

# Supplemental Parenteral Nutrition



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Providing nutrition to patients on the intensive care unit (ICU) has the potential to save lives, reduce infection rates, improve ventilation and reduce length of stay on the ICU and in hospital. Although the amount, route and timing of nutritional support remain controversial, recent studies have allowed us to make some reasonably firm conclusions about optimal feeding on ICU. Meeting the estimated target of energy provision at the appropriate time may be particularly important.

Anyone who has worked on ICU will be aware that ICU patients have a tendency to rapidly lose lean weight and it is tempting to give as much energy as possible. However, this practice, which was common in the 1980s and often referred to as hyperalimentation, may be particularly harmful. Due to changes in metabolism, overfeeding can lead to hyperglycaemia, raised energy expenditure, increased oxygen consumption and carbon dioxide production, hepatic steatosis (fatty liver) and hyperlipidaemia.<sup>1</sup> Hyperlipidaemia may in turn lead to fatty infiltration of lung tissue and the hepatic reticuloendothelial system, impairing gas exchange and antibody production respectively.<sup>2,3</sup> It is likely that at best hyperalimentation may lead to fat weight gain and studies on enforced bed rest have suggested that positive energy balance in immobility leads to increased loss of lean mass.<sup>4</sup>

Although overfeeding is harmful, failure to meet target requirements and under provision can also be dangerous especially in the malnourished. In one study a cumulative negative energy was associated with increased complications and infections<sup>5</sup> and, in another, a daily energy deficit of around 1200 kcal/day lead to greater mortality and morbidity.<sup>6</sup> It could be argued that this is because sicker patients are harder to feed but never the less there seems to be a growing consensus that energy debt is associated with poor outcome.

In the light of the risks of under and overprovision of energy it can be concluded that a modest provision of energy to metabolically

stressed patients is the best solution.<sup>7</sup> Indeed, a retrospective study by Krishnan<sup>8</sup> found that patients who received 9-18 kcal/kg did better than those who received more or less energy in terms of morbidity and mortality. However, it is important to realise that energy requirements will change throughout ICU stay and while only a modest provision of energy is probably best in the initial stages of critical illness, patients will be able to effectively utilise more energy as they recover, their inflammatory response resolves and their metabolism reverts to a more normal anabolic state. It seems likely that while it is inevitable that patients will lose lean mass during critical illness they may be able to replenish losses as they recover, and the importance of adjusting energy provision to account for this cannot be understated. This point was made by ESPEN in their 2006 guidelines on enteral feeding<sup>9</sup> where they recommended that we should avoid giving more than 20-25 kcal/kg in the initial stages of critical illness but that we should increase to 30-35 kcal/kg in the 'anabolic flow phase' or recovery in other words. Unfortunately ESPEN do not give any guidance on how to recognise 'the anabolic flow phase' but it seems logical that the following can be regarded as signs of recovery: a drop in inflammatory markers such as C Reactive protein (CRP), resolving oedema, reduced hyperglycaemia and insulin requirements and a return of appetite and mobility.<sup>10</sup> In addition, Bernstein suggested that a 40 mg rise in weekly serial prealbumin levels indicates the switch to anabolism.<sup>11</sup>

Estimating energy requirements in the critically ill is complex and should always involve a nutritionally trained member of staff such as a dietitian. Indirect calorimetry is considered the gold standard for measuring energy expenditure, however as few UK units have the necessary equipment predictive formulae or expert recommendations, calories per kg will nearly always have to be used. While some ICU dietitians favour ICU specific formulae – such as Irteon-Jones, Penn State, etc.<sup>12,13</sup> These rely on having an accurate dry weight which can be very difficult to obtain as most critically ill patients will be oedematous from illness and fluid resuscitation. Basal metabolic rate (BMR) by a simple formula such as Henry + 10% or 20-25 kcal/kg based on a pre-ICU weight or that reported by a relative may be as good an initial target as any. This should be built up to gradually in the first few days, with NICE<sup>7</sup> recommending giving 50% of estimated target requirements to metabolically stressed patients over the first 24-48 hours. Once the patient is in a recovery phase as defined previously it is vital adequate energy and nitrogen are delivered and targets are met.

Studies such as ACCEPT<sup>14</sup> have shown that meeting estimated feeding targets is associated with improved outcomes, however, the optimum route for doing so remains controversial. Traditionally enteral nutrition has been favoured in critically ill patients and the PEP UP<sup>15</sup> protocol has been suggested as a way of optimising delivery by this route. However, the recently published findings of the large scale CALORIES<sup>16</sup> trial showed that both parenteral and enteral feeding were associated with similar outcomes especially with respect to 30 day mortality. Interestingly, both methods can be associated with failure to meet feeding targets – with over half the patients in each group failing to meet their estimated energy needs.

Enteral nutrition (EN) where feed is infused into the gut through a tube, most commonly a nasogastric (NG) tube, is reported to have numerous advantages for the critically ill patient. Feeding the gut may preserve gut barrier function and confer a number of immunological benefits.<sup>17</sup> Enteral nutrition may enhance immunoglobulin secretion from the gut associated lymphatic tissue (GALT) and several studies have suggested that establishing early enteral nutrition is associated with a reduction in septic morbidity and improved survival.<sup>17,18</sup> However, many ICU patients may have gastric dysfunction with raised gastric residual volumes (GRVs)<sup>19,20</sup> and establishing full NG feeding can be difficult. Feeding beyond the stomach with a jejunal tube can overcome this, however, placement usually involves endoscopy and feeding poorly resuscitated patients or those with paralytic ileus this way can rarely be associated with fatal bowel necrosis.<sup>18</sup>

Parenteral Nutrition (PN), where feed is infused intravenously, developed a bad reputation on the ICU when a meta-analysis, published in 1998,<sup>21</sup> showed significantly increased septic morbidity in

patients fed this way, leading the authors to conclude that it should not be used in the critically ill. However, it is possible to explain these findings. Most of the studies included in the meta-analysis were carried out when massive overfeeding without careful glycaemic control was the vogue, with feed containing lipid emulsions rich in soybean oil infused through inappropriate lines. Soybean oil-based lipid emulsions have been associated with cholestasis,<sup>22</sup> may contain hepatotoxic phytosterols<sup>23</sup> and are rich in omega 6 fatty acids which are precursors of proinflammatory eicosanoids. Replacing some of the soybean oil with combinations of coconut oil (high in medium chain triglycerides), olive oil and potentially anti-inflammatory fish oil to form the so called third generation lipids has been associated with improved outcomes on the ICU.<sup>24</sup> Modern PN has been shown to be risk neutral compared to EN and failure to give it to malnourished ICU patients who cannot be enterally fed may be associated with increased mortality.<sup>25</sup>

Although modern PN is safe, the general consensus from expert groups is that enteral nutrition should be used as the first line of feeding because of its protective effect on the gut barrier and its favourable influence on GALT and immune function.<sup>16</sup> However, because many patients on the ICU have poor gut function, it may not be possible to meet their full feeding target with EN. In such situations, supplemental parenteral nutrition (SPN) can be considered to give the best of both worlds. Here as much nutrition is given by the enteral route as possible and the deficit made up with PN to meet the full target.<sup>26</sup>

While the rationale for SPN is clearly logical, studies on its use have had variable findings. In the Impact of Early Parenteral Nutrition Completing Enteral Nutrition in Adult Critically Ill Patients (EPaNIC)<sup>27</sup> study, 4640 ICU patients were fed as much EN as possible and then randomised to early (day 2) or late (day 8) initiation of parenteral nutrition to meet a calculated energy target. The late initiation group showed improved outcomes with less infections, less cholestasis, fewer days of mechanical ventilation and renal replacement therapy and showed a relative increase of 6.3% in the likelihood of being discharged from ICU alive. However, in this study patients who were largely not malnourished were fed to a very high energy intake of up to 36 kcal/kg/day in the early stages of their critical illness. Furthermore patients who were likely to benefit from PN such as those with BMI <17 kg/m<sup>2</sup> or those with short bowel syndrome were actually excluded from the study. Many patients had diagnoses that would suggest they could have been enterally fed (61% had heart surgery), had a more aggressive approach to their EN been used. Indeed, the study protocol reveals they used a very low gastric residual volume threshold of 250 mls to define tolerance to enteral feed which is contrary to the recommendations of

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ASPEN,<sup>18</sup> who suggest EN should not be withheld for anything less than a GRV of 500 mls. The EPaNIC study<sup>27</sup> simply serves to reinforce our conclusions from previous studies: that feeding excessive amounts of PN to patients with a functioning gut who are not malnourished in the early stages of critical illness is a bad idea.

In contrast, a Swiss study<sup>26</sup> that carefully introduced SPN at day 3, where EN was clearly not tolerated, showed improved outcomes. In a randomised study of 305 patients indirect calorimetry was used to determine an energy target and SPN used to achieve energy balance in conjunction with tight glycaemic control. Careful use of combined EN and PN resulted in fewer infections, more antibiotic free days and shorter duration of mechanical ventilation.

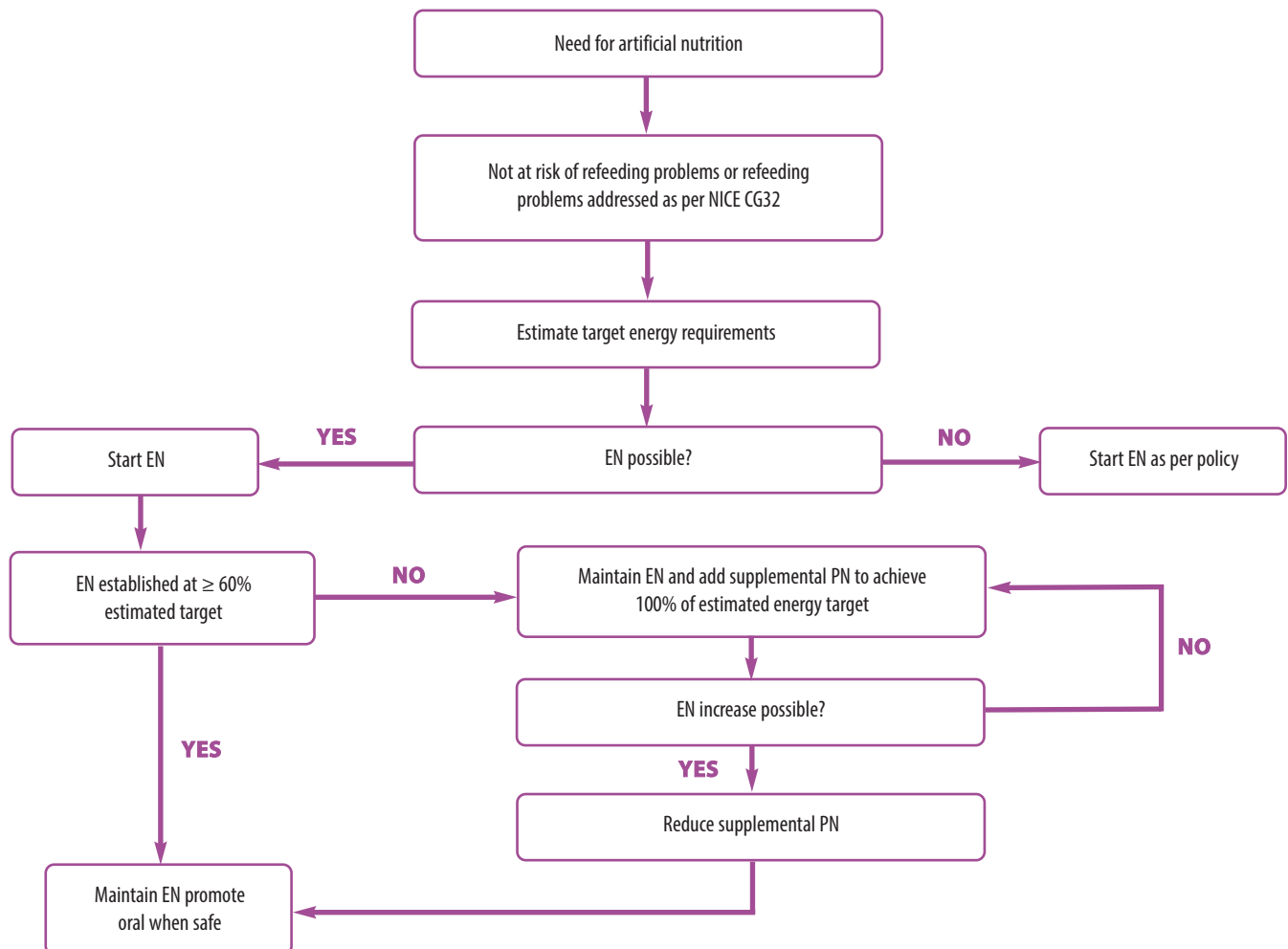
In supplemental feeding the dietitian works out the patient's nutritional requirements and as much of this as possible is fed via the enteral route. The nutritional deficit is then made up by the parenteral route – the amount given adjusted according to the amount of EN tolerated. This can be made a lot easier by using 1 kcal/ml and enteral feed and an approximately 1 kcal/ml PN bag, so that they can be titrated ml for ml according to the amount of EN absorbed. For example, if patient

required 1500 kcal per day but they could only tolerate 25 mls/hr/24hrs of enteral feed (600 kcal), the deficit can be made up by infusing PN at 38 mls/hr/24hrs (approx. 900 kcal). It is important to discard any remaining PN after 24 hrs. Three chamber PN bags for central administration with an energy density of around 1 kcal/ml and third generation lipids are commercially available. An algorithm for supplemental feeding has been published by Heidegger *et al.*<sup>26</sup> and an adapted version is shown in **Figure 1**.

It is becoming clear that achieving appropriate nutritional support at the right time, in the right amounts to specific patient groups is associated with improved outcomes. Overfeeding, particularly in the early phase of critical illness, is harmful. However, failure to meet energy targets is equally as bad, particularly in the malnourished with poor gut function. EN and PN have their pros and cons and both can fail to meet estimated requirements. Berger<sup>28</sup> has hypothesized that, in the future, smart ventilators may determine energy expenditure but even if these do become available, there will always be the need for a nutritionally experienced healthcare professional, such as a dietitian, to carefully monitor and balance feeding by both EN and PN to ensure feeding targets are met.

Figure 1: Supplemental PN Algorithm

Adapted from Heidegger *et al* (2007)<sup>26</sup>





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