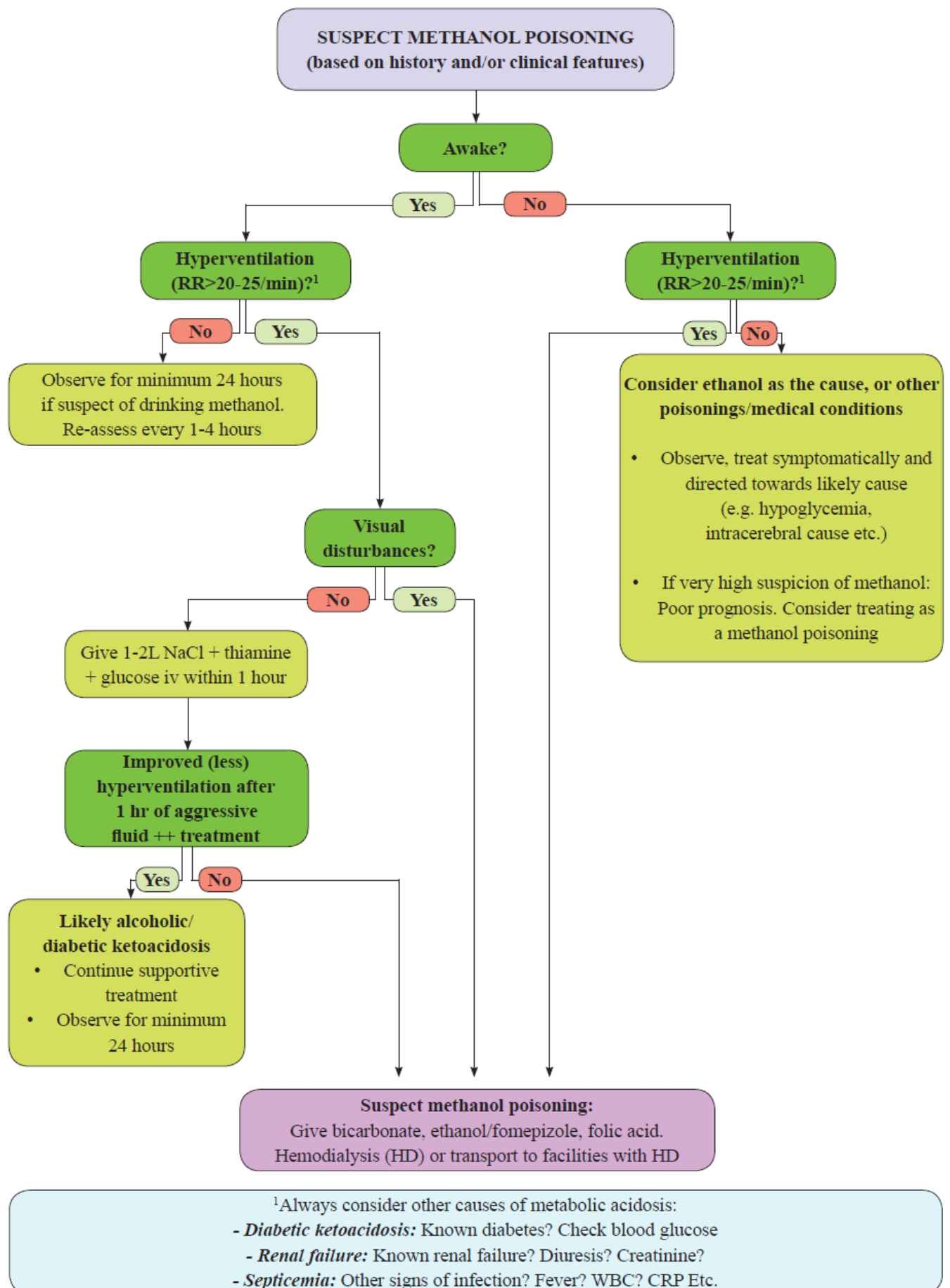
- A) Give **antidote** (Ethanol orally or intravenously or Fomepizole) without delay. *For dosing*: See below
- B) Give **Bicarbonate** ($NaHCO_3$) as soon as possible intravenously. *For dosing*: See below
- C) **Folic acid** (or Folinic acid) 50mg IV or orally (e.g. 10 tablets of 5mg) every 6 hours for 24-48 hours.
- D) **Dialysis**:
 - a) *Intermittent dialysis* (Intermittent Hemodialysis = high-flow dialysis/regular dialysis) for 6-8 hours, or
 - b) *Continuous dialysis* (CRRT/CVVHD/CVVHDF) for minimum 18 hours.
 - c) If dialysis is *not available*: Consider transferal to dialysis unit. Start antidote and bicarbonate if necessary before transport.
 - d) If *peritoneal dialysis* is available: Treat for at least 48 hours (lack of data to support this approach)
 - e) If *limited number of dialysers*: Consider rotating the dialysers between the patients: 1-2 hours each patient for initial stabilization– rotate – then rotate back
- E) If *intubation* is necessary: The patient must be hyperventilated ($RR > 25/min$) (until metabolic acidosis is corrected).

Prognostic aspects:

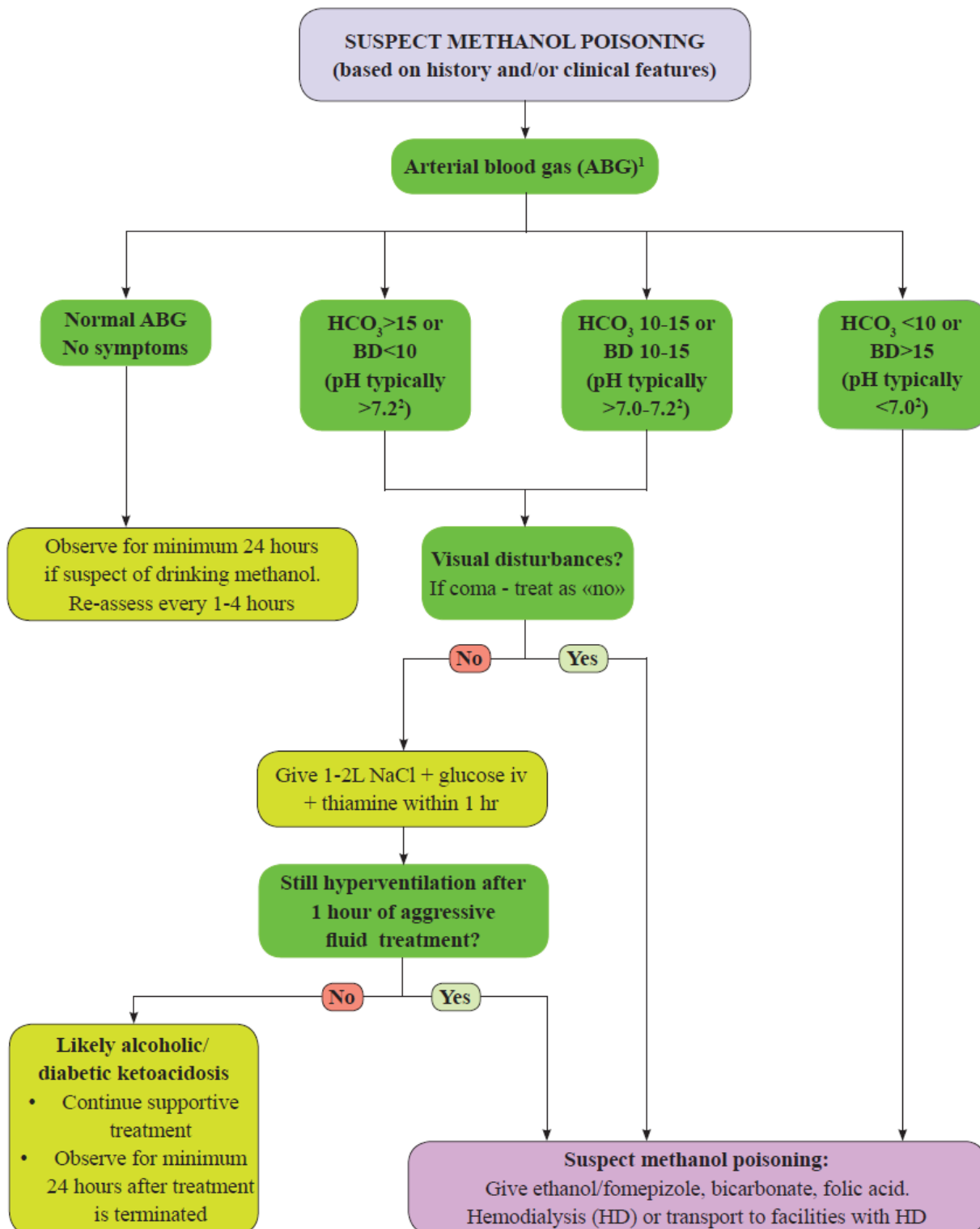
Coma on admission, severe acidosis ($pH < 6.9-7.0$ and $HCO_3^- < 10$ /base deficit > 20) and lack of hyperventilation in spite of the acidosis: Indicates poor prognosis if the patient is suffering from methanol poisoning, but pure ethanol intoxication or a combination of those may be a differential diagnosis.



5. Flow-chart 1: Diagnostic process when blood gas is not available



6. Flow-chart 2: Diagnostic process when blood gas is available



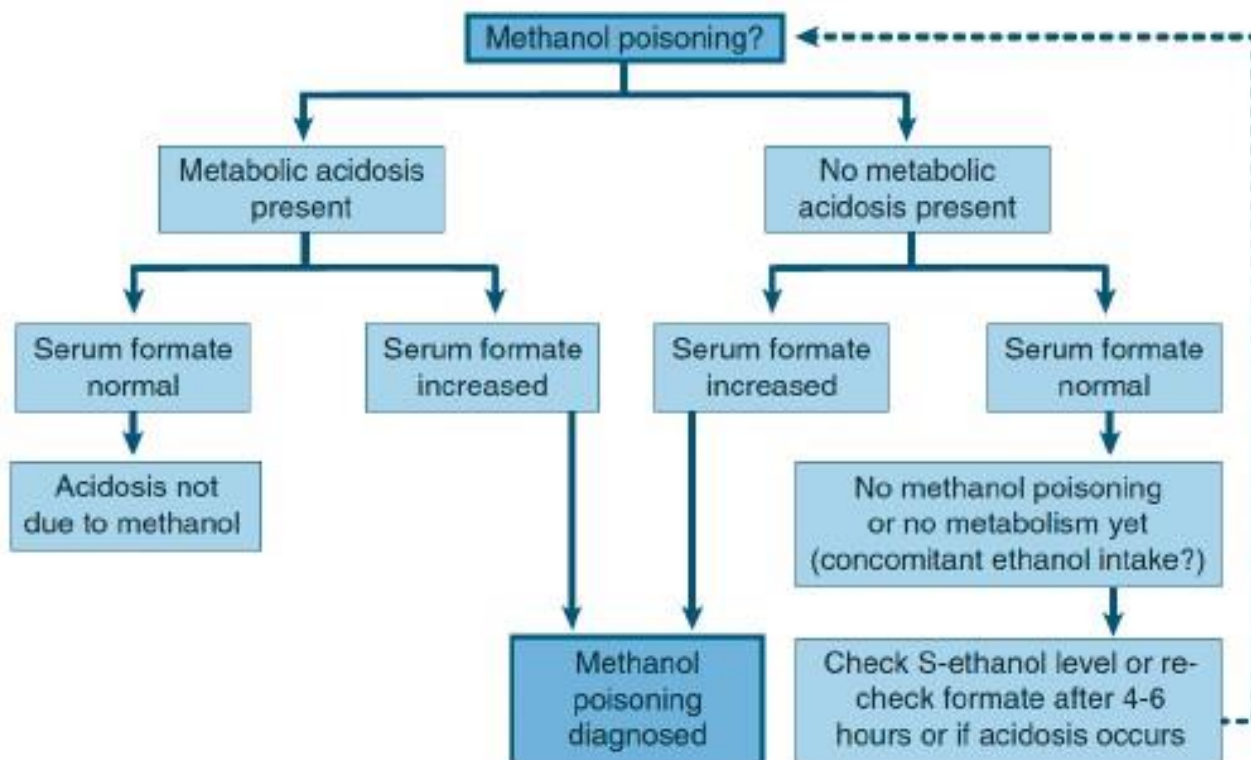
¹ Always consider other causes of metabolic acidosis:

- *Diabetic ketoacidosis*: Known diabetes? Check blood glucose
- *Renal failure*: Known renal failure? Diuresis? Creatinine?
- *Septicemia*: Other signs of infection? Fever? WBC? CRP etc.

² pH will always depend on degree of hyperventilation. therefore focus primarily on base deficit (BD) or HCO₃



7. Flow-chart 3: Clinical use of the formate assay (if available)



From: Hovda KE, McMartin KE, Jacobsen D. Methanol and formaldehyde poisoning.

In: Brent J, Megarbane B, Palmer R, Hatten B, Burkhart K (eds). Critical Care Toxicology, 2nd Edition. Springer Publishing, New York. 2017. 1769-86.



8. Treatment - suggested dosing regimen:

Treatment with antidote should be continued for 5-7 days if no dialysis is given.

Observe and re-assess for 24 hrs after treatment is terminated to make sure no new acidosis develops

Ethanol (be aware of individual differences and frequent under-dosing). Oral = IV dosing.

Rule of thumb: Beer contains 5%, wine 12-14% and spirits 40-45% Ethanol. Higher % can be used, but then dilution is recommended because of gastric irritation.

	5% ethanol	10% ethanol	20% ethanol	40% ethanol
Loading dose	15mL/kg	7.5mL/kg	4mL/kg	2mL/kg
Infusion rate (not regular drinker)	2mL/kg/hr	1mL/kg/hr	0.5mL/kg/hr	0.25mL/kg/hr
Infusion rate (regular drinker)	4mL/kg/hr	2mL/kg/hr	1mL/kg/hr	0.5mL/kg/hr
Infusion rate during HD (not regular drinker)	4mL/kg/hr	2mL/kg/hr	1mL/kg/hr	0.5mL/kg/hr
Infusion rate during HD (regular drinker)	6mL/kg/hr	3mL/kg/hr	1.5mL/kg/hr	0.8mL/kg/hr

HD = hemodialysis

FOMEPIZOLE (If available):

- Give 15mg/kg as a loading dose, then 10mg/kg every 12 hours. Increase dose to 15mg/kg after the 5th dose. *During dialysis: IHD: Dose every 4 hours. CRRT: Dose every 8 hours.*
- If fomepizole availability is limited; Treat primarily only for the first 24 hours (two or max three doses per patient), then continue with ethanol after 24 hours

BICARBONATE

- Calculate needs (based on ABG): **$0.3 \times \text{patient weight (kg)} \times \text{Base deficit} = \text{mmol HCO}_3^-$**
Example: Patient 70kg, Base deficit (BD) 30 mmol/L: $0.3 \times 70 \times 30 = 630 \text{ mmol HCO}_3^-$
- **If no arterial blood gas (ABG) is available:**
 - A) **1000mmol/L (8.4%)** (Cambodia): Give 7-15 ampoules 20mL of NaHCO₃ 8.4% or more within 1-2 hours until hyperventilation is corrected (RF <20 /min).
 - B) **500 mmol/L (4.2%)**: Give 250-500mL or more within 1-2 hours until hyperventilation is corrected (RF <20 /min).

FOLIC ACID:

(or Folinic acid) 50mg iv or orally (e.g. 10 tablets of 5mg) every 6 hours for 24-48 hours



When to call for assistance:

If there are patients with a strong suspicion of methanol poisoning, call the provincial rapid respond team (RRT), local referral hospital or hotline **115**, for advice and to discuss possibilities for intervention.

One of the most important reasons for this is the possibility to identify toxic alcohol in the environment, start early treatment AND *be able to warn the public about the possible danger.*

Where there is one there are usually many.

