# Nutrition in severe illness

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It is well established that serious illness is accompanied by changes in metabolism that effect the nutritional requirements of animals. Traditionally it has been argued that the energetic requirements of seriously ill animals is increased, even in a resting state. This increased metabolic state has been termed "hypermetabolism". The energetic cost of generating a fever, producing and losing exudates, mounting an immune response, tissue inflammation and repair, are presumed to be primarily responsible. Indeed in several experimental studies in rodents, this concept has been supported.

## "No disease benefits from starvation"

The consequences of malnutrition are legion; no body system is left unaffected by starvation. In healthy animals, malnutrition is known to cause several important physiological derangements (Table 1. and Table 2.). In the face of serious illness, the consequences of malnutrition are magnified. Thus, to prevent malnutrition, and to anticipate the increased energetic and nutrient requirements in seriously ill patients, the concept of "illness factors" has arisen and been widely used.

**Table 1:** Known consequences of malnutrition in veterinary patients

| |
|---|
| Muscle wasting |
| Weakness |
| Intestinal ileus |
| Impaired healing |
| Decreased humoral responses |
| Known consequences of malnutrition in veterinary patients |
| Intestinal atrophy |

**Table 2:** Known consequences in human or experimental cases

| |
|---|
| Impaired cellular immunity |
| Bacterial translocation |
| Multiple organ dysfunction |
| Increased hospitalization |
| Increased complications |
| Increased morbidity and mortality when bodyweight loss exceeds 10% |
| Known consequences in human or experimental cases |

## Calculation of maintenance energy requirements (MER) in illness.

The resting energy requirement of an animal is the energy required to maintain all normal body systems at rest in a thermoneutral environment.

The RER of a cat or dog can be calculated by the following formula:

**kJ per day = $BWkg^{0.75}$ x 293**

A more convenient but less accurate formula is:

kJ per day = [(BWkg x 30) + 70] x 4.18

For a healthy active animal, you would normally multiply the RER by an factor that takes into account the energy expended in activity (e.g. 1.4). Animals resting in cages do not require significantly more than their RER.

These equations are derived from observing the energy requirements of large numbers of animals, and on average, they are accurate. However, it is important to realise that between individual animals there is considerable variation. Therefore, the calculated RER for any animal may over or under estimate its actual requirements by as much as 25% (O'Toole et al 2001).

To compensate for the hypermetabolic state, the calculated "healthy" MER is then multiplied by and "illness" or "disease" factor, that range from 1 to 2.

It is important to recognise however, that the illness or disease factors are inventions, and are not based on measured actual energy requirements of dogs and cats in those diseased states.

In an evaluation of the energy requirements of dogs with cancer, it was found that there was no difference between dogs with cancer and healthy dogs, nor was there any difference when the dogs with cancer were treated (surgical excision) (Ogilvie et al 1996).

In another study, the energy requirements of a series of dogs with a variety of mild to severe illnesses were measured. Again, the resting energy requirements measured were not different from those predicted by the "healthy dog" formula. In addition, this study reinforced the inherent variability in the actual energy requirements of dogs, and the relative inaccuracy of the equations (O'Toole et al 2004).

Therefore, there is no support for the use of "disease-specific factors" for estimating MER. Indeed for most hospitalized dogs, the MER ≈ RER.

But, one might ask, does it matter? What harm could come from overfeeding? Surely it is better to give a patient a little more than a little less?

## Metabolic derangements in inflammatory disease states

In serious inflammatory disease, especially chronic inflammatory disease, animals lose muscle more quickly than would be predicted by their food intake. They "waste". This is termed cachexia and has been shown to occur in association with sepsis, non-septic inflammatory disease, neoplasia, and cardiac failure. Cachexia accounts for 30 – 80% of cancer-related deaths in humans (diaphragmatic failure, oedema, immune compromise).

It is characterised by loss of muscle and fat mass and is not explained fully by a caloric deficit and, surprisingly, cannot be corrected by nutrition alone – even forced nutrition. Forced feeding in excess of requirements, results in fat deposition but no change in muscle mass (Kotler 2000).

## Metabolic response to fasting in a normal animal

Fasting results in decreased insulin secretion, production of glucose from the liver, a moderate increase in cortisol, and the release into the circulation of fatty acids and amino acids from fat and muscle respectively. The fatty acids are picked up by the liver, packaged into lipoproteins (VLDL), and exported back out into the circulation for utilization as fuel by the majority of cells in the body. Amino acids are used by the liver to synthesize glucose, and for the synthesis of essential proteins (e.g. clotting proteins).

## Metabolic response to inflammation

In inflammation, there is an increase in insulin secretion in response to feeding, but most cells in the body (especially the liver) are *resistant to the effects*. This resistant prevents utilisation of precious glucose and preserves blood glucose for essential tissues (brain, erythrocytes, leukocytes). There is a massive increase in cortisol which induces a large breakdown of fat and muscle, increasing the delivery of free fatty acids and amino acids to the liver, and greatly increasing muscle and visceral protein breakdown.

Since the liver is resistant to insulin, feeding does little to prevent it from continuing to produce glucose, and hyperglycaemia results.

**Table 3:** Metabolic differences between simple starvation and cachexia

| | Starvation | Inflammation / Cachexia |
|---|---|---|
| Bodyweight | — | — /NC |
| Body fat | — — — | — — |
| RER | — — — | + + |
| MER | — — — | — |
| Protein synthesis | — — — | —/ + |
| Protein degradation | — — | + + + |
| Serum insulin | — — | + + + |
| Serum cortisol | NC | + + + |
| Serum glucose | NC | + + + |
| Serum lipids | + VLDL, + fatty acids, + + + ketones | + + VLDL, + + fatty acids, — ketones |

## Hyperglycaemia – more than a number?

Therefore, any serious acute illness can result in:

- Hyperglycemia
- Insulin resistance
- Increased hepatic glucose production

This has been termed the "Diabetes of injury". It is caused by the constellation of inflammatory signalling factors (cytokines) produced by activated leukocytes, cortisol, adrenaline, and other hormones.

## Diabetes of injury

Previously this insulin resistance and hyperglycaemia was thought to be an adaptive response

- Promotion of glucose uptake in essential tissues and prevention of uptake by muscle
- Moderate hyperglycaemia has been tolerated by veterinary and medical clinicians

In 2001, a study of 1548 human intensive care patients was instigated to determine if there is any benefit to tightly controlling blood glucose in severe illness (van den Berghe et al 2001). Blood glucose was controlled with intensive insulin therapy to less than 6 mmol/L. Amazingly, there was a 43% reduction in mortality in all patients, and even in "long stay" patients, mortality was reduced by 10.6% long stays. In addition there was:

- Shortened hospitalization
- Reduced:
    - Nosocomial infections
    - Acute renal failure
    - Anaemia
    - Liver failure
    - Multiple organ dysfunction
    - Muscle weakness

## Is glucose toxic?

Hyperglycaemia is not normally toxic in the short term. Normally, cells are relatively protected from hyperglycaemia by down-regulation of glucose transporters. However, although the insulin secreted in inflammatory states does not result in reducing blood glucose, it does lead to other signaling effects within cells. Thus the hyperglycaemia stimulates continued insulin release which signals to many cell types to undergo metabolic changes associated with the post-prandial state, that are inappropriate in a diseased state. These alterations have been confirmed in canine sepsis.

In addition, although there is a relative insulin resistance, *some* glucose is forced into some cells leading to cellular glucose overload in neurons, endothelium, alveoli, vascular smooth muscle, and renal tubule cells.

This combination of exaggerated insulin signaling and glucose overload leads to:

- Acute renal failure
- Accelerated removal of erythrocytes and anaemia
- Polyneuropathy, brain oedema, depression, seizures
- Immunosuppression, decreased phagocytosis and killing
- Increased sepsis
- Increased vascular permeability, decreased responsiveness, activation, coagulation, disseminated intravascular coagulation

## Over-feeding in inflammatory disease states

Clearly feeding excessive carbohydrate will exacerbate the hyperglycaemia and *increase morbidity*. Feeding excessive fat exacerbates hepatic load and leads to fatty liver development and liver dysfunction.

Intestinal response to overfeeding:

- Delayed gastric emptying – vomiting
- Risk of aspiration
- Fermentation of undigested nutrients, overgrowth, enterotoxin production (Clostridial spp)
- Maldigestion of disaccharides, peptides
- Osmotic diarrhoea

## Recommendations

1. Feed no more than RER until there is a demonstration of weight loss.

2. BUT – ensure that the RER is being fed!

3. Monitor for hyperglycaemia and hyperlipidaemia
   - reduce intake but keep feeding the gut

4. feed a high protein, high fat diet but consider the possibility of fat malabsorption
   - Euk max cal, Hill's a/d, Hill's p/d feline

Tube feeding
- Hyperosmolar diets poorly tolerated when intestinal motility decreased
- Lactose a poor choice
- Jevity is lactose free, but too low in protein and certain essential amino acids
  - Supplement with whey protein
- Start with 25% RER for first 24 hours, then 50%, then 75%, then 100%.
- Weigh daily

## References

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