Fluid, electrolyte, and acid-base disturbances in Liver Disease

Key Points:

- If kidney ammonia excretion is increased, it leads to a condition in which metabolic acidosis cannot be mitigated by hepatic bicarb production via urea cycle
- Most important variables for albumin production are dietary protein intake and interstitial osmotic pressure sensed by hepatocyte
- Hormonal regulation of Bile formation:
    - Secretin - stimulates basal bile formation and flow
    - Gastrin - increases bile formation and flow
    - Somatostatin - decreases bile formation and flow
-

Bile formation: Composition and flow

- Active transport of osmotically active solutes into canaliculus provides the driving force for bile flow
- Formation into micelles (due to bile acids) prevent the highly concentrated solutes of bile acids from exerting a large osmotic pull within GI tract
- Speed of flow and systemic hydration status will impact the thickness of bile
- High bicarb concentration
    - Influenced by secretin
- Hormonal regulation
    - Secretin - stimulates basal bile formation and flow
    - Gastrin - increases bile formation and flow
    - Somatostatin - decreases bile formation and flow

Ammonia processing

- Ammonia is detoxified by conjugation to glutamate or aspartate and conversion into urea
- Ammonia sources include
    - Portal blood 25%
    - Catabolism of proteins, peptides and amino acids 75%

Ammonia generation role in acid/base:

$CH_3CH(CO_2)NH_3 \rightarrow HCO_3^- + NH_4^+ + H_2O$

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- At physiologic pH, only 1% of NH_4^+ exists in form that can donate proton
- Therefore, protein and amino acid processing leads to alkalosis, but ammonia detoxification prevents systemic changes in pH
- Kidneys can also process and excrete NH_4^+, but do so in a way that does not generate bicarbonate. Therefore:

    - If kidney ammonia excretion is increased, it leads to a condition in which metabolic acidosis cannot be mitigated by hepatic bicarb production via urea cycle

Albumin

- Liver has tremendous safety margin for albumin production
- Most important variables for albumin production are dietary protein intake and interstitial osmotic pressure sensed by hepatocyte
- Most albumin is in the interstitial space
- More significant acute hypoalbuminemia is associated with crystalloid fluid dilution

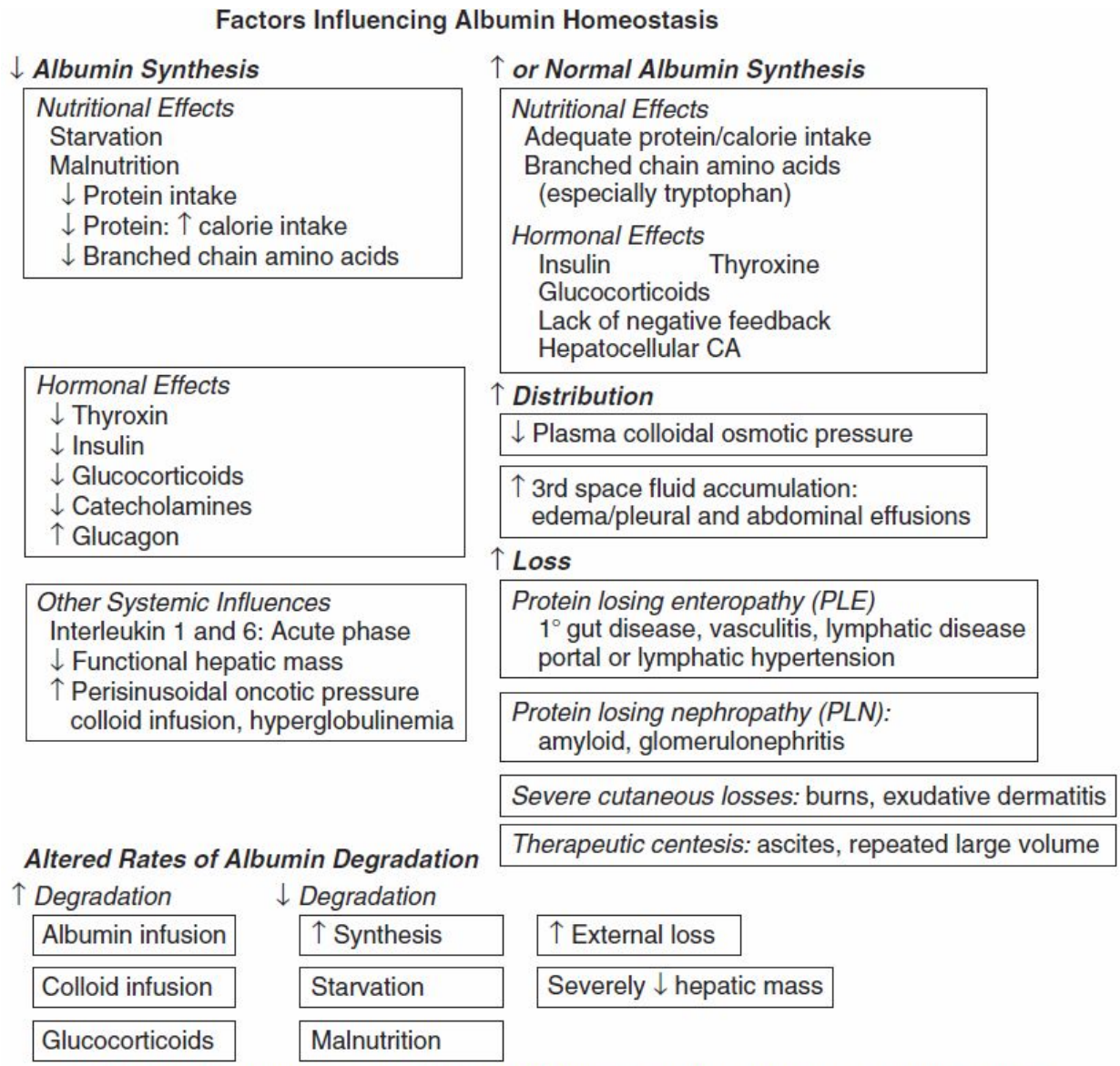


Figure 19-3 Factors and conditions influencing albumin synthesis and degradation.

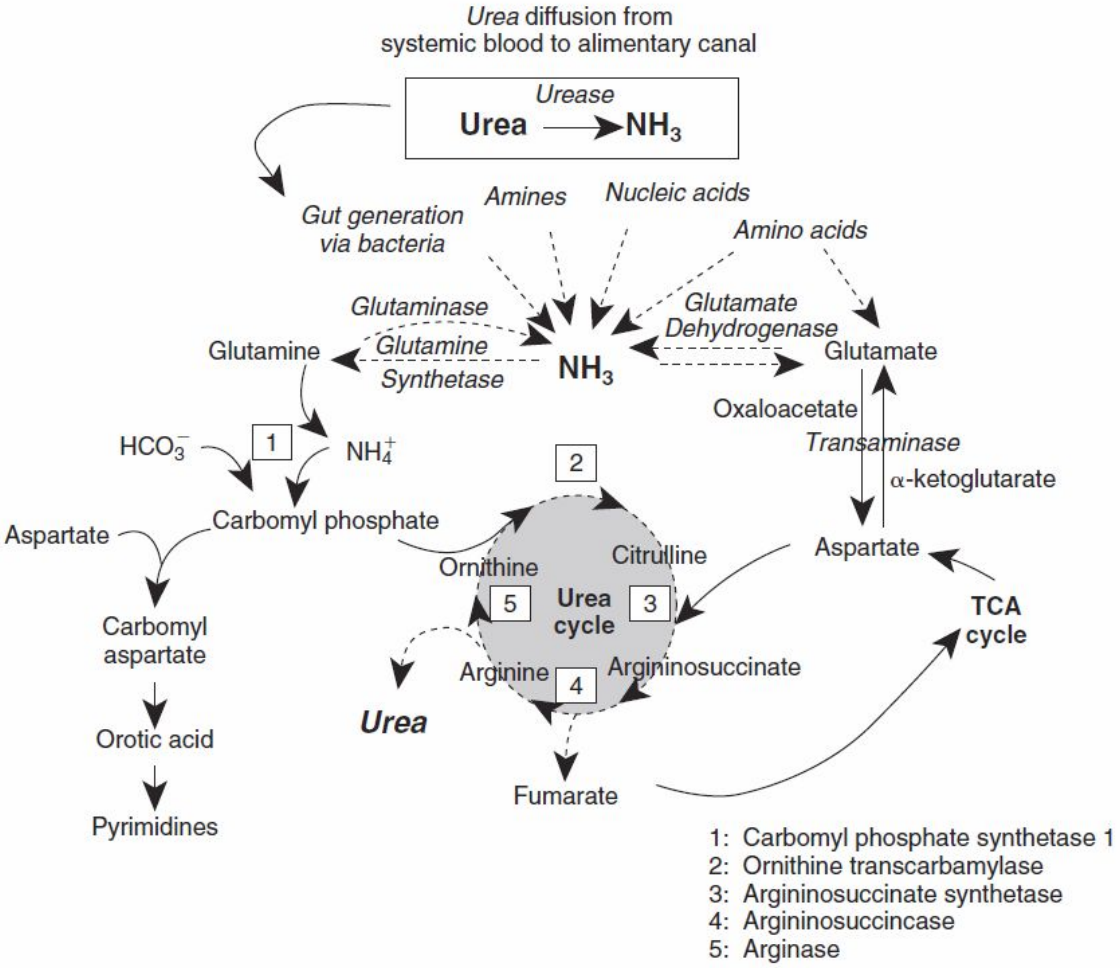
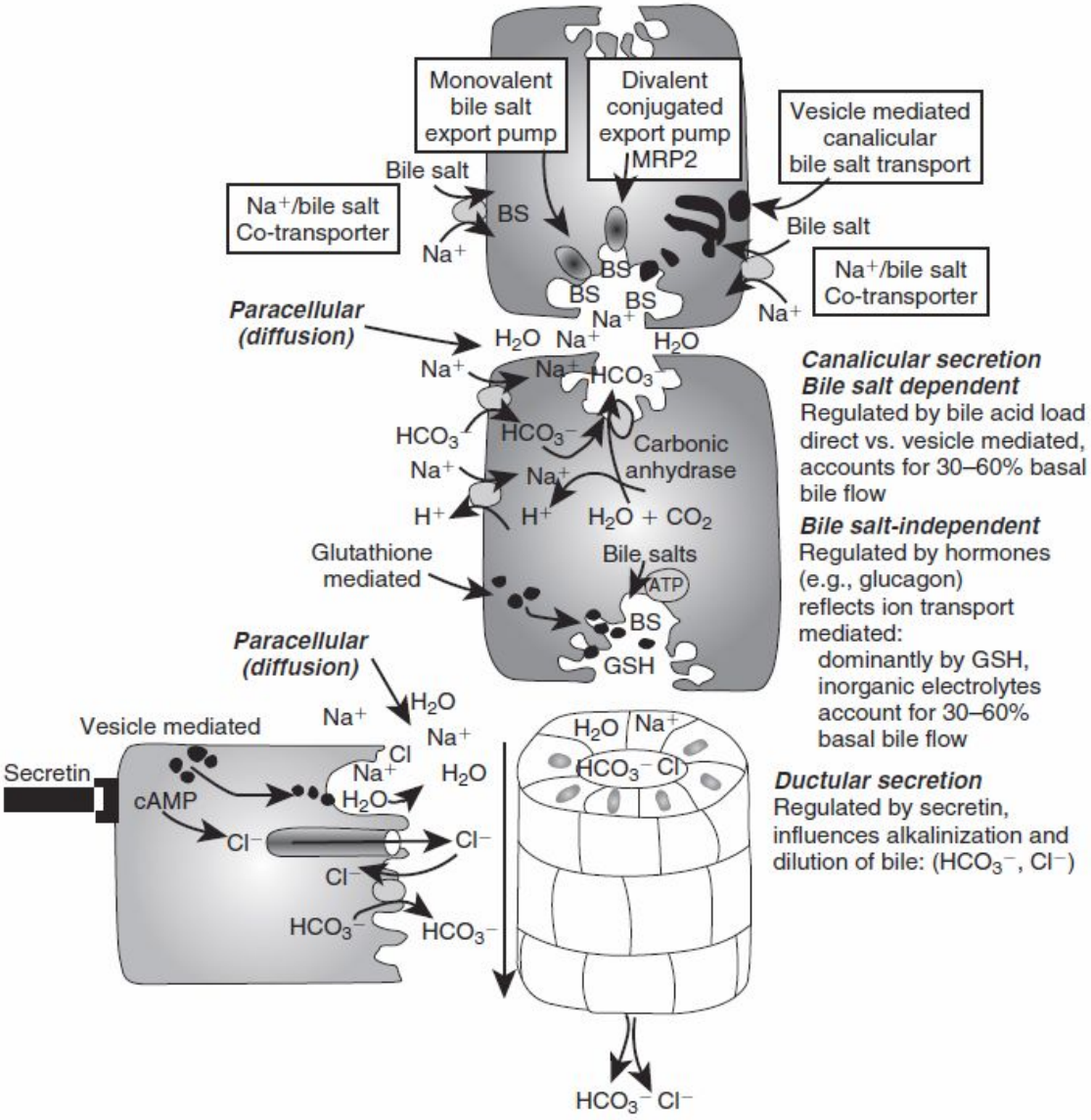


Figure 19-2 Diagram showing the biochemical reactions involved with nitrogenous waste production, detoxification, and elimination in the liver. See text for explanations.


Monovalent bile salt export pump
Divalent conjugated export pump MRP2
Vesicle mediated canalicular bile salt transport
Bile salt
Na+/bile salt Co-transporter
BS
Na+
Bile salt
Na+/bile salt Co-transporter
Paracellular (diffusion)
H2O Na+ H2O
Na+ Na+ HCO3−
HCO3− HCO3−
Carbonic anhydrase
Na+ Na+
H+ H+ H2O + CO2
Glutathione mediated
Bile salts
ATP
BS
GSH
Paracellular (diffusion)
Vesicle mediated
Secretin
cAMP
Na+ H2O
Cl Na+ H2O
Cl−
Cl−
Cl−
HCO3− HCO3−
H2O Na+
HCO3− Cl
HCO3− Cl−
Canalicular secretion
Bile salt dependent
Regulated by bile acid load direct vs. vesicle mediated, accounts for 30–60% basal bile flow
Bile salt-independent
Regulated by hormones (e.g., glucagon) reflects ion transport mediated:
dominantly by GSH, inorganic electrolytes account for 30–60% basal bile flow
Ductular secretion
Regulated by secretin, influences alkalinization and dilution of bile: (HCO3−, Cl−)
Bile salts
Cholesterol
Polyunsaturated
Phosphatidylcholine
BS = Bile salt

Questions:

1. When processing amino acids into ammonia, and then into urea, the liver does does cause a large net change in blood pH. When shifting to more urine excretion of ammonia, the pH of the blood may Increase/decrease. Give a brief explanation of why.
2. Most of the albumin in the body is found:
    a. Within the hepatocytes
    b. Within the blood
    c. Within the interstitium
    d. Within muscle cells
3. Choose whether each of the following hormones increases bile excretion and flow, or decreases it
    a. Somatostatin
    b. Gastrin
    c. Secretin
    d.

Answers

1. When processing amino acids into ammonia, and then into urea, the liver does does not cause a large net change in blood pH. When shifting to more renal processing and excretion of ammonia, the pH of the blood may Increase/decrease. Give a brief explanation of why.

Creation of ammonia creates bicarb along with ammonia. Ammonia is kept from donating proton at physiological pH, so bicarb is 'more' active. However, if kidneys are processing ammonia, liver is less able to produce the bicarb that can titrate acidosis

2. Most of the albumin in the body is found:
    a. Within the hepatocytes
    b. Within the blood
    c. Within the interstitium
    d. Within muscle cells

3. Choose whether each of the following hormones increases bile excretion and flow, or decreases it
    a. Somatostatin - decreases
    b. Gastrin - increases
    c. Secretin - increases (and responsible for basal production)