

## News Summary

### Early enteral nutrition can have a positive impact in the acutely ill patient

- ***Acute illness, trauma and surgery cause muscle loss and significant inflammatory responses with long-term consequences***
- ***Early enteral nutrition maintains the gut structure and motility, allows better nutrient delivery and reduces inflammation***
- ***Tailored nutrition and repeated assessment is needed in long-stay ICU patients to prevent loss of lean body mass***

**Vevey, Switzerland, September 2014** – Acute illness not only has immediate health consequences, it also has negative long-term effects. Cutting edge research presented at a Nestlé Nutrition Institute-sponsored satellite symposium at the European Society of Intensive Care Medicine (ESICM) congress shows that providing these patients with appropriate nutrition, at the right time, can improve outcomes. Professor Rupert Pearse, from Barts and the London School of Medicine and Dentistry, UK, who co-chaired the meeting with Professor Jean-Daniel Chiche from Paris Descartes University, France, explained that all types of acute harm – including trauma, sepsis and major surgery – are characterised by inflammation. This can lead to step-wise loss of organ function, with long-term impact on quality of life and increased mortality. By minimising acute harm with high-quality care that includes proper nutritional intervention, long-term damage can be avoided and the chances of good patient outcomes can be maximised.

#### **Surgery and acute illness cause significant inflammatory responses with long-term consequences**

Professor Rupert Pearse showed that many patients undergoing non-cardiac surgery have post-operative rises in troponin – a protein complex that signals damage to the heart, and this is associated with increased 30-day mortality<sup>1</sup>. Prof Pearse explained that this rise in post-operative deaths is significant: “The mortality rate associated with troponin rises is actually higher than in patients who present in the emergency department with acute chest pain”. The most likely explanation for the rise in troponin is inflammation caused by the surgery itself. It is not just the heart that is affected by surgery-induced acute inflammation, the lungs, gut, kidneys and liver can also be affected. Even if these complications are effectively treated, these patients still have reduced long-term survival. The same appears to be true for acute illness or trauma other than surgery. For example, the severity of acute kidney injury predicts the progression to chronic kidney disease, which is known to lower life expectancy<sup>3</sup>. Prof Pearse highlighted the importance of damage limitation: “It is essential that every measure is taken to limit the severity of acute episodes in patients in intensive care units in order to improve long-term outcomes, and nutrition has a part to play in this care paradigm”.

#### **Muscle loss is significant and rapid in ICU patients**

People who are critically injured and are confined to a bed in an intensive care unit (ICU) can lose 16% of total body protein in the first 21 days, with most (67%) of this coming from muscle<sup>4</sup>, warned Professor Robert Martindale of Oregon Health and Science University, USA. But with the right nutrition, with enteral delivery, and at the right time, the loss of lean body mass can be prevented. Critically ill trauma patients enter a ‘hyperdynamic’ state in which resting metabolic rate is higher than normal. This leads to loss of lean body tissue via a number of mechanisms, including reduced availability of amino acids for muscle protein synthesis, increased breakdown of muscle proteins, and anabolic resistance<sup>5,6</sup>. Prof Martindale described a study of 63 critically ill patients who were expected to remain in the ICU for more than 7 days and be ventilated for more than 48 hours<sup>7</sup>: “Thigh muscle biopsy samples showed that up to 29% of the tissue had been lost in 10 days in these hyperdynamic patients; supplementing amino acids is important to increase protein synthesis and maintain muscle mass”. Adding resistance exercise to the regimen can have additional benefits, including increasing nutrient uptake in muscle and other tissues, reducing inflammation, and lowering insulin resistance.

### **Early enteral nutrition in the critically injured can prevent loss of lean body tissue**

Prof Martindale discussed the known nutritional and non-nutritional benefits of administering nutrients via the enteral route: “They include maintaining the gut structure and motility, better nutrient delivery, reduced gut inflammation, and decreased gut permeability”<sup>8</sup>. Enteral feeding also maintains gut-associated lymphoid tissue and mucosa-associated lymphoid tissue, which play pivotal roles in immunity of the gut and all epithelial surfaces<sup>9</sup>. The timing of enteral nutrition is also important. Several meta-analyses have shown that early enteral nutrition is associated with better health outcomes than delayed enteral nutrition in critically ill patients. Prof Martindale described several studies in which enteral nutrition was given within 24-36 hours of hospitalisation: “We see a decrease in infection rates and reduced length of hospital stay; and importantly, mortality rates are also reduced in ICU and surgical populations”. Decreased mortality has also been seen with early (within 48 hours of ventilator use) enteral nutrition in critically ill patients receiving vasopressor drugs to maintain blood pressure<sup>10</sup>. Enteral feeding is also safe; studies over the last decade show 85-93% success rates when given within 24 hours. In abdominal trauma patients who underwent damage-control laparotomy, enteral feeding within 36 hours allowed sooner abdominal closure and reduced rates of pneumonia compared with later enteral feeding<sup>11</sup>. “Again, this shows us that early feeding via the gut gives us epithelial protection in the lungs” said Prof Martindale.

### **Omega-3 fatty acids as part of early enteral feeding can help reduce inflammation in the critically ill**

The benefits of early enteral nutrition in the critically ill can be achieved with just ‘trophic’ underfeeding rather than full caloric feeding which may be more appropriate for some patients. A study of 525 survivors of acute lung injury found there was no difference in physical function or survival at 12 months after initial trophic or full enteral feeding<sup>12</sup>. Providing nutrients such as vitamins C and E, zinc, arginine and leucine that can help reduce inflammation is important for critically ill patients. Prof Martindale presented recent research showing that perioperative infusions of fish oil can decrease signs of inflammation in cardiac surgery patients and may play a role in cardiac rhythm stabilization and prevention of hepatic steatosis in ICU patients. The omega-3 fatty acids in fish oil, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are enzymatically converted to mediators, including resolvins, which actively fight acute inflammation and prevent progression to the chronic inflammatory state<sup>13</sup>. Summarising the importance of enteral feeding, Prof Martindale said “we need to consider enteral nutrition as a priority once the patient is resuscitated, and the benefits can usually be met with trophic feeding during the first couple of days”.

### **Feed intolerance in neurotrauma patients may be overcome with early nutrition**

In patients who have suffered neurotrauma and need critical care, nutritional support has been shown to be suboptimal according to Professor Peter Andrews of the University of Edinburgh, UK. Evidence shows that early nutrition via the small bowel rather than the gastric route results in reductions in morbidity and mortality. Delayed gastric emptying and feed intolerance is a common problem in the critically ill, and patients with traumatic brain injury (TBI) are at particular risk, with an incidence of up to 80%. An observational study of 797 patients with severe TBI found a four-fold increase in risk of death in those not fed for the first 7 days after injury, and every 10 kcal/kg decrease in energy intake during the first 5 days was associated with a 30-40% increase in mortality<sup>14</sup>. Prof Andrews acknowledged that current guidelines are inadequate: “The Brain Trauma Foundation guidelines recommend that severe TBI patients receive nutritional support within 7 days of injury<sup>15</sup>, but there is limited guidance for the post-acute rehabilitation period”<sup>16</sup>.

### **Achieving nutritional goals in neurotrauma patients is challenging**

A recent systematic review of nutrition in TBI patients found early feeding was associated with lower mortality and reduced incidence of pneumonia<sup>17</sup>. But achieving nutritional goals in this patient population is challenging. A study of over 100 severe TBI patients found that 88% of patients were fed by day 3, via the enteral route in 97% of cases, but on average only 33% of the nutritional target was met. Gastric intolerance was the biggest cause of unsuccessful nutrition<sup>18</sup>. Therapeutic hypothermia is commonly used with sedation to manage acute brain injury, but although this can affect nutritional requirements, patients are still able to absorb enteral nutrition. Prof Andrews recommended caution however: “The reduction in energy requirements with hypothermia treatment are not as large as predicted from calculations, so there is a risk of underfeeding these patients. In contrast, sepsis and shivering significantly increase energy expenditure, so measures need to be taken to prevent these”.

### **Tailored nutrition is needed in long-stay ICU patients to prevent loss of lean body mass**

Long-stay ICU patients are immobile for long periods and so are likely to benefit from individually tailored nutrition, and repeated assessments will ensure that proper nutrition is being delivered. Sarcopenia and hypermetabolism are common problems faced by long-stay (over 10 days) ICU patients, so the main target of nutrition is to limit the loss of lean body mass that is often observed. According to Professor Jan Wernerman of Karolinska Institutet, Stockholm, Sweden, nutritional targets are not being met in this population<sup>20</sup>. Long-stay patients are poorly characterised because very few remain in the ICU for more than 10 days, so the evidence-base for nutrition guidelines is limited. The cause of muscle loss, explained Prof Wernerman, is not reduced synthesis but degradation: “in critically ill patients muscle protein synthesis is usually within the normal range of 1.25 to 2.25% per 24 hours<sup>21</sup> and the myosin, actin and mitochondrial fractions tend to function at a normal level. The overall loss of muscle tends to be due to increased degradation of muscle fibres<sup>22</sup>”.

Recent data suggest that it is important to assess whether ICU patients are being fed appropriately, so nutrition can be tailored to the individual. A study in ICU patients has shown that whole body protein synthesis is higher if they receive 100% of their energy expenditure compared with 50%<sup>23</sup>. Summarising, Prof Wernerman explained that assessing nutritional status should be routine: “Repeated assessments including energy expenditure -easily measured through carbon dioxide elimination, protein status – using urine analysis, and levels of vitamins and trace elements are necessary to ensure that proper nutrition is being delivered”.

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### **Notes to editors:**

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