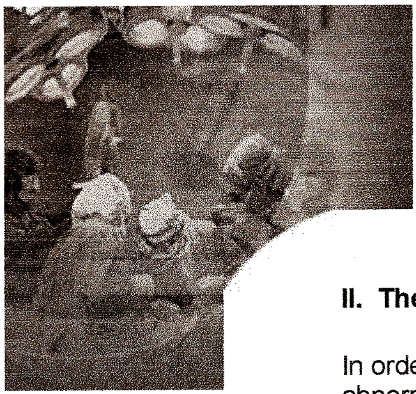


II. The Importance of Maintaining Lean Body Mass

In order to better understand the impact of erosion of lean mass and the normal or abnormal utilization of protein and fat for fuel, a general understanding on normal body composition is required.

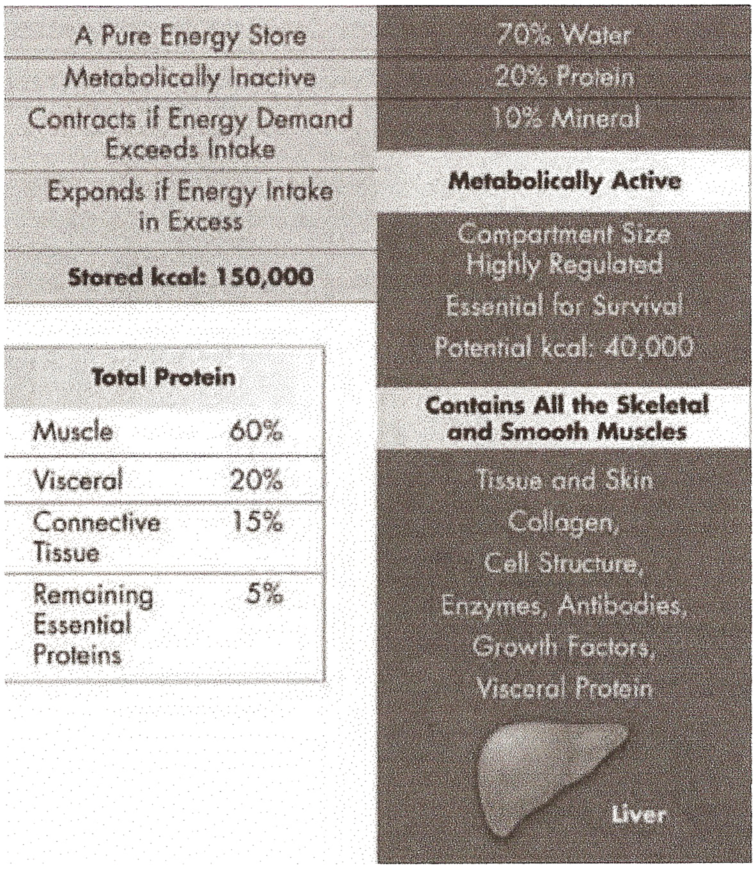
The body composition can be divided into fat and fat-free components. Body protein is present in the fat free or lean body mass (LBM) compartment. Fat mass is usually about 20-30% of total.

The Lean Body Mass is highly active metabolically and physiologically and the size is genetically defined and maintained. The LBM is 75% of body weight and contains all the body protein. There is no real protein store as every protein molecule has a role in maintaining homeostasis. Loss of any body protein is deleterious. The majority of the protein in the lean body mass is in the skeletal muscle mass. Lean body mass is 50-60% muscle mass by weight, the rest is bone and tendon. Protein makes up the critical cell structure in muscle, viscera, red cells and connective tissue. Enzymes which direct metabolism and antibodies which maintain immune functions are also proteins.

It is the loss of body protein which accompanies the injury, not fat loss, that produces the complications of malnutrition.

The majority of fat mass is stored and biologically inactive. Its only role is a reservoir for calories.

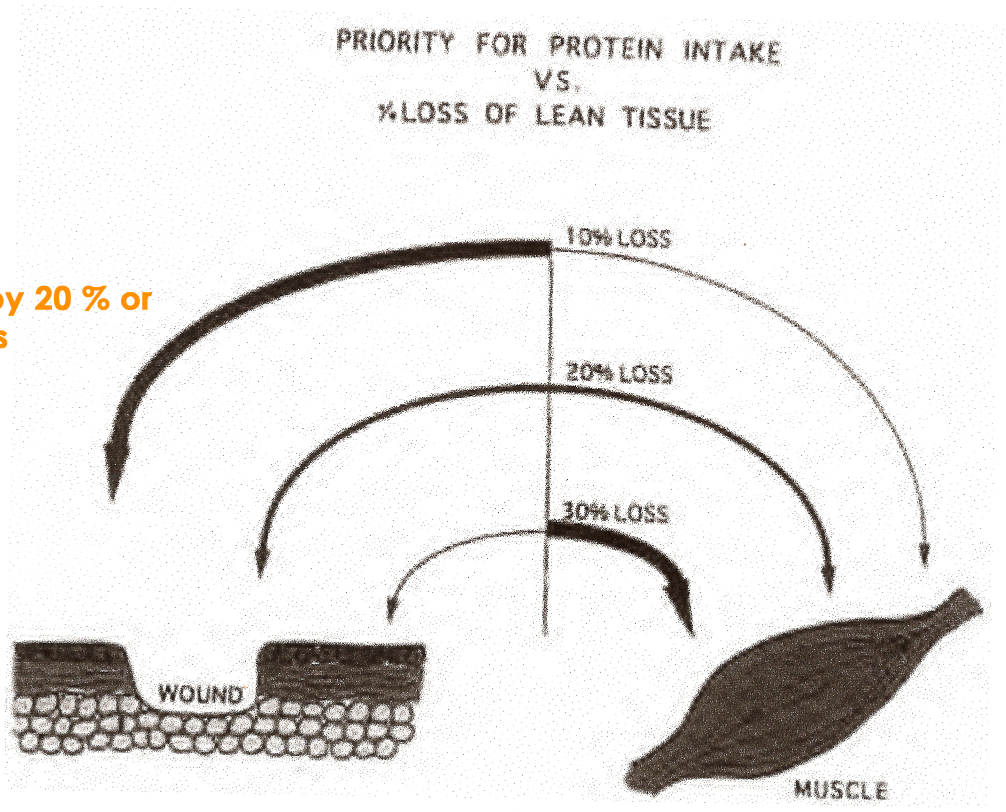
What is Lean Mass and Its Importance?



Complications Relative to Loss of Lean Body Mass *		
Lean Body Mass (% loss of total)	**Complications (Related to lost lean mass)**	**Associated Mortality (%)**
10	Impaired immunity, ..increased infection	10
20	Decreased healing, ..weakness, infection	30
30	Too weak to sit, pressure ..sores, pneumonia, no healing	50
40	Death, usually from ..pneumonia	100

*** Assuming no preexisting loss.**

If muscle mass decreases by 20 % or more, wound healing rate is decreased significantly.



As lean mass decreases, more consumed protein is used to restore LBM with less being available to the wound. Wound healing rate decreases until lean mass is restored.

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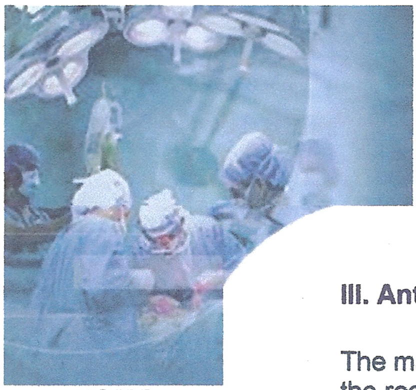


III. Anticatabolic and Anabolic Strategy, (Nutrition)

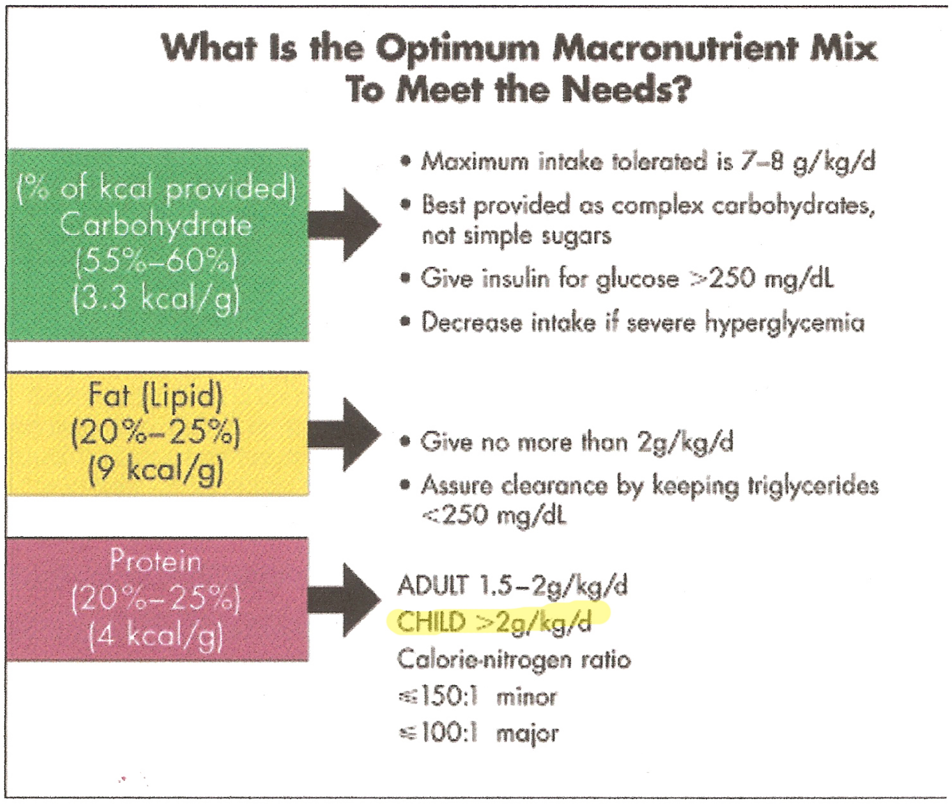
The maintenance of optimum nutrition through both the stress response or catabolic p the recovery or anabolic phase is the most important strategy to decrease lean mass regain lost lean mass.

The remaining strategies are additions to adequate macro and micronutrient intake.

Requirements

- maintain adequate energy 30-35 cal/kg/day
- maintain adequate protein 1.5 to 2 g/kg/day
- maintain adequate micronutrients

What is the Optimum Macronutrient Mix To Meet the Needs?



Growth nutrtion requires more protein (and certain more or less other nutrients) compared to maintenance nutrition.

Notice, a child needs more protein based on body weight compared to adults.

MEETING REQUIREMENTS: THE ROLE OF PROTEIN SUPPLEMENTS APP

STIMULANTS AND INCREASED MICRONUTRIENTS

1. Role of protein supplements
2. Appetite stimulants
3. Anticatabolic micronutrients

1. Protein Supplements

Numerous studies demonstrate the need for increased protein intake during both the and recovery phase after burn injury. The increased protein demands, especially if res depleted body lean mass is required, exceed that which a severe burn injury patient c with intake of food alone. This concept is particularly well documented in the managei burn wound when the addition of protein supplements to maintain intake at 1.5-2.0 g/k significantly increased healing rate.

As described, the protein intake correlates best with healing rate. Nutrient supplemen selected based on the following criteria.

NUTRIENT SUPPLEMENT SELECTION CRITERIA

- Need for high protein content
- Quality of the contained nutrients
- Route of administration, i.e. taken orally or per feeding tube
- Palatability (which equates with compliance)
- Complications

Most high protein supplements are non palatable and not for oral consumption, e.g. C Jevity, etc. and are really used only for tube feeding. There are now available more pa formulations which have a high protein content in a palatable form. In addition, all prot equal. Some proteins and their peptide content have a higher biologic value, i.e. incre nitrogen retention, based on their structure and composition. In addition, specific pept like growth factors or added anabolic stimuli. In a recent randomized trial in burn patie noted the protein composition of a case in hydrolysate (Met-Rx) doubled lean mass ga compared to standard whey hydrolysates, reflecting an added anabolic stimulus prese casein hydrolysate.

It has been demonstrated that bioactive peptides in a hydrolysate of protein have ana activity, wound healing and immunologic effects in excess of that seen with whole pro amino acid intake alone. Bioactive peptides are absorbed intact by the gastrointestina number of peptides have been identified which have anabolic and neuroendocrine act However, the majority of the active growth factor-like peptides in protein hydrolysates been identified.

2. Appetite Stimulating Drugs (Non-anabolic agents)

A critical component in the process of maintaining and restoring lost lean mass is to o nutrient intake. Suppression of appetite is a common characteristic of the stress respc the catabolic phase of injury as well as during recovery. Adequate energy and protein essential for any anabolism to occur, especially with the use of anabolic agents.

The most widely used non-anabolic agents are *megestral acetate*, a synthetic progest steroid and *dronabinol (delta -9 tetra hydro-cannabinol)*

Megestral Acetate

- effective appetite stimulant
- > 85% of weight gain is fat due to progestational steroid effect
- can produce hypogonadism
- decreases lean mass gain
- not beneficial for lean mass gain

Dronabinol

- modest appetite stimulant
- has significant CNS effects
- weight gain mostly fat

To date appetite stimulants which are not anabolic agents, have not been shown to b on the burn or trauma patient to maintain lean mass.

Micronutrient Support

Delivery of increased quantities essential micronutrients is required for the success of anticatabolic or anabolic strategy as micronutrient depletion occurs after burns and tra

Micronutrient Support of the Hypermetabolic State		
VITAMIN B COMPLEX	Energy Production	DAILY DOSE
Thiamine	Oxidation, reduction reactions	10–100 mg
Riboflavin	Oxidative phosphorylation for ATP production	10 mg
Niacin	Electron transfer reactions for energy production	150 mg
Vitamin B6	Transamination for glucose production and breakdown	10–15 mg
Folate	One carbon transfer reaction required for all macronutrient metabolism	0.4–1 mg
Vitamin B12	Coenzyme A reactions for all nutrient use	50 mcg

VITAMIN C	Energy Production	Daily Dose
MINERALS	Carnitine production for fatty acid metabolism	500 mg–2 g
Selenium	Cofactor for fat metabolism	100–150 mcg
Copper	Cofactor for cytochrome oxidase for energy production	1–2 mg
Zinc	Cofactor for DNA, RNA, and polymerase for protein synthesis	4–10 mcg

AMINO ACIDS	Energy Production	Daily Dose
Glutamine	Nitrogen shuttle for glucose amino acid breakdown, urea production, direct source of cell energy	10–20 g

Anticatabolic and Anabolic Micronutrient Support

AMINO ACIDS

Glutamine	Decreases net nitrogen loss Increases net muscle protein synthesis Nitrogen carrier Stimulates HGH release
Arginine	Decreases net nitrogen loss

ANTIOXIDANTS

Vitamin A, C, E, B; Carotene, Zn, Cu, Se	Decreases net oxidant-induced protein degra

PROTEIN SYNTHESIS COFACTORS

Zn, Cu, Mg, Vitamin B Complex	Improve protein synthesis pathways

DAILY DOSE **** See Previous Table***

Micronutrient Support for Wound Healing

AMINO ACIDS	
Glutamine	Primary fuel for fibroblasts Preservation of lean mass Anticatabolic, anabolic properties Stimulates release of HGH
Arginine	Obligatory precursor for wound protein synthesis Increases local wound immune system
Cysteine	Key amino acid for new tissue growth Provider of sulfhydryl bonds
VITAMINS	
Vitamin A	Stimulant for onset of wound-healing process Stimulant of epithelialization and fibroblast deposition of collagen
Vitamin C	Necessary for collagen synthesis
MINERALS	
Zinc	Cofactor for collagen and other wound protein synthesis
Copper	Cofactor for connective tissue production Collagen cross-linking
Manganese	Collagen and ground substance synthesis

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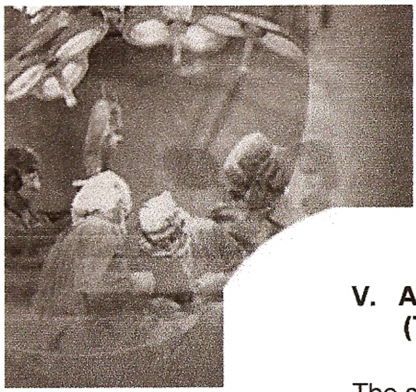


V. ANABOLIC STRATEGY
(The Rationale for the use of Anabolic Hormones)

The successful correction of lean mass loss and prevention of a severe protein deficiency in the presence of catabolic illness requires an increase in overall anabolism.

ROLE OF ANABOLIC HORMONES

- attenuate the catabolic stimulus during stress
- to more rapidly restore lean mass loss
- to restore normal nutrient partitioning such that protein consumed is not converted to energy and weight gained is not fat mass

Even in the recovery phase, endogenous anabolic activity remains depressed. This is the case in elderly patients, those with chronic illness, or patients with involuntary weight loss. Adequacy of substrate (1.5 g/kg/d protein) may not be sufficient to jump-start restoration of lean body mass. However, the machinery is capable of a very rapid rate of protein synthesis that is not age-dependent if stimulated by anabolic agents.

Body composition studies during correction of protein energy malnutrition (PEM) have demonstrated that a significant portion of weight gain after unintentional weight loss from catabolic disease represents the addition of body fat and extracellular fluid, not added protein mass. Inadequate anabolic stimulation is the cause.

The action of all anabolic agents currently in clinical use is twofold. First, amino acids are driven into the protein synthesis channel in the cell thru action of cell surface receptors in lean mass. The metabolic pathways used by anabolic agents to achieve protein synthesis may be different, but the outcome is increased lean mass. The second action is anticatabolic. All anabolic agents appear to decrease protein degradation, possibly by blocking cell cortisol receptors.

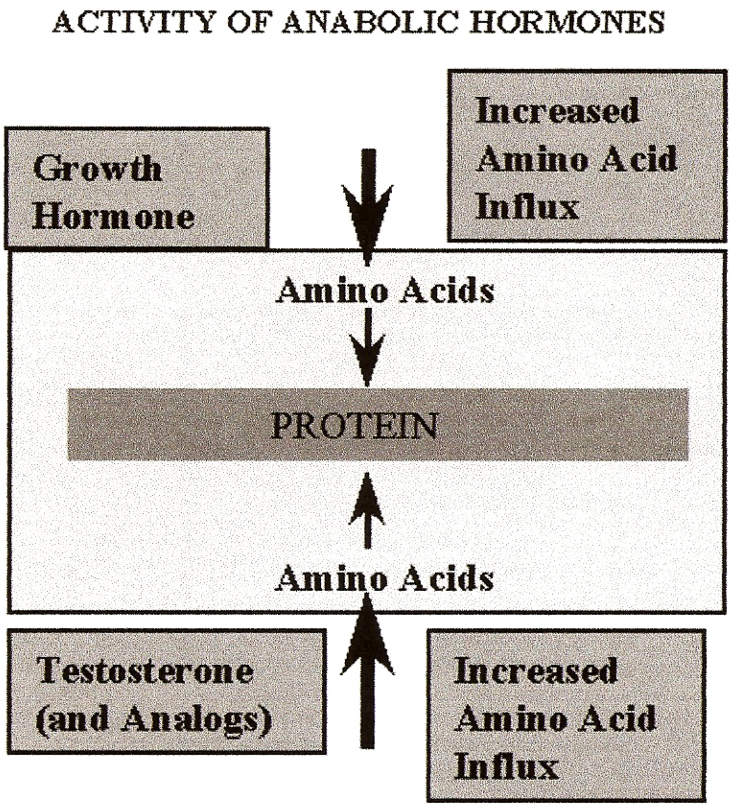
In the absence of a sufficient anabolic activity, the energy-requiring protein synthesis pathway is underused and excess energy is stored as fat.

Actions of Anabolic Hormones

- Anticatabolic by decreasing loss of amino acids from the protein synthesis pathway
- Anabolic by increasing the rate of protein synthesis

* Anabolic hormones are being used with increasing frequency in populations with lean mass loss or existing PEM, along with optimal nutrition and the added anabolic stimulus of resistance exercise.

Activity of Anabolic Hormones



SPECIFIC ANABOLIC HORMONES

A number of approaches to increasing anabolic activity are currently available. Several have been shown to be efficacious for increasing protein synthesis during both the stress and recovery phases of burn injury. The most promising agents are discussed here.

A) HUMAN GROWTH HORMONE

HGH is normally produced by the pituitary gland (0.8 mg/d) and is a potent endogenous anabolic hormone. It is found in highest concentrations in childhood during the growth spurt and gradually decreases with age or chronic illness. HGH binds to specific cell receptors leading to a host of metabolic effects, some due to direct hormone activity on tissues, especially in the liver. Other effects are due to the release of insulin-like growth factor-1, which has potent wound-healing effects.

Metabolic Effects of HGH

- Increase nitrogen retention, protein synthesis
- Increased cell amino acid influx, decreased efflux
- Decreased urea formation
- Increased IGF-levels
- Increased fat oxidation, decreased catabolism
- Increased metabolic rate (10%)
- Insulin resistance, hyperglycemia

Clinical Effects of HGH Therapy in Burn Patients

- Increased muscle formation
- Increased strength (grip) compared to untreated post-operative patients
- Decreased hospital stay (severe burn injury patients)
- Improved wound healing

Clinical Indications for HGH

- Presence of severe catabolism from burn
- Malnourished burn patients with a superimposed catabolism
- Acute loss of > 10% lean body mass (muscle)
- Large burns or wounds with poor healing

- Only FDA approval is for short stature: need to use as orphan drug

Potential Complications

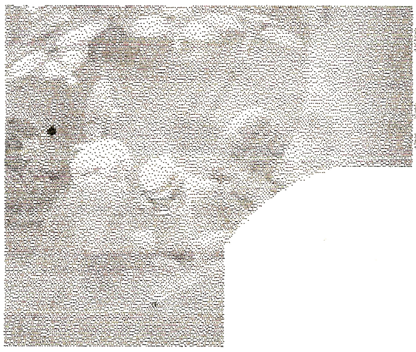
- Insulin resistance (hyperglycemia)
- Fluid retention (usually self-limiting)
- Hypermetabolism
- Increased mortality rate in certain critical care populations

See Section VII for Clinical Research on HGH

The primary stimuli for HGH release are starvation and resistance exercise. Agents such as glutamine and arginine have been reported to increase HGH release. The plasma HGH level is decreased after severe injury or sepsis, thereby decreasing normal anabolic activity. Numerous studies of exogenous HGH use in patients with trauma or burns and other injuries have demonstrated its efficacy for improving anabolism and the wound healing rate. The mechanism for improved outcomes appears to be related to maintenance of lean body mass. The average dose of HGH used is 0.1 to 0.2 mg/kg of body weight, or about 10 times the normal endogenous production. A number of complications have been reported; the most common is hyperglycemia, due to anti-insulin activity. Increased insulin is often required. In addition, HGH is very expensive, and it may increase morbidity and mortality. It must be given parenterally in certain populations at critical care.

Exogenous HGH, now obtained by a genetic engineering process, is only approved by the US Food and Drug Administration (FDA) for use in children with short stature or dwarfism. However, as an orphan drug, it has been used for its anabolic activity, especially in burn patients and patients with impaired wound healing.

Recently, a multi-center study of the use of HGH in critically ill patients (mainly non-trauma and non-burn) demonstrated an increase in mortality rate. The mechanism remains unclear. This response has not been reported with the use of HGH in burn patients.



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Educating the burn care professionals around the world

THE BURN NUTRITION MODULE

Robert H. Demling, M.D. Leslie DeSanti R.N., Dennis P. Orgill, M.D. PhD.

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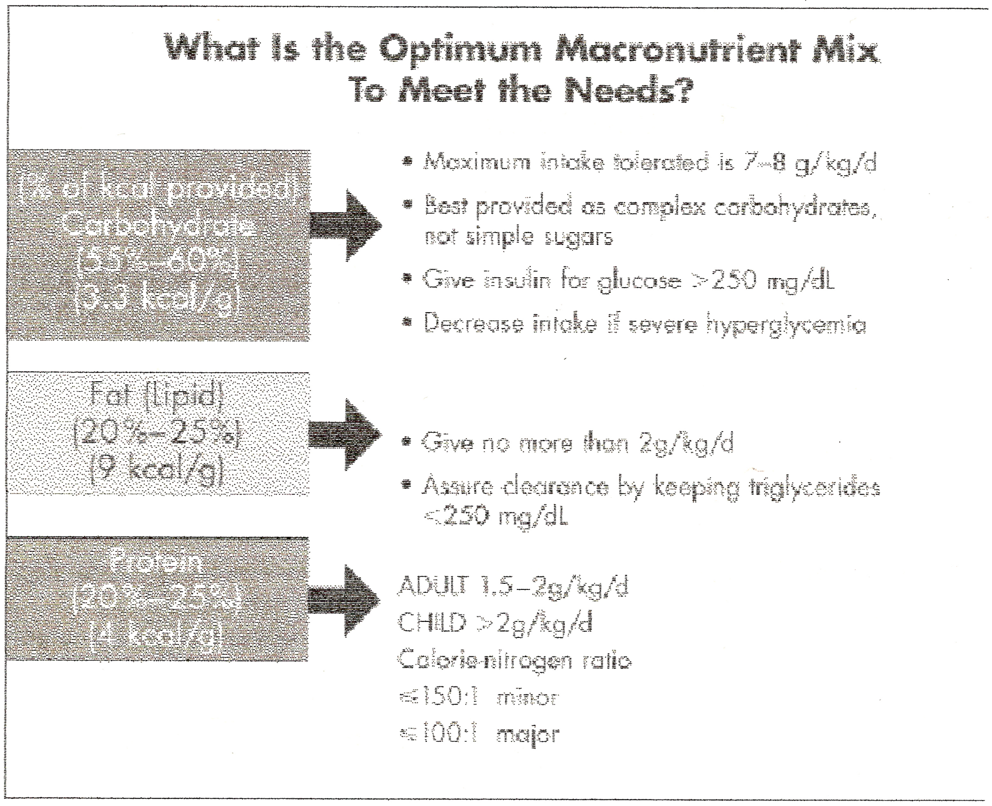
What Is The Optimum Macronutrient Mix To Meet The Needs?



MACRONUTRIENT CHOICES

With the background as to the metabolic changes we can better define the appropria mix of macronutrients, namely carbohydrates, fat and protein. Because of the hormo imbalance favoring excess glucose production, there is a well defined limit as to the quantity of carbohydrates which can be effectively metabolized. That value appears t be 7 to 8 grams/kg/day or 55-60% of Kcals provided, preferably in the form of compl carbohydrates, using the enteral route. Because of intense anti insulin activity, insulir often required. If severe hyperglycemia persists, glucose intake needs to be decreas

Fat or fatty acids are utilized to a limited degree especially when compared to starvat In addition certain fatty acids are immunosuppressive. No more than 25% of Kcals should be provided as lipids.

Protein should makeup 20-25% of Kcals because amino acids are used at an excess rate for fuel and also required for increased protein synthesis. Obviously not all the protein provided will be used for energy but 25% of total Kcals assures sufficient ami acid availability for both energy and synthesis. Micronutrients must be provided as we

Glutamine is the most abundant amino acid in the body composing two thirds of the amino acid pool. Under normal conditions glutamine is a non-essential amino acid an requirements can be met by endogenous production. Synthesis occurs mainly in ske muscle from any of the other amino acids in muscle protein via the generation of alph ketoglutatrate which then can be converted to glutamate and then glutamine. However stress states such as trauma and burns, glutamine is considered a conditionally esse amino acid and exogenous glutamine is essential, as endogenous production is totally inadequate to meet the increased needs. A glutamine deficiency state is well recogni: immediately after burns and trauma or critical illness. They key intra and extra-cellula functions of glutamine are therefore impaired.

KEY FUNCTIONS OF GLUTAMINE

Function in Metabolism Nitrogen shuttle: urea and ammonia clearance Direct source of cell energy	Antioxidant Substrate for the key cellular and plasma antioxidant glutathione
Anabolism: Anti-catabolism Decreases protein breakdown Rate limiting factor for muscle growth Stimulates release of human growth hormone	Immune Function Improves neutrophil bacterial killing and i a lymphocyte fuel Decreases infection rate
Effect on Wound Healing Direct fuel for fibroblast and macrophages Indirectly by preserving lean body mass	Preserves Gut Integrity Primary fuel for gut enterocytes via glutathione antioxidant action

The **Macronutrients** include protein carbohydrates and fat.

Protein intake correlates best with healing and preservation of lean mass. Al proteins are not alike and one should select proteins with the best biologic val This term refers to the quality of the amino acids, i.e. those most commonly us for protein synthesis. Milk proteins and egg albumin re the best. Components proteins include peptides which can either be produced by standard protein breakdown in the GI tract or components of a nutrient supplement, where prote is provided as a hydrolysis. Peptides, besides not requiring energy for absorption, also have biological activities such as anabolic and wound healin properties.

Incorrect →

Carbohydrates are the primary source of energy. Carbohydrates are provided simple sugars and as complex carbohydrates. Sugars are absorbed rapidly and can lead to hyperglycemia especially after a burn. Complex carbohydrates are broken down and
absorbed more slowly, thereby used snore efficiently. Foods and supplements should be chosen which have less sugar and more
complex carbohydrates.

Fat can be provided in a number of forms. Fat in foods is absorbed primarily long chain triglycerides which are carried to the liver in the form of chylomicr Polyunsaturated fats are preferred over saturated fatty acids over the long term but Stake little difference
in the delivery of calories during the stress response.

Ah so! →
S & M CFA's

Medium chain triglycerides (MCT) are all excellent source of calories and are burned like carbohydrates, therefore do not require lipoprotein transport. Hypertriglycendemia, i.e. over 250mg/dl reflects excess fat intake. MCT's do raise triglyceride levels. They
are provided independent of regular foods in man made supplements rich in MCT's or manufactured in the forth of structured lipids which contain a high MCT content. Omega-3 fatty acids are preferred over the more standard Omega 6 because the latter leads to
increased prostaglandins which are immunosuppressive and vasoactive.

MACRONUTRIENT CHOICES

PROTEIN AND PEPTIDES

PROTEINS

WHOLE PROTEIN

- High biologic value - milk, egg albumin best
- Lactalbumin, casein, whey proteins

PEPTIDES

- Small peptides - hydrolyzed proteins with a molecular

weight less than 1000 daltons, typically dipeptides and tripeptides
- Passively absorbed across the brush border of the intestinal mucosa by non-energy-dependent diffusion, whereas free amino acids are absorbed by active transport
- In cases of a compromised intestinal tract, peptides may be better absorbed than free amino acids
- Stimulate better nitrogen retention than do either intact proteins or free amino acid

CARBOHYDRATES

COMPLEX CARBOHYDRATES

- Gut breakdown and absorption is gradual,
- minimizing increases in blood glucose and insulin surges
- Optimum way of delivering carbohydrates

SIMPLE SUGARS

- Rapidly absorbed for immediate energy use
- Increased glucose and insulin producing fat

POLYUNSATURATED FATTY ACIDS (PUFA)

- PUFAs contain two of more double bonds on the carbon chain
- Essential fatty acids required for membrane integrity, eicosanoid synthesis fat soluble vitamin transport, cell-cell interaction
- Can be classified into two major families, w-3 and w-6 (w refers to the location of the first double bond from the terminal methyl end of the carbon chain)
- Both omega-3 and omega-6 fatty acids produce eiconsanoids, prostaglandins, and leukotrienes
- Most current enteral products contain and elevated rationof omega-3 and omega-6 fatty acids

MEDIUM CHAIN TRIGLYCERIDES (MCTs)

- MCT's typically contain eight to 12 carbon chains
- Excellent immediate source of energy
- More readily available as energy source compared to long chain (LCT)
- Do not require chylomicron formation for absorption, rapidly transported tot eh liver for B oxidation
- Do not require carnitine for oxidation

- **MCT's contain 8, 10, or 12 Carbon Atoms**
- **Excellent source of IMMEDIATE ENERGY**
- **More readily available as energy compared to LCFA (Long Chain Fatty Acids)**
- **Do NOT get carried in chylomicrons or liporpteins (eg. LDL or HDL)**
- **Oxidized w/o a need for carnitine.**

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