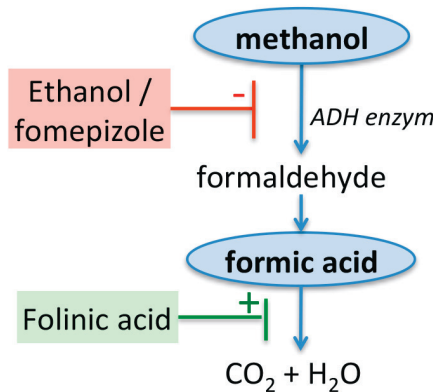


# METHANOL POISONING AT A GLANCE

## Background/Mechanisms of toxicity:



Methanol is not toxic itself, but it is metabolised to the highly toxic formic acid. Treatment focuses on blocking the enzyme (ADH) with antidote formic acid/formate., buffering the metabolic acidosis with bicarbonate, and - if possible - using dialysis to remove methanol and 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 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.**

## 1. 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 with confirmed or suspect methanol poisoning (seriously ill, fatalities, blindness etc.).

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

**Symptoms:** *hyperventilation* (respiration frequency (RF) >20-25/min)/dyspnoea, 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.

## 2. Management

**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, 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, 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.

### **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)  $HCO_3^- > 10$  or  $BD < 15$ , *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 60 min. 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”).

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.*

## **3. 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 hrs.

D) Dialysis:

- a. *Intermittent dialysis* (IHD = 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 transferral 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

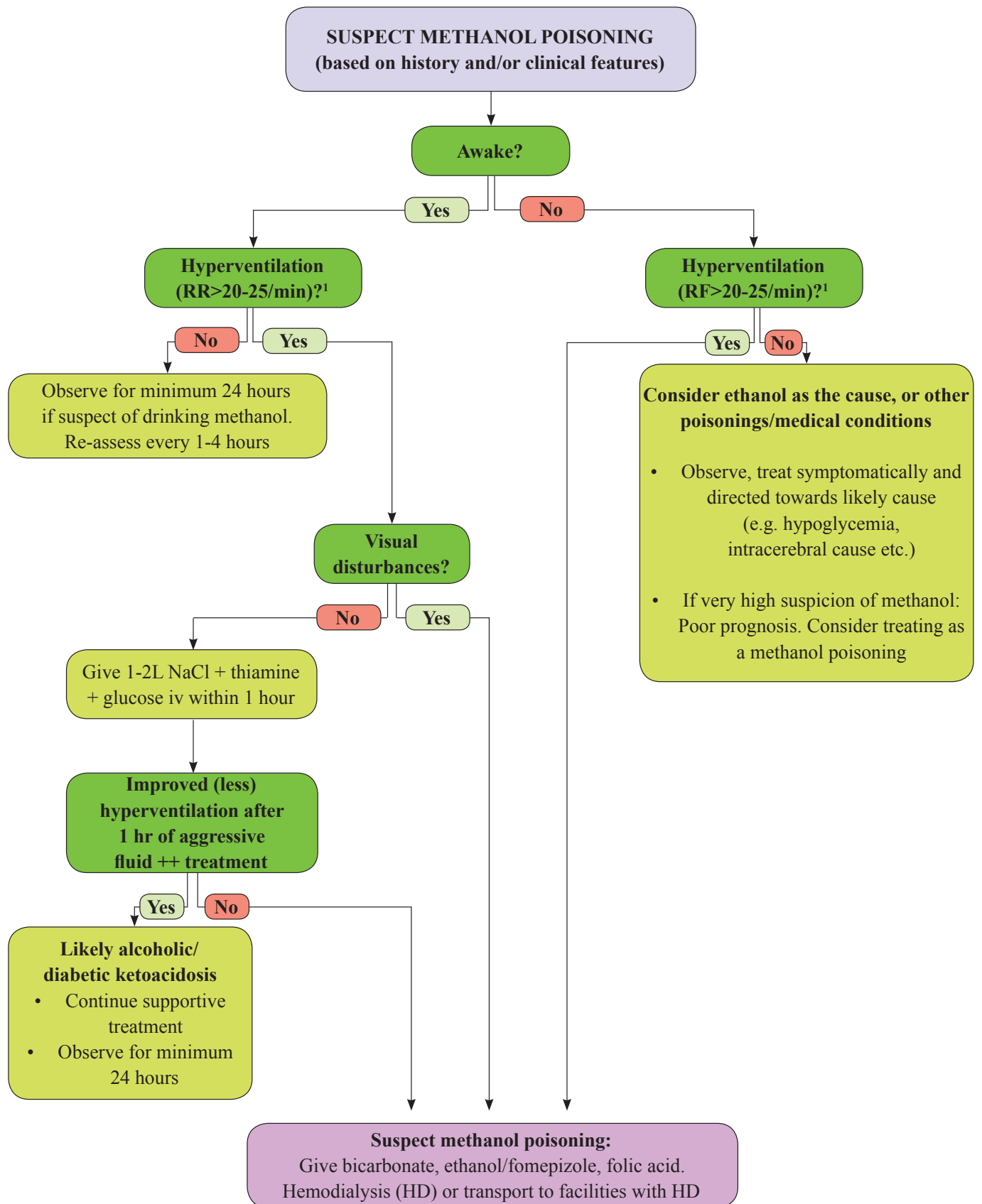
E) If *intubation* is necessary: The patient must be hyperventilated (RF >25/min) (until metabolic acidosis is corrected).

### **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.

## 4. Flow-chart 1

### Diagnostic process when blood gas is not available

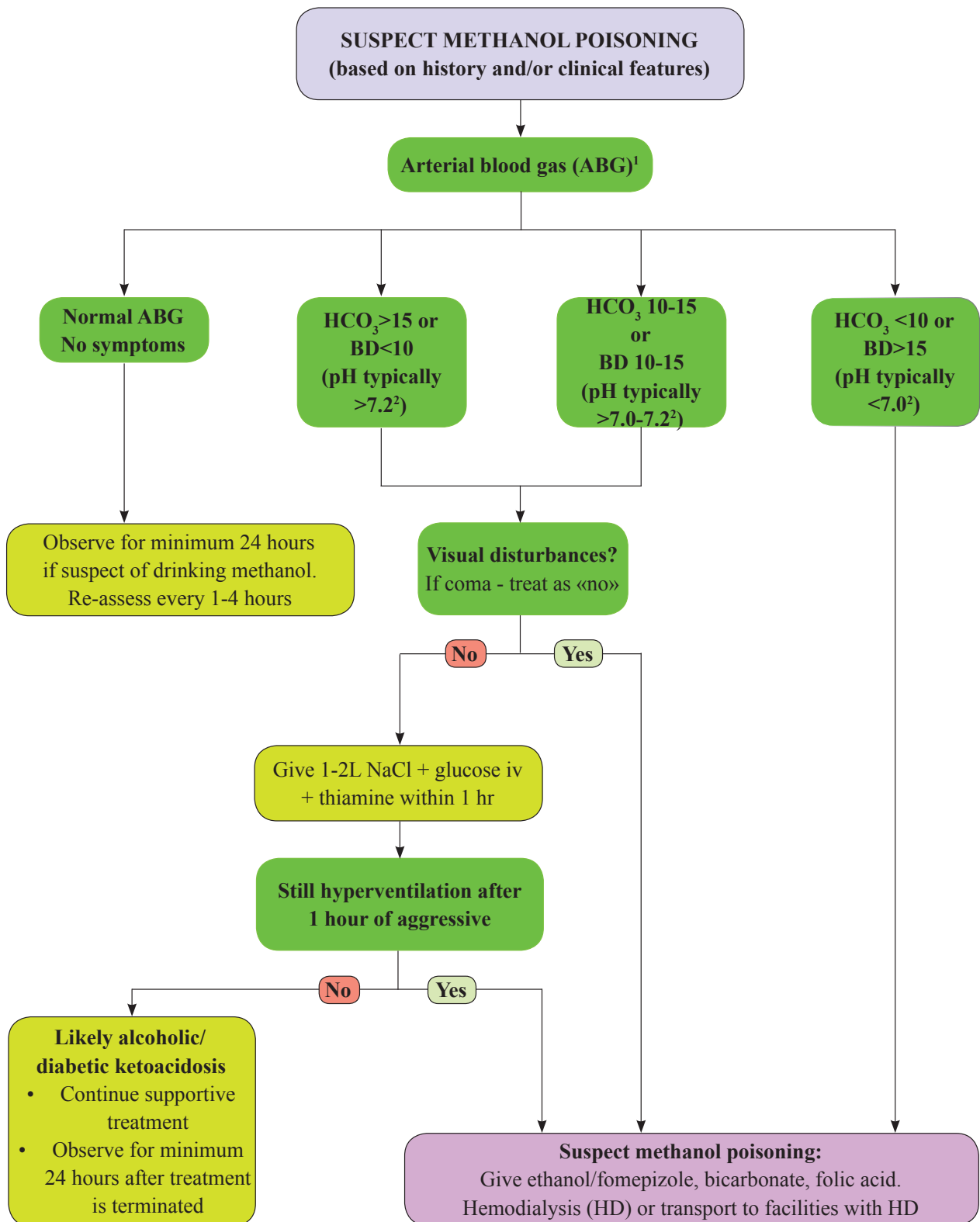


<sup>1</sup>Always consider other causes of metabolic acidosis:

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

## 5. Flow-chart 2

### Diagnostic process when blood gas is not available



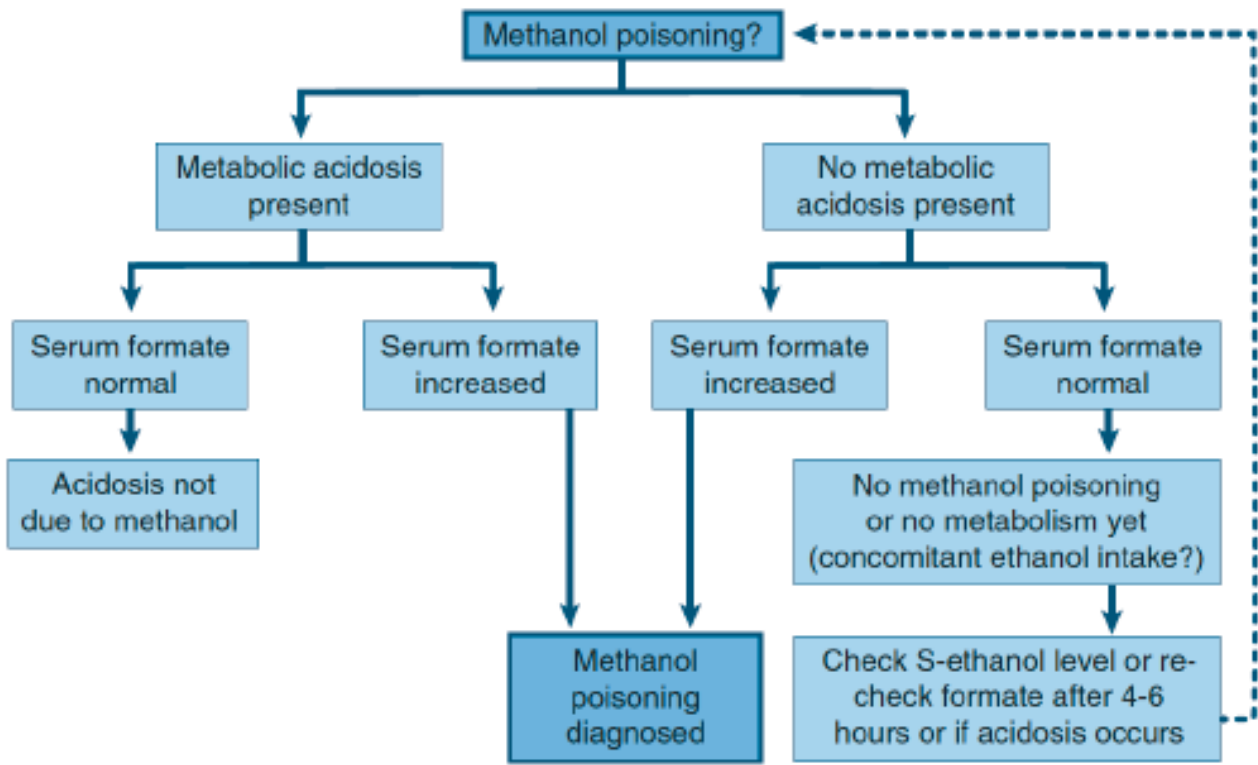
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<sup>2</sup> pH will always depend on degree of hyperventilation. therefore focus primarily on base deficit (BD) or HCO<sub>3</sub>

## 6. 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.

## 7. 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.

|   | 5% ethanol | 10% ethanol | 20% ethanol | 40% ethanol  |
|---|------------|-------------|-------------|--------------|
| <b>Loading dose</b>                                     | 15mL/kg    | 7.5mL/kg    | 4mL/kg      | 2mL/kg       |
| <b>Infusion rate</b><br>(not regular drinker)           | 2mL/kg/hr  | 1mL/kg/hr   | 0.5mL/kg/hr | 0.25mL/kg/hr |
| <b>Infusion rate</b><br>(regular drinker)               | 4mL/kg/hr  | 2mL/kg/hr   | 1mL/kg/hr   | 0.5mL/kg/hr  |
| <b>Infusion rate during HD</b><br>(not regular drinker) | 4mL/kg/hr  | 2mL/kg/hr   | 1mL/kg/hr   | 0.5mL/kg/hr  |
| <b>Infusion rate during HD</b><br>(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 5<sup>th</sup> dose. **During dialysis: IHD:** Dose every 4 hours. **CRRT:** Dose every 8 hrs.
- 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 70 kg, 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%)** : Give 7-15 ampoules 20mL of NaHCO<sub>3</sub> 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 local referral hospital 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.**