



Metabolic Response to Stress, Critical illness and Starvation



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همای اوج سعادت به دام ما افتد

اگر تو را گذری بر مقام ما افتد

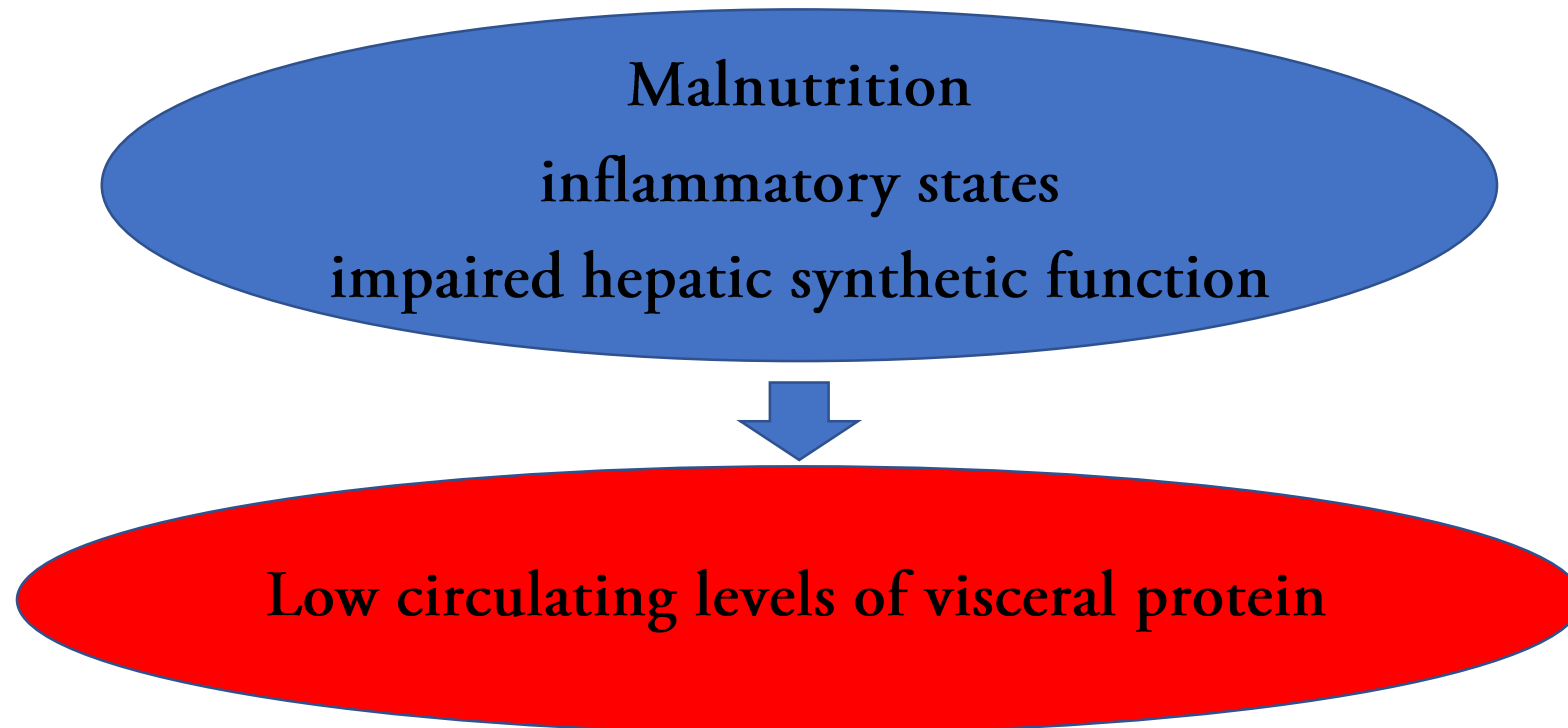
حباب وار براندازم از نشاط کلاه

اگر ز روی تو عکسی به جام ما افتد

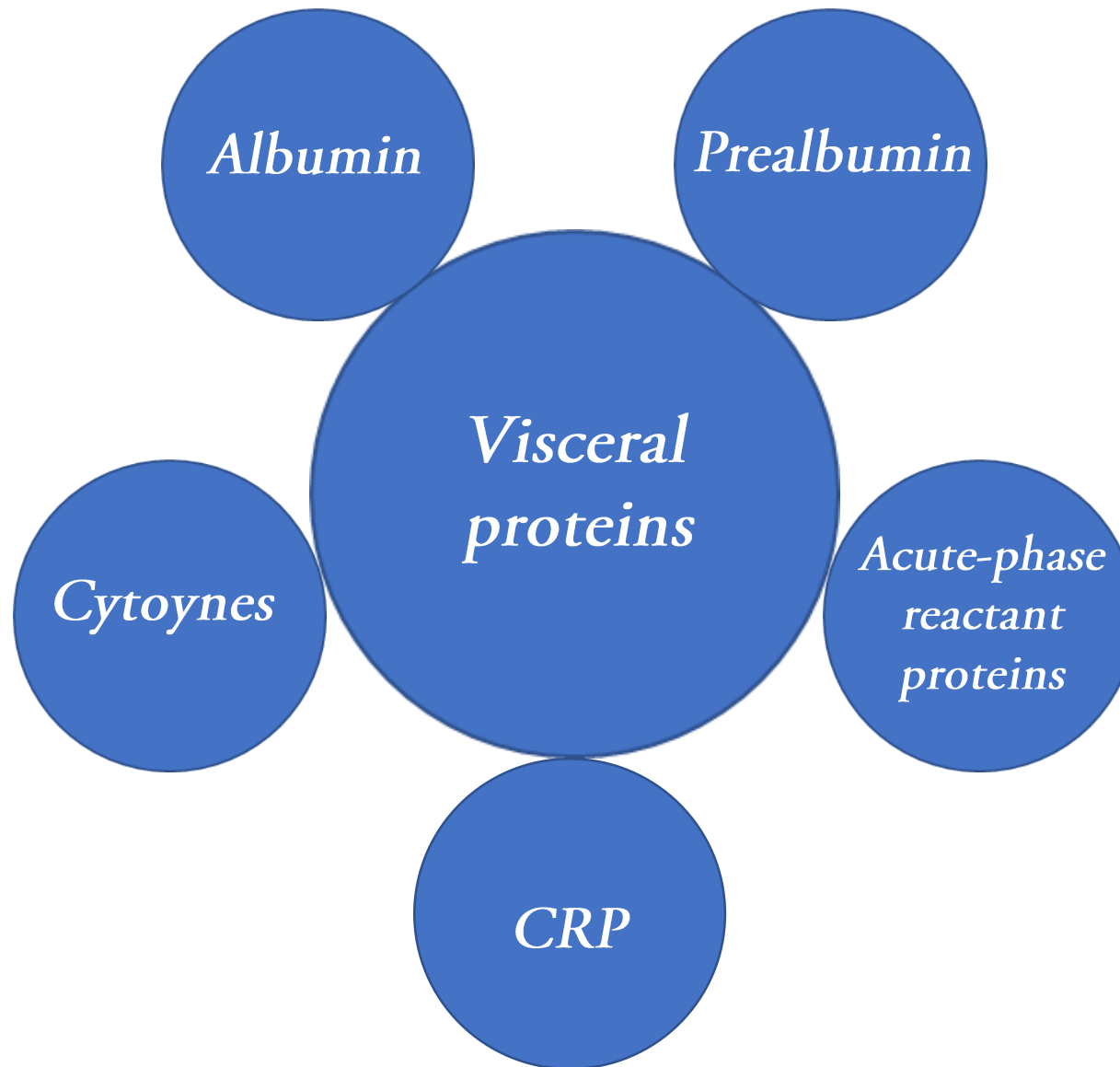
مجلس
عاشقان
مجموعه شعاره آلوده کربلا
شکر کربلا

Body Composition

- The characteristic protein catabolism seen in the metabolic stress response may cause significant alterations in body composition.



Visceral proteins are rapid turnover proteins produced in the liver.



serum albumin

- reliability as a marker of visceral protein status is questionable.
- A large pool
- half-life of 14 to 20 days
- it is not an indicator of the concurrent nutritional status.
- Serum albumin , independent of nutritional status, may be affected by :
 - changes in fluid status
 - albumin infusion
 - sepsis
 - trauma
 - liver disease

prealbumin

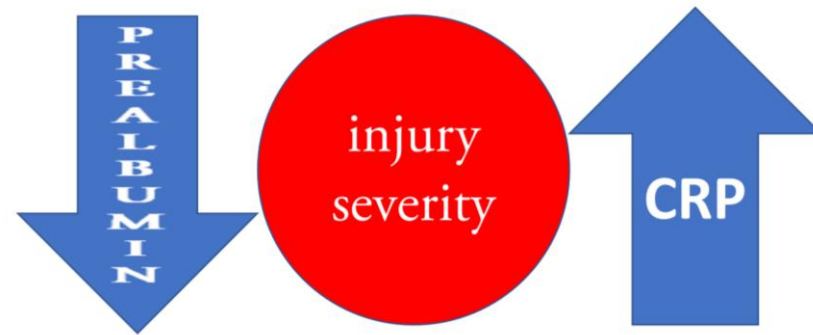


- a circulating glycoprotein synthesized in the liver
- a good marker for the visceral protein pool.
- a half-life of 24 to 48 hours
- reflects more acute nutritional change.
- Prealbumin concentration is diminished in liver disease.

Acute phase reactant proteins

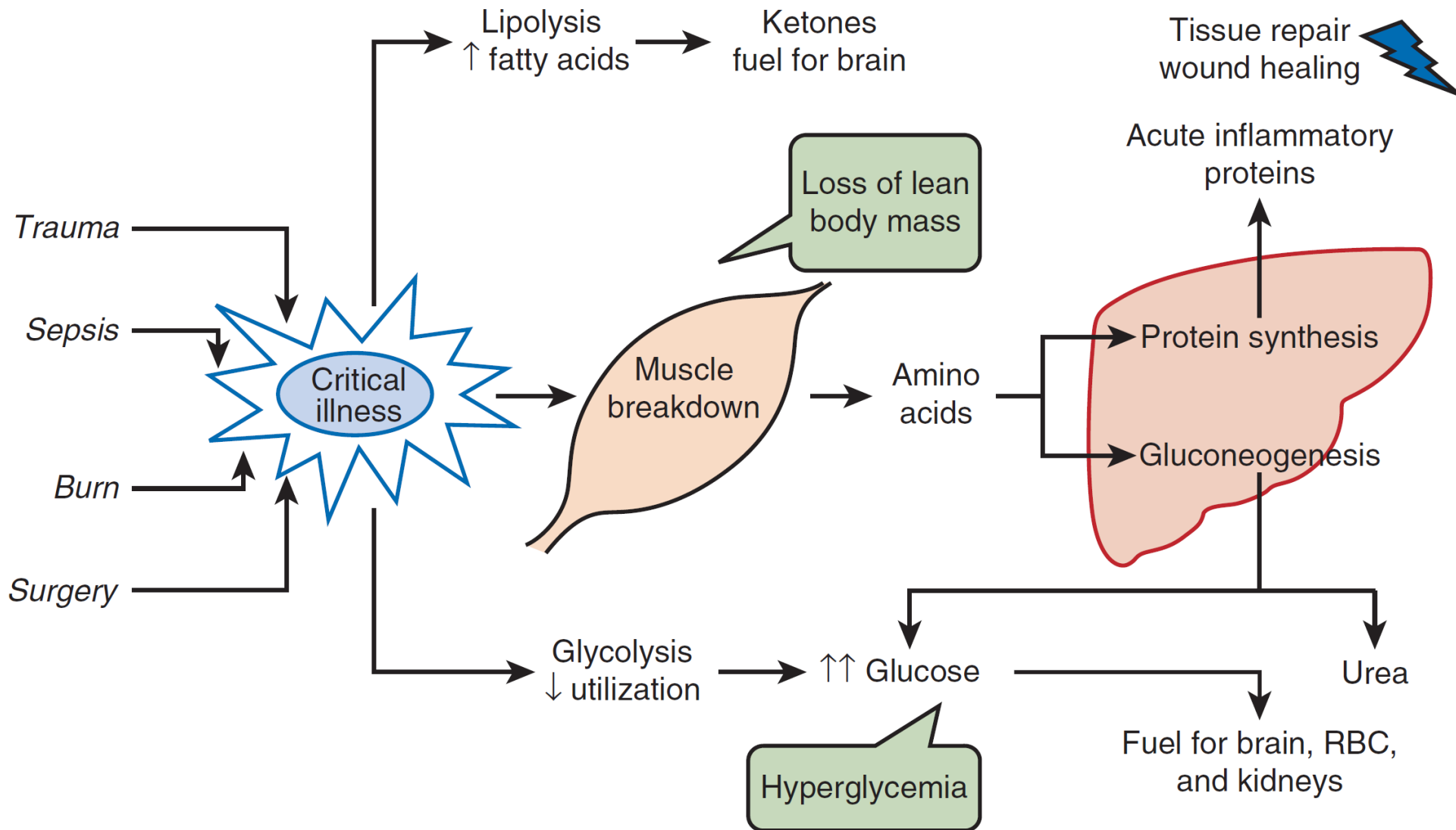
- elevated proportional to the severity of injury
- elevated in response to *cytokines* released during stress response
- have been used to monitor the inflammatory response.

- *prealbumin* and *CRP* are inversely related.



- In infants after surgery, decreases in serum CRP values to less than 2 mg/dL have been associated increases in serum prealbumin levels.

Metabolic Consequences of Critical Illness



Any critical illness
(sepsis trauma, burns, septic shock, etc)

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graph TD; A["Any critical illness (sepsis trauma, burns, septic shock, etc)"] --> B["Hypercatabolic state"]; B --> C["increase in circulating catabolic hormones  
increase in inflammatory cytokines  
insulin resistance (reduced glucose oxidation,  
hyperglycemia , storage as hepatic glycogen)"]; style A fill:#336699,color:#fff; style B fill:#336699,color:#fff; style C fill:#336699,color:#fff;
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Hypercatabolic state

increase in circulating catabolic hormones
increase in inflammatory cytokines
**insulin resistance (reduced glucose oxidation,
hyperglycemia , storage as hepatic glycogen)**

severe infection, trauma, major surgery



**hormonal and metabolic changes ,
systemic inflammatory response**



**activation of sympathetic nervous system
hypothalamic-pituitary-adrenal axis**



Nutritional disturbance



changes in glucose and lipid metabolism , increased protein turnover and breakdown



increased energy expenditure (EE) , negative nitrogen balance , muscle protein loss

Respiratory compromise
(due to loss of respiratory muscle mass)

cardiac dysfunction and arrhythmias
(due to loss of myocardial muscle tissue)

intestinal dysfunction
(due to loss of the gut barrier)

morbidity and
mortality of critical
illness



SO:

large energy imbalances attributable
to underfeeding and overfeeding in
critically ill children must be avoided

Critical Illness :



Insulin

Glucagon

Cortisol

Catecholamines

GH

Aldosteron

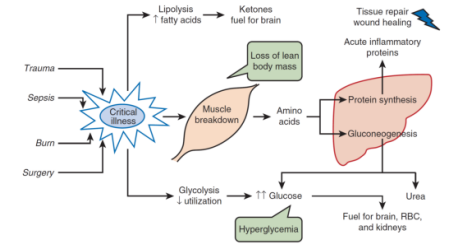
ADH

Proinflammatory cytokines.

Critical Illness :

By interaction between the nervous, endocrine, and immunologic systems:

- Peripheral resistance to growth hormone action
- reduction in insulin-like growth factor (IGF)-1 secretion
- Increased counter-regulating hormone
- insulin- and growth hormone-resistant states (a characteristic sign of stress)
- protein catabolism and the utilization of carbohydrate and fat stores
- increased basal metabolic rate.



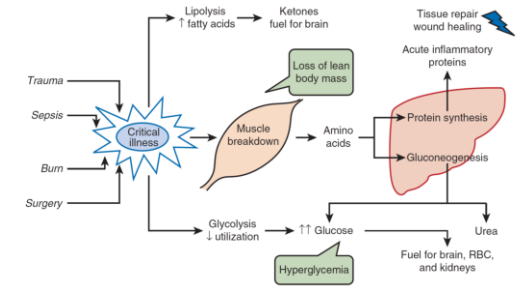
Increased serum counterregulatory hormone concentrations



induce insulin and growth hormone resistance



catabolism of endogenous stores of protein, carbohydrate, and fat

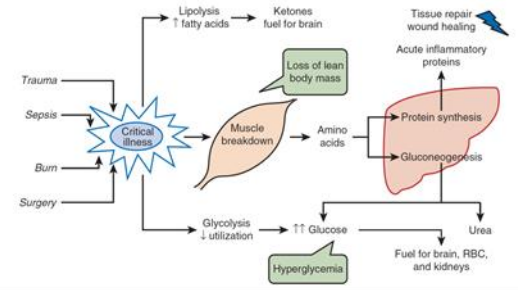


increase in muscle protein degradation
(characteristic of the metabolic stress response)



high concentration of free amino acids in the circulation.

PROTEIN BREAKDOWN



Deamination of branched-chain amino acids

channel the amino acids through the liver

supplies amino acids for the protein synthesis (wound healing, production of Igs and acute-phase reactants)

gluconeogenesis (preferred energy substrate for the brain, erythrocytes, renal medulla)

Overall : net negative protein balance.

**In summary, the metabolic response
to critical illness
results in glucose and lipid
intolerance
and increased protein breakdown**

**Acute phase
reactants**

CRP
 α_1 -acid glycoprotein
haptoglobin
 α_1 -antitrypsin
 α_2 -macroglobulin
ceruloplasmin
fibrinogen

**Reprioritization
of protein
during
metabolic stress,
injury or sepsis**

**transferrin
and
albumin**

Starvation Vs Stress

**TABLE
99.2****Metabolic Stress Versus Starvation**

	Metabolic Stress	Starvation
BMR	↑↑	↔↓
Oxygen consumption (V_{O_2})	↑↑	↓
Protein catabolism	↑↑↑	↔
UUN	↑↑	↔
Weight loss	Rapid	Slow
LBM loss	Early	Late
Response to caloric intake	Protein catabolism continues	Protein catabolism halted
Insulin, cortisol, and catecholamines	↑↑	↓
Ketones	↑↑	↔
Gluconeogenesis	↑	↓

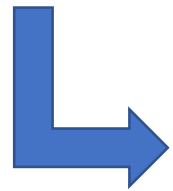
↑, Mildly increased; ↑↑, moderately increased; ↑↑↑, markedly increased; ↓, decreased; ↔, unchanged. *BMR*, Basal metabolic rate; *LBM*, lean body mass; *UUN*, urinary urea nitrogen.

SIMPLE VERSUS STRESS STARVATION

	■ SIMPLE STARVATION (>72 H)	■ STRESS STARVATION
Metabolic rate	↓	↑
Protein catabolism (relatively)	↓	↑
Protein synthesis (relatively)	↓	↑
Protein turnover	↓	↑
Nitrogen balance	↓	↓↓
Gluconeogenesis	↓	↑
Ketosis	↑↑	None
Glucose turnover	↓	↑
Blood glucose	↓	↑
Salt and water retention	?	↑↑↑
Plasma albumin	None	↓↓

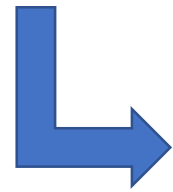
Response of adipose tissue to critical illness

Stress response



Stimulation of lipolysis

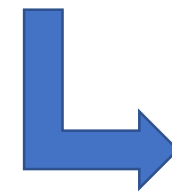
hormone-sensitive lipase



Triglycerides

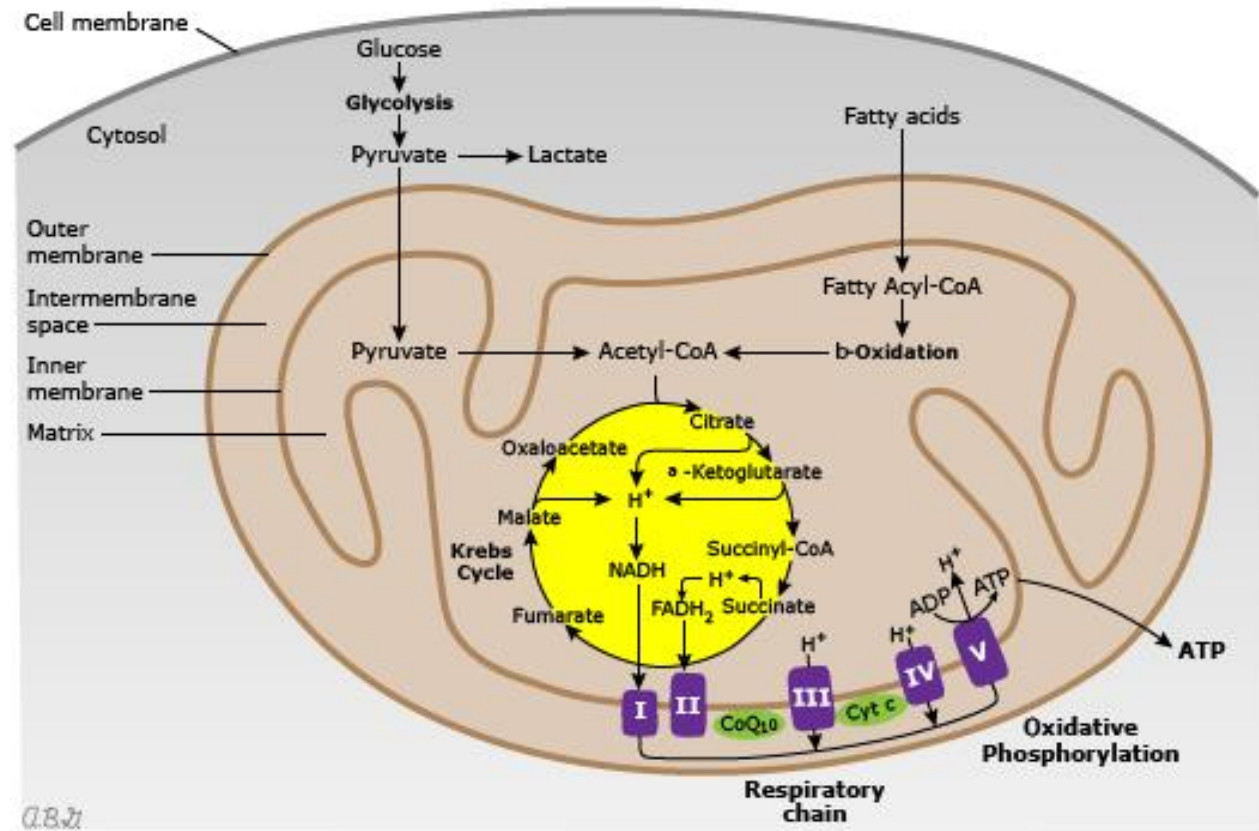


fatty acids and glycerol



gluconeogenesis

- *Fatty acids are oxidized by β -oxidation in the liver generating acetylcoenzyme A for energy production in the tricarboxylic acid cycle and mitochondrial electron transport chain.*
- *the provision of dietary glucose does not decrease fatty acid turnover in times of illness.*



- The **increased demand for lipid use** in the setting of limited lipid stores puts the **metabolically stressed neonate or previously malnourished child** at high risk for the development of **essential fatty acid deficiency**.
- **Preterm infants** are most at risk for developing essential fatty acid deficiency after a short period of a fat-free nutritional regimen.
- **Nutritional therapy** should support the metabolic changes occurring during the **acute catabolic stage**.

And after resolution ...

resolution of a hypermetabolic stress response



anabolic phase



increased release of growth hormone and IGF-1

Supply of adequate nutrition is essential for this recovery phase

