

Metabolic Encephalopathies



Comparative
Neurology
Program

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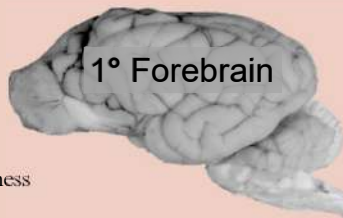
Metabolic Encephalopathy

- Altered brain function due to metabolic dysfunction
 - Acquired metabolic disease
 - Inborn errors of metabolism



Signs of Metabolic Encephalopathy

- Behavior changes
- Altered consciousness
- Seizures
- Ataxia



Metabolic **E**ncephalopathies made **E**asy

- Inborn **E**rrors of metabolism
- E**nergy
- E**lectrolytes
- E**ndocrine
- E**ndogenous toxins

Missy FS DLH

- 10 months old
 - Wax/wane disorientation & imbalance
 - Normal liver function
 - Low protein diet → normal
- 4 years old switched to “Natural” seafood diet
 - Disorientation, imbalance, excessive grooming
 - Progressed to stupor with intact brainstem reflexes



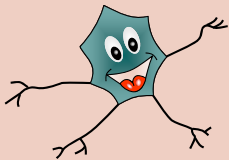
Kelmer, E. *et al.* *JVECC* 17, 299-304 (2007).

Missy

- ↑ Anion gap (26 mmol, ref 10 - 23)
- Venous blood gas
 - ↓pH (7.239 ref 7.300 ± 0.087)
 - ↓pCO₂ (15.1 mmHg, ref 41.8 ± 9.12)
 - ↓HCO₃ (6mmol/L, ref 19.4 ± 4.0)
- 2+ Ketonuria

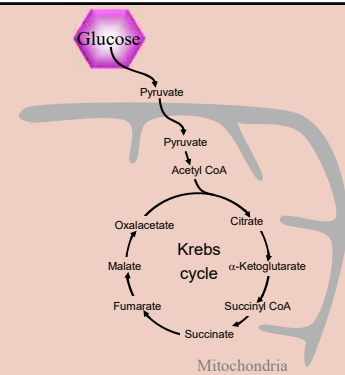


Energy for Excitement



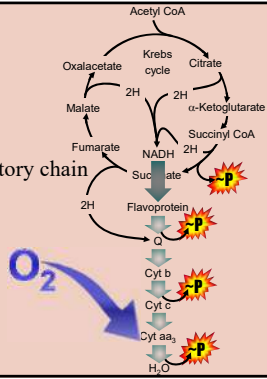
- Neurons are excitable
- Brain ~2% of body wt
- Consumes 20% of energy

Energy

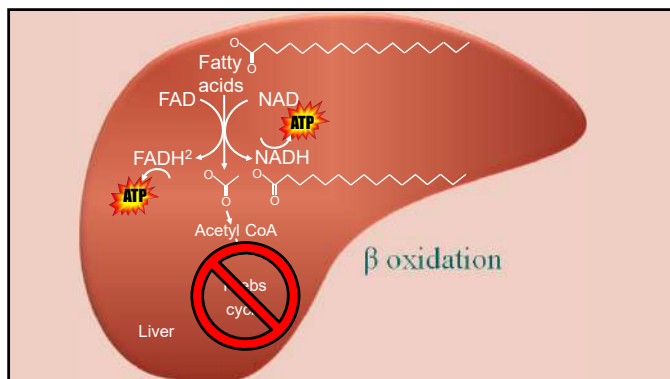
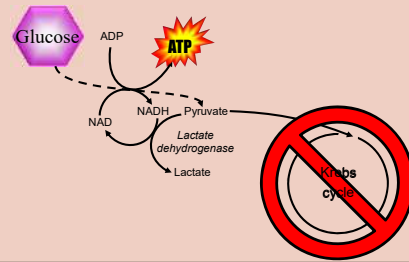


Oxidative phosphorylation

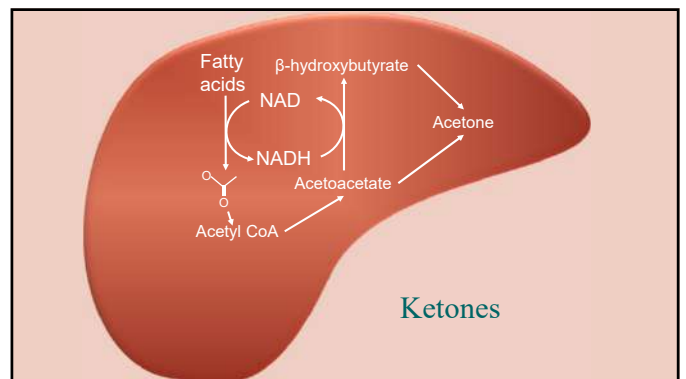
- Protons into respiratory chain



Anaerobic Energy

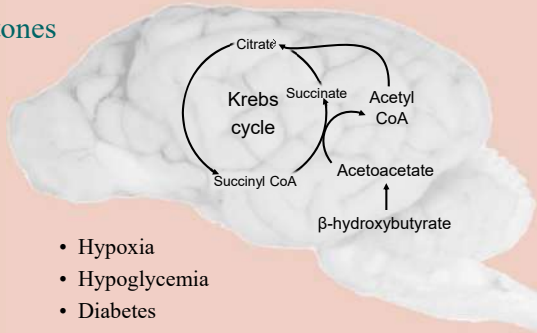


β oxidation



Ketones

Ketones



- Hypoxia
- Hypoglycemia
- Diabetes



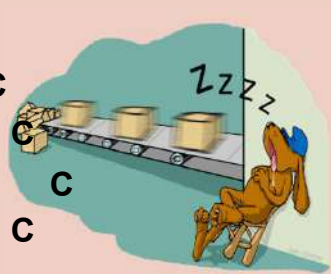
Clues to **E**nergy Errors

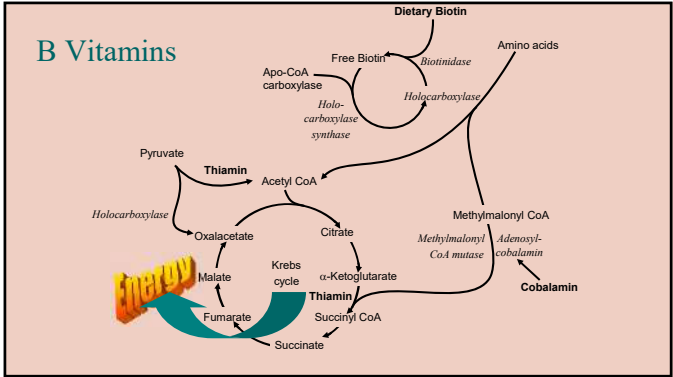
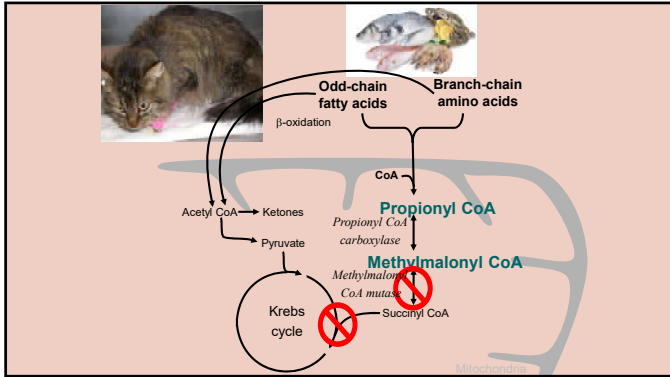
- High anion gap
- Metabolic acidosis
- Ketonuria
- Hypoglycemia

Enzyme A \rightarrow B
Enzyme B \rightarrow C
Enzyme C \rightarrow D
Enzyme D \rightarrow E



Enzyme A \rightarrow B
Enzyme B \rightarrow C
Enzyme C \rightarrow D
Enzyme D \rightarrow E





Missy FS DLH

- Cobalamin undetectable (<100 ng/L, ref 290–1499)

Kelmer, E. et al. *JVECC* 17, 299-304 (2007).

Untreated organic aciduria

- Always try B complex

Cobalamin (B12)

- Dietary intake
- Intrinsic factor
 - Stomach & pancreas in dog
 - Pancreas in cat
- Cubilin
- Transcobalamin

Cobalamin (B12)

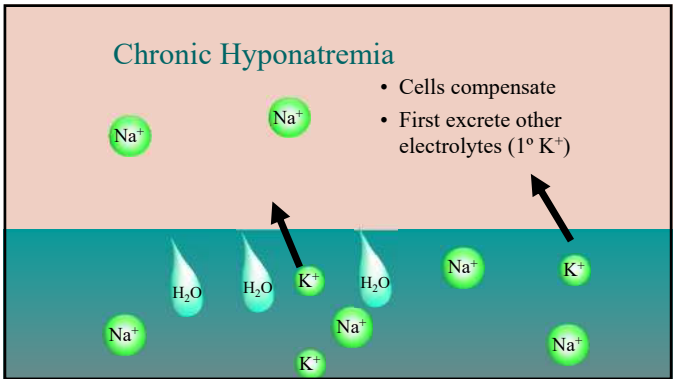
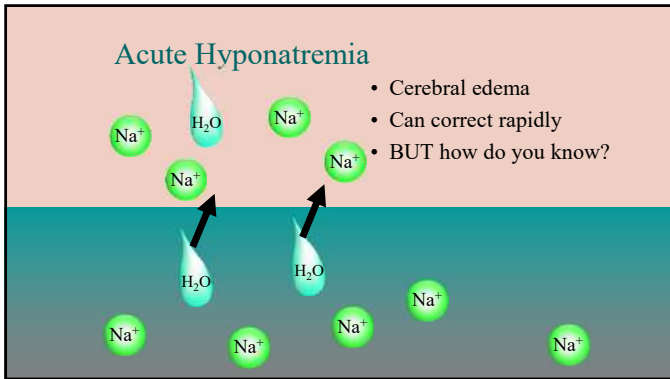
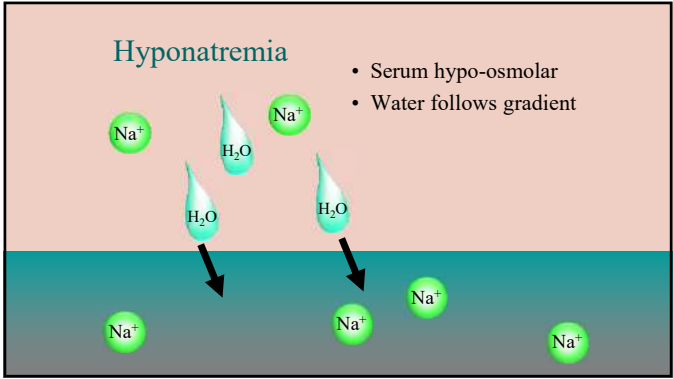
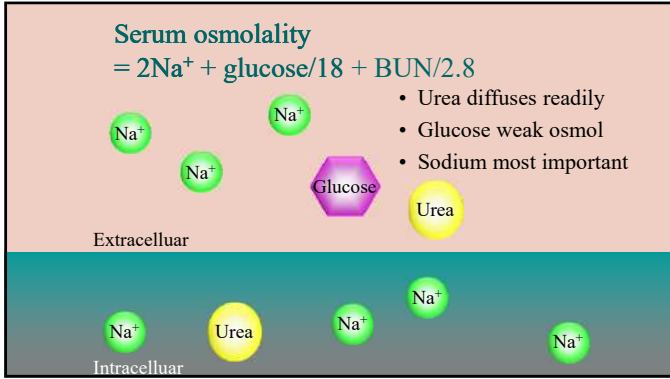
- GI disease
 - Bacterial binding of B12/IF complex
- Pancreatitis
 - Decreased IF production
- Genetic deficiency?

Electrolytes

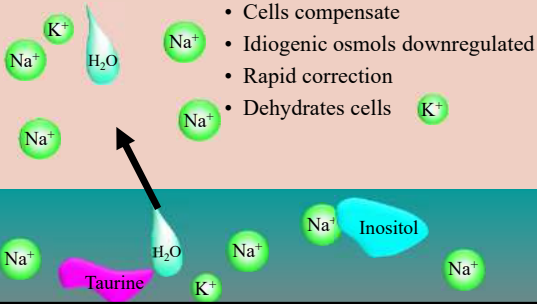
- Potassium } 1° Muscle
- Calcium }
- Sodium }

Sodium

- Critical for...
 - Resting membrane potential
 - Action potential
- Imbalances affect neither!

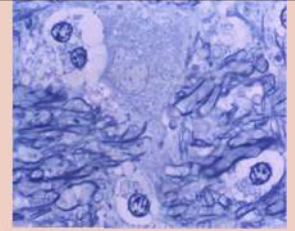


Chronic Hyponatremia



Myelinolysis

- Too rapid correction
- Myelin disruption
- Dehydration of axon?
- Direct damage to oligodendroglia?

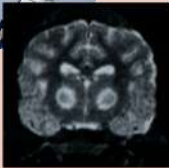


Canine myelinolysis

Laureno 1983 Experimental studies



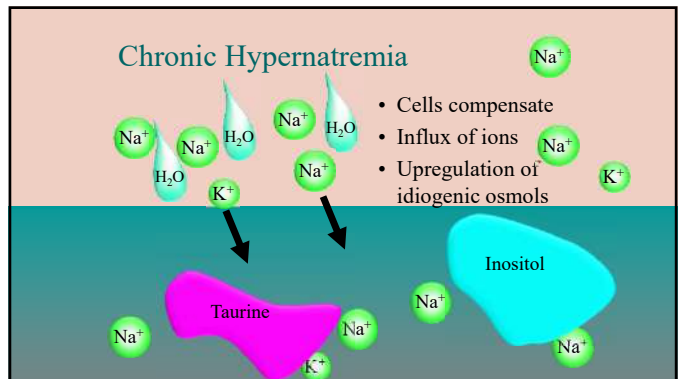
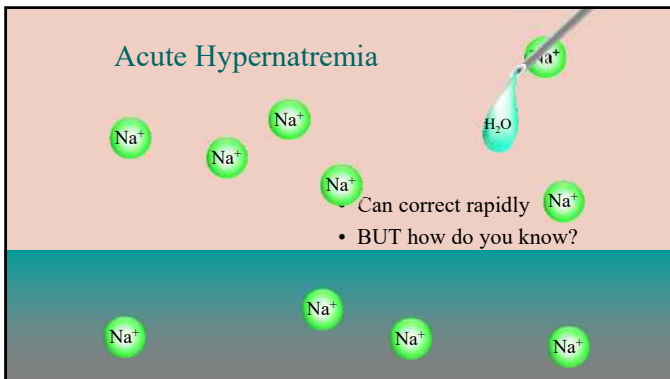
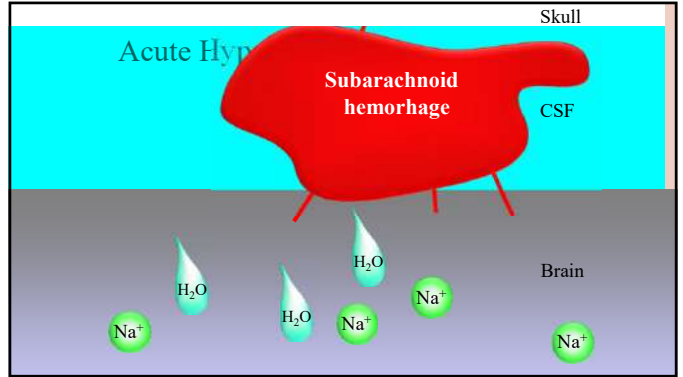
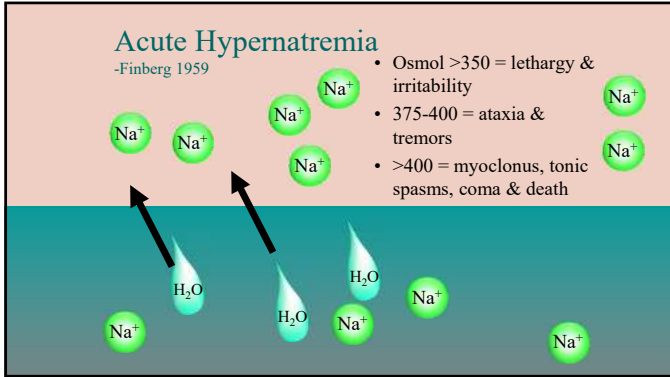
O'Brien et al 1994



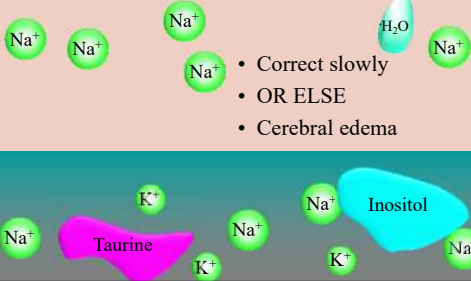
- Depression, ataxia, weakness
- Myoclonus & extensor spasms
- 1° central thalamus

Delayed signs & MRI changes

Sun	Mon	Tue	Wed	Thu	Fri	Sat
						Na ⁺ 101



Chronic Hypernatremia



- Correct slowly
- OR ELSE
- Cerebral edema

First do no harm

- Na^+ deficit in meq =
 $0.6 \times \text{lean wt kg (normal Na - patient's)}$
- Water deficit in liters =
 $0.6 \times \text{lean wt kg} \left(\frac{\text{patient's Na} - 1}{\text{normal}} \right)$
- Keep rate @ ~0.5 meq/l/hour

Metabolic Encephalopathies

Objectives

- Recognize the clues to energy deficiency
- Utilize metabolite screens to identify pathways
- Attempt nutritional end-run around block
- Use caution in correcting sodium imbalances



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