Protein and Amino Acid Metabolism

Protein metabolism during exercise typically ignored, why should we care?

- Estimated amimo acids contribute 5-15% of energy during prolonged exercise
- Because energy demands are so high during exercise, a small percentage is still substantial
- Amino acids essential to integrity of skeletal muscle, their use for energy is of concern

Skeletal Muscle

- ~ 40 % of body weight
- Second largest source of stored energy (fat is first)
  - Glycogen
  - Amino acids

- Skeletal muscle is composed of three sources of amino acids
  - Free amino acid pool
  - Contractile protein
  - Non-contractile protein

Free Amino Acid Pool

- Free amino acids can come from plasma or muscle
- Muscle due to it's mass contains ~75% of the total body free AA
- Still, free AA thought to contribute only ~1% of metabolically active AA

Non-contractile Protein

- Tyrosine and phenylalanine used as indicators of non-contractile protein degradation
- Magnitude of appearance proportional to intensity and duration
- Animal studies have demonstrated up to 25% degradation during prolonged exercise

Contractile Protein

- 3-methyl histidine (3-MH) most common indicator of metabolism
- 3-MH excretion reduced during exercise and elevated afterward
- Indicates contractile protein spared during exercise, but not after

- This biphasic response depends on type of exercise and intensity or duration
- Following light intensity endurance exercise 3-MH is not elevated during recovery
  - Elevated following hi-intensity or prolonged light intensity though
- In animals, 3-MH elevated after eccentric exercise

A brief note

- The liver can contribute significant amounts of amino acids to the total body pool
- Some of the 3-MH degradation is believed to come from this source
- In studies using biopsies, it appears as though 3-MH degradation is suppressed during exercise

Amino Acid Metabolism in Muscle

- Six amino acids can be metabolized by muscle
  - Alanine
  - Aspartate
  - Glutamate
  - BCAA

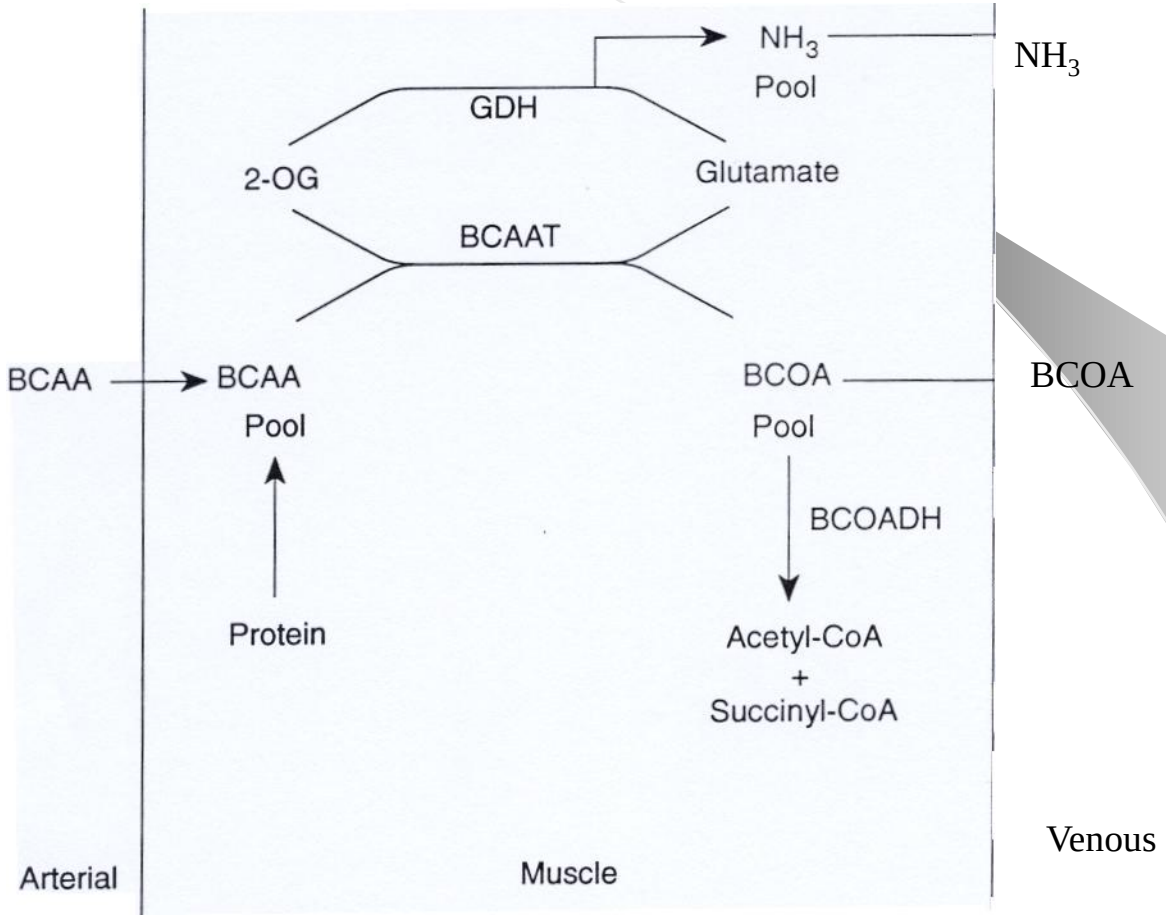
BCAA??

- Branched Chain Amino Acids
- Isoleucine
- Leucine
- Valine
- Important sources of Krebs intermediates under certain conditions

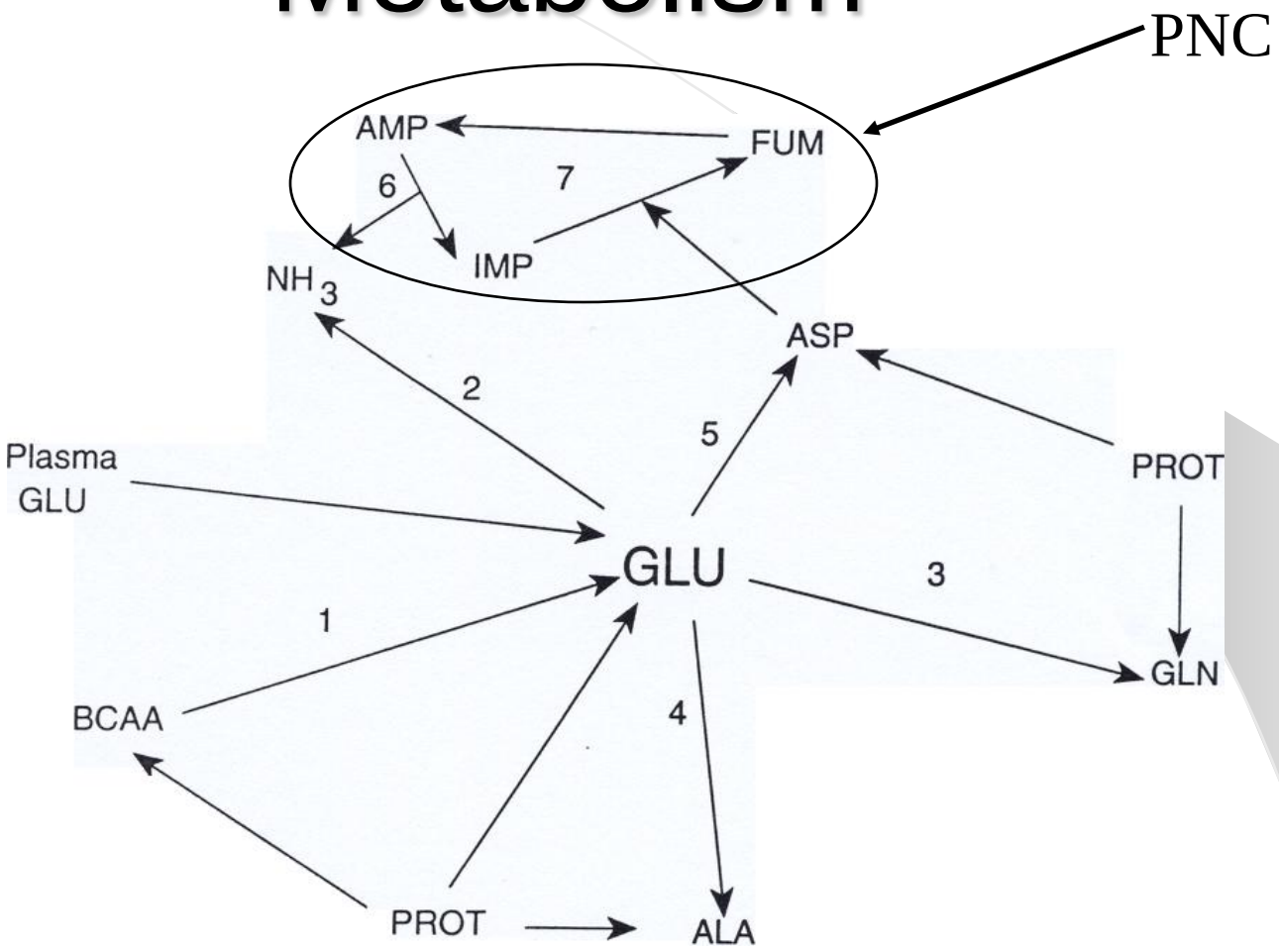
Transamination

- First step in BCAA metabolism
- Donation of NH_3 to form glutamate + BCOA
- BCOA can then form Acetyl-CoA or Succinyl-CoA
  - BCOA can also leave and go to liver

BCAA Transdeamination



Glutamate Central to AA Metabolism



Amino Acid Oxidation During Exercise

- Skeletal muscle can utilize Ala, Asp, Glu and the BCAA
- Ala released from muscle consistently for gluconeogenesis
- Asp donates NH_3 for reamination of IMP to AMP + fumarate (TCA)

- ~4 % BCOADH active in muscle at rest
- Liver BCOADH completely active regardless
- At rest
  - BCAA deaminated >> BCOA in muscle and sent to the liver for oxidation

AA as Energy Source in Skeletal Muscle

- Oxidation of BCAA yield between 32-43 ATP
  - Comparable to complete oxidation of glucose
- AA contribute uup to 18 % energy during prolonged exercise
- BCOADH shown to increase activity up to 66 % in rodents Sk muscle

Measuring AA Flux from Muscle

- At rest net efflux of AA from leg muscle
  - Muscle releasing AA
- During exercise net uptake
  - Prolonged exercise results in release from liver (BCAA)

Evidence

- Mclean et al.- no net accumulation of AA in blood or muscle
  - Indicates skMc uptake and oxidation
- Rennie et al. – during exercise significant drop in efflux of BCOA
  - BCAA being oxidized in muscle

More Evidence

- Henderson et al. – ^{13} C leucine
  - Oxidation to $^{13}CO_2$
  - Showed oxidation proportional to metabolic rate
  - Dependent upon intensity and duration

What's all this mean??

- During exercise amino acids will be oxidized
- Rate of oxidation depends on intensity and duration of the activity
- Long duration, intense activities will result in high rates of AA oxidation
  - Marathon, bike race, triathlon

Remember AMP Deamination?

- AMP >> IMP + NH_3
- Purposes
  - ATP/ADP ratio
  - Prevention of adenine nucleotide loss
  - Production of ammonia to buffer H^+
  - Regulation of carbohydrate metabolism
    - PFK and IMP activation of PHOS

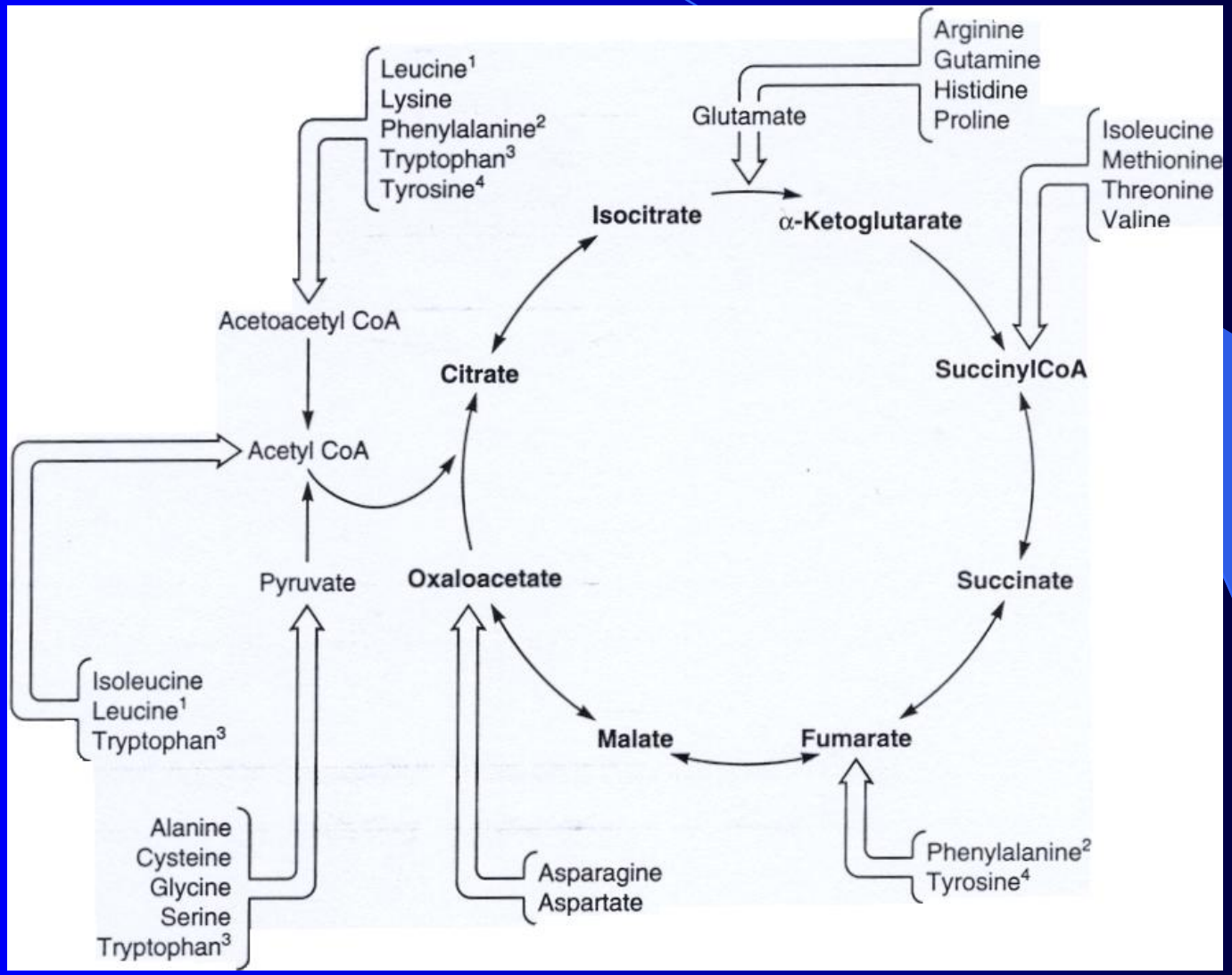
Ammonia as a buffer??

- NH_3 can accept a proton
- $NH_3 + H^+ \leftrightarrow NH4^+$
- Probably not physiologically significant

Purine Nucleotide Cycle

- Reaminates IMP to AMP
- Asp + GTP → Fumarate + NH_3
- NH3 can be used to reaminate IMP
- Fumarate can be used in the Kreb's cycle

Summary of AA Metabolism for Aerobic Intermediates



Infuence of Carbohydrates

- Depletion of glycogen prior to exercise results in elevated plasma NH_3 levels
- Plasma NH_3 levels lower during prolonged exercise when subjects consume CHO

- If glycogen is depleted using prior exercise and diet, plasma BCAA are elevated
- During the subsequent exercise bout, plasma BCAA significantly reduced
- Indicates muscle is taking up and oxidizding BCAA

Influence of FFA

- Infusion of FFA during leg exercise at 80 % $work_{max}$
- Arterial concentration of several AA acids reduced relative to control
- Net release of NH_3 ~ half of control

Ketones

- Infusion of ketones has consistently been shown to reduce leucine oxidation
- No data on NH_3 or other amino acids

Influence of Amino Acids

- When AA are infused or ingested plasma AA will rise
- BCAA will be preferentially taken up by muscle and pass by the liver
- AA oxidation will increase
- Is this good or bad???