

# Macronutrient Metabolism in Starvation and Stress

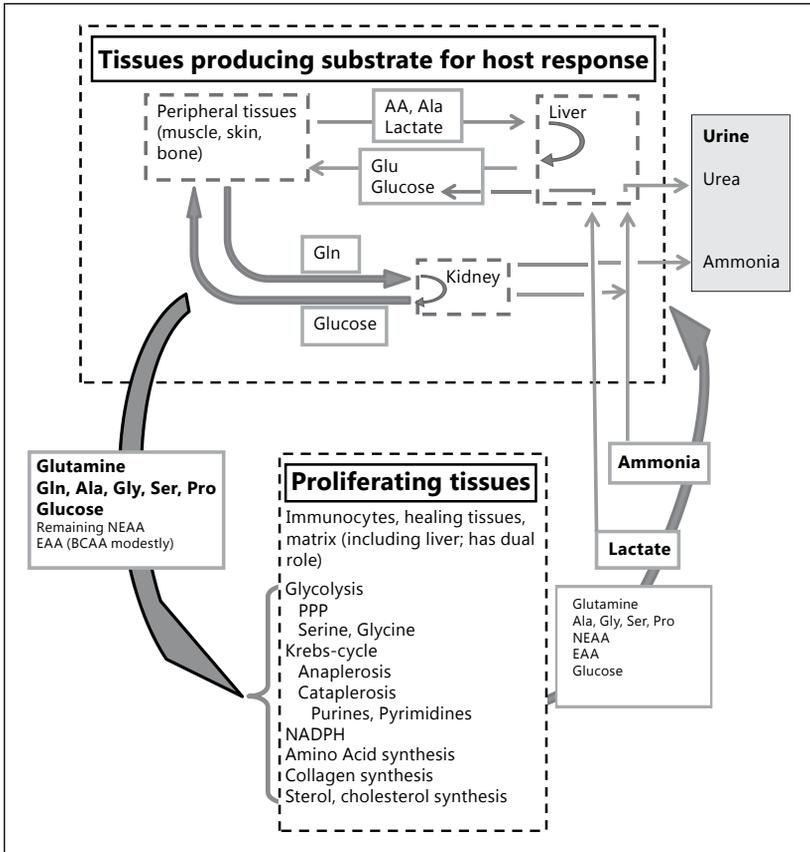
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In starvation and to a lesser extent in stress starvation, the loss of protein mass is spared as much as possible [1–3]. This metabolic arrangement must have developed under the influence of evolutionary pressure in view of the importance of protein mass for function and longevity. Peripheral adipose tissue mass is only limiting when its mass is extremely small.

Protein is the predominant precursor of glucose in (stress) starvation and glucose is an essential substrate for the synthesis and maintenance of cells and matrix and for the control of the redox state. To spare protein, glucose should be used efficiently only for those purposes that cannot be achieved by fat. It is suggested that this is achieved by limiting full glucose oxidation and increasing fatty acid and ketone body oxidation [4], which most likely can also largely cover energy needs of the central nervous system.

In stress states net negative nitrogen balance (catabolism) largely results from net losses of peripheral protein mass, predominantly muscles, whereas central organs (e.g. the liver), the immune system and wound healing are anabolic. A number of factors are responsible for a net negative nitrogen balance which may ultimately lead to death if stress persists. In stress, the amino acid mix derived from peripheral (predominantly muscle) tissues is modified in interplay with the liver and to a minor extent the kidney. This mix is different in nonstressed conditions, containing substantially increased amounts of the non-essential amino acids glutamine, alanine, glycine and (hydroxy)proline. Part of the amino acid skeletons released by muscles are substrates to produce glucose in the liver and kidney. Glucose and the amino acids produced especially serve as substrates for cell proliferation (fig. 1) and matrix deposition.

The catabolic processes in peripheral tissues cannot be countered completely by adequate nutritional support as long as stress persists. This metabolic arrangement dictates a nutritional mix containing liberal amounts of protein and carbohydrates and addition of lipids to cover energy requirements.



**Fig. 1.** Schematic representation of the concerted production of substrates for host response by peripheral tissues (muscle, skin, bone and brain?), liver and kidney and their uptake by proliferating tissues (immune cells, wound healing, matrix and liver). The liver plays a dual role, producing substrates as well as utilizing substrates to synthesize acute phase proteins and immune cells (Kupffer cells). The intermediary metabolism in the intestines and brain is not taken into account. AA = Amino acids; BCAA = branched chain AA; EAA = Essential AA; NEAA = non-EAA; PPP = pentose phosphate pathway.

## References

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- 3 Cherel Y, Robin JP, Heitz A, et al: Relationships between lipid availability and protein utilization during prolonged fasting. *J Comp Physiol B* 1992;162:305–313.
- 4 Soeters MR, Sauerwein HP, Dubbelhuis PF, et al: Muscle adaptation to short-term fasting in healthy lean humans. *J Clin Endocrinol Metab* 2008;93:2900–2903.